23-2553

IN THE

United States Court of Appeals

FOR THE THIRD CIRCUIT

UNITED STATES OF AMERICA EX REL.,
STEPHEN A. KRAHLING; JOAN A. WLOCHOWSKI,

against

MERCK & CO, INC.,

STEPHEN A. KRAHLING; JOAN A. WLOCHOWSKI,

Appellants.

On Appeal from the United States District Court
for the Eastern of District of Pennsylvania
The Honorable Chad F. Kenney, Case No. 2:10-04374-CFK

JOINT APPENDIX
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[1] Exhibits 282 through 299 to the Reilly Declaration have been omitted by consent of the parties.

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serial # 86) and believes that they provide helpful supportive information on the clinical relevance of the chosen ELISA cutoff for seropositivity.

Id. at '30-31 (emphasis added).

334. Merck's April 13, 2005 letter to FDA's Norman Baylor in response to FDA Comment 10 stated:

Response [10]:
We acknowledge that the lower bound of the confidence interval for the group with M-M-R™II with 4.8 $\log_{10}$ $TCID_{50}$ Mumps Virus Potency was below 90%. However, in order to demonstrate that M-M-R™II with 4.1 $\log_{10}$ $TCID_{50}$ Mumps Virus Potency was an acceptable end-expiry potency, the primary hypothesis required that:

- The mumps immune response in children who receive M-M-R™II with 4.1 $\log_{10}$ $TCID_{50}$ be no Mumps Virus Potency group be no more than 5 percentage point lower than mumps immune response in M-M-R™II with 4.8 $\log_{10}$ $TCID_{50}$ Mumps Virus Potency group in order to declare similarity...
- M-M-R™II with 4.1 $\log_{10}$ $TCID_{50}$ Mumps Virus Potency had to induce an acceptable mumps immune response with the lower bound of the ... [Confidence Interval] on the observed response being greater than >90% in subjects who develop neutralizing antibodies.

These hypotheses were met in this study; therefore, 4.1 $\log_{10}$ $TCID_{50}$ Mumps Virus Potency Group (92.2% versus 93.3%) was declared an acceptable end-expiry titer for M-M_R™II. There was not an acceptability hypothesis for the 4.8 $\log_{10}$ $TCID_{50}$ mumps virus potency.

Though the 4.8 $\log_{10}$ $TCID_{50}$ Mumps Potency Group had a slightly lower observed mumps seroconversion rate than the 4.1 $\log_{10}$ $TCID_{50}$ Mumps Virus Potency Group... based on the mumps virus neutralization assay, this difference is not statistically significant ... Due to an unexpectedly higher pre-positive rate in the plaque-reduction neutralization assay (PRN) and a sample storage issue, only 437 subjects were evaluable

in the 4.8 $\log_{10}$ $TCID_{50}$ Mumps Virus Potency Group. If the study had maintained the planned evaluable sample size of 502 subjects in the 4.8 $\log_{10}$ $TCID_{50}$ and the same seroconversion rate of 92.2% was observed, the probability that the true rate was above 90% would have been ~97%.

The current M-M-R™II label states that a single injection of the vaccine induced mumps neutralizing antibodies in 95.8% of susceptible persons. This was based on ... an earlier version of mumps neutralization assay. Since the original mumps neutralization assay was no longer in operation, a new plaque-reduction neutralization assay (PRN) designed to quantitate mumps neutralizing antibody in prevaccination and postvaccination sera was developed for this study to evaluate mumps end expiry potency. Despite the use of a different assay, the seroconversion rate of 92.2% ... for the 4.8 $\log_{10}$ $TCID_{50}$ Mumps Virus Potency Group was inline with that observed in the original clinical studies used in the licensure of M-M-R™II.

The PRN assay was developed and validated by the applicant specifically for this study, and is not the primary assay used by the applicant to evaluate the serologic response to a mumps virus-containing vaccine.[897] Typically, the mumps ELISA is used to detected immunoglobulin gamma antibody (IgG) to mumps virus before and after vaccination. The observed seroconversion rates using the mumps ELISA for the 4.8 and 4.1 $\log_{10}$ $TCID_{50}$ Mumps Virus Potency Groups were 98.1% and 96.9%, respectively. Based on the applicant's broad experience since the late 1980's with this ELISA assay for evaluating the mumps serologic response to M-M-R™II, the observed rate in the 4.8 $\log_{10}$ $TCID_{50}$ Mumps Virus Potency Group is consistent with historical experience.

MRK-KRA00000315 at '44-45 (emphasis added).

[897] *See also* MRK-KRA00051640 (January 17, 2003 email from Dr. David Krah to Dr. Leonard Rubinstein stated: "The M-M-RII Protocol 006 study used a straightforward, non-enhanced neutralization, using several different indicator viruses. The M-M-RII [Protocol 007] study used an anti-IgG enhanced neutralization and the low-passage indicator virus. We would have used the same assay used in 006 for 007 except that we could not achieve the 90% seroconversion sensitivity with any of the wild-type mumps strains without enhancing the assay sensitivity. We could measure >90% seroconversion using the vaccine strain as the indicator, but CBER required use to use a "wild-type" indicator virus for 007.")

335. Merck's April 13, 2005 letter to FDA's Norman Baylor in response to FDA Comment 11 stated:

> Response [11]: …
>
> For the mumps (PRN) per-protocol analyses, 204, 229, and 235 subjects were excluded.... As displayed in Table 11 of the Protocol 007 CSR, the majority of the subjects excluded (>55%) were excluded due to an unknown serostatus at baseline... Subjects whose blood samples were stored at 4C for >1 year prior to testing in the PRN assay (and hence declared invalid...) were considered as having an unknown baseline mumps (PRN) serostatus. Thus, over half of the exclusions due to an unknown serostatus ... resulted from the improper storage of the blood samples. In addition, since baseline and 6-week blood samples were tested in pairs in the PRN assay, subjects who did not have both a baseline and a 6-week blood sample were not tested. ... The second largest reason for being excluded from the per protocol analyses was due to a positive prevaccination serostatus ...
>
> … Of the 204, 229, and 235 subjects excluded from the mumps (PRN) per-protocol analyses in the 3.8, 4.1, and 4.7 $\log_{10}$ $TCID_{50}$ mumps virus potency groups, respectively, greater than 60% ... were included in the mumps (ELISA) per-protocol analyses. The mumps (ELISA) seroconversion rates (SCRs) based on these subjects were 95.4%... 96.3% ..., and 98.2% for the 3.8, 4.1, and 4.8 $\log_{10}$ $TCID_{50}$ mumps virus potency groups, respectively, which were comparable to the mumps (ELISA) SCRs observed for the entire per-protocol population ...

Id. at '47-48 (emphasis added).

335.1. A letter from FDA's Director, Division of Vaccines and Related Products Applications Office of Vaccines Research and Review, CBER, Dr. Karen Goldenthal, to MRL's Associate Director, Worldwide Regulatory Affairs, Dr. Alison Fisher, dated October 17, 2005, stated:

This letter is in regard to the Supplement to your License Application submitted under Section 351 of the Public Health Service Act.

The Center for Biologics Evaluation and Research (CBER) has completed the review of your Supplement received on April 13, 2005, for Measles, Mumps and Rubella Virus Vaccine Live (M-M-R®II), to include a change in the labeled potency of the mumps component of M-M-R®II from 20,000 TCID50 to 12,500 TCID50. Our review finds that the information and data submitted are inadequate for final approval at this time based on the deficiencies described below.

1. The clinical trial described in your supplement is inadequate to support this label change for the mumps component due to the following deficiencies:

a. A substantial amount of sample data was excluded from the analysis. We note that only 437 out of 672 immunized control group subjects contributed to the pre-protocol analysis. This large proportion of missing data precludes a conclusion of success...

c. The control lot failed the acceptability criteria as you acknowledge in your April 13, 2005 response.

If you intend to pursue the proposed changes in labeled potency, we recommend that you support the proposed label change by correlating these study data and/or other relevant mumps vaccine immunogenicity data with the immunogenicity data from the original efficacy studies. You could also consider shortening the end-expiry dating period based upon these data.

MRK-KRA00000479 at '79-80 (emphasis added).

335.2. A letter from MRL's Associate Director, Worldwide Regulatory Affairs, Dr. Alison Fisher, to FDA's Dr. Norman Baylor, Office of Vaccines Research and Review, CBER, regarding "Measles, Mumps and Rubella Vaccine Live (MMRII) STN 101069/5061, RESPONSE TO REQUEST FOR INFORMATION," dated November 15, 2006, stated:

"Reference is made to a letter from CBER on October 17, 2005 regarding the above supplement." MRK-KRA00000393.

335.3. Merck's November 15, 2006 letter, responding to FDA's Comment 1.a stated:

> We acknowledge the deficiency concerning the mumps plaque reduction neutralization (PRN) assay. However, we believe that the clinical trial described in our supplement, and further described in this response, is adequate to support the proposed MMRII label change to revise the mumps end-expiry potency ...
>
> Furthermore, additional analysis performed by MRL has shown a strong correlation (93.6%) between ELISA and PRN serology results suggesting that the majority of the non-evaluable samples would have tested positive by PRN (BB-IND 1016, serial 86, June 2002).
>
> Given that we have mumps ELISA antibody titers for a substantial portion of the subjects with missing (or non-evaluable) PRN data, the observed ELISA results and the strong correlation between ELISA and PRN assay provide indirect evidence about the likely outcome for the missing data.

MRK-KRA00000393 at '99-00 (emphasis added).

335.4. Merck's November 15, 2006 letter, responding to FDA's Comment 1.c, stated:

> … mumps ELISA antibody titers are available for a substantial portion of the subjects with non-evaluable PRN data in all 3 groups, including the control group (subjects immunized with M-M-R™II containing mumps virus potency of 4.8 $\log_{10}$ $TCID_{50}$/dose. The observed mumps ELISA results (98.0%) and the strong correlation between ELISA and PRN assay provide indirect evidence about the likely outcome for the missing data in the 4.8 $\log_{10}$ $TCID_{50}$ mumps potency group.
>
> Additionally, there are several factors relating to the use of a neutralization assay that should be considered:
>
> - Although virus neutralization assays may be the most predictive method for assessing protective immunity, these assays are not standardized making them

poorly suited to evaluate large numbers of human sera due to assay variability (Mauldin et al. 2005. Mumps Virus Specific Antibody Titers from Pre-Vaccine Era Sara: Comparison of the Plaque Reduction Neutralization Assay and Enzyme Immunoassays. J. Clin. Microbiol. 2005; 9:4847-4851). …

- Given the suitability of the internal control group in this clinical trial (see explanation provided in the preceding bullet point), the true performance of the PRN assay used in this clinical trial should be assessed by responses observed in the control group rather than by the arbitrary acceptability criteria (lower bound of the observed response being equal or greater than 90%) set by the applicant.
- The PRN assay used in the study was developed solely for the purpose of this clinical trial. It was not used in any previous nor subsequent clinical trials. It is therefore difficult to ascertain the real performance of this assay other than in the context of this clinical trial.

…

Since the data show that M-M-R™II containing 4.1 $\log_{10}$ $TCID_{50}$ mumps potency induced an acceptable antibody response to mumps, as determined by the seroconversion rate for mumps neutralizing antibodies, which was also noninferior to M-M-R™II containing a release dose of mumps virus (4.8 $\log_{10}$ $TCID_{50}$), a mumps virus potency of 4.1 $\log_{10}$ $TCID_{50}$ was declared an acceptable end-expiry titer for MMRII.

MRK-KRA00000393 at ‘404-405 (emphasis added).

b. WT ELISA Used to Support sBLA for Mumps End Expiry

336. In May 2007 CBER responded to Merck’s November 2006 submission and stated: “the science related to immunogenicity testing of M-M-R®II has substantially evolved since our initial testing requirements. Use of ELISA data to evaluate the effect of differences in product potency on immunogenicity is now acceptable.”[898] Merck prepared an Amendment to the Supplemental Biologics License Application providing additional information to CBER, including

[898] MRK-KRA00000385.

data from rHA Protocol 009 and ProQuad Protocol 012, to support the use of Protocol 007 WT ELISA data in support of the Mumps End Expiry application. In December 2007, FDA approved the reduction in the end expiry claim of the MMRII label to "not less than 4.1" based on the WT ELISA results from the Protocol 007 Clinical Study.[899]

336.1. A letter from FDA's Acting Director, Division of Vaccines and Related Products Applications, Office of Vaccines Research and Review, CBER, Dr. Paul Richman, to MRL Associate Director, Worldwide Regulatory Affairs, Alison Fisher, dated May 18, 2007,[900] stated:

> This letter is in regard to the Supplement to your license Application submitted under Section 351 of the Public Health Services Act.
>
> The Center for Biologics Evaluation and Research (CBER) has completed the review of your Supplement received on April 13, 2005, for Measles, Mumps and Rubella Virus Vaccine Live (M-M-R®II), to include a change in the labeled potency of the mumps component of M-M-R®II from 20,000 $TCID_{50}$ to 12,500 $TCID_{50}$. Our review finds that the information and data submitted are inadequate for final approval at this time. We cannot accept use of multiple imputation analyses of the PRN data to support the lowering of mumps vaccine end-expiry potency.
>
> However, the science related to immunogenicity testing of M-M-R®II has substantially evolved since our initial testing requirements. Use of ELISA data to evaluate the effect of differences in product potency on immunogenicity is now acceptable. The change in end-expiry potency can be supported by the following analyses:
>
> 1. Product consistency

[899] MRK-KRA00000383.

[900] *See* MRK-KRA00552862 (A May 21, 2007 email from Alison Fisher to Luwy Musey, Jonathan Hartzel, and others, subject "FW:" stated: "Please let me know your thoughts here and your timeline for addressing this. Thanks again for your hard work in bringing the FDA to the conclusion that use of ELISA, to evaluate immunogenicity for the mumps end expiry study, can be acceptable given some further analysis." A reply email dated May 21, 2007 from Dr. Hartzel to Dr. Fisher, Dr. Musey, and others stated: "Wow. What a bizarre twist to an already bizarre history for this study. ..." (emphasis added).

> We request a demonstration of consistency between sublot 3 (4.8 $\log_{10}$ $TCID_{50}$ mumps potency) in the present study and two other lots used in previous MMR studies, e.g. Protocols 010-012, with mumps potency of at least 4.8 $\log_{10}$. ...

2. Non-inferiority

> If consistency among the three lots is demonstrated ... the ELISA results of the three lots are pooled to form a control group (C). Noninferiority of Sublot 2 (4.1 $\log_{10}$ $TCID_{50}$ mumps potency) from this supplement will be demonstrated by comparing ELISA results of this sublot (T) with ELISA results of the pooled control group which has at least 4.8 $\log_{10}$ mumps potency...

MRK-KRA00133168 at '170-71 (emphasis added).

336.2. A letter from MRL's Associate Director, Worldwide Regulatory Affairs, Dr. Alison Fisher, to FDA's Norman Baylor, Office of Vaccines Research and Review, CBER, regarding "Measles, Mumps and Rubella Vaccine Live (MMRII) STN 101069/5061, Amendment to Supplemental Biologics License Application Response to FDA Request for Information," dated June 5, 2007, stated:

> In this amendment to the supplement we include responses to CBER's May 18, 2007 questions regarding the change in mumps end expiry potency. These responses include the statistical analysis requested by CBER for product consistency and non inferiority based on the ELISA assay and support the change in mumps end expiry potency to 12,500 $TCID_{50}$.

MRK-KRA00133168.

336.3. Merck's responses to CBER's Question 1 regarding lot consistency stated:

> We were able to demonstrate consistency, based on the statistical methods outlined by CBER, between Sublot 3 (4.8 $\log_{10}$ $TCID_{50}$ mumps virus potency) in the present study (007) and two other lots used in previous studies in which M-M-R™II was administered,

M-M-R™II Protocol 009 and ProQuad™ Protocol 012.[901] Below, we describe how we arrived at selecting the two other lots and the consistency analysis itself.

Lot Selection: The pool of studies used to select two other lots of M-M-R™II was limited to studies in which the Mumps Enzyme-Linked Immunosorbent Assay (ELISA) with a mumps Jeryl Lynn™ 135 antigen was used for mumps immunogenicity testing (to coincide with the assay used for Protocol 007). There were three such studies (see Table 1), one from the M-M-R™II clinical program and two from the ProQuad™ clinical program. Ultimately the two lots that were chosen were 1) the control lot used for M-M-R™II Protocol 009 and 2) ...the control lot used for the ProQuad™ consistency lot study, Protocol 012. All studies measured mumps antibody levels at baseline and at Day 42 postvaccination and used a seroconversion definition of <10 ELISA Ab units at baseline to ≥10 ELISA Ab units at Day 42 postvaccination.

Table 1 provides a summary of the observed, per-protocol mumps immunogenicity results from the pool of studies selected from along with the 4.8 log10 TCID50 mumps virus potency control arm from Protocol 007. The results from Protocol 009 (M-M-R™II with recombinant human albumin [rHA] study) are from the subjects who received M-M-R™II (without rHA) with a mumps potency of 5.4 $\log_{10}$ $TCID_{50}$. The results from the two ProQuad™ studies are from the subjects who received M-M-R™II and VARIVAX concomitantly. Both studies used the same lot of M-M-R™II, which had a mumps potency of 5.0 $\log_{10}$ $TCID_{50}$, but ProQuad™ Protocol 012 was selected over ProQuad™ Protocol 013 ... due to the substantially larger number of subjects tested in that study.

[901] *See* Sections IX.A.6.b and c(1) above regarding MMRII Protocol 009 and ProQuad Protocol 012; *see also* MRK-KRA00140056 at ‘0109 (Protocol 009 using the WT ELISA with 10 Ab cutoff); *see also* MRK-KRA00162963 at ‘3016-17 (Protocol 012 using the WT ELISA with 10 Ab cutoff).

Table 1. Summary of Mumps Immunogenicity Results in Studies Administering M-M-R™II (Mumps Potency[†] ≥4.8 $\log_{10}$ $TCID_{50}$) and Using the Mumps Jeryl Lynn™ 135 ELISA (Per-Protocol)

Program	Protocol Description	Vaccines Administered	Mumps Potency[†] ($\log_{10}TCID_{50}$)	N	n	Observed SCR (95% CI)	Observed GMT (95% CI)
M-M-R™II	007: Mumps End Expiry	M-M-R™II + VARIVAX™	4.8	672	588	98.0% (576/588) (96.5%, 98.9%)	85.2 (78.9, 92.0)
	009: M-M-R™II with rHA	M-M-R™II	5.4	638	533	97.9% (522/533) (96.3%, 99.0%)	85.8 (80.1, 92.0)
ProQuad™	012: Consistency Lot Study	M-M-R™II + VARIVAX™	5.0[‡]	1012	872	97.9% (854/872) (96.8%, 98.8%)	89.7 (84.7, 94.9)
	013: Concomitant Use	M-M-R™II + VARIVAX™		479	145	98.6% (143/145) (95.1%, 99.8%)	98.1 (85.7, 112.3)

[†]Calibrated to the House Standard.
[‡]ProQuad™ Protocols 012 and 013 used the same lot of M-M-R™II.
N=Number of subjects vaccinated.
n=Number of subjects initially seronegative to mumps contributing to the per-protocol population.
SCR=Seroconversion rate.
GMT=Geometric mean titer (in ELISA Ab units).
CI=Confidence Interval
ELISA=Enzyme-linked immunosorbent assay.
rHA=Recombinant human albumin.

MRK-KRA00133172 at '72-74 (emphasis and highlight added).

336.4. Merck's responses to CBER's Question 2 regarding non-inferiority stated:

> Since the three control lots of M-M-R™II were shown to be consistent, these lots were pooled and compared with Sublot 2 (4.1 $\log_{10}$ $TCID_{50}$ mumps virus potency) from Protocol 007. A conclusion of similarity was found between Sublet 2 and the pooled lots for both seroconversion rates and GMTs, as shown in Table 3.

Id. at '177.

336.5. Table 3 in Merck's response to Question 2 stated:

Table 3. Statistical Analysis of the Similarity of Mumps Antibody Responses at 6 Weeks Postvaccination Between Sublot 2 of Protocol 007 and a Control Lot‖ of M-M-R™II in Subjects Initially Seronegative to Mumps (Per Protocol Analysis)

	M-M-R™II 007 Sublot 2 (4.1 $\log_{10}$TCID$_{50}$ mumps virus potency)			Control M-M-R™II‖ (≥4.8 $\log_{10}$TCID$_{50}$ mumps virus potency)			Difference‡ / Fold Difference§ (95% CI)	p-Value†	Conclusion
	N	n	Response	N	n	Response			
SCR	662	583	97.4%	2322	1993	97.9%	-0.5 (-2.2 , 0.7)	<.001*	Similar
GMT†			84.7			87.3	0.97 (0.89 , 1.05)	<.001*	Similar

† GMTs, their fold-differences, associated confidence intervals, and p-values are based on a statistical analysis model with the natural logarithm of the individual titers as the dependent variable and treatment as a fixed effect.

‡M-M-R™II 007 - Control M-M-R™II

§ M-M-R™II 007 / Control M-M-R™II.

‖ The control lot contains subjects who received M-M-R™II (4.8 $\log_{10}$ TCID$_{50}$ mumps virus potency) plus VARIVAX™ from M-M-R™II Protocol 007, M-M-R™II (5.4 $\log_{10}$ TCID$_{50}$ mumps virus potency) from M-M-R™II Protocol 009, and M-M-R™II (5.0 $\log_{10}$ TCID$_{50}$ mumps virus potency) plus VARIVAX™ from ProQuad™ Protocol 012.

* The lower bound of the two-sided 95% CI on the difference or the fold difference being > -5.0 percentage points or > 0.67-fold , respectively, implies that the difference is statistically significantly less than the prespecified clinically relevant decrease of 5 percentage points or 1.5-fold , respectively, and allows for a conclusion of similarity (non-inferiority). This corresponds to a p-value ≤ 0.05 and implies that the difference is statistically significantly less than the prespecified difference of 5 percentage points or 1.5-fold.

N=Number of subjects vaccinated in each group.

n=Number of subjects initially seronegative to mumps contributing to the per-protocol analyses.

CI=Confidence interval.

SCR=Seroconversion rate.

GMT=Geometric mean titer.

Id. at '79 (highlight added).

336.6. A letter from MRL's Director, Worldwide Regulatory Affairs, Dr. Alison Fisher, to FDA's Dr. Norman Baylor, Office of Vaccines Research and Review, CBER, regarding "Measles, Mumps and Rubella Vaccine Live (M-M-R™II) STN 101069/5061, AMENDMENT TO SUPPLEMENTAL BIOLOGICS LICENSE APPLICATION," dated December 3, 2007, stated:

> This submission is an amendment to the supplemental BLA, STN 101069/5061, that was submitted to the FDA on 29 January 2004. … This submission is intended to amend the submission from January 2004 with a new annotated label that is built on the current label (9739302). Revisions are in the DESCRIPTION, the revise the mumps end expiry from 20,000 TCID$_{50}$ to 12,500 TCID$_{50}$, and INDICATIONS AND USAGE sections, minor editorial change, as described in the initial submission (STN 10169/5061).

MRK-KRA00133313.

336.7. The December 3, 2007 AMENDMENT TO SUPPLEMENTAL BIOLOGICS LICENSE APPLICATION included "Proposed Labeling Text of the Package Circular" and

attached a document titled "CURRENT CIRCULAR SHOWING REVISIONS" for M-M-R®II" that stated:

> The reconstituted vaccine is for subcutaneous administration. Each 0.5 mL dose contains not less than 1,000 $TCID_{50}$ (tissue culture infectious doses) of measles virus; ~~20,000~~ 12,500 $TCID_{50}$ of mumps virus; and 1,000 $TCID_{50}$ of rubella virus.

MRK-KRA00133294 (strikeout, underline in original).

336.8. A letter from FDA's Acting Division Director, Division of Vaccines and Related Products Applications, CBER, Dr. Loris D. McVittie, to MRL's Associate Director, Worldwide Regulatory Affairs, Dr. Alison Fisher,[902] dated December 6, 2007, stated:

> We have approved your request to supplement your biologics license application for measles, Mumps, and Rubella Virus Vaccine Live, to include a change in the labeled potency of the mumps component from no less than 20,000 $TCID_{50}$ to no less than 12,500 $TCID_{50}$ per dose at end of expiry.

MRK-KRA00141976.

4. Merck's Statements in Its Applications for Regulatory Approval Were Misleading Because They Omitted That WT ELISA Assay Study Results Were Not Related to Protection

337. In my opinion, the measure of immunogenicity in the five clinical studies cited for support in the three applications were represented to be linked to protection against disease, illustrated by the following statements:[903]

[902] MRK-KRA01300697 at '698 (An email from Alison Fisher to Donna Zacholski, dated December 17, 2008 stated: "It took several rounds of questions from CBER and responses from Merck to get MEE [Mumps End Expiry] approved. We also submitted an additional statistical analysis of ELISA data in place of PRN assay for CBER which was key to approval.") (emphasis added.)

[903] *See also* MRK-KRA00126540 at '40-41 (sBLA for Mumps End Expiry: "One year persistence serology samples will not be tested in the mumps plaque reduction neutralization (PRN) assay. The PRN assay correlates well with the mumps ELISA and therefore only the ELISA testing will be conducted for this time point. Revaccinations will be based solely on ELISA results."); MRK-KRA00138137 at '144 (sBLA for rHA: "A single clinical trial, Protocol 009 … supports the replacement of HSA with rHA … as the study results demonstrated that M-M-R™II with rHA induced acceptable antibody response rates for … mumps …that are similar (noninferior) to those induced by M-M-R™II."); MRK-KRA00140056 at '0196 (sBLA for rHA: "Overall, the study results suggest the M-M-R™II with

- sBLA for Mumps End Expiry (Protocol 007): "The data presented here indicate with a high level of assurance that decreasing the mumps end-expiry titer from 4.3 [20,000] to 4.1 log10 [12,500] TCID50 per dose in children 12 to 18 months of age will ensure that M-M-R™II remains a highly effective vaccine."[904]
- sBLA for rHA (Protocol 009): – "Serum level of antibodies to … mumps … will be determined by enzyme-linked immunosorbent assays (ELISAs). Protective levels of antibody will be defined as ... ≥ 10.0 ELISA antibody units for mumps.[905]
- BLA for ProQuad (Protocol 012, Protocol 013, Protocol 014) – "The data summarized in this clinical summary demonstrate that ProQuad is immunogenic … and is as efficacious as its parent products."[906]

a. The sBLA for Mumps End Expiry

338. The Supplemental Biologics License Application to change the MMRII mumps end expiry specification from "not less than 4.3" to "not less than 4.1" was supported by a single clinical study that included analysis of the subjects using a WT ELISA with a cutoff of 10 Ab units to report a mumps seroconversion rate of 97.4%[907] for children who received the 4.1 $\log_{10}$ [12,500] $TCID_{50}$ dose.

339. With regard to the AIGENT measuring mumps neutralizing antibodies, the sBLA for Mumps End Expiry stated that "[m]umps neutralizing antibodies were measured immediately prior to vaccination and 6 weeks postvaccination using the plaque-reduction neutralization

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rHA is highly immunogenic, well tolerated, and will be as effective as M-M-R™II with HSA in preventing measles, mumps, and rubella."); MRK-KRA00158320 at '350 (BLA for ProQuad: "Merck & Co., Inc. has assessed the correlation between neutralizing antibody … and a wild-type enzyme-linked immunosorbent assay ... These data support the use of the results of a wild-type ELISA as a correlate for protection.")

[904] MRK-KRA00135723 at '46.

[905] MRK-KRA00140056 at '0941.

[906] MRK-KRA00158320 at '338- 339.

[907] MRK-KRA00135759 at '5782 (sBLA for Mumps End Expiry, Module 5, Protocol 007 Clinical Study Report).

(PRN) assay. PRN assay was used as the primary endpoint because it is a functional assay that measures the ability of the vaccine-induced immune response to inhibit viral replication in vitro, and can, therefore, be considered a surrogate for vaccine effectiveness."[908]

340. In my opinion, Merck's statement to FDA is misleading because it omitted that Merck had not performed a formal specificity analysis[909] for the AIGENT assay, and the AIGENT had not been validated as a measure of mumps neutralizing antibodies. Furthermore, the statement omitted that the endpoint measured by the AIGENT had not been demonstrated to have a connection to protection from disease.

341. With regard to the efficacy of a 4.1 mumps dose, the sBLA for Mumps End Expiry stated that that "[t]he data presented here indicate with a high level of assurance that decreasing the mumps end-expiry titer from 4.3 to 4.1 log10 TCID50 per dose in children 12 to 19 months of age will ensure that M-M-R™II remains a highly effective vaccine."[910]

342. In my opinion, Merck's statement to FDA was misleading because it omitted that the assays used in Protocol 007 had not been shown to be connected to protection from disease and therefore the results of the assays could not be used to provide reliable information about the effectiveness of MMRII with a mumps potency of not less than 4.1 log10 TCID50.

343. With regard to the seroconversion rate as a measure of protection, the sBLA for Mumps End Expiry stated that "[l]owering the mumps virus potency to 4.1 log10 TCID50 per dose maintains >90% seroconversion using a neutralization assay, thus preserving the excellent safety and efficacy profile of the vaccine."[911]

[908] MRK-KRA00135723 at '30-31 (emphasis added).
[909] Deposition of Florian Schodel, December 22, 2016, 352:14-365:15.
[910] MRK-KRA00135723 at '46 (emphasis added).
[911] MRK-KRA00135723 at '29.

344. In my opinion, Merck's statement to FDA was misleading because it omitted that the seroconversion rates measured by the AIGENT assay had not been shown to relate to protection from disease. Furthermore, unlike the neutralization assay used in the early efficacy studies to support the licensure of mumps vaccines, the seroconversion rate measured by the AIGENT assay did not "parallel protection from disease."

b. The sBLA for rHA

345. The Supplemental Biologics License Application to replace HSA with rHA in the M-M-R®II manufacturing process was supported by a single clinical study, Protocol 009, that used a WT ELISA with a cutoff of 10 Ab units to report a mumps seroconversion rate of 99.4%.[912]

346. With regard to the effectiveness of MMRII with rHA, the sBLA for rHA stated that "[o]verall, the study results suggest that M-M-R™II with rHA is highly immunogenic… and will be as effective as M-M-R™II with HSA in preventing… mumps…"[913]

347. In my opinion, the statement to the FDA is misleading because it omitted that the Protocol 009 clinical study to support the manufacturing change to rHA used the WT ELISA assay that had not been shown to have a connection to protection. Furthermore, since the WT ELISA assay used was not connected to protection, it is misleading to state that the WT ELISA assay results demonstrate that the manufacturing change from HSA to rHA did not impact the efficacy of the vaccine.

[912] MRK-KRA00140056 at '075 (sBLA for rHA, Module 5, Protocol 009 Clinical Study Report).
[913] MRK-KRA00140056 at '0196 .

c. The ProQuad BLA

348. The Biologics License Application to approve a license to sell ProQuad was based on five clinical studies, three that used a WT ELISA with a cutoff of 10 Ab units to report mumps seroconversion rates in Protocol 012 of 96.0%;[914] in Protocol 013 of 95.4% and 95.2%;[915] and in Protocol 014 of 99.5%.[916] This Biologics License Application stated that the WT ELISA used in Protocols 012, 013, and 014 to support licensure of ProQuad was a "correlate of protection."[917]

349. With regard to the efficacy of ProQuad, the BLA for ProQuad stated that "The data summarized in this clinical summary demonstrate that ProQuad is immunogenic … and is as efficacious as its parent products."[918]

350. In my opinion, the statement to the FDA is misleading because the seroconversion rates reported using the WT ELISA assay that was used in three of the five clinical studies supporting the application were not related to protection and could not support the assertion that ProQuad was as efficacious as its parent products.

351. The BLA for ProQuad stated that "…Merck & Co., Inc. has assessed the correlation between neutralizing antibody (as measured in plaque reduction neutralization [PRN] assay) and a wild-type enzyme-linked immunosorbent assay (ELISA). The overall agreement rate was 93.6% (480/513). These data support the use of the results of a wild-type ELISA as a correlate for protection."[919]

[914] MRK-KRA00158320 at '407 (Protocol 012, Combined Lots Mumps Antibody Responses).
[915] *Id.*, at '420 (Protocol 013, Mumps Antibody Response, Concomitant and Nonconcomitant Use).
[916] *Id.*, at '431 (Protocol 014 Observed Mumps Antibody Response in subjects who previously received MMRII and Varivax).
[917] MRK-KRA00158320 at '47-48, '50.
[918] MRK-KRA00158320 at '338- 339.
[919] MRK-KRA00158320 at '47-48, '50.

352. In my opinion, the statement to FDA was misleading because it omitted that the correlation data comparing the results of Protocol 007 clinical subjects tested by the WT ELISA and AIGENT assays did not demonstrate that the WT ELISA was connected to protection from disease because neither assay had been shown to relate to protection. It was also misleading because Merck's assessment of the correlation between the AIGENT and the WT ELISA provided no reliable data from which to conclude that the WT ELISA results were a correlate for protection.

D. Merck's Labels Are Misleading Because They Omit That the WT ELISA Merck Used Did Not Relate to Protection From Disease

1. MMRII Label 2005

353. In 2005, after Merck obtained approval to use rHA, Merck's label referenced the rHA in the Description section of the label. The one clinical study supporting the manufacturing change was not included in the Clinical Pharmacology section of the label.

353.1. In 2005, the "Description" section in Merck's MMRII label stated:

M-M-R® II
(MEASLES, MUMPS, and
RUBELLA VIRUS VACCINE LIVE)

DESCRIPTION

M-M-R® II (Measles, Mumps, and Rubella Virus Vaccine Live) is a live virus vaccine for vaccination against measles (rubeola), mumps, and rubella (German measles).

M-M-R II is a sterile lyophilized preparation of (1) ATTENUVAX® (Measles Virus Vaccine Live), a more attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and propagated in chick embryo cell culture; (2) MUMPSVAX® (Mumps Virus Vaccine Live), the Jeryl Lynn™ (B level) strain of mumps virus propagated in chick embryo cell culture; and (3) MERUVAX® II (Rubella Virus Vaccine Live), the Wistar RA 27/3 strain of live attenuated rubella virus propagated in WI-38 human diploid lung fibroblasts.[1,2]

The growth medium for measles and mumps is Medium 199 (a buffered salt solution containing vitamins and amino acids and supplemented with fetal bovine serum) containing SPGA (sucrose, phosphate, glutamate, and recombinant human albumin) as stabilizer and neomycin.

The growth medium for rubella is Minimum Essential Medium (MEM) [a buffered salt solution containing vitamins and amino acids and supplemented with fetal bovine serum] containing recombinant human albumin and neomycin. Sorbitol and hydrolyzed gelatin stabilizer are added to the individual virus harvests.

The cells, virus pools, and fetal bovine serum are all screened for the absence of adventitious agents.

The reconstituted vaccine is for subcutaneous administration. Each 0.5 mL dose contains not less than 1,000 $TCID_{50}$ (tissue culture infectious doses) of measles virus, 20,000 $TCID_{50}$ of mumps virus, and 1,000 $TCID_{50}$ of rubella virus. Each dose of the vaccine is calculated to contain sorbitol (14.5 mg), sodium phosphate, sucrose (1.9 mg), sodium chloride, hydrolyzed gelatin (14.5 mg), recombinant human albumin (≤0.3 mg), fetal bovine serum (<1 ppm), other buffer and media ingredients and approximately 25 mcg of neomycin. The product contains no preservative.

Before reconstitution, the lyophilized vaccine is a light yellow compact crystalline plug. M-M-R II, when reconstituted as directed, is clear yellow.

Schedule 1 (collecting MMRII labels including label in effect in 2005).

353.2. In 2005, the Clinical Pharmacology section of Merck's MMRII label stated:

CLINICAL PHARMACOLOGY

Measles, mumps, and rubella are three common childhood diseases, caused by measles virus, mumps virus (paramyxoviruses), and rubella virus (togavirus), respectively, that may be associated with serious complications and/or death. For example, pneumonia and encephalitis are caused by measles. Mumps is associated with aseptic meningitis, deafness and orchitis; and rubella during pregnancy may cause congenital rubella syndrome in the infants of infected mothers.

The impact of measles, mumps, and rubella vaccination on the natural history of each disease in the United States can be quantified by comparing the maximum number of measles, mumps, and rubella cases reported in a given year prior to vaccine use to the number of cases of each disease reported in 1995. For measles, 894,134 cases reported in 1941 compared to 288 cases reported in 1995 resulted in a 99.97% decrease in reported cases; for mumps, 152,209 cases reported in 1968 compared to 840 cases reported in 1995 resulted in a 99.45% decrease in reported cases; and for rubella, 57,686 cases reported in 1969 compared to 200 cases reported in 1995 resulted in a 99.65% decrease.[3]

Clinical studies of 284 triple seronegative children, 11 months to 7 years of age, demonstrated that M-M-R II is highly immunogenic and generally well tolerated. In these studies, a single injection of the vaccine induced measles hemagglutination-inhibition (HI) antibodies in 95%, mumps neutralizing antibodies in 96%, and rubella HI antibodies in 99% of susceptible persons. However, a small percentage (1-5%) of vaccinees may fail to seroconvert after the primary dose (see also INDICATIONS AND USAGE, *Recommended Vaccination Schedule*).

A study[4] of 6-month-old and 15-month-old infants born to vaccine-immunized mothers demonstrated that, following vaccination with ATTENUVAX, 74% of the 6-month-old infants developed detectable neutralizing antibody (NT) titers while 100% of the 15-month-old infants developed NT. This rate of seroconversion is higher than that previously reported for 6-month-old infants born to naturally immune mothers tested by HI assay. When the 6-month-old infants of immunized mothers were revaccinated at 15 months, they developed antibody titers equivalent to the 15-month-old vaccinees. The lower seroconversion rate in 6-month-olds has two possible explanations: 1) Due to the limit of the detection level of the assays (NT and enzyme immunoassay [EIA]), the presence of trace amounts of undetectable maternal antibody might interfere with the seroconversion of infants; or 2) The immune system of 6-month-olds is not always capable of mounting a response to measles vaccine as measured by the two antibody assays.

There is some evidence to suggest that infants who are born to mothers who had wild-type measles and who are vaccinated at less than one year of age may not develop sustained antibody levels when later revaccinated. The advantage of early protection must be weighed against the chance for failure to respond adequately on reimmunization.[5,6]

Efficacy of measles, mumps, and rubella vaccines was established in a series of double-blind controlled field trials which demonstrated a high degree of protective efficacy afforded by the individual vaccine components.[7-12] These studies also established that seroconversion in response to vaccination against measles, mumps, and rubella paralleled protection from these diseases.[13-15]

Following vaccination, antibodies associated with protection can be measured by neutralization assays, HI, or ELISA (enzyme linked immunosorbent assay) tests. Neutralizing and ELISA antibodies to measles, mumps, and rubella viruses are still detectable in most individuals 11 to 13 years after primary vaccination.[16-18] See INDICATIONS AND USAGE, *Non-Pregnant Adolescents and Adult Females*, for Rubella Susceptibility Testing.

The RA 27/3 rubella strain in M-M-R II elicits higher immediate post-vaccination HI, complement-fixing and neutralizing antibody levels than other strains of rubella vaccine[19-25] and has been shown to induce a broader profile of circulating antibodies including anti-theta and anti-iota precipitating antibodies.[26,27] The RA 27/3 rubella strain immunologically simulates natural infection more closely than other rubella vaccine viruses.[27-29] The increased levels and broader profile of antibodies produced by RA 27/3 strain rubella virus vaccine appear to correlate with greater resistance to subclinical reinfection with the wild virus,[27,29-31] and provide greater confidence for lasting immunity.

Schedule 1 (collecting MMRII labels including label in effect in 2005).

354. From 2005 when Merck made the rHA change to MMRII, until December 2007, when Merck changed the mumps end expiry specification, the Clinical Pharmacology Section of the MMRII label cited the efficacy studies supporting the licensure of the monovalent mumps vaccine and stated that these "these studies established that seroconversion in response to vaccination against … mumps … paralleled protection from … disease[]." Furthermore, the

Clinical Pharmacology section stated: "antibodies associated with protection can be measured by neutralization or ELISA assays."

355. In my opinion, the MMRII label from 2005 – 2007 was misleading because it omits that the seroconversion rate measured by the WT ELISA assay used in the clinical study supporting the change from HSA to rHA had not been shown to "parallel protection from disease" as the earlier studies cited in the label had demonstrated. Furthermore, because the WT ELISA assay used in Protocol 009 did not measure "antibodies associated with protection" it is misleading to omit that the WT ELISA assay could not provide reliable information about protection from disease.

2. MMRII Label 2007

356. In 2007, after Merck obtained approval to lower the mumps end expiry potency claim on the MMRII label, Merck's label stated "not less … 12,500 [4.1 log10] TCID50" of mumps in the Description section of the label. The one clinical study supporting the change in potency, Protocol 007, was not included in the Clinical Pharmacology section of the label.

356.1. After the mumps end expiry change to the MMRII label in 2007, the "Description" section of the MMRII label stated:

M-M-R® II
(MEASLES, MUMPS, and
RUBELLA VIRUS VACCINE LIVE)

DESCRIPTION

M-M-R® II (Measles, Mumps, and Rubella Virus Vaccine Live) is a live virus vaccine for vaccination against measles (rubeola), mumps, and rubella (German measles).

M-M-R II is a sterile lyophilized preparation of (1) ATTENUVAX® (Measles Virus Vaccine Live), a more attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and propagated in chick embryo cell culture; (2) MUMPSVAX® (Mumps Virus Vaccine Live), the Jeryl Lynn™ (B level) strain of mumps virus propagated in chick embryo cell culture; and (3) MERUVAX® II (Rubella Virus Vaccine Live), the Wistar RA 27/3 strain of live attenuated rubella virus propagated in WI-38 human diploid lung fibroblasts.[1,2]

The growth medium for measles and mumps is Medium 199 (a buffered salt solution containing vitamins and amino acids and supplemented with fetal bovine serum) containing SPGA (sucrose, phosphate, glutamate, and recombinant human albumin) as stabilizer and neomycin.

The growth medium for rubella is Minimum Essential Medium (MEM) [a buffered salt solution containing vitamins and amino acids and supplemented with fetal bovine serum] containing recombinant human albumin and neomycin. Sorbitol and hydrolyzed gelatin stabilizer are added to the individual virus harvests.

The cells, virus pools, and fetal bovine serum are all screened for the absence of adventitious agents.

The reconstituted vaccine is for subcutaneous administration. Each 0.5 mL dose contains not less than 1,000 $TCID_{50}$ (tissue culture infectious doses) of measles virus; 12,500 $TCID_{50}$ of mumps virus; and 1,000 $TCID_{50}$ of rubella virus. Each dose of the vaccine is calculated to contain sorbitol (14.5 mg), sodium phosphate, sucrose (1.9 mg), sodium chloride, hydrolyzed gelatin (14.5 mg), recombinant human albumin (≤0.3 mg), fetal bovine serum (<1 ppm), other buffer and media ingredients and approximately 25 mcg of neomycin. The product contains no preservative.

Before reconstitution, the lyophilized vaccine is a light yellow compact crystalline plug. M-M-R II, when reconstituted as directed, is clear yellow.

Schedule 1 (collecting MMRII labels including label in effect in 2007).

356.2. After the mumps end expiry change to the MMRII label in 2007 the "Clinical Pharmacology" section of the MMRII label stated:

CLINICAL PHARMACOLOGY

Measles, mumps, and rubella are three common childhood diseases, caused by measles virus, mumps virus (paramyxoviruses), and rubella virus (togavirus), respectively, that may be associated with serious complications and/or death. For example, pneumonia and encephalitis are caused by measles. Mumps is associated with aseptic meningitis, deafness and orchitis; and rubella during pregnancy may cause congenital rubella syndrome in the infants of infected mothers.

The impact of measles, mumps, and rubella vaccination on the natural history of each disease in the United States can be quantified by comparing the maximum number of measles, mumps, and rubella cases reported in a given year prior to vaccine use to the number of cases of each disease reported in 1995. For measles, 894,134 cases reported in 1941 compared to 288 cases reported in 1995 resulted in a 99.97% decrease in reported cases; for mumps, 152,209 cases reported in 1968 compared to 840 cases reported in 1995 resulted in a 99.45% decrease in reported cases; and for rubella, 57,686 cases reported in 1969 compared to 200 cases reported in 1995 resulted in a 99.65% decrease.[3]

Clinical studies of 284 triple seronegative children, 11 months to 7 years of age, demonstrated that M-M-R II is highly immunogenic and generally well tolerated. In these studies, a single injection of the vaccine induced measles hemagglutination-inhibition (HI) antibodies in 95%, mumps neutralizing antibodies in 96%, and rubella HI antibodies in 99% of susceptible persons. However, a small percentage (1-5%) of vaccinees may fail to seroconvert after the primary dose (see also INDICATIONS AND USAGE, *Recommended Vaccination Schedule*).

A study[4] of 6-month-old and 15-month-old infants born to vaccine-immunized mothers demonstrated that, following vaccination with ATTENUVAX, 74% of the 6-month-old infants developed detectable neutralizing antibody (NT) titers while 100% of the 15-month-old infants developed NT. This rate of seroconversion is higher than that previously reported for 6-month-old infants born to naturally immune mothers tested by HI assay. When the 6-month-old infants of immunized mothers were revaccinated at 15 months, they developed antibody titers equivalent to the 15-month-old vaccinees. The lower seroconversion rate in 6-month-olds has two possible explanations: 1) Due to the limit of the detection level of the assays (NT and enzyme immunoassay [EIA]), the presence of trace amounts of undetectable maternal antibody might interfere with the seroconversion of infants; or 2) The immune system of 6-month-olds is not always capable of mounting a response to measles vaccine as measured by the two antibody assays.

There is some evidence to suggest that infants who are born to mothers who had wild-type measles and who are vaccinated at less than one year of age may not develop sustained antibody levels when later revaccinated. The advantage of early protection must be weighed against the chance for failure to respond adequately on reimmunization.[5,6]

Efficacy of measles, mumps, and rubella vaccines was established in a series of double-blind controlled field trials which demonstrated a high degree of protective efficacy afforded by the individual vaccine components.[7-12] These studies also established that seroconversion in response to vaccination against measles, mumps, and rubella paralleled protection from these diseases.[13-15]

Following vaccination, antibodies associated with protection can be measured by neutralization assays, HI, or ELISA (enzyme linked immunosorbent assay) tests. Neutralizing and ELISA antibodies to measles, mumps, and rubella viruses are still detectable in most individuals 11 to 13 years after primary vaccination.[16-18] See INDICATIONS AND USAGE, *Non-Pregnant Adolescents and Adult Females*, for Rubella Susceptibility Testing.

The RA 27/3 rubella strain in M-M-R II elicits higher immediate post-vaccination HI, complement-fixing and neutralizing antibody levels than other strains of rubella vaccine[19-25] and has been shown to induce a broader profile of circulating antibodies including anti-theta and anti-iota precipitating antibodies.[26,27] The RA 27/3 rubella strain immunologically simulates natural infection more closely than other rubella vaccine viruses.[27-29] The increased levels and broader profile of antibodies produced by RA 27/3 strain rubella virus vaccine appear to correlate with greater resistance to subclinical reinfection with the wild virus,[27,29-31] and provide greater confidence for lasting immunity.

Schedule 1 (collecting MMRII labels including label in effect in 2007).

357. From 2007 when Merck's sBLA to lower the end expiry potency of the mumps component of MMRII, through the present (2018), the Clinical Pharmacology Section of the MMRII label cited the efficacy studies supporting the licensure of the monovalent mumps

vaccine and stated that these "these studies established that seroconversion in response to vaccination against … mumps … paralleled protection from … disease[]." Furthermore, the Clinical Pharmacology section stated: "antibodies associated with protection can be measured by neutralization or ELISA assays."

358. In my opinion, the MMRII label from 2007 through the present (2018) was misleading because it omitted that the seroconversion rate measured by the WT ELISA assay used in the clinical study supporting the change in the mumps end-expiry potency had not been shown to "parallel protection from disease" as the earlier studies cited in the label had reported. Furthermore, because the AIGENT and WT ELISA assays used in Protocol 007 did not measure "antibodies associated with protection" it is misleading to omit that Protocol 007 data could not provide reliable information about protection from disease.

359. In my opinion, the MMRII label after 2007 failed to state that the assays used in the clinical study to support a 12,500 [4.1 $\log_{10}$] $TCID_{50}$ potency were not able to assure that the vaccine dose at 12,500 [4.1 $\log_{10}$] $TCID_{50}$ was protective against disease. Furthermore, the reasons why Merck could not assure the vaccine at 4.1 log was protective were:

- Neither the AIGENT nor the WT ELISA measured protection against disease;
- In the AIGENT, the "large proportion of missing data precluded a conclusion of success" at 4.1 log [12,500];[920]

3. ProQuad Label

360. In 2005, after Merck obtained an FDA-approved license to sell ProQuad the ProQuad label has included the following sections: "Description," "Clinical Pharmacology" and "Clinical Studies." From 2005 until 2018, there have been two relevant revisions to the ProQuad

[920] MRK-KRA00000479.

label. The five clinical studies supporting the BLA for ProQuad are cited in the Clinical Studies section of the label.

360.1. In 2005, the "Description" section in Merck's ProQuad label stated:

ProQuad®
[Measles, Mumps, Rubella and Varicella (Oka/Merck) Virus Vaccine Live]

DESCRIPTION

ProQuad® is a combined attenuated live virus vaccine containing measles, mumps, rubella, and varicella viruses. ProQuad is a sterile lyophilized preparation of (1) the components of M-M-R®II (Measles, Mumps and Rubella Virus Vaccine Live): Measles Virus Vaccine Live, a more attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and propagated in chick embryo cell culture; Mumps Virus Vaccine Live, the Jeryl Lynn™ (B level) strain of mumps virus propagated in chick embryo cell culture; Rubella Virus Vaccine Live, the Wistar RA 27/3 strain of live attenuated rubella virus propagated in WI-38 human diploid lung fibroblasts; and (2) Varicella Virus Vaccine Live (Oka/Merck), the Oka/Merck strain of varicella-zoster virus propagated in MRC-5 cells. The cells, virus pools, bovine serum, and human albumin used in manufacturing are all tested to provide assurance that the final product is free of potential adventitious agents.

ProQuad, when reconstituted as directed, is a sterile preparation for subcutaneous administration. Each 0.5-mL dose contains not less than 3.00 $\log_{10}$ $TCID_{50}$ (50% tissue culture infectious dose) of measles virus; 4.30 $\log_{10}$ $TCID_{50}$ of mumps virus; 3.00 $\log_{10}$ $TCID_{50}$ of rubella virus; and a minimum of 3.99 $\log_{10}$ PFU (plaque-forming units) of Oka/Merck varicella virus.

Each 0.5-mL dose of the vaccine contains no more than 21 mg of sucrose, 11 mg of hydrolyzed gelatin, 2.4 mg of sodium chloride, 1.8 mg of sorbitol, 0.40 mg of monosodium L-glutamate, 0.34 mg of sodium phosphate dibasic, 0.31 mg of human albumin, 0.17 mg of sodium bicarbonate, 72 mcg of potassium phosphate monobasic, 60 mcg of potassium chloride; 36 mcg of potassium phosphate dibasic; residual components of MRC-5 cells including DNA and protein; <16 mcg of neomycin, bovine calf serum (0.5 mcg), and other buffer and media ingredients. The product contains no preservative.

MRK-KRA00177125.

360.2. In 2005, the Clinical Pharmacology section of Merck's ProQuad label stated:

CLINICAL PHARMACOLOGY

Background

Measles, mumps, rubella, and varicella are 4 common childhood diseases caused by measles virus, mumps virus, rubella virus, and varicella virus, respectively. These diseases may be associated with serious complications and/or death. For example, measles can be associated with pneumonia and encephalitis; mumps can be associated with aseptic meningitis, deafness, and orchitis; rubella occurring during pregnancy can cause congenital rubella syndrome in the infants of infected mothers; and wild-type varicella can be associated with bacterial superinfection, pneumonia, encephalitis, and Reye's syndrome.

Mechanism of action

In clinical efficacy studies, seroconversion in response to vaccination against measles, mumps, and rubella paralleled protection from these diseases. Also, in previous studies with varicella vaccine, antibody responses against varicella virus ≥5 units/mL in a glycoprotein enzyme-linked immunosorbent assay (gpELISA) (not commercially available) similarly correlated with long-term protection. Clinical studies with a single dose of ProQuad have shown that vaccination elicited rates of antibody responses against measles, mumps, and rubella that were similar to those observed after vaccination with a single dose of M-M-RII (see CLINICAL STUDIES) and seroresponse rates for varicella virus were similar to those observed after vaccination with a single dose of VARIVAX (see CLINICAL STUDIES). The duration of protection from measles, mumps, rubella, and varicella infections after vaccination with ProQuad is unknown.

Persistence of Antibody Responses after Vaccination

The persistence of antibody at 1 year after vaccination was evaluated in a subset of 2107 children enrolled in the clinical trials. Antibody was detected in 98.9% (1722/1741) for measles, 96.7% (1676/1733) for mumps, 99.6% (1796/1804) for rubella, and 97.5% (1512/1550) for varicella (≥5 gpELISA units/mL) of vaccinees following a single dose of ProQuad.

Experience with M-M-RII demonstrates that antibodies to measles, mumps, and rubella viruses are still detectable in most individuals 11 to 13 years after primary vaccination.[1] Varicella antibodies were present for up to ten years post-vaccination in most of the individuals tested who received 1 dose of VARIVAX.

Id. at '125-126.

360.3. In 2005, the Clinical Studies section of Merck's ProQuad label stated:

CLINICAL STUDIES

Formal studies to evaluate the clinical efficacy of ProQuad have not been performed.

Efficacy of the measles, mumps, rubella and varicella components of ProQuad was previously established in a series of clinical studies with the monovalent vaccines. A high degree of protection from infection was demonstrated in these studies.[2-9]

Immunogenicity

Immunogenicity was studied in 5835 healthy children 12 months to 6 years of age with a negative clinical history of measles, mumps, rubella, and varicella who participated in 5 randomized clinical trials. The immunogenicity of ProQuad was similar to that of its individual component vaccines (M-M-RII and VARIVAX), which are currently used in routine immunization.

The presence of detectable antibody was assessed by an appropriately sensitive enzyme-linked immunosorbent assay (ELISA) for measles, mumps (wild type and vaccine type strains), and rubella, and by gpELISA for varicella. For evaluation of vaccine response rates, a positive result in the measles ELISA corresponded to measles antibody concentrations of ≥255 mIU/mL when compared to the WHO II (66/202) Reference Immunoglobulin for Measles.

Children were positive for mumps antibody if the antibody level was ≥10 ELISA units/mL. A positive result in the rubella ELISA corresponded to concentrations of ≥10 IU rubella antibody/mL when compared to the WHO International Reference Serum for Rubella; children with varicella antibody levels ≥5 gpELISA units/mL were considered to be seropositive since a response rate based on ≥5 gpELISA units/mL has been shown to be highly correlated with long-term protection.

Children who received a single dose of ProQuad at 12-23 months of age

In 4 randomized clinical trials, 5446 healthy children 12 to 23 months of age were administered ProQuad, and 2038 children were vaccinated with M-M-RII and VARIVAX given concomitantly at separate injection sites. Subjects enrolled in each of these trials had a negative clinical history, no known recent exposure and no vaccination history for varicella, measles, mumps, and rubella. Children were excluded from study participation if they had an immune impairment or had a history of allergy to components of the vaccine(s). Except for in 1 trial (see *Studies With Other Vaccines*), no concomitant vaccines were permitted during study participation. Following a single dose of ProQuad, the vaccine response rates were 97.4% (95% CI: 96.9, 97.9) for measles, 95.8 (95% CI: 95.1, 96.4) to 98.8% (95% CI: 97.9, 99.4) for mumps, and 98.5% (95% CI: 98.1, 98.8) for rubella. The vaccine response rate was 91.2% (95% CI: 90.3, 92.0) for varicella. These results were similar to the immune response rates induced by concomitant administration of single doses of M-M-RII and VARIVAX at separate injection sites. Fever and measles-like rashes were the only adverse experiences that occurred more frequently in recipients of a single dose of ProQuad compared with recipients of single doses of M-M-RII and VARIVAX (see ADVERSE REACTIONS).

Id. at '126.

360.4. The 2005 ProQuad Clinical Studies section also stated:

Children Who Received a Second Dose of ProQuad

In 2 of the 4 randomized clinical trials described above, a subgroup (N=1035) of the 5446 children administered a single dose of ProQuad were administered a second dose of ProQuad approximately 3 months after the first dose. Children were excluded from receiving a second dose of ProQuad if they were recently exposed to or developed varicella, measles, mumps, and/or rubella prior to receipt of the second dose. No concomitant vaccines were administered to these children. The proportion of initially seronegative vaccinees with positive serological responses following two doses were 99.4% (95% CI: 98.6, 99.8) for measles, 99.9% (95% CI: 99.4, 100) for mumps, 98.3% (95% CI: 97.2, 99.0) for rubella, and 99.4% (95% CI: 98.7, 99.8) for varicella (≥5 gpELISA units/mL). The geometric mean titers (GMTs) following the second dose of ProQuad increased approximately 2-fold each for measles, mumps, and rubella, and approximately 41-fold for varicella.

In these trials, the rates of adverse experiences after the second dose of ProQuad were generally similar to, or lower than, those seen with the first dose. The fever rate was lower after the second dose than after the first dose.

Id. at '126-127.

360.5. The 2005 ProQuad Clinical Studies section also stated:

Children Who Received ProQuad at 4 to 6 Years of Age After Primary Vaccination With M-M-RII and VARIVAX

In a clinical trial involving 799 healthy 4- to 6-year-old children who had received M-M-RII and VARIVAX at least 1 month prior to study entry, 399 received ProQuad and placebo while 205 received M-M-RII and placebo concomitantly at separate injection sites. Another 195 healthy children were administered M-M-RII and VARIVAX concomitantly at separate injection sites. Children were eligible if they were previously administered primary doses of M-M-RII and VARIVAX, either concomitantly or non-concomitantly, at 12 months of age or older. Children were excluded if they were recently exposed to measles, mumps, rubella, and/or varicella, had an immune impairment, or had a history of allergy to components of the vaccine(s). No concomitant vaccines were permitted during study participation.

Following the dose of ProQuad, seropositivity rates were 99.2% (95% CI: 97.6, 99.8) for measles, 99.5% (95% CI: 98.0, 99.9) for mumps, 100% (95% CI: 99.0, 100) for rubella, and 98.9% (95% CI: 97.2, 99.7) for varicella (≥5 gpELISA units/mL). Approximate geometric mean fold-rises in antibody titers (pre-vaccination to post-vaccination) for measles, mumps, rubella, and varicella were 1.2, 2.4, 3.0 and 12, respectively. Post-vaccination GMTs for recipients of ProQuad were similar to those following a second dose of M-M-RII and VARIVAX administered concomitantly at separate injection sites. Additionally, GMTs for measles, mumps, and rubella were similar to those following a second dose of M-M-RII given concomitantly with placebo. The rates of adverse experiences, including the most commonly reported adverse experiences of injection site reactions, nasopharyngitis and cough were generally similar among the 3 treatment groups.

Id. at '127.

360.6. The 2005 ProQuad Clinical Studies section stated:

Studies With Other Vaccines

In a clinical trial involving 1913 healthy children 12 to 15 months of age, 949 received ProQuad plus Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP) and *Haemophilus Influenzae* type b Conjugate (Meningococcal Protein Conjugate) and Hepatitis B (Recombinant) Vaccine concomitantly at separate injection sites. Another 485 healthy children received ProQuad at the initial visit followed by DTaP and *Haemophilus* b Conjugate and Hepatitis B (Recombinant) Vaccine given concomitantly 6 weeks later while 479 children were immunized with M-M-RII and VARIVAX given concomitantly at separate injection sites at the first visit. Seroconversion rates and antibody titers for measles, mumps, rubella, varicella, anti-PRP and hepatitis B were comparable between the 2 groups at approximately 6 weeks post-vaccination indicating the ProQuad and *Haemophilus* b Conjugate (Meningococcal Protein Conjugate) and Hepatitis B (Recombinant) Vaccine may be administered concomitantly at separate injection sites. There are insufficient data to support concomitant immunization with diphtheria, tetanus and acellular pertussis vaccine. No clinically significant differences in adverse experiences were reported between treatment groups.

Id. at '127.

360.7. In 2009 the "Description" section in Merck's ProQuad label stated:

ProQuad®
Measles, Mumps, Rubella and Varicella Virus Vaccine Live 9950900

11 DESCRIPTION

ProQuad (Measles, Mumps, Rubella and Varicella Virus Vaccine Live) is a combined, attenuated, live virus vaccine containing measles, mumps, rubella, and varicella viruses. ProQuad is a sterile lyophilized preparation of (1) the components of M-M-R II (Measles, Mumps, and Rubella Virus Vaccine Live): Measles Virus Vaccine Live, a more attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and propagated in chick embryo cell culture; Mumps Virus Vaccine Live, the Jeryl Lynn™ (B level) strain of mumps virus propagated in chick embryo cell culture; Rubella Virus Vaccine Live, the Wistar RA 27/3 strain of live attenuated rubella virus propagated in WI-38 human diploid lung fibroblasts; and (2) Varicella Virus Vaccine Live (Oka/Merck), the Oka/Merck strain of varicella-zoster virus propagated in MRC-5 cells. The cells, virus pools, bovine serum, and human albumin used in manufacturing are all tested to provide assurance that the final product is free of potential adventitious agents.

ProQuad, when reconstituted as directed, is a sterile suspension for subcutaneous administration. Each 0.5-mL dose contains not less than 3.00 $\log_{10}$ $TCID_{50}$ of measles virus; 4.30 $\log_{10}$ $TCID_{50}$ of mumps virus; 3.00 $\log_{10}$ $TCID_{50}$ of rubella virus; and a minimum of 3.99 $\log_{10}$ PFU of Oka/Merck varicella virus.

Each 0.5-mL dose of the vaccine contains no more than 21 mg of sucrose, 11 mg of hydrolyzed gelatin, 2.4 mg of sodium chloride, 1.8 mg of sorbitol, 0.40 mg of monosodium L-glutamate, 0.34 mg of sodium phosphate dibasic, 0.31 mg of human albumin, 0.17 mg of sodium bicarbonate, 72 mcg of potassium phosphate monobasic, 60 mcg of potassium chloride, 36 mcg of potassium phosphate dibasic, residual components of MRC-5 cells including DNA and protein; <16 mcg of neomycin, bovine calf serum (0.5 mcg), and other buffer and media ingredients. The product contains no preservative.

MRK-KRA01634450 at '465.

360.8. In 2009 the "Clinical Pharmacology" section in Merck's ProQuad label stated:

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

ProQuad has been shown to induce measles-, mumps-, rubella-, and varicella-specific immunity, which is thought to be the mechanism by which it protects against these four childhood diseases.

The efficacy of ProQuad was established through the use of immunological correlates for protection against measles, mumps, rubella, and varicella. Results from efficacy studies or field effectiveness studies that were previously conducted for the component vaccines were used to define levels of serum antibodies that correlated with protection against measles, mumps, and rubella. Also, in previous studies with varicella vaccine, antibody responses against varicella virus ≥5 gpELISA units/mL in a glycoprotein enzyme-linked immunosorbent assay (gpELISA) (not commercially available) similarly correlated with long-term protection. In these efficacy studies, the clinical endpoint for measles and mumps was a clinical diagnosis of either disease confirmed by a 4-fold or greater rise in serum antibody titers between either postvaccination or acute and convalescent titers; for rubella, a 4-fold or greater rise in antibody titers with or without clinical symptoms of rubella; and for varicella, varicella-like rash that occurred >42 days postvaccination and for which varicella was not excluded by either viral cultures of the lesion or serological tests. Specific laboratory evidence of varicella either by serology or culture was not required to confirm the diagnosis of varicella. Clinical studies with a single dose of ProQuad have shown that vaccination elicited rates of antibody responses against measles, mumps, and rubella that were similar to those observed after vaccination with a single dose of M-M-R II *[see Clinical Studies (14)]* and seroresponse rates for varicella virus were similar to those observed after vaccination with a single dose of VARIVAX *[see Clinical Studies (14)]*. The duration of protection from measles, mumps, rubella, and varicella infections after vaccination with ProQuad is unknown.

Id. at '465.

360.9. In 2009 the "Clinical Studies" section in Merck's ProQuad label stated:

14 CLINICAL STUDIES

Formal studies to evaluate the clinical efficacy of ProQuad have not been performed.

Efficacy of the measles, mumps, rubella, and varicella components of ProQuad was previously established in a series of clinical studies with the monovalent vaccines. A high degree of protection from infection was demonstrated in these studies.[10-17]

Id. at '466.

360.10. In 2009 the ProQuad Label also stated:

Immunogenicity in Children 12 Months to 6 Years of Age

Prior to licensure, immunogenicity was studied in 5845 healthy children 12 months to 6 years of age with a negative clinical history of measles, mumps, rubella, and varicella who participated in 5 randomized clinical trials. The immunogenicity of ProQuad was similar to that of its individual component vaccines (M-M-R II and VARIVAX), which are currently used in routine vaccination.

The presence of detectable antibody was assessed by an appropriately sensitive enzyme-linked immunosorbent assay (ELISA) for measles, mumps (wild-type and vaccine-type strains), and rubella, and by gpELISA for varicella. For evaluation of vaccine response rates, a positive result in the measles ELISA corresponded to measles antibody concentrations of •255 mIU/mL when compared to the WHO II (66/202) Reference Immunoglobulin for Measles.

Children were positive for mumps antibody if the antibody level was •10 ELISA units/mL. A positive result in the rubella ELISA corresponded to concentrations of •10 IU rubella antibody/mL when compared to the WHO International Reference Serum for Rubella; children with varicella antibody levels •5 gpELISA units/mL were considered to be seropositive since a response rate based on •5 gpELISA units/mL has been shown to be highly correlated with long-term protection.

Id. at '466.

360.11. In 2009 the ProQuad Label also stated:

Immunogenicity in Children 12 to 23 Months of Age After a Single Dose

In 4 randomized clinical trials, 5446 healthy children 12 to 23 months of age were administered ProQuad, and 2038 children were vaccinated with M-M-R II and VARIVAX given concomitantly at separate injection sites. Subjects enrolled in each of these trials had a negative clinical history, no known recent exposure, and no vaccination history for varicella, measles, mumps, and rubella. Children were excluded from study participation if they had an immune impairment or had a history of allergy to components of the vaccine(s). Except for in 1 trial *[see ProQuad Administered with Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP) and Haemophilus influenzae type b Conjugate (Meningococcal Protein Conjugate) and Hepatitis B (Recombinant) Vaccine below]*, no concomitant vaccines were permitted during study participation. The race distribution of the study subjects across these studies following a first dose of ProQuad was as follows: 66.3% White; 12.7% African-American; 9.9% Hispanic; 6.7% Asian/Pacific; 4.2% other; and 0.2% American Indian. The gender distribution of the study subjects across these studies following a first dose of ProQuad was 52.6% male and 47.4% female. A summary of combined immunogenicity results 6 weeks following administration of a single dose of ProQuad or M-M-R II and VARIVAX is shown in Table 10. These results were similar to the immune response rates induced by concomitant administration of single doses of M-M-R II and VARIVAX at separate injection sites (lower bound of the 95% CI for the risk difference in measles, mumps, and rubella seroconversion rates were >-5.0 percentage points and the lower bound of the 95% CI for the risk difference in varicella seroprotection rates was either >-15 percentage points [one study] or >-10.0 percentage points [three studies]).

Id. at '466.

360.12. The 2009 ProQuad Label Table 10 stated:

Table 10
Summary of Combined Immunogenicity Results 6 Weeks Following the Administration of a Single Dose of ProQuad (Varicella Virus Potency •3.97 $\log_{10}$ PFU) or M-M-R II and VARIVAX (Per-Protocol Population)

Group	Antigen	n	Observed Response Rate (95% CI)	Observed GMT (95% CI)
ProQuad (N=5446†)	Varicella	4381	91.2% (90.3%, 92.0%)	15.5 (15.0, 15.9)
	Measles	4733	97.4% (96.9%, 97.9%)	3124.9 (3038.9, 3213.3)
	Mumps (OD cutoff)‡	973	98.8% (97.9%, 99.4%)	105.3 (98.0, 113.1)
	Mumps (wild-type ELISA)‡	3735	95.8% (95.1%, 96.4%)	93.1 (90.2, 96.0)
	Rubella	4773	98.5% (98.1%, 98.8%)	91.8 (89.6, 94.1)
M-M-R II + VARIVAX (N=2038†)	Varicella	1417	94.1% (92.8%, 95.3%)	16.6 (15.9, 17.4)
	Measles	1516	98.2% (97.4%, 98.8%)	2239.6 (2138.3, 2345.6)
	Mumps (OD cutoff)‡	501	99.4% (98.3%, 99.9%)	87.5 (79.7, 96.0)
	Mumps (wild-type ELISA)‡	1017	98.0% (97.0%, 98.8%)	90.8 (86.2, 95.7)
	Rubella	1528	98.5% (97.7%, 99.0%)	102.2 (97.8, 106.7)

† Includes ProQuad + Placebo followed by ProQuad (Visit 1) (Protocol 009), ProQuad Middle and High Doses (Visit 1) (Protocol 011), ProQuad (Lot 1, Lot 2, Lot 3) (Protocol 012), both the Concomitant and Non-concomitant groups (Protocol 013).

‡ The mumps antibody response was assessed by a vaccine-strain ELISA in Protocols 009 and 011 and by a wild-type ELISA in Protocols 012 and 013. In the former assay, the serostatus was based on the OD cutoff of the assay. In the latter assay, 10 mumps ELISA units was used as the serostatus cutoff.

n = Number of per-protocol subjects with evaluable serology.
CI = Confidence interval.
GMT = Geometric mean titer.
ELISA = Enzyme-linked immunosorbent assay.
PFU = Plaque-forming units.
OD = Optical density.

Id. at '466-467.

360.13. The 2009 ProQuad Label also stated:

Immunogenicity in Children 15 to 31 Months of Age After a Second Dose of ProQuad

In 2 of the 4 randomized clinical trials described above, a subgroup (N=1035) of the 5446 children administered a single dose of ProQuad were administered a second dose of ProQuad approximately 3 to 9 months after the first dose. Children were excluded from receiving a second dose of ProQuad if they were recently exposed to or developed varicella, measles, mumps, and/or rubella prior to receipt of the second dose. No concomitant vaccines were administered to these children. The race distribution across these studies following a second dose of ProQuad was as follows: 67.3% White; 14.3% African-American; 8.3% Hispanic; 5.4% Asian/Pacific; 4.4% other; 0.2% American Indian; and 0.10% mixed. The gender distribution of the study subjects across these studies following a second dose of ProQuad was 50.4% male and 49.6% female. A summary of immune responses following a second dose of ProQuad is presented in Table 11. Results from this study showed that 2 doses of ProQuad administered at least 3 months apart elicited a positive antibody response to all four antigens in greater than 98% of subjects. The geometric mean titers (GMTs) following the second dose of ProQuad increased approximately 2-fold each for measles, mumps, and rubella, and approximately 41-fold for varicella.

Table 11
Summary of Immune Response to a First and Second Dose of ProQuad
in Subjects < 3 Years of Age Who Received ProQuad with a Varicella Virus Dose • 3.97 Log_{10} PFU†

		Dose 1 N=1097			Dose 2 N=1097		
Antigen	Serostatus Cutoff/ Response Criteria	n	Observed Response Rate (95% CI)	Observed GMT (95% CI)	n	Observed Response Rate (95% CI)	Observed GMT (95% CI)
Measles	• 120 mIU/mL‡	915	98.1% (97.0%, 98.9%)	2956.8 (2786.3, 3137.7)	915	99.5% (98.7%, 99.8%)	5958.0 (5518.9, 6432.1)
	• 255 mIU/mL	943	97.8% (96.6%, 98.6%)	2966.0 (2793.4, 3149.2)	943	99.4% (98.6%, 99.8%)	5919.3 (5486.2, 6386.6)
Mumps	• CD Cutoff (ELISA antibody units)	920	98.7% (97.7%, 99.3%)	106.7 (99.1, 114.8)	920	99.9% (99.4%, 100%)	253.1 (237.9, 269.2)
Rubella	• 10 IU/mL	937	97.7% (96.5%, 98.5%)	91.1 (85.9, 96.6)	937	98.3% (97.2%, 99.0%)	158.8 (149.1, 169.2)
Varicella	<1.25 to • 5 gpELISA units	864	86.6% (84.1%, 88.8%)	11.6 (10.9, 12.3)	864	99.4% (98.7%, 99.8%)	477.5 (437.8, 520.7)
	• CD Cutoff (gpELISA units)	695	87.2% (84.5%, 89.6%)	11.6 (10.9, 12.4)	696	99.4% (98.5%, 99.8%)	478.7 (434.8, 527.1)

† Includes the following treatment groups: ProQuad + Placebo followed by ProQuad (Visit 1) (Protocol 009) and ProQuad (Middle and High Dose) (Protocol 011).
‡ Samples from Protocols 009 and 011 were assayed in the legacy format Measles ELISA, which reported antibody titers in Measles ELISA units. To convert titers from ELISA units to mIU/mL, titers for these 2 protocols were divided by 0.1025. The lowest measurable titer postvaccination is 207.5 mIU/mL. The response rate for measles in the legacy format is the percent of subjects with a negative baseline measles antibody titer, as defined by the optical density (OD) cutoff, with a postvaccination measles antibody titer • 207.5 mIU/mL.
Samples from Protocols 009 and 011 were assayed in the legacy format Rubella ELISA, which reported antibody titers in Rubella ELISA units. To convert titers from ELISA units to IU/mL, titers for these 2 protocols were divided by 1.28.
ProQuad (Middle Dose) = ProQuad containing a varicella virus dose of 3.97 log_{10} PFU.
ProQuad (High Dose) = ProQuad containing a varicella virus dose of 4.25 log_{10} PFU.
ELISA = Enzyme-linked immunosorbent assay.
gpELISA = Glycoprotein enzyme-linked immunosorbent assay.
N = Number vaccinated at baseline.
n = Number of subjects who were per-protocol Postdose 1 and Postdose 2 and satisfied the given prevaccination serostatus cutoff.
CI = Confidence interval.
GMT = Geometric mean titer.
PFU = Plaque-forming units.

Id. at '467-468.

360.14. The 2009 ProQuad Label also stated:

Immunogenicity in Children 4 to 6 Years of Age Who Received a First Dose of ProQuad After Primary Vaccination With M-M-R II and VARIVAX

In a clinical trial, 799 healthy 4- to 6-year-old children who had received M-M-R II and VARIVAX at least 1 month prior to study entry were randomized to receive ProQuad and placebo (N=399), M-M-R II and placebo concomitantly at separate injection sites (N=205), or M-M-R II and VARIVAX concomitantly at separate injection sites (N=195). Children were eligible if they were previously administered primary doses of M-M-R II and VARIVAX, either concomitantly or non-concomitantly, at 12 months of age or older. Children were excluded if they were recently exposed to measles, mumps, rubella, and/or varicella, had an immune impairment, or had a history of allergy to components of the vaccine(s). No concomitant vaccines were permitted during study participation. *[See Adverse Reactions (6.1) for ethnicity and gender information.]*

A summary of antibody responses to measles, mumps, rubella, and varicella at 6 weeks postvaccination in subjects who had previously received M-M-R II and VARIVAX is shown in Table 12. Results from this study showed that a first dose of ProQuad after primary vaccination with M-M-R II and VARIVAX elicited a positive antibody response to all four antigens in greater than 98% of subjects. Post-vaccination GMTs for recipients of ProQuad were similar to those following a second dose of M-M-R II and VARIVAX administered concomitantly at separate injection sites (the lower bound of the 95% CI around the fold difference in measles, mumps, rubella, and varicella GMTs excluded 0.5). Additionally, GMTs for measles, mumps, and rubella were similar to those following a second dose of M-M-R II given concomitantly with placebo (the lower bound of the 95% CI around the fold difference for the comparison of measles, mumps, and rubella GMTs excluded 0.5).

Table 12
Summary of Antibody Responses to Measles, Mumps, Rubella, and Varicella at 6 Weeks Postvaccination in Subjects 4 to 6 Years of Age Who Had Previously Received M-M-R II and VARIVAX (Per-Protocol Population)

Group Number (Description)	n	GMT (95% CI)	Seropositivity Rate (95% CI)	% ≥4-Fold Rise in Titer (95% CI)	Geometric Mean Fold Rise (95% CI)
		Measles†			
Group 1 (N=399) (ProQuad + placebo)	387	1985.9 (1817.6, 2169.9)	100% (99.0%, 100%)	4.9% (2.9%, 7.6%)	1.21 (1.13, 1.30)
Group 2 (N=205) (M-M-R II + placebo)	185	2046.9 (1815.2, 2308.2)	100% (98.0%, 100%)	4.3% (1.9%, 8.3%)	1.28 (1.17, 1.40)
Group 3 (N=195) (M-M-R II + VARIVAX)	171	2084.3 (1852.3, 2345.5)	99.4% (96.8%, 100%)	4.7% (2.0%, 9.0%)	1.31 (1.17, 1.46)
		Mumps‡			
Group 1 (N=399) (ProQuad + placebo)	387	206.0 (188.2, 225.4)	99.5% (98.0%, 99.9%)	27.2% (22.8%, 32.1%)	2.43 (2.19, 2.69)
Group 2 (N=205) (M-M-R II + placebo)	185	308.5 (269.6, 352.9)	100% (98.0%, 100%)	41.1% (33.9%, 48.5%)	3.69 (3.14, 4.32)
Group 3 (N=195) (M-M-R II + VARIVAX)	171	295.9 (262.5, 333.5)	100% (97.9%, 100%)	41.5% (34.0%, 49.3%)	3.36 (2.84, 3.97)
		Rubella§			
Group 1 (N=399) (ProQuad + placebo)	387	217.3 (200.1, 236.0)	100% (99.0%, 100%)	32.7% (27.9%, 37.8%)	3.00 (2.72, 3.31)
Group 2 (N=205) (M-M-R II + placebo)	185	174.0 (157.3, 192.6)	100% (98.0%, 100%)	31.9% (25.2%, 39.1%)	2.81 (2.41, 3.27)
Group 3 (N=195) (M-M-R II + VARIVAX)	171	154.1 (138.9, 170.9)	99.4% (96.8%, 100%)	26.9% (20.4%, 34.2%)	2.47 (2.17, 2.81)
		Varicella¶			
Group 1 (N=399) (ProQuad + placebo)	387	322.2 (278.9, 372.2)	98.9% (97.2%, 99.7%)	80.7 (76.2%, 84.6%)	12.43 (10.63, 14.53)
Group 2 (N=205) (M-M-R II + placebo)	185	N/A	N/A	N/A	N/A
Group 3 (N=195) (M-M-R II + VARIVAX)	171	209.3 (171.2, 255.9)	99.4% (96.8%, 100%)	71.9% (64.6%, 78.5%)	8.50 (6.69, 10.81)

† Measles GMTs are reported in mIU/mL; seropositivity corresponds to ≥ 120 mIU/mL.
‡ Mumps GMTs are reported in mumps Ab units/mL; seropositivity corresponds to ≥ 10 Ab units/mL.
§ Rubella titers obtained by the legacy format were converted to their corresponding titers in the modified format. Rubella serostatus was determined after the conversion to IU/mL: seropositivity corresponds to ≥ 10 IU/mL.
¶ Varicella GMTs are reported in gpELISA units/mL; seropositivity rate is reported by % of subjects with postvaccination antibody titers ≥ 5 gpELISA units/mL. Percentages are calculated as the number of subjects who met the criterion divided by the number of subjects contributing to the per-protocol analysis.
gpELISA = Glycoprotein enzyme-linked immunosorbent assay; ELISA = Enzyme-linked immunosorbent assay; CI = Confidence interval; GMT = Geometric mean titer; N/A = Not applicable; N = Number of subjects vaccinated; n = number of subjects in the per-protocol analysis.

Id. at '468-469.

360.15. The 2009 ProQuad Label also stated:

Immunogenicity Following Concomitant Use with Other Vaccines

ProQuad with Pneumococcal 7-valent Conjugate Vaccine and/or VAQTA

In a clinical trial, 1027 healthy children 12 to 15 months of age were randomized to receive ProQuad and pneumococcal 7-valent conjugate vaccine concomitantly (N=510) at separate injection sites or ProQuad and pneumococcal 7-valent conjugate vaccine non-concomitantly (N=517) at separate clinic visits. *[See Adverse Reactions (6.1) for ethnicity and gender information.]* The statistical analysis of non-inferiority in antibody response rates to measles, mumps, rubella, and varicella at 6 weeks postvaccination for subjects are shown in Table 13. In the per-protocol population, seroconversion rates were not inferior in children given ProQuad and pneumococcal 7-valent conjugate vaccine concomitantly when compared to seroconversion rates seen in children given these vaccines non-concomitantly for measles, mumps, and rubella. In children with baseline varicella antibody titers <1.25 gpELISA units/mL, the varicella seroprotection rates were not inferior when rates after concomitant and non-concomitant vaccination were compared 6 weeks postvaccination. Statistical analysis of non-inferiority in GMTs to *S. pneumoniae* serotypes at 6 weeks postvaccination are shown in Table 14. Geometric mean antibody titers (GMTs) for *S. pneumoniae* types 4, 6B, 9V, 14, 18C, 19F, and 23F were not inferior when antibody titers in the concomitant and non-concomitant groups were compared 6 weeks postvaccination.

Table 13
Statistical Analysis of Non-Inferiority in Antibody Response Rates to Measles, Mumps, Rubella, and Varicella at 6 Weeks Postvaccination for Subjects Initially Seronegative to Measles, Mumps, or Rubella, or With Varicella Antibody Titer <1.25 gpELISA units at Baseline in the ProQuad + PCV7* Treatment Group and the ProQuad followed by PCV7 Control Group (Per-Protocol Analysis)

	ProQuad + PCV7 (N=510)		ProQuad followed by PCV7 (N=259)		Difference
Assay Parameter	n	Estimated Response[a]	n	Estimated Response[a]	(percentage points)[a,b] (95% CI)
Measles % ≥255 mIU/mL	406	97.3%	204	99.5%	-2.2 (-4.6, 0.2)
Mumps % ≥10 Ab units/mL	403	96.6%	208	98.6%	-1.9 (-4.5, 1.0)
Rubella % ≥10 IU/mL	377	98.7%	195	97.9%	0.9 (-1.3, 4.1)
Varicella % ≥5 gpELISA units/mL	379	92.5%	192	87.9%	4.5 (-0.4, 10.4)

* PCV7 = Pneumococcal 7-valent conjugate vaccine.
Seronegative defined as baseline measles antibody titer <255 mIU/mL for measles, baseline mumps antibody titer <10 ELISA Ab units/mL for mumps, and baseline rubella antibody titer <10 IU/mL for rubella.
[a] Estimated responses and their differences were based on statistical analysis models adjusting for study center.
[b] ProQuad + PCV7 - ProQuad followed by PCV7.
The conclusion of non-inferiority is based on the lower bound of the 2-sided 95% CI on the risk difference being greater than -10 percentage points (*i.e.* excluding a decrease equal to or more than the prespecified criterion of 10.0 percentage points). This indicates that the difference is statistically significantly less than the prespecified clinically relevant decrease of 10.0 percentage points at the 1-sided alpha = 0.025 level.
N = Number of subjects vaccinated in each treatment group.
n = Number of subjects with measles antibody titer <255 mIU/mL, mumps antibody titer <10 ELISA Ab units/mL, rubella antibody titer <10 IU/mL, or varicella antibody titer <1.25 gpELISA units/mL at baseline and with postvaccination serology contributing to the per-protocol analysis.
Ab = antibody; ELISA = Enzyme-linked immunosorbent assay; gpELISA = Glycoprotein enzyme-linked immunosorbent assay; CI = Confidence interval.

Id. at '469-470.

360.16. The 2009 ProQuad Label also stated:

Table 18
Summary of the Comparison of the Immunogenicity Endpoints for Measles, Mumps, Rubella, Varicella, *Haemophilus influenzae* type b, and Hepatitis B Responses Following Vaccination with ProQuad, *Haemophilus influenzae* type b Conjugate (Meningococcal Protein Conjugate), and Hepatitis B (Recombinant) Vaccine and DTaP Administered Concomitantly Versus Non-Concomitant Vaccination with ProQuad Followed by These Vaccines

		Concomitant Group	Non-Concomitant Group		
		N=949	N=485		
Vaccine Antigen	Parameter	Response	Response	Risk Difference (95% CI)	Criterion for Non-inferiority
Measles	% • 120 mIU/mL	97.8%	98.7%	-0.9 (-2.3, 0.6)	LB >-5.0
Mumps	% • 10 ELISA Ab units/mL	95.4%	95.1%	0.3 (-1.7, 2.6)	LB >-5.0
Rubella	% • 10 IU/mL	98.6%	99.3%	-0.7 (-1.8, 0.5)	LB >-5.0
Varicella	% • 5 gpELISA units/mL	89.6%	90.8%	-1.2 (-4.1, 2.0)	LB >-10.0
HiB-PRP	% • 1.0 mcg/mL	94.6%	96.5%	-1.9 (-4.1, 0.8)	LB >-10.0
HepB	% • 10 mIU/mL	95.9%	98.8%	-2.8 (-4.8, -0.8)	LB >10.0

HiB-PRP = *Haemophilus influenzae* type b, polyribosyl phosphate; HepB = hepatitis B; LB = lower bound, limit for non-inferiority comparison.

Id. at '472-473.

360.17. The current ProQuad package insert states:

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

ProQuad® is a vaccine indicated for active immunization for the prevention of measles, mumps, rubella, and varicella in children 12 months through 12 years of age.

available at https://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm123796.pdf (accessed 2018-02-22)

360.18. The "Description" section of the ProQuad label states:

11 DESCRIPTION

ProQuad (Measles, Mumps, Rubella and Varicella Virus Vaccine Live) is a combined, attenuated, live virus vaccine containing measles, mumps, rubella, and varicella viruses. ProQuad is a sterile lyophilized preparation of (1) the components of M-M-R II (Measles, Mumps, and Rubella Virus Vaccine Live):

Measles Virus Vaccine Live, a more attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and propagated in chick embryo cell culture; Mumps Virus Vaccine Live, the Jeryl Lynn™ (B level) strain of mumps virus propagated in chick embryo cell culture; Rubella Virus Vaccine Live, the Wistar RA 27/3 strain of live attenuated rubella virus propagated in WI-38 human diploid lung fibroblasts; and (2) Varicella Virus Vaccine Live (Oka/Merck), the Oka/Merck strain of varicella-zoster virus propagated in MRC-5 cells. The cells, virus pools, bovine serum, and human albumin used in manufacturing are all tested to provide assurance that the final product is free of potential adventitious agents.

ProQuad, when reconstituted as directed, is a sterile suspension for subcutaneous administration. Each 0.5-mL dose contains not less than 3.00 $\log_{10}$ $TCID_{50}$ of measles virus; 4.30 $\log_{10}$ $TCID_{50}$ of mumps virus; 3.00 $\log_{10}$ $TCID_{50}$ of rubella virus; and a minimum of 3.99 $\log_{10}$ PFU of Oka/Merck varicella virus.

Each 0.5-mL dose of the vaccine contains no more than 21 mg of sucrose, 11 mg of hydrolyzed gelatin, 2.4 mg of sodium chloride, 1.8 mg of sorbitol, 0.40 mg of monosodium L-glutamate, 0.34 mg of sodium phosphate dibasic, 0.31 mg of human albumin, 0.17 mg of sodium bicarbonate, 72 mcg of potassium phosphate monobasic, 60 mcg of potassium chloride; 36 mcg of potassium phosphate dibasic; residual components of MRC-5 cells including DNA and protein; <16 mcg of neomycin, bovine calf serum (0.5 mcg), and other buffer and media ingredients. The product contains no preservative.

Id at '15-16.

360.19. The Clinical Pharmacology section of the ProQuad Package Insert states:

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

ProQuad has been shown to induce measles-, mumps-, rubella-, and varicella-specific immunity, which is thought to be the mechanism by which it protects against these four childhood diseases.

The efficacy of ProQuad was established through the use of immunological correlates for protection against measles, mumps, rubella, and varicella. Results from efficacy studies or field effectiveness studies that were previously conducted for the component vaccines were used to define levels of serum antibodies that correlated with protection against measles, mumps, and rubella. Also, in previous studies with varicella vaccine, antibody responses against varicella virus ≥5 gpELISA units/mL in a glycoprotein enzyme-linked immunosorbent assay (gpELISA) (not commercially available) similarly correlated with long-term protection. In these efficacy studies, the clinical endpoint for measles and mumps was a clinical diagnosis of either disease confirmed by a 4-fold or greater rise in serum antibody titers between either postvaccination or acute and convalescent titers; for rubella, a 4-fold or greater rise in antibody titers with or without clinical symptoms of rubella; and for varicella, varicella-like rash that occurred >42 days postvaccination and for which varicella was not excluded by either viral cultures of the lesion or serological tests. Specific laboratory evidence of varicella either by serology or culture was not required to confirm the diagnosis of varicella. Clinical studies with a single dose of ProQuad have shown that vaccination elicited rates of antibody responses against measles, mumps, and rubella that were similar to those observed after vaccination with a single dose of M-M-R II *[see Clinical Studies (14)]* and seroresponse rates for varicella virus were similar to those observed after vaccination with a single dose of VARIVAX *[see Clinical Studies (14)]*. The duration of protection from measles, mumps, rubella, and varicella infections after vaccination with ProQuad is unknown.

12.4 Persistence of Antibody Responses after Vaccination

The persistence of antibody at 1 year after vaccination was evaluated in a subset of 2107 children enrolled in the clinical trials. Antibody was detected in 98.9% (1722/1741) for measles, 96.7% (1676/1733) for mumps, 99.6% (1796/1804) for rubella, and 97.5% (1512/1550) for varicella (≥5 gpELISA units/mL) of vaccinees following a single dose of ProQuad.

Experience with M-M-R II demonstrates that antibodies to measles, mumps, and rubella viruses are still detectable in most individuals 11 to 13 years after primary vaccination {13}. Varicella antibodies were present for up to ten years postvaccination in most of the individuals tested who received 1 dose of VARIVAX.

Id. at '16.

360.20. The Clinical Studies section of the current ProQuad label states:

14 CLINICAL STUDIES

Formal studies to evaluate the clinical efficacy of ProQuad have not been performed.

Efficacy of the measles, mumps, rubella, and varicella components of ProQuad was previously established in a series of clinical studies with the monovalent vaccines. A high degree of protection from infection was demonstrated in these studies {14-21}.

Immunogenicity in Children 12 Months to 6 Years of Age

Prior to licensure, immunogenicity was studied in 5845 healthy children 12 months to 6 years of age with a negative clinical history of measles, mumps, rubella, and varicella who participated in 5 randomized clinical trials. The immunogenicity of ProQuad was similar to that of its individual component vaccines (M-M-R II and VARIVAX), which are currently used in routine vaccination.

The presence of detectable antibody was assessed by an appropriately sensitive enzyme-linked immunosorbent assay (ELISA) for measles, mumps (wild-type and vaccine-type strains), and rubella, and by gpELISA for varicella. For evaluation of vaccine response rates, a positive result in the measles ELISA corresponded to measles antibody concentrations of ≥255 mIU/mL when compared to the WHO II (66/202) Reference Immunoglobulin for Measles.

Children were positive for mumps antibody if the antibody level was ≥10 ELISA units/mL. A positive result in the rubella ELISA corresponded to concentrations of ≥10 IU rubella antibody/mL when compared to the WHO International Reference Serum for Rubella; children with varicella antibody levels ≥5 gpELISA units/mL were considered to be seropositive since a response rate based on ≥5 gpELISA units/mL has been shown to be highly correlated with long-term protection.

Immunogenicity in Children 12 to 23 Months of Age After a Single Dose

In 4 randomized clinical trials, 5446 healthy children 12 to 23 months of age were administered ProQuad, and 2038 children were vaccinated with M-M-R II and VARIVAX given concomitantly at separate injection sites. Subjects enrolled in each of these trials had a negative clinical history, no known recent exposure, and no vaccination history for varicella, measles, mumps, and rubella. Children were excluded from study participation if they had an immune impairment or had a history of allergy to components of the vaccine(s). Except for in 1 trial *[see ProQuad Administered with Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP) and Haemophilus influenzae type b Conjugate (Meningococcal Protein Conjugate) and Hepatitis B (Recombinant) Vaccine below]*, no concomitant vaccines were permitted during study participation. The race distribution of the study subjects across these studies following a first dose of ProQuad was as follows: 66.3% White; 12.7% African-American; 9.9% Hispanic; 6.7% Asian/Pacific; 4.2% other; and 0.2% American Indian. The gender distribution of the study subjects across these studies following a first dose of ProQuad was 52.6% male and 47.4% female. A summary of combined immunogenicity results 6 weeks following administration of a single dose of ProQuad or M-M-R II and VARIVAX is shown in Table 10. These results were similar to the immune response rates induced by concomitant administration of single doses of M-M-R II and VARIVAX at separate injection sites (lower bound of the 95% CI for the risk difference in measles, mumps, and rubella seroconversion rates were >-5.0 percentage points and the lower bound of the 95% CI for the risk difference in varicella seroprotection rates was either >-15 percentage points [one study] or >-10.0 percentage points [three studies]).

Table 10: Summary of Combined Immunogenicity Results 6 Weeks Following the Administration of a Single Dose of ProQuad (Varicella Virus Potency ≥3.97 $\log_{10}$ PFU) or M-M-R II and VARIVAX (Per-Protocol Population)

Group	Antigen	n	Observed Response Rate (95% CI)	Observed GMT (95% CI)
ProQuad (N=5446*)	Varicella	4381	91.2% (90.3%, 92.0%)	15.5 (15.0, 15.9)
	Measles	4733	97.4% (96.9%, 97.9%)	3124.9 (3038.9, 3213.3)
	Mumps (OD cutoff)†	973	98.8% (97.9%, 99.4%)	105.3 (98.0, 113.1)
	Mumps (wild-type ELISA)†	3735	95.8% (95.1%, 96.4%)	93.1 (90.2, 96.0)
	Rubella	4773	98.5% (98.1%, 98.8%)	91.8 (89.6, 94.1)
M-M-R II + VARIVAX (N=2038*)	Varicella	1417	94.1% (92.8%, 95.3%)	16.6 (15.9, 17.4)

	Measles	1516	98.2% (97.4%, 98.8%)	2239.6 (2138.3, 2345.6)
	Mumps (OD cutoff)†	501	99.4% (98.3%, 99.9%)	87.5 (79.7, 96.0)
	Mumps (wild-type ELISA)†	1017	98.0% (97.0%, 98.8%)	90.8 (86.2, 95.7)
	Rubella	1528	98.5% (97.7%, 99.0%)	102.2 (97.8, 106.7)

* Includes ProQuad + Placebo followed by ProQuad (Visit 1) (Protocol 009), ProQuad Middle and High Doses (Visit 1) (Protocol 011), ProQuad (Lot 1, Lot 2, Lot 3) (Protocol 012), both the Concomitant and Non-concomitant groups (Protocol 013).

† The mumps antibody response was assessed by a vaccine-strain ELISA in Protocols 009 and 011 and by a wild-type ELISA in Protocols 012 and 013. In the former assay, the serostatus was based on the OD cutoff of the assay. In the latter assay, 10 mumps ELISA units was used as the serostatus cutoff.

n = Number of per-protocol subjects with evaluable serology.
CI = Confidence interval.
GMT = Geometric mean titer.
ELISA = Enzyme-linked immunosorbent assay.
PFU = Plaque-forming units.
OD = Optical density.

Id. at '17-19.

360.21. The Clinical Studies section of the current ProQuad label also states:

Immunogenicity in Children 4 to 6 Years of Age Who Received a First Dose of ProQuad After Primary Vaccination With M-M-R II and VARIVAX

In a clinical trial, 799 healthy 4- to 6-year-old children who had received M-M-R II and VARIVAX at least 1 month prior to study entry were randomized to receive ProQuad and placebo (N=399), M-M-R II and placebo concomitantly at separate injection sites (N=205), or M-M-R II and VARIVAX concomitantly at separate injection sites (N=195). Children were eligible if they were previously administered primary doses of M-M-R II and VARIVAX, either concomitantly or non-concomitantly, at 12 months of age or older. Children were excluded if they were recently exposed to measles, mumps, rubella, and/or varicella, had an immune impairment, or had a history of allergy to components of the vaccine(s). No concomitant vaccines were permitted during study participation. *[See Adverse Reactions (6.1) for ethnicity and gender information.]*

A summary of antibody responses to measles, mumps, rubella, and varicella at 6 weeks postvaccination in subjects who had previously received M-M-R II and VARIVAX is shown in Table 12. Results from this study showed that a first dose of ProQuad after primary vaccination with M-M-R II and VARIVAX elicited a positive antibody response to all four antigens in greater than 98% of subjects. Postvaccination GMTs for recipients of ProQuad were similar to those following a second dose of M-M-R II and VARIVAX administered concomitantly at separate injection sites (the lower bound of the 95% CI around the fold difference in measles, mumps, rubella, and varicella GMTs excluded 0.5). Additionally, GMTs for measles, mumps, and rubella were similar to those following a second dose of M-M-R II given concomitantly with placebo (the lower bound of the 95% CI around the fold difference for the comparison of measles, mumps, and rubella GMTs excluded 0.5).

Table 12: Summary of Antibody Responses to Measles, Mumps, Rubella, and Varicella at 6 Weeks Postvaccination in Subjects 4 to 6 Years of Age Who Had Previously Received M-M-R II and VARIVAX (Per-Protocol Population)

Group Number (Description)	n	GMT (95% CI)	Seropositivity Rate (95% CI)	% ≥4-Fold Rise in Titer (95% CI)	Geometric Mean Fold Rise (95% CI)
		Measles*			
Group 1 (N=399) (ProQuad + placebo)	367	1985.9 (1817.6, 2169.9)	100% (99.0%, 100%)	4.9% (2.9%, 7.6%)	1.21 (1.13, 1.30)
Group 2 (N=205) (M-M-R II + placebo)	185	2046.9 (1815.2, 2308.2)	100% (98.0%, 100%)	4.3% (1.9%, 8.3%)	1.28 (1.17, 1.40)
Group 3 (N=195) (M-M-R II + VARIVAX)	171	2084.3 (1852.3, 2345.5)	99.4% (96.8%, 100%)	4.7% (2.0%, 9.0%)	1.31 (1.17, 1.46)
		Mumps†			

Group 1 (N=399) (ProQuad + placebo)	367	206.0 (188.2, 225.4)	99.5% (98.0%, 99.9%)	27.2% (22.8%, 32.1%)	2.43 (2.19, 2.69)
Group 2 (N=205) (M-M-R II + placebo)	185	308.5 (269.6, 352.9)	100% (98.0%, 100%)	41.1% (33.9%, 48.5%)	3.69 (3.14, 4.32)
Group 3 (N=195) (M-M-R II + VARIVAX)	171	295.9 (262.5, 333.5)	100% (97.9%, 100%)	41.5% (34.0%, 49.3%)	3.36 (2.84, 3.97)
		Rubella[‡]			
Group 1 (N=399) (ProQuad + placebo)	367	217.3 (200.1, 236.0)	100% (99.0%, 100%)	32.7% (27.9%, 37.8%)	3.00 (2.72, 3.31)
Group 2 (N=205) (M-M-R II + placebo)	185	174.0 (157.3, 192.6)	100% (98.0%, 100%)	31.9% (25.2%, 39.1%)	2.81 (2.41, 3.27)
Group 3 (N=195) (M-M-R II + VARIVAX)	171	154.1 (138.9, 170.9)	99.4% (96.8%, 100%)	26.9% (20.4%, 34.2%)	2.47 (2.17, 2.81)
		Varicella[§]			
Group 1 (N=399) (ProQuad + placebo)	367	322.2 (278.9, 372.2)	98.9% (97.2%, 99.7%)	80.7 (76.2%, 84.6%)	12.43 (10.63, 14.53)
Group 2 (N=205) (M-M-R II + placebo)	185	N/A	N/A	N/A	N/A
Group 3 (N=195) (M-M-R II + VARIVAX)	171	209.3 (171.2, 255.9)	99.4% (96.8%, 100%)	71.9% (64.6%, 78.5%)	8.50 (6.69, 10.81)

* Measles GMTs are reported in mIU/mL; seropositivity corresponds to ≥120 mIU/mL.
† Mumps GMTs are reported in mumps Ab units/mL; seropositivity corresponds to ≥10 Ab units/mL.
‡ Rubella titers obtained by the legacy format were converted to their corresponding titers in the modified format. Rubella serostatus was determined after the conversion to IU/mL: seropositivity corresponds to ≥10 IU/mL.
§ Varicella GMTs are reported in gpELISA units/mL; seropositivity rate is reported by % of subjects with postvaccination antibody titers ≥5 gpELISA units/mL. Percentages are calculated as the number of subjects who met the criterion divided by the number of subjects contributing to the per-protocol analysis.
gpELISA = Glycoprotein enzyme-linked immunosorbent assay; ELISA = Enzyme-linked immunosorbent assay; CI = Confidence interval; GMT = Geometric mean titer; N/A = Not applicable; N = Number of subjects vaccinated; n = number of subjects in the per-protocol analysis.

Id. at '19-20.

360.22. The Clinical Studies section of the current ProQuad label also states:

Immunogenicity Following Concomitant Use with Other Vaccines

ProQuad with Pneumococcal 7-valent Conjugate Vaccine and/or VAQTA

In a clinical trial, 1027 healthy children 12 to 15 months of age were randomized to receive ProQuad and pneumococcal 7-valent conjugate vaccine concomitantly (N=510) at separate injection sites or ProQuad and pneumococcal 7-valent conjugate vaccine non-concomitantly (N=517) at separate clinic visits. *[See Adverse Reactions (6.1) for ethnicity and gender information.]* The statistical analysis of non-inferiority in antibody response rates to measles, mumps, rubella, and varicella at 6 weeks postvaccination for subjects are shown in Table 13. In the per-protocol population, seroconversion rates were not inferior in children given ProQuad and pneumococcal 7-valent conjugate vaccine concomitantly when compared to seroconversion rates seen in children given these vaccines non-concomitantly for measles, mumps, and rubella. In children with baseline varicella antibody titers <1.25 gpELISA units/mL, the varicella seroprotection rates were not inferior when rates after concomitant and non-concomitant vaccination were compared 6 weeks postvaccination. Statistical analysis of non-inferiority in GMTs to *S. pneumoniae* serotypes at 6 weeks postvaccination are shown in Table 14. Geometric mean antibody titers (GMTs) for *S. pneumoniae* types 4, 6B, 9V, 14, 18C, 19F, and 23F were not inferior when antibody titers in the concomitant and non-concomitant groups were compared 6 weeks postvaccination.

Table 13: Statistical Analysis of Non-Inferiority in Antibody Response Rates to Measles, Mumps, Rubella, and Varicella at 6 Weeks Postvaccination for Subjects Initially Seronegative to Measles, Mumps, or Rubella, or With Varicella Antibody Titer <1.25 gpELISA units at Baseline in the ProQuad + PCV7* Treatment Group and the ProQuad Followed by PCV7 Control Group (Per-Protocol Analysis)

Assay Parameter	ProQuad + PCV7 (N=510) n	ProQuad + PCV7 (N=510) Estimated Response†	ProQuad followed by PCV7 (N=259) n	ProQuad followed by PCV7 (N=259) Estimated Response†	Difference (percentage points)†,‡ (95% CI)
Measles % ≥255 mIU/mL	406	97.3%	204	99.5%	-2.2 (-4.6, 0.2)
Mumps					

% ≥10 Ab units/mL	403	96.6%	208	98.6%	-1.9 (-4.5, 1.0)
Rubella % ≥10 IU/mL	377	98.7%	195	97.9%	0.9 (-1.3, 4.1)
Varicella % ≥5 gpELISA units/mL	379	92.5%	192	87.9%	4.5 (-0.4, 10.4)

* PCV7 = Pneumococcal 7-valent conjugate vaccine.
Seronegative defined as baseline measles antibody titer <255 mIU/mL for measles, baseline mumps antibody titer <10 ELISA Ab units/mL for mumps, and baseline rubella antibody titer <10 IU/mL for rubella.
† Estimated responses and their differences were based on statistical analysis models adjusting for study center.
‡ ProQuad + PCV7 - ProQuad followed by PCV7.
The conclusion of non-inferiority is based on the lower bound of the 2-sided 95% CI on the risk difference being greater than -10 percentage points (*i.e.*, excluding a decrease equal to or more than the prespecified criterion of 10.0 percentage points). This indicates that the difference is statistically significantly less than the prespecified clinically relevant decrease of 10.0 percentage points at the 1-sided alpha = 0.025 level.
N = Number of subjects vaccinated in each treatment group.
n = Number of subjects with measles antibody titer <255 mIU/mL, mumps antibody titer <10 ELISA Ab units/mL, rubella antibody titer <10 IU/mL, or varicella antibody titer <1.25 gpELISA units/mL at baseline and with postvaccination serology contributing to the per-protocol analysis.
Ab = antibody; ELISA = Enzyme-linked immunosorbent assay; gpELISA = Glycoprotein enzyme-linked immunosorbent assay; CI = Confidence interval.

Id at '20-21.

360.23. The Clinical Studies section of the current ProQuad label also states:

ProQuad Administered with Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP) and Haemophilus influenzae type b Conjugate (Meningococcal Protein Conjugate) and Hepatitis B (Recombinant) Vaccine

In a clinical trial, 1913 healthy children 12 to 15 months of age were randomized to receive ProQuad plus diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed (DTaP) and *Haemophilus influenzae* type b conjugate (meningococcal protein conjugate) and hepatitis B (recombinant) vaccine concomitantly at separate injection sites (N=949), ProQuad at the initial visit followed by DTaP and *Haemophilus* b conjugate and hepatitis B (recombinant) vaccine given concomitantly 6 weeks later (N=485), or M-M-R II and VARIVAX given concomitantly at separate injection sites (N=479) at the first visit. *[See Adverse Reactions (6.1) for ethnicity and gender information.]* Seroconversion rates and antibody titers for measles, mumps, rubella, varicella, anti-PRP, and hepatitis B were comparable between the 2 groups given ProQuad at approximately 6 weeks postvaccination indicating that ProQuad and *Haemophilus* b conjugate (meningococcal protein conjugate) and hepatitis B (recombinant) vaccine may be administered concomitantly at separate injection sites (see Table 18 below). Response rates for measles, mumps, rubella, varicella, *Haemophilus influenzae* type b, and hepatitis B were not inferior in children given ProQuad plus *Haemophilus influenzae* type b conjugate (meningococcal protein conjugate) and hepatitis B (recombinant) vaccines concomitantly when compared to ProQuad at the initial visit and *Haemophilus influenzae* type b conjugate (meningococcal protein conjugate) and hepatitis B (recombinant) vaccines given concomitantly 6 weeks later. There are insufficient data to support concomitant vaccination with diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed (data not shown).

Table 18: Summary of the Comparison of the Immunogenicity Endpoints for Measles, Mumps, Rubella, Varicella, *Haemophilus influenzae* type b, and Hepatitis B Responses Following Vaccination with ProQuad, *Haemophilus influenzae* type b Conjugate (Meningococcal Protein Conjugate), and Hepatitis B (Recombinant) Vaccine and DTaP Administered Concomitantly Versus Non-Concomitant Vaccination with ProQuad Followed by These Vaccines

		Concomitant Group	Non-Concomitant Group		
		N=949	N=485		
Vaccine Antigen	Parameter	Response	Response	Risk Difference (95% CI)	Criterion for Non-inferiority
Measles	% ≥120 mIU/mL	97.8%	98.7%	-0.9 (-2.3, 0.6)	LB >-5.0
Mumps	% ≥10 ELISA Ab units/mL	95.4%	95.1%	0.3 (-1.7, 2.6)	LB >-5.0
Rubella	% ≥10 IU/mL	98.6%	99.3%	-0.7 (-1.8, 0.5)	LB >-5.0
Varicella	% ≥5 gpELISA units/mL	89.6%	90.8%	-1.2 (-4.1, 2.0)	LB >-10.0
HiB-PRP	% ≥1.0 mcg/mL	94.6%	96.5%	-1.9 (-4.1, 0.8)	LB >-10.0
HepB	% ≥10 mIU/mL	95.9%	98.8%	-2.8 (-4.8, -0.8)	LB >10.0

HiB-PRP = *Haemophilus influenzae* type b, polyribosyl phosphate; HepB = hepatitis B; LB = lower bound, limit for non-inferiority comparison.

Id. at '23-24.

361. From 2005, when Merck obtained a license to sell ProQuad, through the present (2018), the Clinical Pharmacology Section of the ProQuad label stated:

> Clinical studies with a single dose of ProQuad have shown that vaccination elicited rates of antibody responses against measles, mumps, and rubella that were similar to those observed after vaccination with a single dose of M-M-R II.

362. In my opinion, Merck's ProQuad label was misleading because it omitted that the antibody responses measured using the WT ELISA assay in the clinical studies supporting the licensure of ProQuad did not have a connection to protection from disease, and could therefore not be used to assess the similarity of MMRII and ProQuad as they relate to protection from disease.

363. From 2005, when Merck obtained a license to sell ProQuad, through the present (2018), the "Clinical Studies" Section of the ProQuad label stated:

> Formal studies to evaluate the clinical efficacy of ProQuad have not been performed. Efficacy of the measles, mumps, rubella, and varicella components of ProQuad was

> previously established in a series of clinical studies with the monovalent vaccines. A high degree of protection from infection was demonstrated in these studies.[921]

364. In my opinion, Merck's ProQuad label was misleading because it omitted that the ProQuad clinical study results using the WT ELISA assay could not be used to demonstrate that ProQuad afforded the same "high degree of protection" from mumps as a component vaccine because the clinical study data using WT ELISA did not reflect protection from disease.

365. From 2009 through the present (2018), "Clinical Pharmacology" section of the ProQuad label stated:

> Results from efficacy studies or field effectiveness studies that were previously conducted for the component vaccines were used to define levels of serum antibodies that correlated with protection against measles, mumps, and rubella... In these efficacy studies, the clinical endpoint for ... mumps was a clinical diagnosis of ... disease confirmed by a 4-fold or greater rise in serum antibody titers...[922]

366. In my opinion, Merck's ProQuad label was misleading because it omitted that the WT ELISA used in the clinical studies to support the licensure of ProQuad did not include the 4-fold rise criteria reported to be correlated with protection against mumps infection. Furthermore, the label omitted that the WT ELISA assay with a 10 Ab cutoff did not have a connection to whether a subject was protected from disease. Moreover, the label is misleading because it did not state that the seroconversion rates measured in the clinical studies to support ProQuad were not measured using the 4-fold rise criteria used in previous clinical studies that reported a correlation between the 4-fold rise criteria and protection from disease.

[921] *See* Schedule 2 (ProQuad label).
[922] *See id.*

367. In my opinion, from 2005, when Merck obtained a license to sell ProQuad, through today (2018), the ProQuad label has failed to state that the WT ELISA assay used in three of the clinical studies to support the application, Protocol 012, Protocol 013, and Protocol 014, did not measure protection because the WT ELISA used in the three clinical studies had not been correlated to an assay that measured protection from mumps.[923] Furthermore, the Clinical Pharmacology section of the ProQuad label has failed to state that the reported "rates of antibody response against ... mumps ... that were similar to those observed after vaccination with a single dose of M-M-R II" were not obtained from studies that employed a clinically relevant assay.[924] Moreover, the "Clinical Studies" section of the ProQuad label has failed to state that because Merck's WT ELISA did not measure protection from mumps, seroconversion measured by WT ELISA did not demonstrate that ProQuad offered the same "high degree of protection from infection" as its component vaccines, as stated in the Clinical Studies section of the ProQuad label.[925]

4. Merck's Misleading Statements Summarized

368. As described in the paragraphs above, Merck's Supplemental Biologics License Applications for MMRII and its Biologics License Application for ProQuad and the labels for MMRII and ProQuad supported by these applications are misleading because they omitted that the assays used did not relate to protection. The misleading statements can be summarized as follows:

[923] *See* Schedule 2 (ProQuad labels).
[924] *See id.*
[925] *See id.*

- "The data presented ... indicate with a high level of assurance that decreasing the mumps end-expiry titer from 4.3 [20,000] to 4.1 log10 [12,500] TCID50 per dose ...will ensure that M-M-R™II remains a highly effective vaccine."[926]
- "Serum level of antibodies to … mumps … will be determined by ... (ELISAs). Protective levels of antibody will be defined as ... ≥ 10.0 ELISA antibody units for mumps.[927]
- "[m]umps neutralizing antibodies were measured ...using the plaque-reduction neutralization (PRN) assay. PRN assay ... is a functional assay that measures the ability of the vaccine-induced immune response to inhibit viral replication in vitro, and can... be considered a surrogate for vaccine effectiveness."[928]
- "[l]owering the mumps virus potency to 4.1 log10 TCID50 per dose maintains >90% seroconversion using a neutralization assay, thus preserving the excellent ... efficacy profile of the vaccine."[929]
- "...study results suggest that M-M-R™II with rHA ... will be as effective as M-M-R™II with HSA in preventing… mumps…"[930]
- "antibodies associated with protection can be measured by neutralization or ELISA assays."[931]
- "Seroconversion in response to vaccination against ... mumps ... paralleled protection from ... disease[]."[932]
- "The data ... demonstrate that ProQuad ... is as efficacious as its parent products."[933]
- "…Merck ... has assessed the correlation between neutralizing antibody (as measured in ... [PRN] assay) and a wild-type ... ELISA ... These data support the use of the results of a wild-type ELISA as a correlate for protection."[934]

[926] MRK-KRA00135723 at '46.
[927] MRK-KRA00140056 at '0941.
[928] MRK-KRA00135723 at '30-31 (emphasis added).
[929] MRK-KRA00135723 at '29.
[930] MRK-KRA00140056 at '0196 .
[931] *See* Schedule 1 (Labels)
[932] *Id*.
[933] MRK-KRA00158320 at '338- 339.
[934] *See* Schedule 1 (Labels)

- "Efficacy of the ... mumps... component[] of ProQuad was previously established in a series of clinical studies with the monovalent vaccines. A high degree of protection from infection was demonstrated in these studies."[935]

X. FDA LICENSING OF MUMPS VACCINES BY OTHER MANUFACTURERS

369. As described in Section III.A above, since the approval of Mumpsvax in 1967 Merck has been the only manufacturer licensed to sell a mumps containing vaccine in the United States. Starting in the 1990's, SmithKline Beecham, now GlaxoSmithKline (GSK)[936], has sought FDA approval to license Priorix, another measles, mumps and rubella vaccine, in the United States. According to the testimony of GSK's corporate designee, April Cohen, in these cases [redacted].[937]

A. Mumps Immunogenicity Testing as Part of Efforts to License Priorix in the United States

370. Beginning in the 1990's a question arose regarding mumps immunogenicity testing in the clinical studies that would support a Biologic License Application for Priorix.[938] Specifically, FDA required SmithKline Beecham (now GSK) to use a serologic assay[939] that would be a predictor of protection in its mumps immunogenicity testing.

[935] *Id*.
[936] In this section GSK refers to both SmithKline Beecham and GlaxoSmithKline as the manufacturer of Priorix.
[937] *See* Deposition of April Cohen, January 4, 2018, 22:5-22:12 ([redacted]).
[938] *See* Section V.B.3 above discussing the Biologics License Application process.
[939] *See* Section III.B.3.b.(1) above describing a serologic assay.

370.1. A SmithKline Beecham Pharmaceuticals document titled: "[redacted]," dated December 18, 1997, stated:

[redacted]

GSK-MMR-IND-00047687 at '88 (original bold removed, underline added).

370.2. A letter from FDA's Director, Office of Vaccine Research and Review, CBER, Carolyn Hardegree, to SmithKline Beecham's Assistant Director, US Regulatory Affairs, Dr. Angus J. Grant, with the reference "[redacted], dated March 2, 1998, stated:

[redacted]

[redacted]

GSK-MMR-IND-0000221 at '21-22 (emphasis added).

370.3. A SmithKline Beecham Pharmaceuticals document titled: "[redacted]," dated March 26, 1998, stated:

[redacted]

GSK-MMR-IND-0047707 at '07-08 (emphasis added).

370.4. A SmithKline Beecham Pharmaceuticals document titled: [redacted]," dated November 3, 1998, stated:

[redacted]

[redacted]

GSK-MMR-IND-0002235 at '36 (emphasis added).

371. In my opinion, [redacted]. Furthermore, [redacted]. Moreover, [redacted].

372. Today, GSK has not obtained an FDA-approved license to sell Priorix in the United States.

B. Effect of Merck's Mumps Vaccine Labels on Merck's Competitors

373. In deposition testimony in these cases, GSK's corporate designee testified how Merck's MMRII label, and the statements in it, relate to GSK's attempt to license Priorix in the United States. An internal Merck powerpoint presentation, described above, also evidences how Merck's MMRII label relates to GSK's attempt to license Priorix in the United States.

373.1. GlaxoSmithKline's corporate designee, April D. Cohen, testified as follows:

[redacted]

[redacted]

Deposition of April D. Cohen, January 4, 2018, 96:21-99:2 (emphasis added).

373.2. GlaxoSmithKline's corporate designee, April D. Cohen, further testified as follows:

[redacted]

[redacted]

Deposition of April D. Cohen, January 4, 2018, 217:16-221:5 (emphasis added).

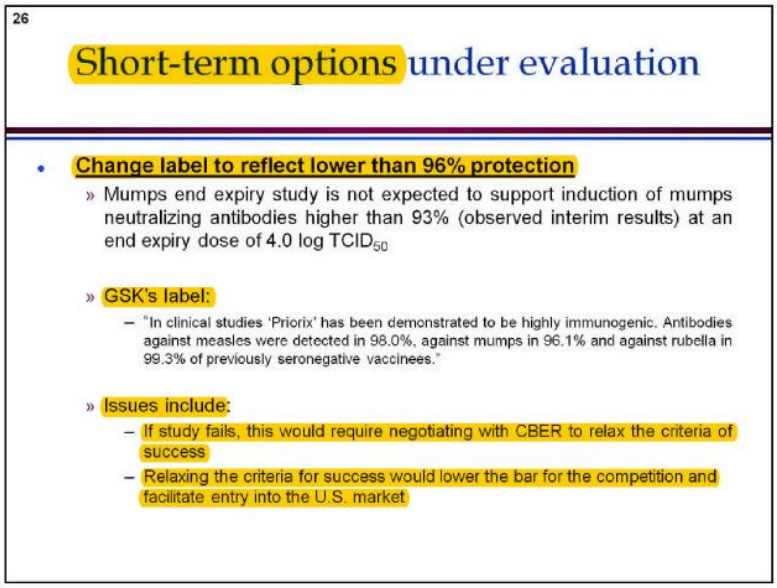
373.3. GlaxoSmithKline's corporate designee, April D. Cohen, further testified as follows:

[redacted]

[redacted]

Deposition of April D. Cohen, January 4, 2018, 243:24-244:15 (emphasis added).

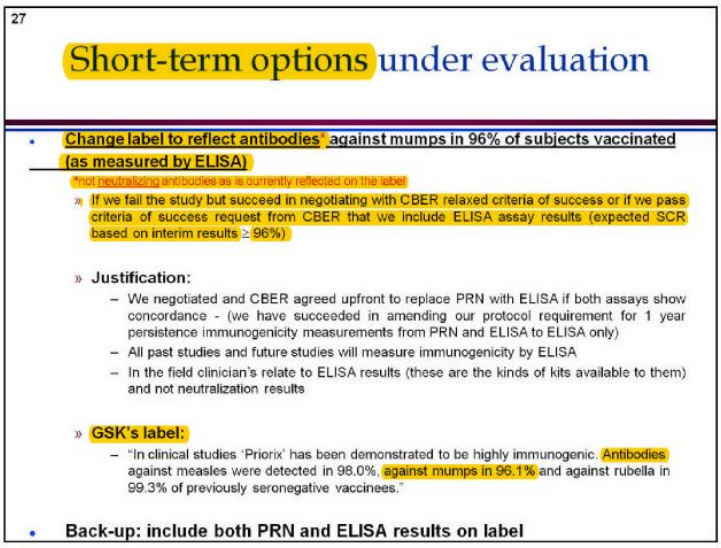
373.4. A powerpoint presentation titled "M-M-R®II Mumps End Expiry study status & Regulatory implications"[940] with Dr. Manal Morsy as presenter, "GRSRC [Global Regulatory Strategic Review Committee] dated October 11, 2002," stated:



MRK-KRA00040705 at '26 (highlight added).

373.5. The powerpoint also stated:

[940] As discussed above in Section VIII.N.5 in October 2002 Merck evaluated the option of changing its MMRII as part of a corrective action to assure compliance with its label when it could not assure mumps potency of "not less than 4.3" through end expiry.



Id. at '27 (highlight added).

373.6. In sum, the Merck presentation stated:

- Merck evaluated changing its MMRII label to reflect "antibodies" instead of "neutralizing antibodies" against mumps in 96% of subjects vaccinated (as measured by ELISA) if Merck relaxed the criteria of success in the trial and used ELISA assay results showing greater than 96%
- Relaxing the criteria for Merck's success "would lower the bar for competition and facilitate entry into the U.S. market."

374. In my opinion, it is not unusual for efficacy claims in existing products to be used by FDA as the standard for other similar products, especially with products that impact the public health. While relative effectiveness has generally not been viewed on the surface as part of the Federal Food Drug and Cosmetics Act, the determination of safety does encompass the concept of relative effectiveness when dealing with serious public health issues.

In evaluating effectiveness, FDA reviews new drug products and devices on their merits.[941] FDA does not require new drug products or devices to be more effective than their approved therapies for the same disease or condition. In general, both new drug products and class III devices must be shown to be effective through evidence consisting of clinical investigations that provide a basis on which it can be concluded that the new drug product or class III device will be safe and have the effect that it is represented to have.

For most new drug products and new class III devices intended to treat serious illness or provide symptomatic relief, a showing of effectiveness is usually based on a clinical trial comparing the product to a placebo. Such a showing does not necessarily involve a comparison to another active treatment or a product that is known to be effective.

In certain circumstances, however, it may be important to consider whether a new product is less effective than available alternative therapies, when less effectiveness could present a danger to the patient or to the public. For example, it is essential for public health protection that a new therapy be as effective as alternatives that are already approved for marketing when:

1. the disease to be treated is life- threatening or capable of causing irreversible morbidity (e.g., stroke or heart attack); or

[941] "[B]iological products subject to regulation under section 351 of the Public Health Service Act, are also drugs, within the meaning of Section 201(g)(1) of the Federal Food, Drug and Cosmetic Act, and are therefore also subject to regulation under that Act." Biological Products: Procedures for Review of Safety, Effectiveness and Labeling, 38 Fed. Reg. 4319.

2. the disease to be treated is a contagious illness that poses serious consequences to the health of others (e.g., sexually transmitted diseases).

Statement Regarding the Demonstrations of Effectiveness of Human Drug Products and Devices, 60 Fed Reg 39180 at 39180-81 (notice August 1, 1995) (emphasis added).

375. In my opinion, the claims set forth in Merck's MMRII and ProQuad labels could and do impact the standards for relative effectiveness that other manufacturers would have to meet to obtain FDA approval to market similar products in the United States.

XI. THE RESURGENCE OF MUMPS CASES AND MUMPS OUTBREAKS IN THE UNITED STATES AMONG HIGHLY VACCINATED POPULATIONS

376. Since 2006 there has been a resurgence of mumps cases and mumps outbreaks amount highly vaccinated populations in the United States. The Centers for Disease Control ("CDC") publishes *Morbidity, Mortality Weekly Reports* ("MMWR"), which include tables that identify the numbers of reported cases of certain notifiable diseases, including mumps.[942] Dr. Stanley Plotkin, a noted virologist and academician, has called for the development of a new mumps vaccine. FDA's Dr. Steven Rubin, someone with extensive experience with mumps vaccines and mumps virology, has also stated that the resurgence of mumps in the United States has made it "quite clear that newer, more immunogenic vaccines are needed." While the cause

[942] The CDC notes, with respect to "Notifiable Infectious Diseases and Conditions Data," that "[t]hese data are useful for analyzing infectious disease or condition trends and determining relative infectious disease or condition numbers. However, reporting practices affect how these data should be interpreted. Infectious disease and condition reporting is likely incomplete, and completeness might vary depending on the infectious disease or condition and reporting state." "About Notifiable Infectious Diseases and Conditions Data," https://www.cdc.gov/nndss/infectious.html. The CDC also notes that "[t]he NNDSS [National Notifiable Diseases Surveillance System] surveillance data likely represent an underestimate of the true number of cases of a given condition because of under-recognition and under-reporting of disease." Notifiable Infectious Diseases and Conditions Tables, https://www.cdc.gov/nndss/infectious-tables html.

of the resurgence of mumps cases and outbreaks is not known,[943] whether young adults getting mumps now may have received low potency mumps vaccine as children has not been made known to the public health community, including the CDC.[944]

376.1. The CDC's MMWR, published January 7, 2011, Volume 59, No. 52, Pg. 1673-1720, Notifiable Diseases and Mortality Tables, Table I, stated:

> TABLE I. Provisional cases[945] of infrequently reported notifiable diseases (<1,000 cases reported during the preceding year) – United States, week ending January 1, 2011 (52nd week)*[946]

Disease	Current Week	Cum 2010	5-year weekly average†	Total cases reported for previous years					States reporting cases during current week (No.)
				2009	2008	2007	2006	2005	
…	…	…	…	…	…	…	…	…	…
Mumps	5	2,528	56	1,991	454	800	6,584	314	PA (1), MD (1), FL (2), CO (1)
…	…	…	…	…	…	…	…	…	…

> * Case counts for reporting year 2010 are provisional and subject to change. For further information on interpretation of these data, *see* http://www.cdc.gov/ncphi/disss/nndss/phs/files/ProvisionalNationa%20NotifiableDiseasesSurveillanceData20100927.pdf.[947]
> † Calculated by summing the incidence counts for the current week, the 2 weeks preceding the current week, and the 2 weeks following the current week, for a total of 5 preceding years. Additional information is available at http://www.cdc.gov/ncphi/disss/nndss/phs/files/5yearweeklyaverage.pdf.

[943] *See* Schedule 17 (collecting studies identifying possible confounders for mumps outbreaks).
[944] Deposition of CDC's Director, Division of Viral Diseases, Dr. Mark Pallansch, October 13, 2018, 148:11-149:10.
[945] "Provisional data on the reported occurrence of nationally notifiable infectious diseases and conditions are published weekly in MMWR. After each reporting year, staff in state and territorial health departments finalize reports of cases for that year with local or county health departments and reconcile the data with reports previously sent to CDC throughout the year." https://www.cdc.gov/mmwr/volumes/64/wr/mm6453a1 htm?s_cid=mm6453a1_w
[946] *See* "Mumps," https://www.cdc.gov/mmwr/volumes/64/wr/mm6453a1 htm?s_cid=mm6453a1_w ("A total of 1,724 cases occurred January 1, 2010 through June 27, 2010. … Among the patients for whom vaccination status was reported, 90% had received at least 1 dose of mumps-containing vaccine, and 74% had received 2 doses. This was the largest mumps outbreak to occur in the United States since 2006 (2)."
[947] *See id.*, "Interpreting Data" for 2010.

available at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5952md.htm?s_cid=mm5952md_w. (highlight added).

376.2. The CDC's MMWR, published January 6, 2012, Volume 60, No. 52, Pg. 1729-1776, Notifiable Disease and Mortality Tables, Table II, stated:

TABLE II. (*Continued*) Provisional cases of selected notifiable diseases, United States, weeks ending December 31, 2011, and January 1, 2011 (52nd week)*

Reporting Area	…	Mumps				…
		Current week	Previous 52 weeks Med	Max	Cum 2011	Cum 2010
United States		3	7	47	370	2,612
…		…	…	…	…	…

* Case counts for reporting year 2011 are provisional and subject to change. For further information on interpretation of these data, see http://www.cdc.gov/osels/ph_surveillance/nndss/phs/files/ProvisionalNationa%20NotifiableDiseasesSurveillanceData20100927.pdf. Data for TB are displayed in Table IV, which appears quarterly.

available at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6052md.htm?s_cid=mm6052md_w. (highlight added).

376.3. The CDC's MMWR, published January 8, 2016, Volume 64, No. 52, ND-923-ND-940, Notifiable Diseases and Mortality Tables, Table II, stated:

TABLE II. (Continued) Provisional cases of selected notifiable diseases (≥1,000 cases reported during the preceding year), and selected* low frequency diseases, United States, weeks ending January 2, 2016, and December 27, 2014 (52nd week)† (Export data)

Reporting Area	Mumps				…
	Current week	Previous 52 weeks Med	Max	Cum 2015	Cum 2014
United States	2	16	74	1,057	1,196
…	…	…	…	…	…

† Case counts for reporting year 2015 are provisional and subject to change. For further information on interpretation of these data, see http://wwwn.cdc.gov/nndss/document/ProvisionalNationaNotifiableDiseasesSurveillanceData20100927.pdf. Data for TB are displayed in Table IV, which appears quarterly.

available at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6452md.htm?s_cid=mm6452md_w. (highlight added).

376.4. The CDC's MMWR, published January 6, 2017, Volume 65, No. 52, Notifiable Diseases and Mortality Tables, Table II, stated:

TABLE II. (Continued) Provisional cases of selected notifiable diseases (≥1,000 cases reported during the preceding year), and selected* low frequency diseases, United States and U.S. territories, weeks ending December 31, 2016, and January 2, 2016 (52nd week)† (Export data)

Reporting Area	Mumps				…
	Current week	Previous 52 weeks Med	Max	Cum 2016	Cum 2015
United States	63	66	390	5,311	1,329
…	…	…	…	…	…

† Case counts for reporting year 2016 are provisional and subject to change. For further information on interpretation of these data, see http://wwwn.cdc.gov/nndss/document/ProvisionalNationaNotifiableDiseasesSurveillanceData20100927.pdf. Data for TB are displayed in Table IV, which appears quarterly.

available at https://www.cdc.gov/mmwr/volumes/65/wr/mm6552md.htm?s_cid=mm6552md_w. (highlight added).

376.5. The CDC's MMWR, published January 5, 2018, Volume 66, No. 52, Notifiable Diseases and Mortality Tables, Table II, stated:

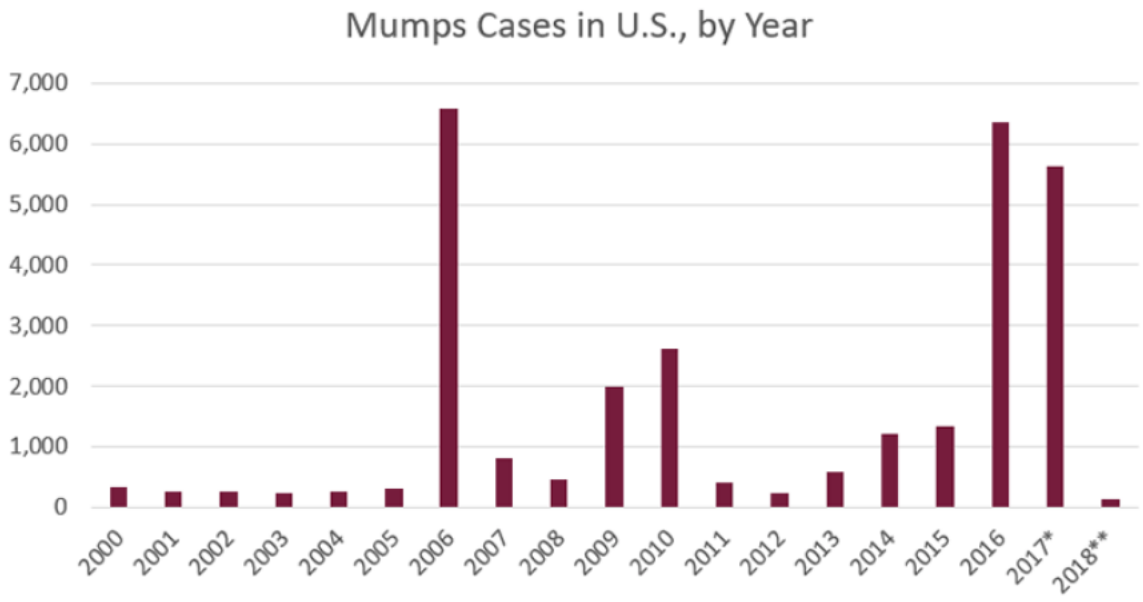
TABLE II. (Continued) Provisional cases of selected notifiable diseases (≥1,000 cases reported during the preceding year), and selected* low frequency diseases, United States and U.S. territories, weeks ending December 30, 2017, and December 31, 2016 (52nd week)† (Export data)

Reporting Area	…	Mumps					…
		Current week	Previous 52 weeks Med	Max	Cum 2017	Cum 2016	
United States		9	97	519	5,629	6,369	
…		…	…	…	…	…	

† Case counts for reporting year 2017 are provisional and subject to change. For further information on interpretation of these data, see http://wwwn.cdc.gov/nndss/document/ProvisionalNationaNotifiableDiseasesSurveillanceData20100927.pdf. Data for tuberculosis are displayed in Table III, which appears quarterly.

available at https://www.cdc.gov/mmwr/volumes/66/wr/mm6652md.htm?s_cid=mm6652md_w. (highlight added).

376.6. The CDC website charts "Mumps Cases in U.S., by Year" as follows:



* Case count is preliminary and subject to change.

** Cases as of January 27, 2018. Case count is preliminary and subject to change.

Source: Morbidity and Mortality Weekly Report (MMWR), Notifiable Diseases and Mortality Tables.

available at https://www.cdc.gov/mumps/outbreaks.html

376.7. The CDC's tables identifying the number of reported cases of mumps can be summarized as follows:

2006	2010	2014	2015	2016	2017
6,584	2,612	1,196	1,329	6,369	5,629

376.8. An email from the CDC's William Bellini to the FDA's Steve Rubin, and MRL's Executive Director, Biologics/Vaccines Clinical Research, Florian Schodel, and David Krah, among others, with the subject: "Conference Call," dated April 16, 2006, stated:

> I would like to propose that we have a conference call on Tuesday or Wednesday afternoon to discuss the most expeditious course for resolving the questions regarding the relative ability of vaccine induced mumps antibody to neutralize vaccine virus versus mumps genotype G virus. As most of you know by now, there are many cases of mumps in alleged 2-dose MMR recipients.[948]
>
> While this is not altogether unexpected, the number of cases in the population between 18-25 years-of-age that report having 2-doses of vaccine is a bit troublesome. I am not at all suggesting that there is something wrong with the vaccine or that vaccine efficacy or effectiveness is not as expected for MMR. I believe that we have to get this study done so that we have some lab confirmation to point to.

MRK-KRA00069487 at '88 (emphasis added).

376.9. In a "Press Briefing On Mumps Outbreak in the Midwest with Dr. Julie Gerberding and Dr. Jane Seward," dated April 19, 2006, then Director of the CDC, Dr. Gerberding, stated:

> I have to emphasize that the best protection against mumps is the vaccine. There is a lot of confusion right now about whether or not this outbreak is related to some problem with the vaccine, and I really want to emphasize that while we are of course investigating the outbreak and we will learn more about the efficacy of the vaccine in this particular setting, we have absolutely no information to suggest that there is any problem with the vaccine.

Centers for Disease Control and Prevention, *Transcript of Press Briefing on Mumps Outbreak In the Midwest with Dr. Julie Gerberding, and Dr. Jane Seward* (Apr. 19, 2006), available at https://www.cdc.gov/media/transcripts/t060419.htm (emphasis added).

376.10. A document titled "Mumps Research Priorities Meeting – CDC – February 25, 2010, Meeting Summary, stated:

[948] *See* Section IV above. CDC recommends two doses of mumps vaccine, one at 18 months of age, the second at 4-5 years of age.

Mumps Research Priorities, Opportunities and Resources

- Participants agreed on the need to improve the understanding of correlates of immune protection against mumps in order to understand vaccine failure
    - Limited data on anti-mumps virus antibodies suggest there may be a protective level, but what that level is and how sharply it divides protected from unprotected individuals is unknown. . . .
- Studies in the context of the current outbreak should continue to attempt to describe spectrum of illness, and correlate of protection following household exposure to mumps. Outbreak based studies are also needed to assess viral shedding in sub-clinical infections.

MRK-KRA00091458 at '60. (emphasis added).

376.11. A letter from FDA's Acting Principal Investigator, Division of Viral Products, CBER, Dr. Steven Rubin, to Dr. Biao He, Professor and GRA Distinguished Investigator, Department of Infectious Diseases, University of Georgia College of Veterinary Medicine, dated October 19, 2011, stated:

> I am pleased to support your proposal to investigate the rationale approaches to attenuation of mumps virus for vaccine development. … The proposed studies are of public health significance and are timely considering the recent resurgence of mumps in highly vaccinated populations in the United States and elsewhere, making it quite clear that newer, more immunogenic vaccines are needed. …
>
> As someone with extensive experience with mumps vaccines and mumps virology, I … very much look forward to our future collaborations.

NIH000007 (emphasis added).

376.12. In 2016, an article titled "Safety and Immunogenicity of M-M-RII (Combination Measles-Mumps-Rubella Vaccine) in Clinical Trials of Healthy Children Conducted between 1988-2009" in the Pediatric Infectious Disease Journal, by Barbara Kuter,

Michelle Brown, Richard Wiedmann, Jonathan Hartzel, and Luwy Musey, dated April 18, 2016, stated:

> **Background:** M-M-RII, a combination measles, mumps and rubella vaccine, was licensed in the United States in 1978 based on data from several clinical trials that demonstrated that the safety and immunogenicity of the vaccine were comparable to the component monovalent vaccines and to the previous trivalent combination vaccine.
>
> **Methods:** Safety and immunogenicity data from 23 postlicensure clinical trials conducted with M-M-RII between 1988 and 2009 were summarized. A total of 12,901 children who received only a first dose, 920 children who received a first and second dose and 400 children who received only a second dose were evaluated.
>
> **Results:** The vaccine was generally well tolerated among children who received a first and/or second dose of M-M-RII. During the 28–42-day follow-up after dose 1 and dose 2, the median rate of temperatures ≥102°F (oral equivalent) was 24.8% and 13.0% and the median rate of measles/rubella-like rash was 3.2% and 0.5%, respectively. The median rate of injection-site reactions during the first 5 days postdose 1 and postdose 2 was 17.3% and 42.7%, respectively. The seroconversion rates (enzyme-linked immunosorbent assay) after dose 1 were remarkably consistent from study to study between 1988 and 2009 (92.8%–100% for measles, 97.7%–100% for mumps and 92.8%–100% for rubella). A trend test showed that there was no change in the immunogenicity of the vaccine over the 21-year period.

> **Conclusions:** The results of this analysis demonstrate that M-M-RII is well tolerated and immunogenic. The vaccine performed consistently over 21 years of evaluation in clinical trials.

Barbara J. Kuter et al., Safety and Immunogenicity of M-M-RII (Combination Measles–Mumps–Rubella Vaccine) in Clinical Trials of Healthy Children Conducted Between 1988 and 2009, 35 PEDIATRIC INFECTIOUS DISEASE J. 1011 (2016).[949]

376.13.An article titled "*Commentary: Mumps Vaccines: Do We Need A New One?*," in The Pediatric Infectious Disease Journal by Dr. Stanley A. Plotkin, accepted for publication on December 4, 2012 and published in April 2013, stated:

> We need a new mumps vaccine. I come to that conclusion because of the numerous examples we have that mumps is resurgent in older previously vaccinated adolescents, particularly when they come together in groups into which mumps virus is introduced. …
>
> The Centers for Disease Control attributed the resurgence of mumps in the United States to the accumulation of susceptible adolescents from rural areas in crowded circumstances such as colleges, with the introduction of mumps virus from outside. However, more recent outbreaks have occurred in less rural areas and it is evident that vaccine failure plays a big role in them. Why is the mumps vaccine partially failing? There are 2 main hypotheses: strain change and waning immunity. …[950]
>
> I would argue as others have, that a new vaccine is needed. Mumps can cause meningitis and orchitis, and the expenses of dealing with an outbreak are considerable. …
>
> However, pharmaceutical companies have to make choices of which vaccines to develop, considering the fact that in the United States at least half a billion dollars are necessary to

[949] *See also* MRK-KRA00352365 (draft of manuscript dated Jan. 20, 2014).

[950] Confounders for the resurgence of mumps cases and outbreaks can be summarized as follows: close contact/crowded environment/conditions that foster frequent high intensity exposure; delayed recognition and diagnosis; diminished vaccine effectiveness; waning immunity; unrecognized importation of mumps; differences between the mumps vaccine strain and the circulating mumps wild strain; and accumulation of susceptible individuals. *See* Schedule 17 (Confounders for Mumps Outbreaks collecting studies discussing possible causes for outbreaks).

> license 1 vaccine. It is therefore not appealing for companies to develop a better form of an already licensed vaccine, compared with the development of a new vaccine. Under these circumstances, the only way forward is if the National Institute of Health provides funding to academic centers for the preclinical development of a new mumps vaccine strain. Subsequently it may be possible to convince a vaccine manufacturer to introduce the strain as part of a new MMR. Although the practical difficulties are considerable, so is the cost of continued outbreaks of mumps.

Plotkin SA, "*Commentary: Mumps vaccines: do we need a new one?*" 32 PEDIATRIC INFECTIOUS DISEASE 381-82 (April 2013) (emphasis added).

376.14. The treatise *Plotkin's Vaccines* by Stanley A. Plotkin, Walter A. Orenstein, Paul A. Offit, and Kathryn M. Edwards (7th ed. 2018) includes a chapter, on "Mumps Vaccines" by Dr. Steven Rubin that stated:

> The ACIP first recommended inclusion of MMR in the national immunization schedule as a single dose in 1971, and then as a two-dose regimen in 1989.

Steven A. Rubin, *Mumps Vaccines* in Plotkin's VACCINES 663-688 at 670 (Elseveir, 7th ed. 2017).

376.15. The chapter on "Mumps Vaccines" also stated:

> Failure to vaccinate or use of only one of the two recommended doses of MMR is also not a likely factor [in the outbreaks] given that recent outbreaks are characterized by very high two-dose coverage.

Rubin, *id*. at 678 (emphasis added).

376.16. Dr. Rubin's chapter on "Mumps Vaccines" in *Plotkin's Vaccines* by Stanley A. Plotkin, Walter A. Orenstein, Paul A. Offit, and Kathryn M. Edwards (7th ed. 2018), stated:

> A critical issue for further study concerns the extent and duration of protection conferred by two doses of mumps vaccine per the current administration schedule. Widespread use

of the live virus mumps vaccine since U.S. licensure in 1967 has resulted in an exceptional decrease in the incidence of mumps, but continuing outbreaks in highly vaccinated populations worldwide illustrate the potential for continued epidemics regardless of vaccine coverage. A review of the literature shows that close to 95% of children respond to their first dose of mumps vaccine with virus-neutralizing antibodies, and nearly all those who do not will seroconvert following a second dose. However, as reviewed in this chapter, a substantial proportion of vaccinees become seronegative or demonstrate significant declines in antibody titers over time (see "Persistence of Antibodies" above). In parallel, the effectiveness of mumps vaccines seems to decline with time postvaccination as well (see "Risk Factors for Vaccine Failure and Recent Outbreaks" above). These observations are suggestive of waning immunity. In the context of low levels of virus-neutralizing antibody, antigenic differences between vaccine strains and contemporary circulating viruses may be of more significance than previously appreciated. Together, these concerns indicate possible utility of an additional dose of vaccine during adolescence or later. The potential effectiveness of an additional dose later in life was suggested in studies where the MMR vaccine was used as a control measure in school-based outbreaks (see "Postexposure Prophylaxis" above). Although the mumps attack rates in students receiving the intervention declined substantially in these studies, conclusions could not be drawn because of study power as well as the caveat of the intervention being initiated after the outbreak started to decline. Nonetheless, use of an additional dose of vaccine during an outbreak would seem prudent. This notion is supported by data on the immunogenicity of a third dose of MMR among 685 young adults in a non-outbreak setting as reported by Fiebelkorn and colleagues. In that study, the GMT of virus-neutralizing antibody titers was observed to significantly increase in response to the third dose when measured 1 month after vaccination. However, at 1 year postvaccination, the GMT retreated close to baseline, suggesting only a transient benefit of a third dose of vaccine, making it difficult to justify a change to the current MMR vaccine schedule for routine vaccine use. Unfortunately, other biological indicators of improved immunity, such as more robust B-cell memory or higher antibody avidity, were not examined.

Rubin, *id*. at 687 (emphasis added).

376.17.Dr. Rubin's Chapter in *Plotkin's Vaccines* stated:

> As a consequence of the resurgence of mumps over the past decade despite high vaccine coverage, changes to the current vaccination schedule or development of new, more effective vaccines have been suggested. As described in "Disease Control Strategies and Possible Eradication" above, changing from a two-dose to a three-dose MMR schedule was evaluated, but the results raised doubt whether this or any other change to the vaccination schedule would improve the long-term effectiveness of the vaccine. This leaves development of new vaccines as the only practical approach to improving vaccine performance; however, prospectively designing improved vaccines is predicated on knowing what is responsible for the less-than-desirable performance of existing vaccines, as well as knowledge of reliable markers of vaccine efficacy, neither of which are known. In the absence of a clear understanding of factors that influence the kinetics, robustness, and duration of meaningful immune responses to mumps vaccination, and how these parameters can be reliably measured, there is little promise of new vaccines performing any better than existing vaccines.

Id. (emphasis added).

376.18. The CDC's Director, Division of Viral Diseases, Dr. Mark Pallansch, testified as follows:

> *Q. Now, if there had been manufacturing changes, in what way would that have been relevant to ACIP's determinations?*
> *A. It would depend upon the nature of the change, so I don't know. There's not a general answer to that.*
> *Q. Suppose there were changes made to potency.*
> *A. Again we'd want to know what clinical data was, you know, looked at in terms of a change in potency, and what was FDA's reaction to that.*
> *Q. And why would that be relevant?*

A. I mean, it has to affect -- it affects how we interpret data being provided, because we look at data for a specific product as the product hasn't changed unless we're aware of it. So, again, if we knew the potency change occurred at such and such a date, we would deliberately analyze data, you know, with that date in mind.

Q. And as far as you know, the CDC has not engaged in any kind of analysis in connection with any potency changes in Merck's mumps-containing vaccines?

A. We can't because we're not aware of potency changes.

Deposition of CDC's Director, Division of Viral Diseases, Dr. Mark Pallansch, October 13, 2018, 148:11-149:10 (emphasis added).

377. In my opinion, the causes for the resurgence of mumps cases and mumps outbreaks has not been established. The issues identified in this report and the possibility that some young adults who are at risk for mumps received lower potency vaccine has not been publicly disclosed by Merck. If these young adults received lower potency vaccines as children this information would be relevant for evaluating potential causes of the resurgence of mumps cases and mumps outbreaks since 2006.

XII. CONCLUSIONS[951]

In my opinion:

378. The Section 314 Review was different than the FDA review conducted in 1973 when responsibility for regulation of vaccines was transferred to the FDA, described above, because the NCVIA's no-fault compensation program for vaccine-related injuries was related to the manufacturers' responsibility to ensure their vaccines are safe and effective and have labeling that is not false or misleading.

[951] This is a summary of my conclusions. Please see report for all conclusions cited.

379. This duty is continuous, and the manufacturer must provide updates with any information it later discovers, or in the exercise of reasonable care, should have discovered about its vaccine. The material information that a manufacturer must provide would include any aspects of the vaccine identified as important by the National Vaccine Advisory Committee, such as vaccine efficacy, including duration of protection, immunogenicity, vaccine improvements which would improve utilization and administration, and stability of vaccine storage characteristics.

380. The Section 314 Review of MMRII was consistent with the goals set forth by Congress to enact the NCVIA, including focus on stability and potency, among other vaccine characteristics.

381. By 1998, any assertion by Merck that the 20,000 TCID50 [4.3 log10] mumps potency claim on its MMRII label was anything but an end expiry claim was rejected by FDA. In response, Merck stated that it could determine the potency titers present at the end of shelf life and proposed to reduce the mumps potency claim to 5,000 [3.7 log10] TCID50. Furthermore, to support the change in the labeling to state "at expiry, no less than 5,000 . . ." Merck needed clinical data to demonstrate the clinical effectiveness of MMRII with the proposed lower mumps potency. Merck began preparing and reviewing a clinical protocol to support the proposed mumps end expiry label change.

382. In 1998, according to Merck's documents, Merck did not have clinical data to support a correlation between an ELISA and a neutralization assay when it initiated Protocol 007.

383. For Merck to use ELISA for mumps immunogenicity testing in Protocol 007, or future clinical trials, it had to correlate the ELISA to a highly-specific neutralization assay designed as a measure of protection against circulating wild-type mumps infection.

384. As of September 1999: (a) Merck needed to conduct an end expiry study of mumps immunogenicity promptly; (b) FDA required Merck to use a neutralization assay in the end expiry study and did not believe modification to a neutralization assay was necessary; (c) Merck could not use an ELISA test unless it was correlated to a neutralization assay; (d) reporting seroconversion rates of lower than 96% in the end expiry trial could require Merck to change the 96% seroconversion rate in the MMRII label. A reasonable and prudent vaccine manufacturer presented with this information would use a neutralization assay that measures protection against disease, and report the results of that study as promptly as possible.

385. The objective of Protocol 007 was to measure MMRII's ability to protect against currently circulating wild-type mumps, especially at a potency lower than the 4.3 log10 [20,000] TCID50 stated on the MMRII label. A reasonable and prudent manufacturer would design a serologic assay that would accomplish the stated goal of the study.

386. Whatever "enhancements," modifications or changes to a serologic assay a manufacturer evaluates in the design of a clinical study, it is ultimately the manufacturer's obligation to design and conduct an adequate and well-controlled study that meets the stated objectives. Furthermore, as stated previously, the objective of Protocol 007 was to measure protection against wild-type mumps disease at a potency less than the 4.3 log 10 [20,000] TCID50 stated on the MMRII label.

387. As FDA has noted, false positive and false negative results are frequently observed when ELISA assays using mumps virus are used to assess antibody response. Furthermore, if an ELISA assay was going to be used instead of a neutralization assay in mumps immunogenicity testing, it would be important to minimize the risk of reporting false positive or false negative

results by ELISA. Moreover, one way to minimize this risk, which would have been acceptable to FDA, was to correlate the ELISA to a neutralization assay.

388. The regulatory communications from FDA to Merck from 1998-2000, described above, evidence that mumps immunogenicity testing required the use of a serologic assay that had some connection to protection against disease. Furthermore, the "gold standard" was a neutralization assay using a wild-type indicator virus, but an ELISA assay could be used if it was correlated to a neutralization assay. A correlation to a neutralization assay would minimize the risk of reporting false positive or false negative results by ELISA. Moreover, FDA's requirements to assess protection afforded by vaccination, and the duration of the protection, in mumps immunogenicity testing was consistent with the National Vaccine Advisory Committee's priorities for evaluating whether a vaccine is safe and effective. These requirements would apply to any mumps immunogenicity testing conducted as part of a clinical study to support an existing license of a mumps vaccine, or an application for the license of a new mumps vaccine.

389. To use an ELISA assay as an appropriate measure of protection against circulating wild-type mumps infection, it must be correlated to an assay that measures protection, such as a neutralization assay.

390. I have considered the 1999 email documenting a conversation between Merck's Dr. Wonnacott and FDA's Dr. Baylor and Dr. Baylor's purported agreement that Merck did not need to report lots manufactured before September 1999 that had titers below the MMRII label claim before the 24 month expiration as being "out of specification." Merck's summary of the purported agreement is not consistent with FDA's Dr. Carbone's subsequent statement to Dr. McKee documented in the August 2000 memo that "neither a conclusion has been drawn nor a

commitment made" regarding mumps potency/stability. Moreover, since the reporting of out of specification product is a compliance issue, I would expect the FDA's position regarding Merck's reporting obligations would be appropriately addressed in the Team Biologics inspection. I note the agenda for Day 2 of the August 2000 Team Biologics inspection included review of Error and Accident Reporting and Out of Specification Results.

391. It is the vaccine manufacturer who is responsible for assuring that its overall operation and the products it manufactures are in compliance with the law and that the products released to the market are safe and effective. This is not a requirement unique to mumps potency, or even to Merck.

392. Merck's response to FDA's Form 483 and the separate submission of mumps stability data, which did not include analysis of product manufactured after May, 1998, did not provide assurance that mumps containing vaccines manufactured after May 1998 would have "not less than 4.3 log" at end expiry. Furthermore, since product manufactured after May 1998 was within the 24-month shelf life in October 2000, there was risk that some product on the market would not meet the "not less than 4.3 log" end expiry specification. Moreover, because potency is tied to effectiveness, a risk of lower potency vaccine on the market necessarily includes a risk of less effective vaccine on the market.

393. Merck's response to the October 2000 Form 483 did not provide the FDA sufficient assurance that corrective actions had been taken to fix the cited deficiencies, including with regard to mumps potency. The Warning Letter was the next regulatory mechanism after the Form 483 before FDA could initiate an enforcement action to assure Merck's compliance with the law.

394. In responding to the February 2001 Warning Letter, Merck needed to demonstrate appropriate corrective actions to ensure compliance regarding the mumps potency issue identified in Observation #3, or it would face potential regulatory action.

395. In response to the pending Warning Letter, I would expect Merck to provide the FDA with similar information to that provided to Drs. Scolnick and Greene, including the following:

- Merck identified 225 lots still within the 24-month dating period with estimated end expiry potencies below 4.3 log 10 [20,000] TCID50/dose.
- Merck identified 213 of those lots to still be within the 24 month dating period on February 23, 2001 when Dr. Margolskee sent her email, and 212 of the lots would still be within the 24 month dating period on March 8, 2001 (when the Warning Letter response was due).
- Merck identified six lots with an estimated end expiry potency of 3.4 [2,500] to 3.7 log10 [5,000] TCID50/dose.
- Merck identified 101 lots with an estimated an end expiry potency between 3.7 [5,000] and 3.9 log10 8,000] TCID50/dose.
- Merck identified 118 lots with an estimated end expiry potency between 4.0 [10,000] and 4.2 log10 [16,000] TCID50/dose.
- The lots projected to fall below 4.0 log 10 [10,000] TCID50 at end expiry "will be a compliance issue with the Agency."
- From the results of the AIGENT Drs. Margolskee and Sadoff felt "3.7 [was] medically ok and may be defensible."
- Lots which would have potency lower than 3.7 at 24 months would not have data from the end expiry trial to support effectiveness.
- Complete data from the end expiry trial will take several more months.
- For lots manufactured at least since the summer of 1998, a total of ~1.0 log is lost over 24 months. Given this new analysis, lots manufactured since September

1999 have 24 month end expiry titers projected to be at or above 4.0 log, not 4.3 log as stated on the label.

- Attachment #4 estimated total doses of low mumps titer lots within expiry released to the United States to be approximately 12 Million doses.
- The medical assessment of the 101 lots between 3.7 and 4.0 depended on the neutralization data in Protocol 007, amongst other things.
- Merck was going to test a set of non-responders from the Protocol 007 preliminary subset analysis outside the protocol to evaluate responses in other assays to get assurance it did not have from the AIGENT testing alone.
- Merck proposed a set of surveillance investigations.
- Merck initiated a "Fact Finding" as a prelude to a potential product recall.
- Merck attempted to identify how long a lot may be on the market before it is used.
- Merck proposed to confirm findings from the Worldwide Adverse Events System with a retrospective HMO database study.
- Merck proposed to set up a prospective surveillance study if it could map the lots of interest to an HMO with the appropriate infrastructure.
- The results of testing the nonresponders outside the protocol would be used to evaluate whether Merck needed to have a "high level of concern."
- If nonresponders were truly not responding to the vaccine, Merck would need to consider further assessment, including potential revaccination of large infant cohorts.

396. The results of assay testing outside of protocol should have been disclosed to the FDA. Furthermore, Merck should have disclosed to the FDA that the assay testing outside of protocol, according to Dr. Margolskee, was to provide Merck reassurance of the results it was sending to the FDA as assurance that lower potency MMRII would be effective. Moreover, comparing the results of the ten children who were selected for re-test in assay testing outside of protocol shows the children responding differently depending on which assay was used. Most importantly, children who were non-responders by neutralization were responders in the ELISA,

tending to show that the ELISA did not give similar results to a neutralization assay, especially for children with low level responses.

397. I would expect Merck to provide the information contained in the draft responses to the Warning Letter in the final response to the FDA, particularly the sections disclosing the 223 lots. Furthermore, I would expect Merck to provide the FDA with the same information Dr. Margolskee provided to Drs. Scolnick, Greene and Kim in her March 5, 2001 email, including the following:

- Comparing the ELISA and AIGENT results for children who were non-responders by the AIGENT, Merck identified that children who received the lowest potency of 3.7 were not responding by either assay, suggesting children who got doses at that potency were not sufficiently protected.
- Merck's overfilled MMRII lots (manufactured after September 1999) complied with a 4.0 end expiry, not the 4.3 log on the MMRII label.
- Merck identified an "urgent need" to change the label and intended to do that by using ELISA testing, which would be available more quickly than the neutralization data.
- There were 107 lots filled before the overfill potentially still on the market with projected potencies lower than 4.0 at 24 months and the clinical data from the preliminary subset analysis in Protocol 007 did not support the effectiveness of MMRII at a dose below 4.0.
- Merck identified 6 retention samples to test potency at 24 months and was discussing testing the other 101 lots for potency at 24 months.
- Merck was investigating where the lower potency lots were sold. It could trace them to distributors and large HMOs but not individual doctors' offices.
- Merck was conducting a risk assessment for children who had received MMRII in recent years analyzing the probability of a child (1) getting a dose of < 4.0 log, (2) being a nonresponder, and (3) subsequently being exposed to mumps. The

assessment depended on how quickly vaccines were used from the time they were sold (the "burn rate") and the risk of mumps exposure.

- Needing to revaccinate children was a potential outcome of the risk assessment and since tracing lots and assessing when the lots were used (i.e. what potency a child received) was likely impossible, the need to revaccinate would "probably mean large scale initiative."
- Children in the Protocol 007 study who were negative by ELISA or neutralization would be offered revaccination.
- The "further steps" Merck would take as a result of its investigation.

398. As of February 27, 2001, the date of Mr. Bennett's email to Dr. Keith Chirgwin and Dr. Roberta McKee that stated: "Current Product … Given our current minimum release specification limit of 5.0, we have 95% confidence that each lot released will be at or above 4.0 through expiry," Merck did not have adequate assurances that MMRII could meet the product specification of not less than 4.3 through going forward, even after the overfill implemented in September 1999.

399. Merck's response to the Warning Letter was inadequate. A reasonable and prudent manufacturer would have included: (1) the identification of the low potency lots summarized in the draft responses; (2) the medical assessment of children getting MMRII doses with low potency mumps, including the need for potential surveillance studies and revaccination of large groups of children; (3) the assay testing outside of the protocol to provide reassurance of the results of Protocol 007 cited in the Warning Letter to justify the efficacy of lower potency product; and (4) the calculations showing the "process change to increase the mumps content of the product to ensure compliance to the labeled titer" did not assure MMRII could meet the 4.3 mumps end expiry going forward, even after the overfill.

400. Merck's BPDR 01-003 was inadequate. In light of the public health significance of the issues involved, a reasonable and prudent manufacturer would have included investigation of other single-dose vial MMRII lots manufactured in 1998, the same year as M-M-R®II Lot# 0628706. Furthermore, since some of the 225 lower potency lots identified in Attachment #4 were manufactured in 1998, the investigation I would have expected to see in this BPDR would have included those lots.

401. BPDR 01-003 was also inadequate because it stated that "[t]o ensure that [future] lots will meet the mumps potency specification of 4.3 TCID50/dose at expiry, the minimum specification was revised from 4.3 to 5.0 logTCID50/dose at release." A reasonable and prudent manufacturer would have reported that it did not have adequate assurances that future lots would meet the mumps potency specification of 4.3 TCID50/dose at expiry even after the overfill.

402. The submission of Serial 63 to the FDA, including the results of the AIGENT testing of the Protocol 007 preliminary subset analysis, were part of the response to the February 2001 Warning Letter. Furthermore, Merck provided that interim analysis "to justify the efficacy of lower potency product."

403. With regard to the proposal to complete the end expiry study using WT ELISA testing, a reasonable and prudent manufacturer would have informed the FDA that it did not have assurances that it could meet the mumps end expiry specification of 4.3 on the MMRII label, and that the request to bridge to ELISA and complete the end expiry study using ELISA proposed in Serial 63 was to expedite a label change to reduce the end expiry claim.

404. With regard to product manufactured before the overfill (September 1999) Merck's BPDR 01-005 was inadequate in light of the public health significance of the issues involved.

Merck tested lots 0538J, 0539J, 0926J, 1070J and 1071J. The only lot that met the end expiry specification was 0926J. A reasonable and prudent manufacturer would have investigated other single-dose vial MMRII lots manufactured in the same years as lots 0538J, 0539J, 1070J and 1071J. Furthermore, since all five lots were on the list of 225 "Low Mumps Titer Lots Within Expiry" in Attachment #4 to Dr. Margolskee's February 23, 2001 email to Drs. Scolnick and Greene, I would have expected to see an investigation reported in this BPDR to include the lots in that list. While Dr. Margolskee's March 5, 2001 email to Drs. Scolnick and Greene stated that discussions were "underway" to assay 101 lots of the lots identified, none of those lots are reported or discussed in this BPDR or elsewhere. Moreover, the remaining lots on the list of 225, also predicted below the label claim, were also not reported or discussed in the BPDR or elsewhere.

405. Merck used the results of the preliminary subset analysis of Protocol 007's AIGENT testing as part of the medical assessment in BPDR-005 for why no further action was required in response to Merck's reporting of four MMRII lots out of specification for failing to meet the end expiry potency specification for mumps at 24 months. Furthermore, the submission of clinical data from the testing conducted in Dr. Krah's lab was inadequate to support the medical assessment of the risk of receiving lower potency vaccine because raw data was changed without justification during the testing in Dr. Krah's lab.

406. BPDR 01-005 was also inadequate because it stated the September 1999 overfill and other "changes were implemented to ensure that, in the future, potency for lots at expiry would meet the current specification of 4.3 logTCID50/dose" when Merck did not have assurance that the overfill would ensure not less than 4.3 at end expiry. A reasonable and prudent manufacturer would have disclosed that, at the time it was reporting these out of

specification lots, it did not have adequate assurances that future lots of product would meet the mumps potency specification of 4.3 TCID50/dose at expiry.

407. Mr. Krahling's account of events, as recorded in the Merck workbook, are serious accusations of fraud in a clinical trial, particularly in light of the public health significance of the issues involved.

408. The Form 483 observation that "raw data is being changed with no justification" in the Protocol 007 testing rendered that data unreliable. Furthermore, Merck had already relied on that data, "changed with no justification," on at least three instances: (1) in response to the 2001 Warning Letter to "justify the efficacy of lower potency product;" (2) in its Serial 63 submission of the results of the preliminary analysis from Protocol 007; and (3) in Biological Product Deviation Report 01-005.

409. Because a reasonable and prudent manufacturer must assure submissions to the FDA are accurate, Merck's prior submissions relying on the Protocol 007 data changed without justification should have been amended. Furthermore, after two Form 483s, a Warning Letter and two BPDRs within twelve months all relating in some way to the mumps potency issue, a reasonable and prudent manufacturer would have described to the FDA that it was unable to assure the mumps end expiry specification in MMRII even after the overfill and while it did not have clinical data to support lowering the end expiry specification.

410. Merck continued to be unable to assure compliance with its MMRII label in April 2002 and the Protocol 007 AIGENT data was necessary to resolve the compliance issue.

411. FDA's Dr. Carbone's statement documented in Dr. Chirgwin's record of conversation that "'there is nothing really scientifically wrong' with our mumps PRN assay" is

consistent with Dr. Carbone's notes from the unannounced inspection to Dr. Krah's lab in August 2001 that resulted in the Form 483 in which she stated: "As the immunological correlate for efficacy of mumps vaccination Merck has developed an assay to measure anti-mumps antibodies in the serum of vaccinated subjects." Furthermore, according to Merck's documents, if Merck's proposed WT ELISA cutoff of 10Ab was not accepted by the FDA, the seroconversion rates Merck would report in clinical studies using the WT ELISA would be lower than the seroconversion rates on the MMRII label.

412. Based on Dr. Antonello's testimony that neither the 1:32 cutoff in the AIGENT nor the 10 Ab cutoff used in the WT ELISA reflected a protective level, the 10 Ab WT ELISA cutoff did not meet the FDA's requirement that it "relate to seroprotection."

413. If the cutoff in Merck's WT ELISA had been set higher (i.e. 40 ab using a four-fold rise criterion), the seroconversion rates Merck would have reported by its WT ELISA would have been lower than those reported using 10 Ab.

414. In response to FDA's request to identify individual titers "in the relative range around the cutoff in the P[laque]R[eduction]N[eutralization] and ELISA in order to confirm the AIGENT and WT ELISA are categorizing sera in a comparable fashion," I would expect Merck to provide the FDA with the following information relevant to samples with titers around the cutoff:

- The tables Merck prepared in March 2001 comparing the results of the approximately 60 low level responders and non responders in the preliminary subset by AIGENT and WT ELISA broken out by potency dose showing seroconversion rates as follows:
  The 4.9 dose: seroconversion rate by WT ELISA was 81% and 43% by AIGENT.

The 4.0 dose: seroconversion rate by WT ELISA was 93% and 26% by AIGENT.
The 3.7 dose: seroconversion rate by WT ELISA was 40% and 20% by AIGENT.

- The results of assay testing outside the protocol in assay 46-01, showing the following results for the ten children retested:
  None of the ten responded in a standard neutralization assay using JL-135.
  Seven of the ten responded in the WT ELISA (also using JL-135).

415. In response to the April 2002 Form 483, finding a deficiency in the underlying report from March 2001, a reasonable and prudent manufacturer would have investigated other single-dose vial MMRII lots manufactured in 1998. A reasonable and prudent manufacturer would have also reported that it did not have adequate assurances that future lots would meet the mumps potency specification of 4.3 TCID50/dose at expiry.

416. With regard to MMRII lots manufactured from September 1999 – September 2002, Merck never informed the FDA that "approx[imately] 7% of the lots [we]re expected to be < 4.3 at expiry" or that Merck could "statistically predict that a certain number of lots will fail on stability," even after the manufacturing change implemented in September 1999 to "overfill" the mumps component to ensure Merck could "provide a high level of assurance that the minimum titers would be maintained through expiry." Furthermore, since this was never reported to the FDA, to the best of my understanding, no one has investigated which lots released were the 7% Merck that would fail to have 4.3 log10 [20,000] TCID50/dose at end expiry. Moreover, with regard to children immunized in the United States with vaccines manufactured from September 1999- September 2002, no one can determine which of the children, who are now young adults (approximately 17-22 years old), were immunized from the 7% of lots Merck predicted would

fail to have 4.3 log10 [20,000] TCID50/dose at end expiry to evaluate whether they have been sufficiently immunized because the end expiry potency fell below Merck's specification.

417. Dr. Rosolowsky's telephone conversation with FDA's Dr. Phil Krause apparently notifying Dr. Krause of Merck's intention to file a Prior Approval Supplement as a corrective action for the mumps potency issue, as documented in a December 2002 email, does not change Merck's obligation to ensure the products that it releases to the market are safe and effective and meet the specifications on the label. Furthermore, a verbal notification to FDA personnel of a corrective action that will take place in the future does not change the manufacturer's obligation to implement an immediate corrective action to correct the problem identified and prevent its recurrence. It is the manufacturer's responsibility to ensure that its products meet the specifications on the label and to comply with all provisions of the Federal Food, Drug, and Cosmetic Act, the Public Health Services Act, and all applicable regulations.

418. Merck did not execute the corrective action it represented to FDA's Dr. Krause that it would take in January 2003, or any time thereafter. Merck's "alternative strategy" was to use Protocol 007 data instead of changing the MMRII label to reduce the shelf-life and ensure currently marketed product met the label specification of "not less than 4.3" for mumps at end expiry.

419. With regard to FDA requirements, a vaccine is adulterated if a manufacturer does not have procedures that are designed to assure that the product has the identity, strength, purity or potency it purports or represents it to have. From at least 1998 – December 2007, Merck did not have adequate procedures to assure that MMRII vaccine had "not less than 4.3 log10 [20,000] TCID50" per dose through end expiry. My opinions with regard to Merck's ability to

assure the MMRII potency specification for mumps of not less than 4.3 $\log_{10}$ [20,000] $TCID_{50}$ for the shelf life of the vaccine are as follows:

419.1. From at least 1998 – September 1999, Merck did not have adequate procedures to assure that MMRII vaccine had "not less than 4.3 log10 [20,000] TCID50" per dose through end expiry. Merck's actions with regard to the identification of product manufactured before the overfill for which it could not assure "not less than 4.3 log10 [20,000]" at end expiry can be summarized as follows:

− Merck identified 225 lots it predicted could not meet the end expiry specification of "not less than 4.3" on the MMRII label	MRK-KRA00549518
− Merck identified six of the lots with predicted lowest potency identified on the list of 225 lots	MRK-KRA00616007 at '08
− Merck tested five of the six lots, 0538J, 0539J, 0926J, 1070J and 1071J, and reported the results in BPDR 01—005: − Lot 0538J (117,970 doses) was out of specification − Lot 0539J (115,320 doses) was out of specification − Lot 1070J (118,040 doses) was out of specification − Lot 1071J (117,550 doses) was out of specification − Lot 0926J (57,720 doses) was within specification	MRK-KRA00754233; MRK-KRA00549518
− The sixth lot, Lot 0517J (115,400 doses) was not tested or reported to the FDA. Merck documents indicate it was exported outside the United States.	MRK-KRA00548824; MRK-KRA00548114

With regard to the remaining 219 lots (225-6= 219), Merck could not assure those lots met the end expiry claim of 4.3 log10 [20,000] TCID50/dose, and never informed the FDA. Moreover, with regard to children immunized in the United States with vaccines from lots Merck manufactured from May 1998 – September 1999 for which Merck did not have adequate

assurance, no one can determine whether these children who are now young adults (approximately 18-23 years old) have been sufficiently immunized because the end expiry potency fell below Merck's specification.

419.2. By the end of 2000, Merck could not ensure MMRII lots manufactured after September 1999, after the overfill, met the label potency specification of "not less than 4.3 log" for mumps. Furthermore, Merck could not ensure MMRII lots manufactured before the overfill and still within the 24-month shelf life, met the label potency specification of "not less than 4.3" for mumps. Moreover, in December 2000 Merck did not have clinical data to support lowering the end expiry claim on the MMRII label, or adequate data to provide reassurance of the efficacy of lower potency product.

419.3. After the overfill implemented in September 1999 and as long as the MMRII label stated "not less than 4.3 $\log_{10}$ [20,000]" $TCID_{50}$ Merck was required to have adequate procedures to assure that MMRII vaccine had that amount of mumps virus per dose through end expiry.

419.4. In April 2001, Merck still did not have adequate assurance that MMRII would have "not less than 4.3" mumps potency at the end of the 24 month shelf life. Furthermore, Mr. Bennett's conclusion that "expiry dating needs to be 12 months in order to provide 95% confidence that a lot released at 5.0 will be above 4.3 at expiry" was relevant to the April 4, 2001 discussion with FDA about the ongoing questions of mumps stability/potency in MMRII that started with the Section 314 Review in 1996. A reasonable and prudent manufacturer would have described the results of Mr. Bennett's analysis to the FDA personnel in attendance. Moreover, a reasonable and prudent manufacturer would have updated its response to the Warning Letter four weeks earlier that had stated: "we believe that the actions taken to date

comprehensively address all concerns raised during the referenced inspection as well as in the subsequent Warning Letter."

419.5. In August 2001, Merck could not assure the end expiry potency of the mumps component of MMRII [4.3 log10/20,000 TCID50], even after the overfill initiated in September 1999, because Merck's stability data only supported an end expiry potency of 4.0. With an end-expiry potency of 4.3, Mr. Bennett calculated that MMRII's shelf life was less than 12 months, not the 24 months in MMRII's labeling. A reasonable and prudent manufacturer would have described this issue to the FDA, and not waited for "the clinical efficacy data that was being generated."

419.6. In December 2001, Merck still could not ensure the mumps end expiry specification of 4.3 that continued to be on the MMRII label because, according to Mr. Bennett, the "expiry dating need[ed] to be 12 months in order to provide 95% confidence that a lot released at 5.0 will be above 4.3 at expiry," and, according to Mr. Schofield, "the [stability] plan works with 4.0 but not 4.3." Furthermore, according to Merck's summary of the December 7, 2001 teleconference, FDA's Dr. Carbone raised the potency/stability issue with Mr. Schofield and other recipients of Mr. Bennett's email on the call. A reasonable and prudent manufacturer would have described to FDA's Dr. Carbone and other FDA personnel on the call that Merck was unable to assure the mumps end expiry specification in MMRII even after the overfill and it did not have clinical data to support lowering the end expiry specification because of the deficiencies cited in the Protocol 007 testing.

419.7. Until Merck had clinical data from an adequate and well-controlled study and FDA's approval to lower the mumps end expiry claim on the MMRII label, Merck remained

obligated to ensure that all product met the "not less than 4.3 log [20,000]" mumps end expiry claim. Furthermore, Mr. Bennett's analysis documents Merck's ongoing inability to ensure all MMRII products complied with that label specification even after the overfill. Merck continued to have inadequate assurance that MMRII met the label specification for mumps through end expiry in March 2002.

419.8. As of July 2002, Merck still did not have adequate assurances that that all MMRII product met the "not less than 4.3 log [20,000]" potency claim for mumps on the label, even after the overfill implemented in September 1999. Furthermore, until Merck actually implemented any of the proposed "fixes" it contemplated, it remained obligated to ensure compliance with its label.

419.9. In September 2002, according to Merck's documents, Merck did not have adequate procedures to assure that MMRII met that standard, even after the overfill implemented in September 1999.

419.10. In December 2002, Merck still did not have adequate controls to ensure that mumps potency of MMRII would be "not less than 4.3" at end expiry, even the overfill.

419.11. MRL's Executive Director, Worldwide Regulatory Affairs, Dr. Keith Chirgwin's September 2003 email regarding "a call" from FDA's Dr. Baylor did not change Merck's obligation to ensure the products that it releases to the market are safe and effective. Through the end of 2003, Merck still could not ensure that MMRII vaccine had "not less than 4.3 log10 [20,000] TCID50" of mumps virus per dose through end expiry.

419.12. Through the end of 2004, Merck still could not ensure that MMRII had "not less than 4.3 log10 [20,000] TCID50" mumps virus per dose through end expiry.

419.13. Consistent with the opinions of Dr. Stark and Dr. Schenerman, from July 2005-2007 Merck could not ensure that MMRII met its mumps end expiry potency specification of "not less than 4.3."

419.14. From May 1998-December 2007, MMRII was adulterated because Merck was unable to assure the potency specification for mumps of not less than 4.3 $\log_{10}$ [20,000] $TCID_{50}$ for the shelf life of the vaccine.

420. After conducting the comparison between the AIGENT and WT ELISA, Merck made repeated representations to FDA that the comparison supported the cutoff used in the WT ELISA assay. FDA requested specific, additional information from Merck about the 10 Ab cutoff in the WT ELISA assay after Merck's submission in Serial 86. FDA requested "the mumps ELISA seropositive cutoff be justified via use of known mumps neutralizing and non-neutralizing sera. Furthermore, CBER recommended an analysis of the ELISA predictive value in identifying sera that tested positive in the neutralization assay." In response to FDA's request, Merck stated "Serial 86 … we believe provided information on the clinical relevance of the chosen ELISA cutoff for seropositivity." Merck made this statement in BB-IND 7068 and in BB-IND 1016. These statements were misleading for the following reasons:

- Merck's statements suggest that Serial 86 answered FDA's questions regarding the clinical relevance of the WT ELISA assay cutoff when Merck had not determined the clinical relevance of the WT ELISA cutoff to use in the clinical studies to support its three pending applications.
- Merck's statements omitted that the AIGENT assay had not been demonstrated to be a reliable measure of the presence of mumps neutralizing antibodies or validated as a sufficiently specific assay to measure mumps neutralizing antibodies.

- Merck's statements omitted that the AIGENT assay had not been shown to be a reliable measure of clinical protection and that Merck senior management "[did not] know what a clinically protective level [was]" using either the AIGENT or WT ELISA.
- Merck's statements omitted that seroprotection had not been considered in determining the WT ELISA assay's 10 Ab cutoff.

421. The AIGENT assay results from Protocol 007 could not be used to provide reliable information about protection from disease. Moreover, according to Merck's documents, if the biological relevance of the chosen cutoff continued to be in question, a four-fold rise criteria may have been required to "demonstrate significant response to the vaccine."

422. The measure of immunogenicity in the five clinical studies cited for support in the three applications were represented to be linked to protection against disease, illustrated by the following statements:[952]

- sBLA for Mumps End Expiry (Protocol 007): "The data presented here indicate with a high level of assurance that decreasing the mumps end-expiry titer from 4.3 [20,000] to 4.1 log10 [12,500] TCID50 per dose in children 12 to 18 months of age will ensure that M-M-R™II remains a highly effective vaccine."
- sBLA for rHA (Protocol 009): – "Serum level of antibodies to … mumps … will be determined by enzyme-linked immunosorbent assays (ELISAs). Protective levels of antibody will be defined as ... ≥ 10.0 ELISA antibody units for mumps.

[952] *See also* MRK-KRA00126540 at '40-41 (sBLA for Mumps End Expiry: "One year persistence serology samples will not be tested in the mumps plaque reduction neutralization (PRN) assay. The PRN assay correlates well with the mumps ELISA and therefore only the ELISA testing will be conducted for this time point. Revaccinations will be based solely on ELISA results."); MRK-KRA00138137 at '144 (sBLA for rHA: "A single clinical trial, Protocol 009 … supports the replacement of HSA with rHA … as the study results demonstrated that M-M-R™II with rHA induced acceptable antibody response rates for … mumps …that are similar (noninferior) to those induced by M-M-R™II."); MRK-KRA00140056 at '0196 (sBLA for rHA: "Overall, the study results suggest the M-M-R™II with rHA is highly immunogenic, well tolerated, and will be as effective as M-M-R™II with HSA in preventing measles, mumps, and rubella."); MRK-KRA00158320 at '350 (BLA for ProQuad: "Merck & Co., Inc. has assessed the correlation between neutralizing antibody … and a wild-type enzyme-linked immunosorbent assay ... These data support the use of the results of a wild-type ELISA as a correlate for protection.")

- BLA for ProQuad (Protocol 012, Protocol 013, Protocol 014) – "The data summarized in this clinical summary demonstrate that ProQuad is immunogenic … and is as efficacious as its parent products."

423. With regard to the AIGENT measuring mumps neutralizing antibodies, the sBLA for Mumps End Expiry stated that "[m]umps neutralizing antibodies were measured immediately prior to vaccination and 6 weeks postvaccination using the plaque-reduction neutralization (PRN) assay. PRN assay was used as the primary endpoint because it is a functional assay that measures the ability of the vaccine-induced immune response to inhibit viral replication in vitro, and can, therefore, be considered a surrogate for vaccine effectiveness." Merck's statement to FDA is misleading because it omitted that Merck had not performed a formal specificity analysis[953] for the AIGENT assay, and the AIGENT had not been validated as a measure of mumps neutralizing antibodies. Furthermore, the statement omitted that the endpoint measured by the AIGENT had not been demonstrated to have a connection to protection from disease.

424. With regard to the efficacy of a 4.1 mumps dose, the sBLA for Mumps End Expiry stated that that "[t]he data presented here indicate with a high level of assurance that decreasing the mumps end-expiry titer from 4.3 to 4.1 log10 TCID50 per dose in children 12 to 19 months of age will ensure that M-M-R™II remains a highly effective vaccine." Merck's statement to FDA was misleading because it omitted that the assays used in Protocol 007 had not been shown to be connected to protection from disease and therefore the results of the assays could not be used to provide reliable information about the effectiveness of MMRII with a mumps potency of not less than 4.1 log10 TCID50.

[953] Deposition of Florian Schodel, December 22, 2016, 352:14-365:15.

425. With regard to the seroconversion rate as a measure of protection, the sBLA for Mumps End Expiry stated that "[l]owering the mumps virus potency to 4.1 log10 TCID50 per dose maintains >90% seroconversion using a neutralization assay, thus preserving the excellent safety and efficacy profile of the vaccine." Merck's statement to FDA was misleading because it omitted that the seroconversion rates measured by the AIGENT assay had not been shown to relate to protection from disease. Furthermore, unlike the neutralization assay used in the early efficacy studies to support the licensure of mumps vaccines, the seroconversion rate measured by the AIGENT assay did not "parallel protection from disease."

426. With regard to the effectiveness of MMRII with rHA, the sBLA for rHA stated that "[o]verall, the study results suggest that M-M-R™II with rHA is highly immunogenic… and will be as effective as M-M-R™II with HSA in preventing… mumps…" Merck's statement to the FDA is misleading because it omitted that the Protocol 009 clinical study to support the manufacturing change to rHA used the WT ELISA assay that had not been shown to have a connection to protection. Furthermore, since the WT ELISA assay used was not connected to protection, it is misleading to state that the WT ELISA assay results demonstrate that the manufacturing change from HSA to rHA did not impact the efficacy of the vaccine.

427. With regard to the efficacy of ProQuad, the BLA for ProQuad stated that "The data summarized in this clinical summary demonstrate that ProQuad is immunogenic … and is as efficacious as its parent products." Merck's statement to the FDA is misleading because the seroconversion rates reported using the WT ELISA assay that was used in three of the five clinical studies supporting the application were not related to protection and could not support the assertion that ProQuad was as efficacious as its parent products.

428. The BLA for ProQuad stated that "…Merck & Co., Inc. has assessed the correlation between neutralizing antibody (as measured in plaque reduction neutralization [PRN] assay) and a wild-type enzyme-linked immunosorbent assay (ELISA). The overall agreement rate was 93.6% (480/513). These data support the use of the results of a wild-type ELISA as a correlate for protection." Merck's statement to FDA was misleading because it omitted that the correlation data comparing the results of Protocol 007 clinical subjects tested by the WT ELISA and AIGENT assays did not demonstrate that the WT ELISA was connected to protection from disease because neither assay had been shown to relate to protection. It was also misleading because Merck's assessment of the correlation between the AIGENT and the WT ELISA provided no reliable data from which to conclude that the WT ELISA results were a correlate for protection.

429. The MMRII label from 2005 – 2007 was misleading because it omits that the seroconversion rate measured by the WT ELISA assay used in the clinical study supporting the change from HSA to rHA had not been shown to "parallel protection from disease" as the earlier studies cited in the label had demonstrated. Furthermore, because the WT ELISA assay used in Protocol 009 did not measure "antibodies associated with protection" it is misleading to omit that the WT ELISA assay could not provide reliable information about protection from disease.

430. The MMRII label from 2007 through the present (2018) was misleading because it omitted that the seroconversion rate measured by the WT ELISA assay used in the clinical study supporting the change in the mumps end-expiry potency had not been shown to "parallel protection from disease" as the earlier studies cited in the label had reported. Furthermore, because the AIGENT and WT ELISA assays used in Protocol 007 did not measure "antibodies

associated with protection" it is misleading to omit that Protocol 007 data could not provide reliable information about protection from disease.

431. The MMRII label after 2007 failed to state that the assays used in the clinical study to support a 12,500 [4.1 $\log_{10}$] $TCID_{50}$ potency were not able to assure that the vaccine dose at 12,500 [4.1 $\log_{10}$] $TCID_{50}$ was protective against disease. Furthermore, the reasons why Merck could not assure the vaccine at 4.1 log was protective were:

- Neither the AIGENT nor the WT ELISA measured protection against disease;
- In the AIGENT, the "large proportion of missing data precluded a conclusion of success" at 4.1 log [12,500];[954]

432. From 2005, when Merck obtained a license to sell ProQuad, through the present (2018), the Clinical Pharmacology Section of the ProQuad label stated that "[c]linical studies with a single dose of ProQuad have shown that vaccination elicited rates of antibody responses against measles, mumps, and rubella that were similar to those observed after vaccination with a single dose of M-M-R II." Merck's ProQuad label was misleading because it omitted that the antibody responses measured using the WT ELISA assay in the clinical studies supporting the licensure of ProQuad did not have a connection to protection from disease, and could therefore not be used to assess the similarity of MMRII and ProQuad as they relate to protection from disease.

433. From 2005, when Merck obtained a license to sell ProQuad, through the present (2018), the "Clinical Studies" Section of the ProQuad label stated that "[f]ormal studies to evaluate the clinical efficacy of ProQuad have not been performed. Efficacy of the measles, mumps, rubella, and varicella components of ProQuad was previously established in a series of clinical studies with the monovalent vaccines. A high degree of protection from infection was

[954] MRK-KRA00000479.

demonstrated in these studies." Merck's ProQuad label was misleading because it omitted that the ProQuad clinical study results using the WT ELISA assay could not be used to demonstrate that ProQuad afforded the same "high degree of protection" from mumps as a component vaccine because the clinical study data using WT ELISA did not reflect protection from disease.

434. From 2009 through the present (2018), "Clinical Pharmacology" section of the ProQuad label stated that "[r]esults from efficacy studies or field effectiveness studies that were previously conducted for the component vaccines were used to define levels of serum antibodies that correlated with protection against measles, mumps, and rubella... In these efficacy studies, the clinical endpoint for ... mumps was a clinical diagnosis of ... disease confirmed by a 4-fold or greater rise in serum antibody titers..." Merck's ProQuad label was misleading because it omitted that the WT ELISA used in the clinical studies to support the licensure of ProQuad did not include the 4-fold rise criteria reported to be correlated with protection against mumps infection. Furthermore, the label omitted that the WT ELISA assay with a 10 Ab cutoff did not have a connection to whether a subject was protected from disease. Moreover, the label is misleading because it did not state that the seroconversion rates measured in the clinical studies to support ProQuad were not measured using the 4-fold rise criteria used in previous clinical studies that reported a correlation between the 4-fold rise criteria and protection from disease.

435. From 2005, when Merck obtained a license to sell ProQuad, through today (2018), the ProQuad label has failed to state that the WT ELISA assay used in three of the clinical studies to support the application, Protocol 012, Protocol 013, and Protocol 014, did not measure protection because the WT ELISA used in the three clinical studies had not been correlated to an assay that measured protection from mumps. Furthermore, the Clinical Pharmacology section of

the ProQuad label has failed to state that the reported "rates of antibody response against ... mumps ... that were similar to those observed after vaccination with a single dose of M-M-R II" were not obtained from studies that employed a clinically relevant assay. Moreover, the "Clinical Studies" section of the ProQuad label has failed to state that because Merck's WT ELISA did not measure protection from mumps, seroconversion measured by WT ELISA did not demonstrate that ProQuad offered the same "high degree of protection from infection" as its component vaccines, as stated in the Clinical Studies section of the ProQuad label.

436. [redacted]. Furthermore, [redacted]. Moreover, [redacted].

437. It is not unusual for efficacy claims in existing products to be used by FDA as the standard for other similar products, especially with products that impact the public health. While relative effectiveness has generally not been viewed on the surface as part of the Federal Food Drug and Cosmetics Act, the determination of safety does encompass the concept of relative effectiveness when dealing with serious public health issues.

> In evaluating effectiveness, FDA reviews new drug products and devices on their merits. FDA does not require new drug products or devices to be more effective than their approved therapies for the same disease or condition. In general, both new drug products and class III devices must be shown to be effective through

evidence consisting of clinical investigations that provide a basis on which it can be concluded that the new drug product or class III device will be safe and have the effect that it is represented to have.

For most new drug products and new class III devices intended to treat serious illness or provide symptomatic relief, a showing of effectiveness is usually based on a clinical trial comparing the product to a placebo. Such a showing does not necessarily involve a comparison to another active treatment or a product that is known to be effective.

In certain circumstances, however, it may be important to consider whether a new product is less effective than available alternative therapies, when less effectiveness could present a danger to the patient or to the public. For example, it is essential for public health protection that a new therapy be as effective as alternatives that are already approved for marketing when:

1. the disease to be treated is life- threatening or capable of causing irreversible morbidity (e.g., stroke or heart attack); or

2. the disease to be treated is a contagious illness that poses serious consequences to the health of others (e.g., sexually transmitted diseases).[955]

438. The claims set forth in Merck's MMRII and ProQuad labels could and do impact the standards for relative effectiveness that other manufacturers would have to meet to obtain FDA approval to market similar products in the United States.

[955] Statement Regarding the Demonstrations of Effectiveness of Human Drug Products and Devices, 60 Fed Reg 39180 at 39180-81 (notice August 1, 1995).

439. The causes for the resurgence of mumps cases and mumps outbreaks has not been established. The issues identified in this report and the possibility that some young adults who are at risk for mumps received lower potency vaccine has not been publicly disclosed by Merck. If these young adults received lower potency vaccines as children this information would be relevant for evaluating potential causes of the resurgence of mumps cases and mumps outbreaks since 2006.

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David A. Kessler, M.D.

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March 14, 2018

Appendix A

Curriculum Vitae

DAVID A. KESSLER

1969-1973	AMHERST COLLEGE, Amherst, Massachusetts Bachelor of Arts, *magna cum laude* (B.A. Independent Scholar, 1973)
1973-1979	HARVARD MEDICAL SCHOOL, Boston, Massachusetts Doctor of Medicine (M.D. 1979)
1975-1977	UNIVERSITY OF CHICAGO LAW SCHOOL, Chicago, Illinois Doctor of Law (J.D., 1978), Harvard Law School, 1977-1978
1984-1986	NEW YORK UNIVERSITY GRADUATE SCHOOL OF BUSINESS ADMINISTRATION (Manhattanville), Purchase, New York Advanced Professional Certificate in Management

EMPLOYMENT

2003-present	UNIVERSITY OF CALIFORNIA, SAN FRANCISCO Professor of Pediatrics, Epidemiology and Biostatistics
2003-2007	Dean, School of Medicine Vice Chancellor of Medical Affairs
1997-2003	YALE UNIVERSITY SCHOOL OF MEDICINE Dean Professor of Pediatrics, Internal Medicine, and Public Health
1990-1997	UNITED STATES FOOD AND DRUG ADMINISTRATION Commissioner (Appointed by President George H. W. Bush, Reappointed by President William J. Clinton)
1984-1990	THE HOSPITAL OF THE ALBERT EINSTEIN COLLEGE OF MEDICINE Medical Director
1986-1990	COLUMBIA UNIVERSITY Julius Silver Program in Law, Science and Technology Lecturer on Law
1982-1984	MONTEFIORE MEDICAL CENTER Special Assistant to the President
1981-1984	UNITED STATES SENATE COMMITTEE ON LABOR AND HUMAN RESOURCES, Consultant to the Chairman

HONORARY DEGREES

1992 AMHERST COLLEGE, Amherst, Massachusetts
Doctor of Science *honoris causa*

1992 GEORGE WASHINGTON UNIVERSITY, Washington, D.C.
Doctor of Science *honoris causa*

1993 PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE, Philadelphia, Pennsylvania, Doctor of Science *honoris causa*

1993 DICKINSON COLLEGE OF LAW, Carlisle, Pennsylvania
Doctor of Laws *honoris causa*

1995 ALBANY MEDICAL COLLEGE, Albany, New York
Doctor of Science *honoris causa*

1997 NORTHEASTERN UNIVERSITY, Boston, Massachusetts
Doctor of Science *honoris causa*

1998 MOUNT SINAI SCHOOL OF MEDICINE, New York, New York
Doctor of Humane Letters *honoris causa*

1998 COLGATE UNIVERSITY, Hamilton, New York
Doctor of Science *honoris causa*

1998 YALE UNIVERSITY, New Haven, Connecticut
Master of Arts *privation*

1999 CONNECTICUT COLLEGE, New London, Connecticut
Doctor of Humane Letters *honoris causa*

2001 DICKINSON COLLEGE, Carlisle, Pennsylvania
Doctor of Science, *honoris causa*

2001 UNION COLLEGE, Schenectady, New York
Doctor of Laws, *honoris causa*

2002 UNIVERSITY OF LOUISVILLE, Louisville, Kentucky
Doctor of Public Service, *honoris causa*

2005 STATE UNIVERSITY OF NEW YORK, Syracuse, NY
Doctor of Science, *honoris causa*

2012 DREXEL UNIVERSITY, Philadelphia, PA
Doctor of Science, *honoris causa*

2013 CLAREMONT GRADUATE UNIVERSITY, Claremont, CA
Doctor of Science, *honoris causa*

HONORS

NATIONAL ACADEMY OF SCIENCES, Public Welfare Medal,
Honorary Member

INSTITUTE OF MEDICINE, Member

AMERICAN SOCIETY OF CLINICAL ONCOLOGY
Distinguished Service Award for Scientific Achievement

AMERICAN ACADEMY OF ARTS AND SCIENCES, Fellow

PHI BETA KAPPA, Amherst College

UNIVERSITY OF CHICAGO LAW REVIEW, Associate Editor

2008 PUBLIC HEALTH HERO AWARD, UC Berkeley

SIGMA XI, The Scientific Research Society of North America

BARNARD COLLEGE Barnard
Medal of Distinction

CASPAR PLATT AWARD, The University of Chicago Law School

HARVARD BLODGETT AWARD IN BIOLOGY, Amherst College

WHITING FOUNDATION GRANT-IN-AID for research at
Sloan-Kettering Institute

NATIONAL SCIENCE FOUNDATION FELLOWSHIP (declined)

JOHN WOODRUFF SIMPSON FELLOWSHIP, awarded by Amherst
College for the study of medicine

ALVAN T.--VIOLA D. FULLER AMERICAN CANCER SOCIETY
JUNIOR RESEARCH FELLOW (declined)

NATIONAL INSTITUTES OF HEALTH TRAINING FELLOWSHIP
RECIPIENT for physiology research at the Marine Biological Laboratory,

Woods Hole, Massachusetts

PHI DELTA THETA SCHOLARSHIP
DISTINGUISHED PUBLIC SERVICE AWARD
The George Washington University School of Medicine and Health Sciences

UNITED STATES DEPARTMENT OF JUSTICE, CIVIL DIVISION
Special Citation

AMERICAN SOCIETY OF PUBLIC ADMINISTRATION
National Capitol Area Chapter
President's Award for Outstanding Achievement

AMERICAN FEDERATION FOR AIDS RESEARCH (AmFAR)
Sheldon W. Andelson Public Policy Achievement Award

THE WOODROW WILSON AWARD FOR DISTINGUISHED
GOVERNMENT SERVICE Johns Hopkins University

HAL OGDEN AWARD
Association of State and Territorial Directors of Health Promotion and
Public Health Education and the U. S. Centers for Disease Control

NATIONAL ORGANIZATION FOR RARE DISEASES (NORD)
Outstanding Service to the Public Health Award

MARCH OF DIMES
Franklin Delano Roosevelt Leadership Award

CHILDREN'S HOSPITAL NATIONAL MEDICAL CENTER
Children's Research Institute Award of Academic Excellence

AMERICAN HEART ASSOCIATION
National Public Affairs Special Recognition Award for Food Labeling

ISRAEL CANCER RESEARCH FOUNDATION
President's Award

INSTITUTE FOR ADVANCED STUDIES IN IMMUNOLOGY AND AGING
Lifetime Public Service Award

AMERICAN LUNG ASSOCIATION
Special Recognition Award

UNIVERSITY OF CHICAGO ALUMNI ASSOCIATION
Professional Achievement Award (Washington, D.C. Chapter)

U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Secretary's Award for Excellence in Public Service

NATIONAL KIDNEY CANCER ASSOCIATION
Progressive Leadership Award

JOHNS HOPKINS UNIVERSITY SCHOOL OF PUBLIC HEALTH
Dean's Medal

AMERICAN CANCER SOCIETY
Medal of Honor

AMERICAN HEART ASSOCIATION
Meritorious Achievement Award

WORLD HEALTH ORGANIZATION Pan
American World Health Organization World
No Tobacco Day Award

AMERICAN HEART ASSOCIATION
National Public Affairs Special Recognition Award for Tobacco

PROFESSIONAL ACHIEVEMENT CITATION, University of
Chicago Alumni Association

PENNSYLVANIA HOSPITAL Molly
and Sidney N. Zubrow Award

AMERICAN LUNG ASSOCIATION OF CONNECTICUT
Humanitarian Award

AMERICAN COLLEGE OF PREVENTIVE MEDICINE
Special Recognition Award

ASSOCIATION OF AMERICAN MEDICAL COLLEGES AND THE ROBERT WOOD JOHNSON FOUNDATION
David E. Rogers Award for Improving Health and Healthcare of the American People

JACOBS INSTITUTE OF WOMEN'S HEALTH
Excellence in Women's Health Award

NARAL PRO-CHOICE AMERICA
Lifetime Achievement Award

THE ASSOCIATION OF STATE AND TERRITORIAL CHRONIC DISEASE PROGRAM DIRECTORS
Joseph W. Cullen Award for Outstanding Contributions to Chronic Disease Prevention and Control

THE COLLEGE OF WILLIAM & MARY LAW SCHOOL
2005 Benjamin Rush Medal

CALIFORNIA CENTER FOR PUBLIC HEALTH ADVOCACY
David Kessler Award for Extraordinary Contribution to the Public Health

BOOKS FOR A BETTER LIFE AWARD

INTERNSHIP & RESIDENCY

1981-1982	SENIOR ASSISTANT RESIDENT, Department of Pediatrics, The Johns Hopkins Hospital
1980-1981	ASSISTANT RESIDENT, Department of Pediatrics, The Johns Hopkins Hospital
1979-1980	INTERN, Department of Pediatrics, The Johns Hopkins Hospital

ACADEMIC APPOINTMENTS

2003-present	UNIVERSITY OF CALIFORNIA, SAN FRANCISCO Professor of Pediatrics Professor of Epidemiology and Biostatistics
1997-2003	YALE UNIVERSITY Professor of Pediatrics Professor of Internal Medicine Professor of Public Health
1990-1997 (On leave)	ALBERT EINSTEIN COLLEGE OF MEDICINE Department of Pediatrics Department of Epidemiology and Social Medicine Associate Professor of Pediatrics Associate Professor of Epidemiology and Social Medicine
1988-1990	ALBERT EINSTEIN COLLEGE OF MEDICINE Department of Epidemiology and Social Medicine Assistant Professor
1986-1990	COLUMBIA UNIVERSITY SCHOOL OF LAW Julius Silver Program in Law, Science and Technology Lecturer on Law

1982-1990 ALBERT EINSTEIN COLLEGE OF MEDICINE
Department of Pediatrics
Assistant Professor

SPECIAL STUDY

June 1987 JOHNS HOPKINS SCHOOL OF HYGIENE AND PUBLIC HEALTH
Graduate Summer Program in Epidemiology - Pharmacoepidemiology

June 1985 YALE SCHOOL OF ORGANIZATION AND MANAGEMENT
Advanced Management Studies in Health Care Management

1977-1978 HARVARD LAW SCHOOL, Special Student

RESEARCH EXPERIENCE

Summers 1970-1972 SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH
Division of Drug Resistance, New York, New York
Research Asst

Summer 1972 MARINE BIOLOGICAL LABORATORY, Woods Hole, Massachusetts
Physiology course

1974-1975 CHILDREN'S HOSPITAL MEDICAL CENTER
Department of Surgical Research, Boston, Massachusetts
Research Associate

Summer 1976 DEPARTMENT OF HEALTH, EDUCATION and WELFARE
Office of the General Counsel, Chicago, Illinois
Law Clerk

VISITING COMMITTEE

1992-1994 UNIVERSITY OF CHICAGO LAW SCHOOL

UNIVERSITY ACCREDITATION

2008-2012 WESTERN ASSOCIATION OF SCHOOLS AND COLLEGES,
Chair of LLU Accreditation Committee

2013; 2016 NORTHWEST COMMISSION ON COLLEGES AND UNIVERSITIES
University of Washington; Washington State University

SPECIAL PROJECTS

1982-1988 THE ROBERT WOOD JOHNSON FOUNDATION
Program for Hospital Initiatives in Long-Term Care,

1989-1990 THE PEW CHARITABLE TRUSTS
THE ROBERT WOOD JOHNSON FOUNDATION
Program to Strengthen Hospital Nursing Co-Director

CORPORATE BOARD AND ADVISORY POSITIONS AND COMMITTEES

2011 - Present IMMUCOR
Member of Board, Chairman of Compliance Committee

2008 - Present TPG
Senior Advisor

2011 - 2014 APTALIS HOLDINGS
Member of Board, Chairman of Compliance Committee

2009 –2017 TOKAI
Member of Board

2007 GOOGLE HEALTH ADVISORY COUNCIL

2007 REVOLUTION HEALTH GROUP
Medical Advisory Board

2007 PERSEUS LLC
Advisory Board

2003 – 2014 FLEISHMAN HILLARD INTERNATIONAL COMMUNICATIONS
International Advisory Board

2000 - 2003 PERSEUS-SOROS BIOTECHNOLOGY FUND Scientific Advisory Board

ADVISORY COMMITTEES

2007 THE RHODES TRUST, THE RHODES SCHOLARSHIPS
Chair, California Selection Committee

2006	CENTER FOR THE ADVANCED STUDIES ON AGING, UNIVERSITY OF MIAMI External Advisory Group
2005 -2015	BROAD MEDICAL RESEARCH PROGRAM Advisory Board
2005	CLINTON SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES National Advisory Board
2003, 2013	HEINZ AWARDS (HEINZ FAMILY FOUNDATION) Awards Juror
2003	MARCH OF DIMES Chair, Prematurity Campaign in Northern California
2002 - 2004	CENTER ON ALCOHOL MARKETING AND YOUTH AT GEORGETOWN UNIVERSITY Advisory Board
2001 -	UNIVERSITY OF CHICAGO LAW REVIEW Editorial Advisory Board
2000 - 2005	JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION Oversight Committee
2000	GOVERNOR'S BLUE RIBBON COMMISSION ON MENTAL HEALTH, STATE OF CONNECTICUT Honorary Chair
2000	FILM AID INTERNATIONAL, INTERNATIONAL RESCUE COMMITTEE Advisory Board
1999	WORLD HEALTH ORGANIZATION Expert Panel on Tobacco
1997	ADVISORY COMMITTEE ON TOBACCO AND PUBLIC HEALTH (Co-Chairman with C. Everett Koop)
1993	GOVERNMENT UNIVERSITY INDUSTRY ROUNDTABLE National Academy of Sciences
1990	ADVISORY COMMITTEE ON THE FOOD AND DRUG ADMINISTRATION Chairman, Drugs and Biologics Subcommittee
1988 - 1989	NATIONAL ADVISORY COUNCIL ON HEALTH CARE TECHNOLOGY ASSESSMENT, Department of Health and Human Services, Washington, D.C. Chairman, Patient Outcomes Subcommittee

PRIOR FEDERAL COMMITTEE MEMBERSHIPS

WHITE HOUSE COMMISSION ON PRESIDENTIAL SCHOLARS

NATIONAL COUNCIL ON SCIENCE AND TECHNOLOGY
Committee on Health, Safety and Food R&D, Vice Chair

INSTITUTE OF MEDICINE
Forum On Drug Development and Regulation

INSTITUTE OF MEDICINE
AIDS Roundtable

NATIONAL TASK FORCE ON AIDS DRUG DEVELOPMENT

OFFICE OF SCIENCE AND TECHNOLOGY POLICY Federal Coordinating Council for Science, Engineering and Technology Committee on Life Science and Health Biotechnology Research Subcommittee, Member ex officio

BOARDS OF DIRECTORS

Current:

CENTER FOR SCIENCE IN THE PUBLIC INTEREST

DRUG STRATEGIES

Past:

AMHERST COLLEGE BOARD OF TRUSTEES

ELIZABETH GLASER PEDIATRIC AIDS FOUNDATION
Chairman, Board of Directors

NATIONAL CENTER FOR ADDICTION AND SUBSTANCE ABUSE
COLUMBIA UNIVERSITY

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES INDEPENDENT CITIZENS OVERSIGHT COMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

HENRY J. KAISER FAMILY FOUNDATION

DOCTORS OF THE WORLD

YALE-NEW HAVEN HOSPITAL

CONSUMERS UNION

NATIONAL COMMITTEE FOR QUALITY ASSURANCE

NEW YORK COUNTY HEALTH SERVICE REVIEW ORGANIZATION

COMPREHENSIVE MEDICAL REVIEW ORGANIZATION

FELLOWSHIP

YALE COLLEGE Fellow,
Calhoun College

LECTURESHIPS

THE REGIS J. FALLON LECTURE SERIES ON HEALTH AND LAW
University of Chicago

GRAYSON DISTINGUISHED LECTURE
Southern Illinois University School of Law

WEINBERG SYMPOSIUM LECTURE
Harvard Medical School

THE THOMAS B. FERGUSON LECTURE
Society of Thoracic Surgeons

GEORGE E. ALTMAN, M.D. LECTURE
Beth Israel Hospital

BETH AND RICHARD SACKLER LECTURE
University of Pennsylvania

MARTIN W. WITTE LECTURE
Newport Beach Public Library and Newport Beach Public Library Foundation

HERBERT L. ABRAMS LECTURE
Harvard Medical School

GEORGE GOODMAN LECTURE
State University of New York at Stony Brook

EVNIN LECTURE
Princeton University, Woodrow Wilson School

BOYARSKY LECTURE
Law, Medicine, and Ethics, Kenan Ethics Program, Duke University

CHARTER LECTURE
The University of Georgia

GARDERE & WYNNE LECTURE
Health Law and Policy Institute, University of Houston

DISTINGUISHED LECTURE IN NATIONAL SERVICE
University of Miami

TENTH ANNUAL JOHN O. VIETA, MD LECTURE
Lenox Hill Hospital

HARPER FELLOWSHIP LECTURE
Yale Law School

DR. JAMES STEWART KAUFMAN MEMORIAL LECTURE
The Mt. Sinai Health Care Foundation

DULCY B. MILLER MEMORIAL LECTURE
Smith College

JEAN MAYER LECTURE IN NUTRITION AND FOOD POLICY
Tufts University

HENRY BARNETT DISTINGUISHED LECTURESHIP
Albert Einstein College of Medicine

MARTIN A. CHERKASKY DISTINGUISHED LECTURESHIP
Robert Wagner Graduate School of Public Service New York University

ALPHA OMEGA ALPHA DISTINGUISHED LECTURESHIP
Cornell Medical School--New York Hospital

ST. GEORGE SOCIETY LECTURESHIP
Johns Hopkins Medical School

GOVERNOR WINTHROP ROCKEFELLER DISTINGUISHED LECTURESHIP University of Arkansas Medical School

MOLLY AND SIDNEY N. ZUBROW LECTURE
Pennsylvania Hospital

LEROY HOECK M.D. DISTINGUISHED LECTURESHIP
Children's Hospital National Medical Center

JULES AND JANE HIRSH HEALTH POLICY ADDRESS
George Washington University

JOHN S. LATTA LECTURESHIP
University of Nebraska Medical
School

PAUL K. SMITH MEMORIAL LECTURE
George Washington University

WOLK HEART FOUNDATION LECTURE
Colgate University

HASTINGS LECTURE
Association for the Advancement of Medical Instrumentation
National Heart, Lung and Blood Institute

INSTITUTE OF MEDICINE 25TH DISTINGUISHED LECTURESHIP University of Washington

RALPH CAZORT LECTURESHIP
Meharry Medical School

DAVID M. IFSHIN MEMORIAL LECTURE
Potomac, Maryland

CHARLES C. LEIGHTON MEMORIAL LECTURE
Leonard David Institute of Health Economics
University of Pennsylvania

D. W. HARRINGTON LECTURE State
University of New York At Buffalo School of
Medicine and Biomedical Sciences

SAMUEL RUBIN LECTURE FOR THE ADVANCEMENT OF LIBERTY
Columbia University

LEO S. WEIL MEMORIAL LECTURE
Tulane Medical Center, Touro Infirmary,
and Louisiana State University School of Medicine

THOMAS PARRIN LECTURE
University of Pittsburgh School of Public Health

DAVID PACKARD LECTURE
Uniformed Services University of the Health Sciences

NORMAN E. ZINBERG LECTURE
Harvard Medical School

JOHN H. ERSKINE LECTURE
St. Jude's Children's Research Hospital

MARTIN V. BONVENTRE MEMORIAL LECTURE
The Brooklyn Hospital Center

PURVES LECTURE
Woodbridge Library, Woodbridge, Connecticut

VISITING SCHOLAR LECTURE University of Oklahoma - Board of Regents Oklahoma Scholar Leadership Extension Program

J. ROSWELL GALLAGHER LECTURER
Society of Adolescent Medicine

KATHERINE BOUCOT STURGIS LECTURESHIP
American College of Preventive Medicine

HELMUT SCHUMANN LECTURE
Dartmouth-Hitchcock Medical Center

50TH ANNIVERSARY COMMUNICATION LECTURE
Centers for Disease Control and Prevention

5TH JAMES BORDLEY III MEMORIAL LECTURE
Mary Imogene Bassett Hospital

TURNER LECTURE
University of California

MARIE SHULSKY MEMORIAL LECTURE ON HEALTH AND SOCIAL RESPONSIBILITY
Fifth Avenue Synagogue, New York, New York

GERTRUDE AND G.D. CRAIN, JR. LECTURE SERIES
Medill School of Journalism, Northwestern University

GEORGE ARMSTRONG LECTURE
Ambulatory Pediatric Society

ARCO FORUM OF PUBLIC AFFAIRS
Institute of Politics, John F. Kennedy School of Government
Harvard University

PAUL LEVINGER LECTURE AND PROFESSORSHIP PRO TEM IN THE ECONOMICS OF HEALTH CARE Brown University

ARNOLD J. SCHWARTZ MEMORIAL HEALTH LECTURE
Robert F. Wagner Graduate School of Public Service New York University

RONALD ALTMAN MEMORIAL LECTURE
Festival of Arts, Books and Culture, Cherry Hills, New Jersey

SAMUEL MARTIN, M.D. III MEMORIAL LECTURE Division of General Internal Medicine and Leonard Davis Institute University of Pennsylvania

CARL J. MARTINSON, M.D. MEMORIAL LECTURESHIP ON HEALTH PROMOTION AND DISEASE PREVENTION University of Minnesota

LEONARD SILK MEMORIAL LECTURE Mt.
Desert Island Biological Laboratories

CALDWELL LECTURE
American Roentgen Ray Society

RICHARD H. DENT LECTURE St.
George's School

ROBERT T. WONG DISTINGUISHED PROFESSORSHIP
University of Hawaii, Manoa

NIDA/American Psychiatric Association Obesity Symposium

HARVARD OBESITY COURSE

STANFORD BARIATRIC COURSE

AMERICAN BARIATRIC SOCIETY

RHODES ENDOWED LECTURE

STAFFORD LITTLE LECTURE PUBLIC LECTURES AT PRINCETON

GERALD AND SALLY DENARDO LECTURESHIP, SANTA CLARA UNIVERSITY

ALEX AND LENA CASPER MEMORIAL LECTURE, MIAMI UNIVERSITY

UNIVERSITY OF VERMONT FOOD SYSTEMS LEADERSHIP

GOOGLE LECTURE

GLOBAL STUDIES SYMPOSIUM, WHITMAN COLLEGE
Excellence in Public Service

DONALD DUNPHY LECTURE, MCCONE HOSPITAL, UNIVERSITY OF NORTH CAROLINA

CENTER FOR GLOBAL HEALTH, STANFORD MEDICAL SCHOOL

STANFORD UNIVERSITY: THE ETHICS OF FOOD & THE ENVIRONMENT

STANFORD MEDICAL SCHOOL, DEPARTMENT OF MEDICINE, GRAND ROUNDS

LEGACY WARNER SERIES LECTURE ON IMPACT OF FAMILY AND SMOKING PREVENTION AND CONTROL ACT

LEADING VOICES IN PUBLIC HEALTH, EAST TENNESSEE STATE UNIVERSITY

92ND STREET YMCA PUBLIC LECTURE, NEW YORK

COMMONWEALTH CLUB OF CALIFORNIA

SAN FRANCISCO PUBLIC LIBRARY LECTURE

KANSAS CITY PUBLIC LIBRARY

YALE ROBERT WOOD JOHNSON CLINICAL SCHOLARS PROGRAM

COMMUNITY/PUBLIC SERVICE AWARDS

NATIONAL ASSOCIATION FOR THE ADVANCEMENT OF COLORED PEOPLE
Montgomery County Chapter
Person of the Year

LEAGUE OF WOMEN VOTERS, NEW YORK
Carrie Chapman Catt Award

COMMON CAUSE
Public Service Achievement Award

AMERICAN ACADEMY OF PEDIATRICS
Excellence in Public Service

BUSINESS WEEK
Best in Public Service

GEORGE ORWELL AWARD FOR HONESTY AND CLARITY
IN PUBLIC LANGUAGE
National Conference of Teachers of English

ANTI-DEFAMATION LEAGUE OF B'NAI BRITH
Man of Achievement Five Towns, New York

GOLDEN SLIPPER CLUB OF PHILADELPHIA
Golden Slipper Award

NATIONAL FATHER'S DAY COMMITTEE
Father of the Year Award

UNITED SENIORS HEALTH COOPERATIVE
Seniors Advocate Award

NATIONAL ASSOCIATION OF GOVERNMENT COMMUNICATORS
Communicator of the Year Award

NATIONAL CONSUMERS LEAGUE
Trumpeter Award

THE INTERNATIONAL PLATFORM ASSOCIATION
George Crile Award

AMERICAN LUNG ASSOCIATION of New York
Life and Breath Award in Public Health

CONSUMER FEDERATION OF AMERICA
Philip Hart Public Service Award

CAMPAIGN FOR TOBACCO FREE KIDS
Distinguished Service Award

MEDICAL SOCIETY OF NEW YORK, 1st District Branch
Public Service Award

ONCOLOGY NURSING SOCIETY
Public Service Award

PUBLIC VOICE FOR FOOD & HEALTH POLICY
Special Recognition Award for Advancing the Consumer Interest in Food and Agriculture Policy

ATTENDING PEDIATRICIAN

2003 - 2013	UNIVERSITY OF CALIFORNIA, SAN FRANCISCO MEDICAL CENTER
1997-2003	YALE-NEW HAVEN HOSPITAL
1982-1990	BRONX MUNICIPAL HOSPITAL CENTER
1982-1990	NORTH CENTRAL BRONX HOSPITAL
1982-1990	MONTEFIORE MEDICAL CENTER
1982-1990	HOSPITAL OF THE ALBERT EINSTEIN COLLEGE OF MEDICINE

COMMUNITY ACTIVITIES

SCARSDALE SCHOOL DISTRICT, Scarsdale, New York

1986-1990	Legislative Affairs Advisory Committee 1988-1990 Buildings and Facilities Advisory Committee
1990	SCARSDALE STUDENT TRANSFER EDUCATION PLAN, Board of Trustees

GENERAL INFORMATION

Address:
2715 Steiner Street
San Francisco, CA 94123

Office Phone:
(415) 929 1121

Married:
Paulette Kessler
Two children - Elise and Ben

Born:
May 31, 1951

MEDICAL LICENSURE

California
Connecticut (non-active)
Maryland (non-active)
New York (non-active)

PUBLICATIONS

Books

Kessler, David A., CAPTURE: UNRAVELING THE MYSTERY OF MENTAL SUFFERING, Harper, Pub. date: April 2016 Paperback: April, 2017

Kessler, David A. THE END OF OVEREATING: TAKING CONTROL OF THE INSATIABLE AMERICAN APPETITE, Rodale, 2009

Translated and Adapted:
過食にさようなら-止まらない食欲をコントロール [単行本]
K0HEЦ 06Ж0CTBЖУ
이 페이지 번역하기
Perché mangianmo troppo (e come fare per smetteria
Laat je niet volvreten: Hoe de voedselindustgrie schade toebrengt ann onze gexondheid
Das Ende des groben Fressens Wie die Nahrungsmittelindustrie Sie zu ubermaBigem Essen berleitet und was Sie dagegen tun konnen
Muszáj annyit enni? Hadüzenet a só, a zsír és a cukor ellen
Also: Romania, Canada, UK, Australia, India
Your Food is Fooling You: How Your Brain is Hijacked by Sugar Fat and Salt (US Young Adult Version)
Hijacked: How Your Brain is Fooled by Food (Canadian Young Adult Version)

Kessler, David A., A QUESTION OF INTENT: A GREAT AMERICAN BATTLE WITH A DEADLY INDUSTRY, Public Affairs (Hardcover 2001) (Paperback 2002)

Edited Books

Eisdorfer, Carl, Kessler, David A., Spector, Abby (eds.), CARING FOR THE ELDERLY: RESHAPING HEALTH POLICY, Johns Hopkins University Press, 1989. Includes chapter by Coombs, C., Eisdorfer, C., Feiden, K., and Kessler, D.A. "Lessons from the Program for Hospital Initiatives in Long-Term Care."

Articles

Kessler, David A., Nesbit, J.A., Westmoreland, T.M., Albright, M.B., "A Tribute to C. Everett Koop," PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, 110(18):7108-9 (April 30, 2013)

Articles

McClellan M, Benner J, Schilsky R, Epstein D, Woosley R, Friend S, Sidransky D, Geoghegan C, Kessler D. An accelerated pathway for targeted cancer therapies. NATURE DRUG DISCOVERY. 2011 10(2):79-80

Kessler, David A., "Towards More Comprehensive Food Labeling," NEW ENGLAND JOURNAL OF MEDICINE, 371:193-195 (July 27, 2014)

Kessler DA, Mande JR, Scarbrough FE, Schapiro R, Feiden K. Developing the "nutrition facts" food label. HARVARD HEALTH POLICY REVIEW 2003;4:13-24

Kessler, David A., Nesbit, J.A., Westmoreland, T.M., Albright, M.B., "A Tribute to C. Everett Koop," PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, 110(18):7108-9 (April 30, 2013)

Naleid, A.M., Grimm, J.W., Kessler, David A., Sipols, A.J., Aliakbari, S., Bennett, J.L., Wells, J., Figlewicz, D.P., "Deconstructing the Vanilla Milkshake: the Dominant Effect of Sucrose on Self-administration Flavor Mixtures," APPETITE, 50(1):128-38 (January 2008)

Halme, Dina J. and Kessler, David A., "FDA Regulation of Stem Cell-Based Therapies", NEW ENGLAND JOURNAL OF MEDICINE, 355 (16): 1730-1735 (October 19, 2006)

Kessler, David A., "Alcohol Marketing and Youth: The Challenge for Public Health," JOURNAL OF PUBLIC HEALTH POLICY, 26(3):292-295 (Autumn 2005)

Kessler, David A., "The Tobacco Settlement," NEW ENGLAND JOURNAL OF MEDICINE, 337:1082-1083 (October 9, 1997)

Kessler, David A., Wilkenfeld, J.P., Thompson. L.J. "The Food and Drug Adminstration's Rule on Tobacco: Blending Science and Law," PEDIATRICS, 99(6):884-887 (June 1997)

Kessler, David A., Natanblut, Sharon L., Wilkenfeld, Judith P., Lorraine, Catherine C., Mayl, Sharon Lindan, Bernstein, Ilisa B.G. and Thompson, Larry, "Nicotine Addiction: A Pediatric Disease," JOURNAL OF PEDIATRICS, 130:518-524 (April 1997)

Kessler, David A., Barnett, Philip S., Witt, Ann, Zeller, Mitchell R., Mande, Jerold R. and Schultz, William B., "The Legal and Scientific Basis for FDA's Assertion of Jurisdiction Over Cigarettes and Smokeless Tobacco," JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, 277:405-409 (February 5, 1997)

Kessler, David A., Hass, Arthur E., Feiden, Karyn L. , Lumpkin, Murray and

Temple, Robert, "Approval of New Drugs in the United States: Comparison with the United Kingdom, Germany and Japan," JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, 276:1826-1831 (December 11, 1996)

Kessler, David A., Witt, Ann, Barnett, Philip S., Zeller, Mitchell R., Natanblut, Sharon, Wilkenfeld, Judith, Lorraine, Catherine C., Thompson, Larry J. and Schultz, William B., "The Food and Drug Administration's Regulation of Tobacco Products," NEW ENGLAND JOURNAL OF MEDICINE, 335:988-994 (September 26, 1996)

Silverman, Barbara G., Brown, S. Lorie, Bright, Roslie A., Kaczmarek, Ronald G., Arrowsmith-Lowe, Janet B., Kessler, David A., "Reported Complications of Silicone Gel Breast Implants: An Epidemiologic Review," ANNALS OF INTERNAL MEDICINE, 124:744-756 (April 15, 1996)

Kessler, David A., "Nicotine Addiction in Young People," NEW ENGLAND JOURNAL OF MEDICINE, 333:186-189 (July 20, 1995)

Kessler, David A., "Accelerating the Approval of Drugs for Life-Threatening and Serious Diseases," SCIENTIFIC AMERICAN, 272:48-52 (March 1995)

Kessler, David A., Rose, Janet L., Temple, Robert J., Schapiro, Renie and Griffin, Joseph, "Therapeutic Class Wars: Drug Promotion in a Competitive Marketplace," NEW ENGLAND JOURNAL OF MEDICINE, 331:1350 (November 17, 1994)

Kessler, David A., Merkatz, Ruth B., Schapiro, Renie, "A Call for Higher Standards for Breast Implants," JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, 270:2607-2608 (December 1, 1993)

Kessler, David A., Siegel, Jay P., Noguchi, Philip D., Zoon, Kathryn C., Feiden, Karyn L., and Woodcock, Janet, "Regulation of Somatic Cell Therapy and Gene Therapy by the Food and Drug Administration," NEW ENGLAND JOURNAL OF MEDICINE, 329:1169-1173 (October 14, 1993)

Merkatz, Ruth B., Temple, Robert, Sobel, Solomon, Feiden, Karyn, Kessler, David A., and members of the working group on Women in Clinical Trials, "Women in Clinical Trials of New Drugs: A Change in FDA Policy," NEW ENGLAND JOURNAL OF MEDICINE, 329:292-296 (July 22, 1993)

Kessler, David A. for the Working Group, "A New Approach to Reporting Medication and Device Adverse Effects and Product Problems," JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, 269:2765-2768 (June 2, 1993)

Kessler, David A., Taylor, Michael A., Maryanski, James H., Flamm, Eric L., and Kahl, Linda S., "The Safety of Foods Developed by Biotechnology," SCIENCE, 256:1747-1749 (June 26, 1992)

Kessler, David A., "The Basis for the FDA's Decision on Breast Implants,"

NEW ENGLAND JOURNAL OF MEDICINE, 326:1713-1715 (June 18, 1992)

Kessler, David A., "Communicating to Patients About Their Medication," NEW ENGLAND JOURNAL OF MEDICINE, 325:1650-1652 (December 5, 1991)

Kessler, David A., "Drug Promotion and Scientific Exchange," NEW ENGLAND JOURNAL OF MEDICINE, 325:201-203 (July 18, 1991)

Kessler, David A. and Pines, Wayne L., "The Federal Regulation of Prescription Drug Advertising and Promotion," JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, 264:2409-2415 (November 14, 1990)

Kessler, David A., "The Federal Regulation of Food Labeling: Promoting Foods to Prevent Disease," NEW ENGLAND JOURNAL OF MEDICINE, 321:717-725 (September 14, 1989)

Kessler, David A., "The Regulation of Investigational Drugs," NEW ENGLAND JOURNAL OF MEDICINE, 320:281-288 (February 2, 1989)

Kessler, David A., Pape, Stuart, and Sundwall, David, "The Federal Regulation of Medical Devices," NEW ENGLAND JOURNAL OF MEDICINE, 317:357-366 (August 6, 1987)

Kessler, David A., "Food Safety: Revising the Statute," SCIENCE, 223:1034-1040 (March 1984)

Kessler, David A., "Regulating the Prescribing of Human Drugs for Nonapproved Uses Under the Food, Drug and Cosmetic Act," HARVARD JOURNAL OF LEGISLATION, 693-760 (1978)

Kessler, David A., "Implementing the Anticancer Clauses of the Food, Drug and Cosmetic Act," THE UNIVERSITY OF CHICAGO LAW REVIEW, 44:817-850 (1977)

Kessler, David A., Langer, Robert S., Pless, Naomi A., and Folkman, Judah, "Mast Cells and Tumor Angiogenesis," INTERNATIONAL JOURNAL OF CANCER, 18:703-709 (November 15, 1976)

Kessler, David A., "Experimental Activation of the Herpes Virus Associated with the Lucke Renal Adenocarcinoma of the Leopard Frog, Rana Pipiens," unpublished thesis, Amherst College (1973)

Editorials

Kessler, David A., Myers, Matthew, "Beyond the Tobacco Settlement," NEW ENGLAND JOURNAL OF MEDICINE, 345:535-537 (August 16, 2001) (editorial)

Kessler, David A., "Cancer and Herbs," NEW ENGLAND JOURNAL OF MEDICINE, 342 (23):1742-43 (June 8, 2000) (editorial)

Koop, C. Everett, Kessler, David A., Lundberg, George D., "Reinventing American Tobacco Policy - Sounding the Medical Community's Voice," JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, 279:550-552 (February 18, 1998) (editorial)

Kessler, David A., "Addressing the Problem of Misleading Advertising," ANNALS OF INTERNAL MEDICINE, 116:950-951 (June 1, 1992) (editorial)

Published Speeches

Kessler, David A., "Remarks by the Commissioner of Food and Drugs," FOOD AND DRUG LAW JOURNAL, 52:1-5, presented at the Food and Drug Law Institute's 39th Annual Educational Conference, Washington, D.C. (December 10-11, 1996)

Kessler, David A., "Remarks by the Commissioner of Food and Drugs," FOOD AND DRUG LAW JOURNAL, 51:207-216 (1996), presented at the Food and Drug Law Institute's 38th Annual Educational Conference, Washington, D.C. (December 12-13, 1995)

Kessler, David A., "Remarks by the Commissioner of Food and Drugs," FOOD AND DRUG LAW JOURNAL, 50:327-334 (1995), presented at the Food and Drug Law Institute's 37th Annual Educational Conference, Washington, D.C.(December 13-14, 1994)

Kessler, David A., "Statement on Nicotine-Containing Cigarettes," TOBACCO CONTROL, 3:148-158 (1994)

Kessler, David A., "Issues in Approving Drugs for AIDS Treatment," REGULATORY AFFAIRS, 6:189-200 (1994), presented at the Institute of Medicine's 25th anniversary lecture series, Seattle, Washington

Kessler, David A., "FDA's Revitalization of Medical Device Review and Regulation," BIOMEDICAL INSTRUMENTATION AND TECHNOLOGY, May/June 1994:220-226, presented at the AAMI/NIH Cardiovascular Science and Technology Conference, Rockville, Maryland (December 10, 1993)

Kessler, David A., "Harmonization," PHARMACEUTICAL ENGINEERING, 14:38-40 (January/February 1994), presented at the Second International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, Orlando, Florida (October 27, 1993)

Kessler, David A. "The Academic/Industry Interface: The Risks of Scientists Becoming Entrepreneurs," HOPKINS MEDICAL NEWS, Fall 1993:58

Kessler, David A., "Controlled Release and Rational Drug Development," presented at the Controlled Release Society Meeting, July 27, 1993, FOOD AND DRUG REPORTS, 4:9 (1993)

Kessler, David A., "Remarks by the Commissioner of Food and Drugs," FOOD DRUG COSMETIC LAW JOURNAL, 48:1-10 (1993), presented at The Food and Drug Law Institute's 35th Annual Educational Conference, Washington, D.C. (December 8, 1992)

Kessler, David A., "Reinvigorating the Food and Drug Administration," FOOD TECHNOLOGY, 46:20 (August 1992), presented at the Annual Meeting of Institute of Food Technologists, New Orleans, LA (June 20-24, 1992)

Kessler, David A., "A Challenge for American Pharmacists," AMERICAN PHARMACY, 33-36 (January 1992)

Kessler, David A., "Remarks--1991 Annual DIA Meeting," DRUG INFORMATION JOURNAL (October 1991)

Kessler, David A., "Remarks by the Commissioner of Food and Drugs," FOOD DRUG COSMETIC LAW JOURNAL, 46:773-779 (November 1991), presented at the Association of Food and Drug Officials' Annual Conference, Grand Rapids, MI (June 17, 1991)

Kessler, David A., "Restoring the FDA's Preeminence in Regulation of Food," FOOD DRUG COSMETIC LAW JOURNAL (May 1991)

Kessler, David A., "Remarks Upon Taking the Oath of Office," JOURNAL OF THE ASSOCIATION OF FOOD AND DRUG OFFICIALS, 55:7-10 (April 1991)

Kessler, David A., "Remarks by the Commissioner of Food and Drugs," FOOD DRUG COSMETIC LAW JOURNAL, 46:21-26 (January, 1991), presented at the Food and Drug Law Institute's 33rd Annual Educational Conference, Washington, D.C. (December 11, 1990)

Appendix B

Prior Testimony & Expert Witness Fee

APPENDIX B

PRIOR TESTIMONY

Dr. David Kessler testified at trial or deposition in the following cases over the last seven years through March 2018:

- ***In re Risperdal***, Philadelphia, PA and Texas cases, including No. 2012CCV-61916-1 (Tex. Dist. Ct. filed Oct. 2, 2012 and Pledger and Walker); Wolken JCCP 4775
- ***Wells v. Allergan, Inc.*** No. 12-973 (W.D. Okla. filed Sept. 4, 2012); ***Drake v. Allergan***, Case No. 2013 vv00234 (U.S. Dist. Ct. Burlington, Vermont)
- ***In re C.R. Bard, Inc., Pelvic Repair Sys. Prods. Liab. Litig.***, MDL No. 2187 (S.D.W.V. filed July 15, 2010)
- ***SB v. Ortho-McNeil-Janssen Pharm., Inc. (In re Risperdal Litig.)***, No. 100503629 (Pa. Ct. Com. Pl. filed May 27, 2010)
- ***In re Yaz & Yasmin (Drospirenone) Marketing, Sales Practices & Prods. Lib. Litig.***, MDL No. 2100 (J.P.M.L. filed July 30, 2009)
- ***In re Flonase Antitrust Litigation*** (American Sales Company, Inc. v. Smithkline Beecham Corp.), 08-cv-3149, United States District Court, Eastern District of Pennsylvania
- ***Pharmathene, Inc. v. Siga Techs., Inc.***, No. 2627 (Del. Ch. filed Dec. 20, 2006)
- ***Commonwealth v. Merck & Co.***, No. 09-1671 (Ky. Cir. Ct. filed Sept. 28, 2009) (and Utah)
- ***State v. Merck & Co.***, No. 05-3700 (E.D. La. filed Aug. 5, 2005)
- ***Commonwealth Care Alliance v. AstraZeneca Pharm. L.P.***, No. SUCV2005-269 (Mass. Super. Ct. filed Jan. 25, 2005)
- ***Smith & Nephew, Inc. v. N.H. Ins. Co.***, No. 04-3027 (W.D. Tenn. filed Dec. 17, 2004)
- ***In re Neurontin Marketing, Sales Practices & Prods. Liab. Litig.,*** MDL No. 1629 (D. Mass. filed June 9, 2004)
- ***Brown v. Am. Brands, Inc.***, No. 711400 (Cal Super. Ct. filed June 10, 1997)
- ***In re: Actos (Pioglitazone) Prods. Lib. Litig.***, No. 11-md-2299 (W. D. La. filed Dec. 29, 2011)
- ***Brown v RJ Reynolds Tobacco Company et al.***, No. 2007 CA 002855 (Fla. Cir. Ct. filed Nov. 28, 2007)
- ***In re Merck & Co., Inc. Sec., Deriv. & "ERISA" Litig.***, MDL No. 1658, No. 05-2367 (D.N.J. filed May 5, 2005)
- ***In re Prograf Antitrust Ligation*** MDL2242, United States District Court of Massachusetts
- ***In re Nexium Antitrust Litigation*** MDL 2419 United States District Court, District of Massachusetts
- ***Cabana v. Stryker.*** Superior Court of State of California, Los Angeles
- ***In Re: Fosamax Litigation,*** Civil Action No. 282, (Superior Court of New Jersey, Atlantic County) and Case No. 30-2012-00547764 (Superior Court of California, Orange County)
- ***Western Sugar Coop et al v. Archer-Daniels-Midland Co, et al***, U.S. District Court, Central District of California, No. 11-03473
- ***H.B., et al. v. Abbott Laboratories***, No. #15-cv-702-NJR-SCW (U.S District Court, Southern District of Illinois filed June 26, 2015)
- ***In re New England Compounding Pharmacy, Inc. Products Liability Litigation***, MDL No. 2419 (United States District Court of Massachusetts filed 2/14/13)
- ***In re: DePuy Orthopaedics, Inc., Pinnacle Hip Implant Prods. Liab. Litig.***, MDL No. 3:11-md-02244 (N.D. Tex. filed May 24, 2011)
- ***In re: Tropicana Orange Juice Mktg. & Sales Practices Litig.***, MDL No. 2353, No. 2:11-cv-07382 (D.N.J. filed Aug. 10, 2012)
- ***In re Cipro Cases I and II*****,** Nos. 4154 & 4220 (Cal. Super. Ct., filed Feb. 25, 2002)
- ***Anders v. Medtronic, Inc., et al.,*** No. 1322-CC10219-02 (Mo Cir. Ct.)
- ***Austin v. C.R. Bard, Inc., et al.***, Case No. 15-cv-8373 (Circuit Court of the 17th Judicial Circuit (Div. 7), Broward County, Florida). ***In re Bard IVC Filters Products Liability Litigation***, Case No. 2:15-MD-02641-DGC.
- ***In re: Zoloft Litigation***, JCCP No. 4771 (Superior Court of California, Orange County)
- ***In re: Testosterone Replacement Therapy Product Liability Litigation***, MDL No. 2545 (U.S. District Court, Northern District of Illinois – Eastern Division)
- ***In re: Xarelto Products Liability Litigation***, MDL No. 2592 (U.S. District Court, Eastern District of Louisiana – New Orleans Division); Philadelphia County Court of Common Pleas

- ***In re: Benicar (Olmesartan) Product Liability Litigation***, Civil No. 15-2606 (U.S. District Court, District of New Jersey)
- ***In re: Cook Medical, Inc. IVC Filters Marketing, Sales Practices and Product Liability Litigation***, MDL No. 2570 (U.S. District Court, Southern District of Indiana – Indianapolis Division)
- ***State of Texas, ex rel. v. AstraZeneca LP, et al.***, Case No. D-1-GN-13-003530 (District Court of Travis County, Texas)
- ***Council for Education and Research on Toxics v. Starbucks Corp***. et al., case number BC435759
- ***In Re Asacol Antitrust*** *(*U.S. District Court for the District of Massachusetts)
- ***Tinsley v. Streich*** (Circuit Court City of Charlottesville, Virginia))

Dr. David Kessler provided sworn expert statements in the following cases over the last five years:

- ***DePuy ASR Hip System Cases***, No. CJC-10-4649 (Cal. Super. Ct. filed Dec. 22, 2010)
- ***Cordero v. Endoscopy Ctr. of S. Nev. LLC (In the Matter of Endoscopy Ctr. & Associated Businesses)***, No. 08-A-558091-C (Nev. Dist. Ct. filed Feb. 28, 2008)
- ***Jenkins et. al. v. Medtronic, Inc. et al.***, Case No. 2:13cv02985 (W.D. Tenn.)

1,000/hr

Appendix C

Materials Provided

Appendix C - Production Documents

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Appendix C - Production Documents

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Appendix C - Merck's FDA Regulatory File

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DEPOSITION TRANSCRIPTS & EXHIBITS
Deposition of Katalin Abraham dated May 18, 2017 including Exhibits and any errata
Deposition of Joseph Antonello, Ph.D. dated August 3, 2017 including Exhibits and any errata
Deposition of Philip S. Bennett dated May 24, 2017 including Exhibits and any errata
Deposition of Joye L. Bramble, Ph.D. dated January 6, 2017 including Exhibits and any errata
Deposition of Keith D. Chirgwin, M.D. dated January 26, 2017 including Exhibits and any errata
Deposition of April D. Cohen dated January 4, 2018 including Exhibits and any errata
Deposition of Michael Dekleva, Ph.D. dated February 9, 2017 including Exhibits and any errata
Deposition of James Donald, M.D. dated March 23, 2017 including Exhibits and any errata
Deposition of Colleen Duffy dated December 12, 2016 including Exhibits and any errata
Deposition of Emilio Emini, Ph.D. dated June 6, 2017 including Exhibits and any errata
Deposition of Alison L. Fisher, Ph.D. dated November 1, 2016 including Exhibits and any errata
Deposition of Jonathan Hartzel, Ph.D. dated June 23, 2017 including Exhibits and any errata
Deposition of Amy R. Keegan dated April 27, 2017 including Exhibits and any errata
Deposition of Amy R. Keegan dated February 9, 2018 including Exhibits and any errata
Deposition of Chester J. Kitchen, Jr. dated April 25, 2017 including Exhibits and any errata
Deposition of Andrew Klein, M.D. dated December 19, 2016 including Exhibits and any errata
Deposition of David Krah, Ph.D. dated July 11, 2017 including Exhibits and any errata
Deposition of David Krah, Ph.D. dated July 12, 2017 including Exhibits and any errata
Deposition of Stephen Krahling dated May 2, 2017 including Exhibits and any errata
Deposition of Stephen Krahling dated May 3, 2017 including Exhibits and any errata
Deposition of Barbara J. Kuter, Ph.D. dated December 14, 2016 including Exhibits and any errata
Deposition of Barbara J. Kuter, Ph.D. dated February 9, 2018 including Exhibits and any errata
Deposition of Dorothy Margolskee, M.D. dated April 21, 2017 including Exhibits and any errata
Deposition of Tabitha Martin dated May 23, 2017 including Exhibits and any errata
Deposition of Roberta L. McKee, Ph.D. dated March 30, 2017 including Exhibits and any errata
Deposition of Eric Metzger dated June 11, 2015 including Exhibits and any errata
Deposition of Cynthia Morrisey dated July 27, 2017 including Exhibits and any errata
Deposition of Manal A. Morsy, M.D., Ph.D. dated August 5, 2016 including Exhibits and any errata
Deposition of Luwy Musey, M.D. dated October 7, 2016 including Exhibits and any errata
Deposition of Mark Pallansch, Ph.D. dated October 13, 2017 including Exhibits and any errata
Deposition of Robyn Reynolds dated October 27, 2016 including Exhibits and any errata
Deposition of Florian Schodel, M.D. dated December 22, 2016 including Exhibits and any errata
Deposition of Tim Schofield dated March 20, 2017 including Exhibits and any errata
Deposition of Alan W. Sims dated October 12, 2017 including Exhibits and any errata
Deposition of Mark Stannard dated December 13, 2016 including Exhibits and any errata
Deposition of John I. Sutter, M.D. dated November 10, 2016 including Exhibits and any errata
Deposition of Michele Taylor dated May 9, 2017 including Exhibits and any errata
Deposition of Jorge Troncoso dated May 26, 2017 including Exhibits and any errata
Deposition of Henrietta Ukwu, M.D. dated May 31, 2017 including Exhibits and any errata
Deposition of Joan Wlochowski dated June 13, 2017 including Exhibits and any errata
Deposition of Joan Wlochowski dated June 14, 2017 including Exhibits and any errata
Deposition of Mary K. Yagodich dated August 18, 2016 including Exhibits and any errata
ADDITIONAL MATERIALS
15 U.S.C. § 2, Monopolizing trade a felony; penalty15 U.S.C. § 2, Monopolizing trade a felony; penalty
21 CFR § 1.21, Failure to reveal material fact

21 CFR § 10.65, Meetings and Correspondence, available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=10.65.
21 CFR § 1271.440, Orders of Retention, Recall, Destruction, and Cessation of Manufacturing
21 CFR § 200.5, Mailing of important information about drugs
21 CFR § 201.1, Drugs; name and place of business of manufacturer, packer, or distributor, available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=201.1.
21 CFR § 201.56, General requirements on content and format of labeling for human prescription drugs (2000), available at https://www.gpo.gov/fdsys/pkg/CFR-2000-title21-vol4/pdf/CFR-2000-title21-vol4-sec201-56.pdf.
21 CFR § 201.56, Requirements on content and format of labeling for human prescription drug and biological products, (2012), available at https://www.gpo.gov/fdsys/pkg/CFR-2012-title21-vol4/pdf/CFR-2012-title21-vol4-sec201-56.pdf.
21 CFR § 201.57, Specific requirements on content and format of labeling for human prescription drug and biological products described in 201.56(b)(1)
21 CFR § 201.57, Specific requirements on content and format of labeling for human prescription drugs (2000) available at https://www.gpo.gov/fdsys/pkg/CFR-2000-title21-vol4/pdf/CFR-2000-title21-vol4-sec201-57.pdf.
21 CFR § 201.57, Specific requirements on content and format of labeling for human prescription drugs and biological products described in § 201.56(b)(1) (2012), available at https://www.gpo.gov/fdsys/pkg/CFR-2012-title21-vol4/pdf/CFR-2012-title21-vol4-sec201-57.pdf.
21 CFR § 201.80, Specific Requirements on Content and Format of labeling for human prescription drug and biological products; older drugs not described in § 201.56(b)(1), available at https://www.gpo.gov/fdsys/pkg/CFR-2012-title21-vol4/pdf/CFR-2012-title21-vol4-sec201-80.pdf.
21 CFR § 211.192, Production record review
21 CFR § 312.20, Requirement for an IND Application
21 CFR § 312.21, FDA Phases of an Investigation
21 CFR § 312.23, FDA IND Content and Format
21 CFR § 312.42, Clinical Holds and Requests for Modification
21 CFR § 312.70, Disqualification of a clinical investigator, available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.70.
21 CFR § 314.125, Refusal to approve an NDA
21 CFR § 314.126, Adequate and well-controlled studies, available at https://www.gpo.gov/fdsys/pkg/CFR-2012-title21-vol5/pdf/CFR-2012-title21-vol5-sec314-126.pdf.
21 CFR § 314.22 Submitting an abbreviated application, or a 505(j)(2)(c) petition that relies on, a listed drug that is no longer marketed, available at https://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol5/pdf/CFR-2011-title21-vol5-sec314-122.pdf.
21 CFR § 314.3, Definitions, available at https://www.gpo.gov/fdsys/pkg/CFR-2012-title21-vol5/pdf/CFR-2012-title21-vol5-sec314-3.pdf.
21 CFR § 314.50, Content and Format of an Application, available at https://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol5/pdf/CFR-2011-title21-vol5-sec314-50.pdf.
21 CFR § 314.70, Supplements and other changes to an approved application, available at https://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol5/pdf/CFR-2011-title21-vol5-sec314-70.pdf.
21 CFR § 600.14, Reporting of biological product deviations by licensed manufacturers
21 CFR § 600.3, Definitions, available at https://www.gpo.gov/fdsys/pkg/CFR-2017-title21-vol7/pdf/CFR-2017-title21-vol7-sec600-3.pdf.
21 CFR § 601.2, FDA Applications for Biologics Licenses; Procedures for Filing
21 CFR § 601.22, Licensing

21 CFR § 601.25, Review Procedures to Determine that licensed biological products are safe, effective, and not misbranded under prescribed, recommended, or suggested conditions of use, available at https://www.gpo.gov/fdsys/pkg/CFR-2012-title21-vol7/pdf/CFR-2012-title21-vol7-sec601-25.pdf.
21 CFR § 601.27, Pediatric studies, 1998, available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=601.27.
21 CFR § 601.5(b), Revocation of License
21 CFR § 601.6(a), Suspension of License
21 CFR § 610, "Biological Products; Bacterial Vaccines and Toxoids; Implementation of Efficacy Review," *Federal Register* , 70(242), December 19, 2005, pp. 75018-75028.
21 CFR § 630.51, Clinical Trials to Qualify for License
21 CFR § 812.119, Disqualifications of clinical investigator, available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.119.
21 CFR §§ 310.3-310.6, New Drugs and Biologics
21 CFR pt 211, Current Good Manufacturing Practice for Finished Pharmaceuticals
21 CFR pt 314, Applications for FDA Approval to Market a New Drug
21 CFR pt. 11, Electronic System Compliance
21 CFR pt. 210, cGMP General
21 CFR pt. 211, cGMP Detailed
21 CFR pt. 314, Drug Applications
21 CFR pt. 50, Protection of Human Subjects
21 CFR pt. 56, Institutional Review Boards
21 CFR pt. 600, GMP Biological Products
21 CFR pt. 600-680, Biologics
21 CFR pt. 601, Licensing Biologicals
21 CFR pt. 610, Biological Product Standards
21 U.S.C. § 301 et seq., Federal Food, Drug, and Cosmetic Act
21 U.S.C. § 321, Definitions; generally
21 U.S.C. § 334, Seizure – Grounds and Jurisdiction
21 U.S.C. § 351, Adulterated drugs and devices
21 U.S.C. § 352, Misbranded drugs and devices
21 U.S.C. § 355 et seq.
21 U.S.C. § 355, New drugs
31 U.S.C. § 3729, False claims
32 PEDIATRIC INFECTIOUS DISEASE 381-82 (April 2013), Plotkin SA, "Commentary: Mumps vaccines: do we need a new one?"
35 PEDIATRIC INFECTIOUS DISEASE J. 1011 (2016), Safety and Immunogenicity of M-M-RII (Combination Measles–Mumps–Rubella Vaccine) in Clinical Trials of Healthy Children Conducted Between 1988 and 2009
38 Fed. Reg. 4319, Biological Products: Procedures for Review of Safety, Effectiveness and Labeling
42 CFR 493; Clinical Laboratory Improvement Act of 1967 (CLIA), Clinical Laboratory Improvement Amendments of 1988, Food and Drug Administration Modernization Act of 1997, and Taking Essential Steps for Testing Act of 2012, available at https://www.gpo.gov/fdsys/search/searchresults.action?st=42+CFR+493+.
42 U.S.C. § 247b, Project grants for preventative health services
42 U.S.C. § 262, Regulation of biological products
42 U.S.C. § 262, Regulation of biological products, available at http://uscode.house.gov/view.xhtml?req=(title:42%20section:262%20edition:prelim).
42 U.S.C. § 300aa-1 et seq., National Vaccine Injury Act

42 U.S.C. § 300aa-1, Establishment
42 U.S.C. § 300aa-14, Vaccine Injury Table
42 U.S.C. § 300aa–15, Compensation.
42 U.S.C. § 300aa-19, Advisory Commission on Childhood Vaccines
42 U.S.C. § 300aa-2, Program responsibilities
42 U.S.C. § 300aa-22, Standards of responsibility
42 U.S.C. § 300aa-23, Trial
42 U.S.C. § 300aa-5, National Vaccine Advisory Committee
60 Fed Reg 39180, Statement Regarding the Demonstrations of Effectiveness of Human Drug Products and Devices
About FDA, 100 Years of Biologics Regulation-FDA Consumer Magazine, FDA Consumer Magazine, July-Aug. 2002, available at https://www.fda.gov/AboutFDA/WhatWeDo/History/ucm064476.htm.
Abrams et al, "Assessing Mumps Outbreak Risk in Highly Vaccinated Populations Using Spatial Seroprevalence Data." American Journal of Epidemiology, Volume 179, Issue 8, 15 April 2014, Pages 1006-1017, https://doi.org/10.1093/aje/kwu014.
Adams et al. "Summary of Notifiable Infectious Diseases and Conditions - United States, 2015". MMWR Morb Mortal Wkly Rep 2017;64:1-143. DOI: http://dx.doi.org/10.15585/mmwr.mm6453a1.
Afzal, M. A., A. R. Pickford, T. Forsey and P. D. Minor (1992). "Heterogeneous mumps vaccine." Lancet 340(8825): 980-981.
Afzal, M. A., A. R. Pickford, T. Forsey, A. B. Heath and P. D. Minor (1993). "The Jeryl Lynn vaccine strain of mumps virus is a mixture of two distinct isolates." J Gen Virol 74 (Pt 5): 917-920.
Albertson, "Mumps outbreak at a university and recommendation for a third dose of measles-mumps-rubella vaccine-Illinois, 2015-2016," Morbidity and Mortality Weekly Report, 2016 July 29;65(29):731-734
Allwinn, R., B. Zeidler, K. Steinhagen, E. Rohwader, S. Wicker, H. F. Rabenau and H. W. Doerr (2011). "Assessment of mumps virus-specific antibodies by different serological assays: which test correlates best with mumps immunity?" Eur J Clin Microbiol Infect Dis 30(10): 1223-1228.
Alsheikhly, A. R., C. Orvell, B. Wahlin, T. Andersson and P. Perlmann (1984). "The role of viral glycoproteins in mumps virus-mediated antibody-dependent cellular cytotoxity in vitro." Scand J Immunol 20(5): 449-460.
Alsheikhly, A. R., T. Andersson, U. Andersson and P. Perlmann (1985). "Mumps virus-induced enhancement of the in vitro cytotoxicity of cord blood lymphocytes." Scand J Immunol 21(4): 321-328.
Als-Nielsen, B., W. Chen, C. Gluud and L. L. Kjaergard (2003). "Association of funding and conclusions in randomized drug trials: a reflection of treatment effect or adverse events?" JAMA 290(7): 921-928.
Amanna, I. J., N. E. Carlson and M. K. Slifka (2007). "Duration of humoral immunity to common viral and vaccine antigens." N Engl J Med 357(19): 1903-1915.
Amarasinghe, G. K., Y. Bao, C. F. Basler, S. Bavari, M. Beer, N. Bejerman, K. R. Blasdell, A. Bochnowski, T. Briese, A. Bukreyev, C. H. Calisher, K. Chandran, P. L. Collins, R. G. Dietzgen, O. Dolnik, R. Durrwald, J. M. Dye, A. J. Easton, H. Ebihara, Q. Fang, P. Formenty, R. A. M. Fouchier, E. Ghedin, R. M. Harding, R. Hewson, C. M. Higgins, J. Hong, M. Horie, A. P. James, D. Jiang, G. P. Kobinger, H. Kondo, G. Kurath, R. A. Lamb, B. Lee, E. M. Leroy, M. Li, A. Maisner, E. Muhlberger, S. V. Netesov, N. Nowotny, J. L. Patterson, S. L. Payne, J. T. Paweska, M. N. Pearson, R. E. Randall, P. A. Revill, B. K. Rima, P. Rota, D. Rubbenstroth, M. Schwemmle, S. J. Smither, Q. Song, D. M. Stone, A. Takada, C. Terregino, R. B. Tesh, K. Tomonaga, N. Tordo, J. S. Towner, N. Vasilakis, V. E. Volchkov, V. Wahl-Jensen, P. J. Walker, B. Wang, D. Wang, F. Wang, L. F. Wang, J. H. Werren, A. E. Whitfield, Z. Yan, G. Ye and J. H. Kuhn (2017). "Taxonomy of the order Mononegavirales: update 2017." Arch Virol 162(8): 2493-2504.
Amexis, G., S. Rubin, V. Chizhikov, F. Pelloquin, K. Carbone and K. Chumakov (2002). "Sequence diversity of Jeryl Lynn strain of mumps virus: quantitative mutant analysis for vaccine quality control." Virology 300(2): 171-179.

Anderson et al, "Mumps Epidemiology and Immunity The Anatomy of a Modern Epidemic", Pediatr Infect Dis J. 2008 Oct;27(10 Suppl):S75-9.
Anderson et al, "Vaccination and herd immunity to infectious diseases." Nature 318.6044 (1985): 323.
Andzhaparidze, OG, "Chronic non-cytopathic infection of human continuous cell lines with mumps virus," Acta Virologica, 1983 Jul; 27(4):318-28.
Anis et al, "Mumps outbreak in Israel's highly vaccinated society: are two doses enough?", Epidemiol Infect. 2012 Mar;140(3):439-46.
Antibody-dependent enhancement of severe dengue disease in humans Katzelnick LC, Gresh L, Halloran ME, Mercado JC, Kuan G, Gordon A, Balmaseda A, Harris E.
Approval History, Letters, Reviews, and Related Documents, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM573996.zip.
Arnould R.J., and L. DeBrock, "An Overview of the Market for Vaccines in the United States," Background Paper Prepared for the Committee on the Evaluation of Vaccine Purchase Financing in the United States, August 2002.
Assay of humoral immunity to mumps virus. Pipkin PA, Afzal MA, Heath AB, Minor PD. J Virol Methods. 1999 May
Audsley, M. D. and G. W. Moseley (2013). "Paramyxovirus evasion of innate immunity: Diverse strategies for common targets." World J Virol 2(2): 57-70.
August 19, 2009 Approval Letter, available at http://wayback.archive-it.org/7993/20170723024951/https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm179531.htm.
B.J. Kuter, et al., *Safety and Immunogenicity of M-M-RII (Combination Measles-Mumps-Rubella Vaccine) in Clinical Trials of Healthy Children Conducted Between 1998 and 2009,* The Pediatric Infectious Disease Journal, 35(9), (Sept.) 2016.
Backhouse, J. L., H. F. Gidding, P. B. McIntyre and G. L. Gilbert (2006). "Evaluation of two enzyme immunoassays for detection of immunoglobulin G antibodies to mumps virus." Clin Vaccine Immunol 13(7): 764-767.
Bakalar N., "New Shingles Vaccine is Cost-Effective," *The New York Times,* January 4, 2018, available at https://www.nytimes.com/2018/01/04/well/live/new-shingles-vaccine-is-cost-effective.html?rref=collection%2Fsectioncollection%2Fwell.
Barskey, "Mumps Outbreak in Orthodox Jewish communities in the United States," New England Journal of Medicine, 2012 Nov 1;367(18):1704-13;
Barskey, A. E. et al.: *Mumps Outbreak in Orthodox Jewish communities in the United States* , New England Journal of Medicine, 367(18): 1704-13, (Nov. 1) 2012.
Barskey, A. E. et al.: *Mumps resurgences in the United States A historical perspective* , Vaccine, 27: 6186-6195, (2009).
Bashe, W. J., Jr., T. Gotlieb, G. Henle and W. Henle (1953). "Studies on the prevention of mumps. VI. The relationship of neutralizing antibodies to the determination of susceptibility and to the evaluation of immunization procedures." J Immunol 71(2): 76-85.
Begg, C., M. Cho, S. Eastwood, R. Horton, D. Moher, I. Olkin, R. Pitkin, D. Rennie, K. F. Schulz, D. Simel and D. F. Stroup (1996). "Improving the quality of reporting of randomized controlled trials. The CONSORT statement." JAMA 276(8): 637-639.
Bektas, A., S. H. Schurman, R. Sen and L. Ferrucci (2017). "Human T cell immunosenescence and inflammation in aging." J Leukoc Biol 102(4): 977-988.
Berger, R. J., M. (1980). "Comparison of five different tests for mumps antibodies." Infection 8(5): 180-183.

Berkowska, M. A., G. J. Driessen, V. Bikos, C. Grosserichter-Wagener, K. Stamatopoulos, A. Cerutti, B. He, K. Biermann, J. F. Lange, M. van der Burg, J. J. van Dongen and M. C. van Zelm (2011). "Human memory B cells originate from three distinct germinal center-dependent and -independent maturation pathways." Blood 118(8): 2150-2158.
Berndt E.R., R.N. Denoncourt and A.C. Warner, "U.S. Markets for Vaccines: Characteristics, Case Studies and Controversies," AEI Press, Washington, DC, 2009.
Berndt E.R., T.G. McGuire, and J.P. Newhouse, "A Primer on the Economics of Prescription Pharmaceutical Pricing in Health Insurance Markets," *Forum for Health Economics & Policy* , 14(2), 2011, Article 10.
Bernstein, "Comparison of the Safety and Immunogenicity of a Refrigerator-Stable Versus a Frozen Formulation of ProQuad (Measles, Mumps, Rubella, and Varicella Virus Vaccine Live)," Pediatrics, 2007 June; 119(6)
Berry, A. A., R. Abu-Elyazeed, C. Diaz-Perez, M. A. Mufson, C. J. Harrison, M. Leonardi, J. D. Twiggs, C. Peltier, S. Grogg, A. Carbayo, S. Shapiro, M. Povey, C. Baccarini, B. L. Innis and O. Henry (2017). "Two-year antibody persistence in children vaccinated at 12-15 months with a measles-mumps-rubella virus vaccine without human serum albumin." Hum Vaccin Immunother 13(7): 1516-1522.
Beveridge, W. I. and P. E. Lind (1946). "Mumps; virus haemagglutination and serological reactions." Aust J Exp Biol Med Sci 24: 127-132.
Biedel, C. W. (1978). "Recurrent mumps parotitis following natural infection and immunization." Am J Dis Child 132(7): 678-680.
Bioanalytical method validation, An updated review, available at http://www.phmethods.net/sites/default/files/10.4103-2229-4708.72226.pdf.
Bioanalytical Method Validation, FDA Guidance for Industry, available at https://www.fda.gov/downloads/Drugs/Guidance/ucm070107.pdf.
Biological Products Regulated under Section 351 of the Public Health Service Act; Implementation of Biologics License; Elimination of Establishment License and Product License, 64 Fed. Reg. 56441 (Oct. 20, 1999).
Biological Products: Corrections and Technical Amendments, 51 Fed. Reg. 15606 (Apr. 25, 1986) (to be codified at 21 CFR pt. 601, 610, 620, 630, 640, 650, 660, and 680).
Biological Products: Procedures for Review of Safety, Effectiveness and Labeling, 38 Fed. Reg. 4319 (Feb. 13, 1973) (to be codified at 21 CFR pt. 273).
Biological Products: Reporting of Biological Product Deviations in Manufacturing (Final Rule), 65 Fed. Reg. 66,621, 66,623 (Nov. 7, 2000).
BioPharm International, "After the Consent Decree - An Uphill Battle for Affected Companies," June 1, 2004, available at http://www.biopharminternational.com/print/243232?page=full.
BLA Approval Letter from Dr. Marion Gruber, FDA to Dr. Jody Gould, GSK Biologicals, Oct. 20, 2017, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM581750.pdf.
BLA Clinical Review Memorandum, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM584811.zip.
BlueCross BlueShield of South Carolina's "2009 Comprehensive Formulary: List of Covered Drugs" for MedBlueRx, pp. 1-59.
Bonanni, P., M. Grazzini, G. Niccolai, D. Paolini, O. Varone, A. Bartoloni, F. Bartalesi, M. G. Santini, S. Baretti, C. Bonito, P. Zini, M. T. Mechi, F. Niccolini, L. Magistri, M. B. Pulci, S. Boccalini and A. Bechini (2017). "Recommended vaccinations for asplenic and hyposplenic adult patients." Hum Vaccin Immunother 13(2): 359-368.
Branche, A. R. and A. R. Falsey (2016). "Parainfluenza Virus Infection." Semin Respir Crit Care Med 37(4): 538-554.
Brunell, "The Effectiveness of Evaluating Mumps Vaccine Effectiveness", Clin Infect Dis. 2007 Aug 15;45(4):467-9. Epub 2007 Jul 10.

Brunell, P. A., A. Brickman, S. Steinberg and E. Allen (1972). "Parotitis in children who had previously received mumps vaccine." Pediatrics 50(3): 441-444.
Bulati, M., C. Caruso and G. Colonna-Romano (2017). "From lymphopoiesis to plasma cells differentiation, the age-related modifications of B cell compartment are influenced by "inflamm-ageing"." Ageing Res Rev 36: 125-136.
Burnet, F. M. (1945). "Haemagglutination by mumps virus; relationship to Newcastle disease and influenza viruses." Aust J Sci 8: 81-83.
Business Wire, Sanofi Pasteur and Merck (Known as MSD Outside the United States and Canada) Announce Intent to End Joint Vaccines Operations in Europe, Sanofi Pasteur MSD, to Pursue Their Own Distinct Growth Strategies, Mar. 8, 2016, available at https://www.businesswire.com/news/home/20160308005897/en/Sanofi-Pasteur-Merck-MSD-United-States-Canada.
Buynak EB, Whitman JE Jr, Roehm RR, Morton DH, Lampson GP, Hilleman MR. Proc Soc Exp Biol Med. 1967
Buynak, Comparison of Neutralization and Hemagglutination-Inhibition Tec.
Buynak, E. B., et al.: *Combined Live Measles, Mumps, Rubella Vaccine* , J. Am. Med. Assoc., 207:2259-2262, (Mar. 24) 1969.
Buynak, E. B., et al.: *Live Attenuated Mumps Virus Vaccine: 1. Vaccine Development* , Proc Soc Exp Biol Med, 123:768-775 (Dec), 1966.
Buynak, E. B., J. E. Whitman, Jr., R. R. Roehm, D. H. Morton, G. P. Lampson and M. R. Hilleman (1967). "Comparison of neutralization and hemagglutination-inhibition techniques for measuring mumps antibody." Proc Soc Exp Biol Med 125(4): 1068-1071.
Buynak, E.B., et al.: *Jeryl Lynn Strain Live Attenuated Mumps Virus Vaccine* , J. Am. Med. Assoc., 203(1):63-67 (Jan 1), 1968.
Bylander J., "The United States' Piecemeal Approach to Vaccine Policy," *Health Affairs* , 35(2), February 2016, pp. 195-198.
C. Grady, H.P. Forster, E. Emanuel, *The 2000 Revision of the Declaration of Helsinki: A Step Forward or More Confusion?* , The Lancet, 358(9291):1449–1453, (Oct.) 2001.
Calain, P. and L. Roux (1988). "Generation of measles virus defective interfering particles and their presence in a preparation of attenuated live-virus vaccine." J Virol 62(8): 2859-2866.
Can BioShield Effectively Procure Medical Countermeasures That Safeguard the Nation?: Hearing Before the Subcomm. on Emerging Threats, Cybersecurity and Science and Technology of the Comm. on Homeland Security, 110th Cong. (2007), at 36-41 (statement of Jesse Goodman, M.D., MPH, Director, Center for Biologics Evaluation and Research, HHS), available at https://www.gpo.gov/fdsys/pkg/CHRG-110hhrg43559/pdf/CHRG-110hhrg43559.pdf and https://web.archive.org/web/20161104011329/http://www.hhs.gov/asl/testify/2007/04/t20070418c.html.
Carbone, K. M. R. S. (2007). Mumps virus. Fields Virology. P. M. H. D.M. Knipe, Lippincott Williams & Wilkins. 1527-1550.
Cardemil et al, "Effectiveness of a Third Dose of MMR Vaccine for Mumps Outbreak Control" N Engl J Med 2017;377:947-56.
Cardemil, C. V. et al.: *Effectiveness of a Third Dose of MMR Vaccine for Mumps Outbreak Control* , New Eng J Med., 377(10): 947-956, (Sept. 7, 2017).
CBER Clinical Review Of Studies Submitted In Support Of Licensure Of ProQuadTM, available at http://wayback.archiveit.org/7993/20170723030938/https:/www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM123800.pdf.
CDC, "2016 Recommended Immunizations for Children from Birth Through 6 Years Old," available at https://www.cdc.gov/vaccines/schedules/.

CDC, "A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP) Part 1: Immunization of Infants, Children and Adolescents," *Morbidity and Mortality Weekly Report* , 54(RR-16), December 23, 2005, available at https://www.cdc.gov/mmwr/PDF/rr/rr5416.pdf.
CDC, "ACIP votes down use of LAIV for 2016-2017 flu season," available at https://www.cdc.gov/media/releases/2016/s0622-laiv-flu.html.
CDC, "Archived CDC Vaccine Price List as of February 24, 2015," available at https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/2015/2015-02-24.html#modalIdString_CDCTable_0.
CDC, "Archived CDC Vaccine Price List as of January 1, 2018," available at https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/2018/2018-01-01.html.
CDC, "Archived CDC Vaccine Price List as of September 1, 2017," available at https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/2017/2017-09-01.html#modalIdString_CDCTable_0.
CDC, "Archived CDC Vaccine Price List as of September 23, 2008," available at https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/archive.html.
CDC, "CDC Vaccine Price List," prices last updated December 1, 2004.
CDC, "CDC Vaccine Price List," prices last updated December 4, 2001.
CDC, "CDC Vaccine Price List," prices last updated November 2, 2002.
CDC, "CDC Vaccine Price List," prices last updated November 21, 2003.
CDC, "CDC Vaccine Price List," prices last updated September 27, 2000.
CDC, "Combination Vaccines for Childhood Immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP)," *Morbidity and Mortality Weekly Report* , 48(RR-5), 1999, pp. 1–15.
CDC, "Epidemiology and Prevention of Vaccine-Preventable Diseases: Mumps," available at http://www.cdc.gov/vaccines/pubs/pinkbook/mumps.html.
CDC, "Signs & Symptoms of Mumps," available at https://www.cdc.gov/mumps/about/signs-symptoms.html.
CDC, "The VFC Program: At a Glance," February 14, 2014, available at https://www.cdc.gov/vaccines/programs/vfc/about/.
CDC, "Transmission of Mumps," available at https://www.cdc.gov/mumps/about/transmission.html.
CDC, "Vaccine Prices," effective date October 1, 1995.
CDC, "Vaccine Tracking System (VTrckS)," available at https://www.cdc.gov/vaccines/programs/vtrcks/index.html.
CDC, "VFC CDC Vaccine Price List Archives," available at http://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/archive.html.
CDC, *Epidemiology and Prevention of Vaccine-Preventable Diseases* (Pinkbook) (13th ed.), Appendix E.
CDC, Epidemiology and Prevention of Vaccine-Preventable Diseases, 12th Ed., Ch. 14 Mumps (2012)
CDC, Epidemiology and Prevention of Vaccine-Preventable Diseases, 13th Ed., Ch. 15 Mumps (2015)
CDC, Measles prevention: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 1989; 38(No. S-9):1-18.
CDC, Measles, Mumps, and Rubella – Vaccine Use and Strategies for Elimination of Measles, Rubella, and Congenital Rubella Syndrome and Control of Mumps: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 1998; 47(RR-8); 1-57.
CDC, Measles, Mumps, Rubella, and Varicella Diseases and How to Protect Against Them, available at https://www.cdc.gov/vaccinesafety/vaccines/mmrv-vaccine.html.

CDC, Mumps Surveillance: January 1972-June 1974. Atlanta, GA: U.S. Department of Health, Education, and Welfare, Public Health Service, 1974.
CDC, Mumps: For Healthcare Providers, available at https://www.cdc.gov/mumps/hcp.html.
CDC, Notice to Readers: Updated Recommendations of the Advisory Committee on Immunization Practices (ACIP) for the Control and Elimination of Mumps. MMWR 2006; 55(22):629-30.
CDC, Press Briefing Transcripts: Press Briefing on Mumps Outbreak in the Midwest, Apr. 19, 2006, available at https://www.cdc.gov/media/transcripts/t060419.htm.
CDC, Q&As about Monovalent M-M-R Vaccines, https://www.cdc.gov/vaccines/hcp/clinical-resources/mmr-faq-12-17-08.html.
CDC, Questions Answered on Vaccines Purchased with 317 Funds - Important Immunization Information for Parents & Healthcare Providers, available at https://www.cdc.gov/vaccines/imz-managers/guides-pubs/qa-317-funds.html (last updated: July 19, 2013).
CDC, Recommendation of the Advisory Committee on Immunization Practices for Use of a Third Dose of Mumps Virus – Containing Vaccine in Persons at Increased Risk for Mumps During an Outbreak. MMWR 2018; 67(1); 33-38.
CDC, Recommendation of the Immunization Practices Advisory Committee (ACIP): mumps vaccine. MMWR 1980; 29:87-8,93-4.
CDC, Recommendation of the Public Health Service Advisory Committee on Immunization Practices: mumps vaccine. MMWR 1967; 16:430-1.
CDC, Recommendation of the Public Health Service Advisory Committee on Immunization Practices: mumps vaccine. MMWR 1968; 17:419.
CDC, Recommendation of the Public Health Service Advisory Committee on Immunization Practices: mumps vaccine. MMWR 1977; 26:393-4.
CDC, Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger, UNITED STATES, 2018 (Jan. 1, 2018).
CDC, Selected U.S. Discontinued Vaccines, available at https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/b/discontinued_vaccines.pdf.
CDC, *Summary of Notifiable Diseases --- United States, 2006* , MMWR 55(53):1-94. (Available at : https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5553a1.htm).
CDC, *Summary of Notifiable Infectious Diseases and Conditions – United States, 2015* , MMWR, 64(53): 1-143, (Aug. 11) 2017.
CDC, U.S. Vaccines & Immunizations, available at https://www.cdc.gov/vaccines/terms/usvaccines.html.
CDC, Vaccines for Children Program, available at https://www.cdc.gov/vaccines/programs/vfc/index.html.
CDC. (2018). "Mumps for Healthcare Providers." Retrieved 09 March, 2018, from https://www.cdc.gov/mumps/hcp.html.
CDC. Use of Combination Measles, Mumps, Rubella, and Varicella Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2010; 59(RR03); 1-12.
Center for Disease Control. *Epidemiologic Notes and Reports – Mumps in an Elementary School – New York.* MMWR 1973;22(22): 185-90.
Center for Disease Control. *Recommendation of the Immunization Practices Advisory Committee (ACIP) – Mumps Vaccine.* MMWR 1980;29(8): 87-93.
Center for Disease Control. *Recommendation of the Public Health Service Advisory Committee on Immunization Practices – Mumps Vaccine.* MMWR 1977;26(48): 393-94.
Center for Disease Control. *Surveillance Summary – Mumps Surveillance 1973 – the United States.* MMWR 1974;23(50): 431-32.
Centers for Disease Control and Prevention (CDC), "2016 Annual Tables of Infectious Disease Data," National Notifiable Diseases Surveillance System, 2017, https://www.cdc.gov/nndss/infectious-tables.html;

Centers for Disease Control and Prevention (CDC), "Epidemiology and Prevention of Vaccine-Preventable Diseases" Chapter on Mumps The Pink Book: Course Textbook - 13th Edition (2015)
Centers for Disease Control and Prevention (CDC), "Mumps Cases and Outbreaks," 2018 Mar 6, https://www.cdc.gov/mumps/outbreaks.html
Centers for Disease Control and Prevention (CDC), "Mumps Outbreak --- New York, New Jersey, Quebec, 2009" Morbidity and Mortality Weekly Report, November 12, 2009 / 58(Dispatch);1-4
Centers for Disease Control and Prevention (CDC), "Mumps Outbreak at a University and Recommendation for a Third Dose of Measles-Mumps-Rubella Vaccine - Illinois, 2015-2016" Morbidity and Mortality Weekly Report, July 29, 2016 / 65(29);731-734
Centers for Disease Control and Prevention (CDC), "Mumps Outbreak on a University Campus - California, 2011" Morbidity and Mortality Weekly Report, December 7, 2012 / 61(48);986-989
Centers for Disease Control and Prevention (CDC), "National Notifiable Diseases Surveillance System, Weekly Tables of Infectious Disease Data," National Notifiable Diseases Surveillance System, 2018, https://www.cdc.gov/nndss/infectious-tables.html
Centers for Disease Control and Prevention (CDC), "Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, of 2013: Summary Recommendations of the Advisory Committee of Immunization Practices (ACIP)," Morbidity and Mortality Weekly Report, 2013 June 14; 62(RR04):1-34
Centers for Disease Control and Prevention (CDC), "Recommendation of the Advisory Committee on Immunization Practices for Use of a Third Dose of Mumps Virus-Containing Vaccine In Persons at Increased Risk for Mumps During an Outbreak," Morbidity and Mortality Weekly Report, 2018 Jan 12;67(1):33-38
Centers for Disease Control and Prevention (CDC), "Summary of Notifiable Infectious Diseases and Conditions - United States, 2014," Morbidity and Mortality Weekly Report, 2016 Oct 14;63(54):31;
Centers for Disease Control and Prevention (CDC), "Summary of Notifiable Infectious Diseases and Conditions - United States, 2015," Morbidity and Mortality Weekly Report, 2017 Aug 11;64(53):32
Centers for Disease Control and Prevention (CDC), "Update: Mumps Outbreak --- New York and New Jersey, June 2009--January 2010" Morbidity and Mortality Weekly Report, February 12, 2010 / 59(05);125-129
Centers for Disease Control and Prevention (CDC), Epidemiology and Prevention of Vaccine-Preventable Diseases, Appendix E (Washington D.C. Public Health Foundation 13th Ed. 2015)
Centers for Disease Control and Prevention (CDC), National Center for Health Statistics. (2012 Dec) "Healthy People 2010 Final Review", DHHS publication ; no. (PHS)2012-1038.
Centers for Disease Control and Prevention (CDC). "Mumps epidemic--Iowa, 2006." MMWR Morb Mortal Wkly Rep. 2006 Apr 7;55(13):366-8.
Centers for Disease Control and Prevention (CDC). (1999, April 2) "Achievements in Public Health, 1900-1999 Impact of Vaccines Universally Recommended for Children -- United States, 1990-1998", MMWR 48(12);243-248.
Centers for Disease Control and Prevention (CDC). (2017, Aug 11) "Summary of Notifiable Infectious Diseases and Conditions - United States, 2015", MMWR 64(53)
Centers for Disease Control and Prevention (CDC); National Health and Nutrition Examination Survey; 2003?2004 Data Documentation, Codebook, and Frequencies; Mumps Antibody ? Serum (Surplus) (SSMUMP_C); First Published: April 2008; Last Revised: June 2009; downloaded 8/10/2017 from https://wwwn.cdc.gov/nchs/nhanes/2003-2004/SSMUMP_C.htm
Centers for Disease Control and Prevention (CDC); National Health and Nutrition Examination Survey; 2009?2010 Data Documentation, Codebook, and Frequencies; Measles, Mumps, Rubella & Varicella (MMRV_F); First Published: December 2011; Last Revised: NA; downloaded 8/10/2017 from https://wwwn.cdc.gov/nchs/nhanes/2009-2010/MMRV_F.htm

Centers for Disease Control and Prevention (formerly National Communicable Disease Center). *Collected Recommendations of the Public Health Service Advisory Committee on Immunization Practices – Mumps Vaccine.* MMWR SUPPLEMENT 1969;18(43): 12-13.
Centers for Disease Control and Prevention (formerly National Communicable Disease Center). *Immunization Practices – Mumps Vaccine.* MMWR 1967;16(51): 430-35.
Centers for Disease Control and Prevention (formerly National Communicable Disease Center). *Recommendation of the Public Health Service Advisory Committee on Immunization Practices – Mumps Vaccine.* MMWR 1968;17(45): 419-23.
Centers for Disease Control and Prevention. *Absence of Asymptomatic Mumps Virus Shedding Among Vaccinated College Students During a Mumps Outbreak – Washington, February – June 2017.* MMWR 2017;66(47): 1307-08.
Centers for Disease Control and Prevention. *Brief Report: Update: Mumps Activity – United States, January 1-October 7, 2006.* MMWR 2006;55(42): 1152-153.
Centers for Disease Control and Prevention. *Complications of Mumps During a University Outbreak Among Students Who Had Received 2 Doses of Measles-Mumps-Rubella Vaccine – Iowa, July 2015 – May 2016.* MMWR 2017;66(14): 390-91.
Centers for Disease Control and Prevention. *Current Trends Mumps – United States, 1980-1983.* MMWR 1983;32(42): 545-7.
Centers for Disease Control and Prevention. *Current Trends Mumps – United States, 1984-1985.* MMWR 1986;35(13): 216-9.
Centers for Disease Control and Prevention. *Current Trends Mumps – United States, 1985-1988.* MMWR 1989;38(7): 101-5.
Centers for Disease Control and Prevention. *Current Trends Mumps – United States, 1985-1988* . MMWR 1989;38(7):101-05.
Centers for Disease Control and Prevention. *Epidemiologic Notes and Reports Mumps – United States, 1985-1986.* MMWR 1987;36(10): 151-5.
Centers for Disease Control and Prevention. *Epidemiologic Notes and Reports Mumps in the Workplace – Chicago.* MMWR 1988;37(35): 533-8.
Centers for Disease Control and Prevention. *Epidemiologic Notes and Reports Mumps in the Workplace – Chicago* . MMWR 1988;37(35):533-38.
Centers for Disease Control and Prevention. *Exposure to Mumps During Air Travel – United States, April 2006.* MMWR 2006;55(14): 401-2.
Centers for Disease Control and Prevention. *Measles, Mumps, and Rubella -- Vaccine Use and Strategies for Elimination of Measles, Rubella, and Congenital Rubella Syndrome and Control of Mumps: Recommendations of the Advisory Committee on Immunization Practices (ACIP).* MMWR 1998;47(RR-8): 1-57.
Centers for Disease Control and Prevention. *Mumps – United States, 1983-1984.* MMWR 1984;33(38): 533-5.
Centers for Disease Control and Prevention. *Mumps Epidemic – Iowa, 2006.* MMWR 2006;55(13): 366-8.
Centers for Disease Control and Prevention. *Mumps Epidemic – United Kingdom, 2004-2005.* MMWR 2006;55(7): 173-5.
Centers for Disease Control and Prevention. *Mumps Outbreak – New Jersey* . MMWR 1984;33(29): 421-2, 427-30.
Centers for Disease Control and Prevention. Mumps Outbreak – New York, New Jersey, Quebec, 2009. MMWR 2009;58(45): 1270-74.
Centers for Disease Control and Prevention. *Mumps Outbreak at a Summer Camp – New York, 2005* . MMWR 2006;55(7): 175-7.
Centers for Disease Control and Prevention. Mumps Outbreak at a University and Recommendation for a Third Dose of Measles-Mumps-Rubella Vaccine – Illinois, 2015-2016. MMWR 2016;65(29): 731-4.

Centers for Disease Control and Prevention. *Mumps Outbreak on a University Campus – California 2011.* MMWR 2012;61(48): 986-89.
Centers for Disease Control and Prevention. *Mumps Outbreaks on University Campuses – Illinois, Wisconsin, South Dakota* . MMWR 1987;36(30): 496-8, 503-5.
Centers for Disease Control and Prevention. *Mumps Surveillance – United States, 1988-1993* . MMWR 1995;44(SS-3):1-14.
Centers for Disease Control and Prevention. *Notice to Readers: Licensure of a Combined Live Attenuated Measles, Mumps, Rubella, and Varicella Vaccine.* MMWR 2005;54(47): 1212-1214.
Centers for Disease Control and Prevention. *Notice to Readers: Updated Recommendations of the Advisory Committee on Immunization Practices (ACIP) for the Control and Elimination of Mumps.* MMWR 2006;55(22): 629-30.
Centers for Disease Control and Prevention. *Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, 2013: Summary Recommendations of the Advisory Committee on Immunization Practices (ACIP).* MMWR 2013;62(RR04): 1-34.
Centers for Disease Control and Prevention. *Recommendation of the Advisory Committee on Immunization Practices for Use of a Third Dose of Mumps Virus-Containing Vaccine in Persons at Increased Risk for Mumps During an Outbreak.* MMWR 2018;67(1): 33-8.
Centers for Disease Control and Prevention. *Recommendations of the Immunization Practices Advisory Committee Measles Prevention: Supplementary Statement.* MMWR 1989;38(1): 11-14.
Centers for Disease Control and Prevention. *Recommendations of the Immunization Practices Advisory Committee Mumps Prevention.* MMWR 1989;38(22): 388-92, 397-400.
Centers for Disease Control and Prevention. *Update: Multistate Outbreak of Mumps – United States, January 1-May 2, 2006* . MMWR 2006;55(20):559-63.
Centers for Disease Control and Prevention. *Update: Mumps Outbreak – New York and New Jersey, June 2009-January 2010.* MMWR 2010;59(5): 125-50.
Centers for Disease Control and Prevention. *Update: Recommendations from the Advisory Committee on Immunization Practices (ACIP) Regarding Administration of Combination MMRV Vaccine.* MMWR 2008;57(10): 258-60
Centers for Disease Control and Prevention. *Updated Recommendations for Isolation of Persons with Mumps.* MMWR 2008;57(40): 1103-05.
Centers for Disease Control and Prevention. *Use of Combination Measles, Mumps, Rubella, and Varicella Vaccine – Recommendations of the Advisory Committee on Immunization Practices (ACIP).* MMWR 2010;59(RR03): 1-12.
Centers for Disease Control, MMWR, *Summary of Notifiable Infectious Diseases and Conditions – United States, 2014* , 63(54), 20 (2016).
Centers for Disease Control, MMWR, *Summary of Notifiable Infectious Diseases and Conditions – United States, 2015* , 64(53), 22 (2017).
Cerutti, A., X. Qiao and B. He (2005). "Plasmacytoid dendritic cells and the regulation of immunoglobulin heavy chain class switching." Immunol Cell Biol 83(5): 554-562.
Ch. 4 Key Regulatory Guidelines for the Development of Biologics in the United States and Europe, available at https://www.cov.com/-/media/files/corporate/publications/2013/10/chapter4_key_regulatory_guidlines_for_the_development_of_biologics_in_the_united_states_and_europe.pdf.
Chaiken, B. P. et al.: *The Effect of a School Entry Law on Mumps Activity in a School District* , JAMA, 257(18): 2455-58, (May 8) 1987.
Chambers, P., B. K. Rima and W. P. Duprex (2009). "Molecular differences between two Jeryl Lynn mumps virus vaccine component strains, JL5 and JL2." J Gen Virol 90(Pt 12): 2973-2981.

Changes to be Reported for Product and Establishment License Applications; Guidance, 60 Fed Reg 17535 (Apr. 6, 1995).
Chatom Primary Care, P.C. v. Merck & Co. , Inc., No. 2:12-cv-03555-CDJ (E.D. Pa.), Consolidated Amended Class Action Complaint, at Dkt. No. 26.
Chatom Primary Care, P.C. v. Merck & Co. , Inc., No. 2:12-cv-03555-CDJ (E.D. Pa.), Protective Order, at Dkt. No. 84.
Chiba, Y., J. L. Dzierba, A. Morag and P. L. Ogra (1976). "Cell-mediated immune response to mumps virus infection in man." J Immunol 116(1): 12-15.
Christenson, B. and M. Bottiger (1990). "Methods for screening the naturally acquired and vaccine-induced immunity to the mumps virus." Biologicals 18(3): 213-219.
Chu W.L., "GSK purchases Wyeth's vaccine facility," September 1, 2005, available at https://www.outsourcing-pharma.com/Article/2005/09/02/GSK-purchases-Wyeth-s-vaccine-facility.
CLIA standards, available at https://www.gpo.gov/fdsys/pkg/STATUTE-102/pdf/STATUTE-102-Pg2903.pdf.
Clinical Review Memo, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM429166.pdf.
Clinical Review of Biologics License Application for GlaxoSmithKline Biologicals Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate) (proposed proprietary name: Hiberix), available at https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM579091.zip.
CLINICAL REVIEW OF NEW BIOLOGICS LICENSE APPLICATION STN #125122 ROTATEQ®, Jan. 30, 2006, available at http://wayback.archive-it.org/7993/20170723031531/https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142304.pdf.
Cohen, J. (2017). "New evidence that dengue antibodies trigger life-threatening infections," available at https://www.sciencemag.org/news/2017/11/new-evidence-dengue-antibodies-trigger-life-threatening-infections.
Coleman M.S., N. Sangrujee, F. Zhou, and S. Chu, "Factors Affecting U.S. Manufacturers' Decisions to Produce Vaccines," *Health Affairs* , Vol. 24, No. 3, 2005, pp. 635-642.
Collins, A. M. and K. J. Jackson (2013). "A Temporal Model of Human IgE and IgG Antibody Function." Front Immunol 4: 235.
"Combination Vaccine for Hepatitis A and B," available at http://www.webmd.com/hepatitis/combination-vaccine-for-hepatitis-a-and-b.
Committee On, B. (2016). "Informed Consent in Decision-Making in Pediatric Practice." Pediatrics 138(2).
Company Overview of Merck & Co., Inc., Bloomberg, available at https://www.bloomberg.com/research/stocks/private/snapshot.asp?privcapId=288502.
Comparison of Hemagglutination Inhibition Assay and Enzyme Immunoassay for Determination of Mumps Kumakura_et_al-2013-Journal_of_Clinical_Laboratory_Analysis
Connaughton, S. M., J. X. Wheeler, E. Vitkova, P. Minor and S. Schepelmann (2015). "In vitro and in vivo growth alter the population dynamic and properties of a Jeryl Lynn mumps vaccine." Vaccine 33(36): 4586-4593.
CONSORT 2010 Checklist.doc, available at https://osf.io/pz748/.
CONSORT 2010 Explanation and Elaboration, updated guidelines, available at https://www.academia.edu/10159568/CONSORT_2010_Explanation_and_Elaboration_updated_guidelines_for_reporting_parallel_group_randomised_trials.
Cooper, L. Z., B. Matters, J. K. Rosenblum and S. Krugman (1969). "Experience with a modified rubella hemagglutination inhibition antibody test." JAMA 207(1): 89-93.

Corrales-Aguilar, E., M. Trilling, H. Reinhard, V. Falcone, A. Zimmermann, O. Adams, S. Santibanez and H. Hengel (2016). "Highly individual patterns of virus-immune IgG effector responses in humans." Med Microbiol Immunol 205(5): 409-424.
Cortese et al, "Mumps Vaccine Performance among University Students during a Mumps Outbreak", Clinical Infectious Diseases 2008 Apr 15; 46(8):1172-80
Cortese, M. M., A. E. Barskey, G. E. Tegtmeier, C. Zhang, L. Ngo, M. H. Kyaw, A. L. Baughman, J. E. Menitove, C. J. Hickman, W. J. Bellini, G. H. Dayan, G. R. Hansen and S. Rubin (2011). "Mumps antibody levels among students before a mumps outbreak: in search of a correlate of immunity." J Infect Dis 204(9): 1413-1422.
Cortese, M.M. et al.: *Mumps Vaccine Performance among University Students during a Mumps Outbreak* , Clinical Infectious Diseases, 46(8): 1172-80, (Apr. 15) 2008.
Cox, R. and R. K. Plemper (2015). ""The paramyxovirus polymerase complex as a target for next-generation anti-paramyxovirus therapeutics."." Front Microbiol 6: 459.
Cox, R. J. (2013). "Correlates of protection to influenza virus, where do we go from here?" Hum Vaccin Immunother 9(2): 405-408.
CPG § 120.100, Fraud, untrue statements of material facts, bribery, and illegal gratuities, available at https://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm073837.htm.
Cui, A., Z. Zhu, Y. Hu, X. Deng, Z. Sun, Y. Zhang, N. Mao, S. Xu, X. Fang, H. Gao, Y. Si, Y. Lei, H. Zheng, J. He, H. Wu and W. Xu (2017). "Mumps Epidemiology and Mumps Virus Genotypes Circulating in Mainland China during 2013-2015." PLoS One 12(1): e0169561.
Cusi, M. G., P. Correale, M. Valassina, M. Sabatino, P. E. Valensin, M. Donati and R. Gluck (2001). "Comparative study of the immune response in mice immunized with four live attenuated strains of mumps virus by intranasal or intramuscular route." Arch Virol 146(7): 1241-1248.
Cusi, M. G., R. Zurbriggen, M. Valassina, S. Bianchi, P. Durrer, P. E. Valensin, M. Donati and R. Gluck (2000). "Intranasal immunization with mumps virus DNA vaccine delivered by influenza virosomes elicits mucosal and systemic immunity." Virology 277(1): 111-118.
Cusi, M. G., S. Fischer, R. Sedlmeier, M. Valassina, P. E. Valensin, M. Donati and W. J. Neubert (2001). "Localization of a new neutralizing epitope on the mumps virus hemagglutinin-neuraminidase protein." Virus Res 74(1-2): 133-137.
Danzon P.M., and N.S. Pereira, "Vaccine Supply: Effects of Regulation and Competition," *International Journal of the Economics of Business* , 18(2), 2011, pp. 239-271.
Date et al, "Long-Term Persistence of Mumps Antibody after Receipt of 2 Measles-Mumps-Rubella (MMR) Vaccinations and Antibody Response after a Third MMR Vaccination among a University Population", J Infect Dis. 2008 Jun 15;197(12):1662-8.
Date, A. A. et al.: *Long-Term Persistence of Mumps Antibody after Receipt of 2 Measles-Mumps-Rubella (MMR) Vaccinations and Antibody Response after a Third MMR Vaccination among a University Population* , Journal of Infectious Diseases, 197(12): 1662-68, (June 15) 2008.
Davidkin, I., M. Valle and I. Julkunen (1995). "Persistence of anti-mumps virus antibodies after a two-dose MMR vaccination. A nine-year follow-up." Vaccine 13(16): 1617-1622.
Davidkin, Persistence of Measles, Mumps, and Rubella Antibodies in an MMR-Vaccinated Cohort_A 20-Year Follow-up (2008).
Davidkin, Vaccine-induced measles virus antibodies after two doses of combined measles, mumps and rubella vaccine a 12-year follow-up in two cohorts (1998).
Davidson, W. L., E. B. Buynak, M. B. Leagus, J. E. Whitman, Jr. and M. R. Hilleman (1967). "Vaccination of adults with live attenuated mumps virus vaccine." JAMA 201(13): 995-998.

Dayan, G. H. et al.: *Mumps Outbreaks in Vaccinated Populations: Are Available Mumps Vaccines Effective Enough to Prevent Outbreaks?* , Clinical Infectious Diseases, 47: 1458-467, (Dec. 1) 2008.
Dayan, G. H. et al.: *Recent Resurgence of Mumps in the United States* , New England J Med., 358(15): 1580-1589, (Apr. 10) 2008.
de la Fuente Garcia, I., L. Coic, J. M. Leclerc, C. Laverdiere, C. Rousseau, P. Ovetchkine and B. Tapiero (2017). "Protection against vaccine preventable diseases in children treated for acute lymphoblastic leukemia." Pediatr Blood Cancer 64(2): 315-320.
De Laval et al, "Lower long-term immunogenicity of mumps component after MMR vaccine." Pediatr Infect Dis J. 2010 Nov;29(11):1062-3; author reply 1063. doi: 10.1097/INF.0b013e3181f2d864.
De Paula, S. O. and B. A. Fonseca (2004). "Dengue: a review of the laboratory tests a clinician must know to achieve a correct diagnosis." Braz J Infect Dis 8(6): 390-398.
December 10, 2014 Approval Letter - Gardasil 9, available at https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm426520.htm.
Deeks et al, "An assessment of mumps vaccine effectiveness by dose during an outbreak in Canada", CMAJ. 2011 Jun 14;183(9):1014-20.
Defense Health Program Peer Reviewed Medical Research Program Clinical Trial Award Funding Opportunity Number: W81XWH-17-PRMRP-CTA; Catalog of Federal Domestic Assistance Number: 12.420 Military Medical Research and Development
Delegations of Authority and Organization; National Childhood Vaccine Injury Act of 1986, 58 Fed. Reg. 17105 (Apr. 1, 1993).
Delgado, M. F., S. Coviello, A. C. Monsalvo, G. A. Melendi, J. Z. Hernandez, J. P. Batalle, L. Diaz, A. Trento, H. Y. Chang, W. Mitzner, J. Ravetch, J. A. Melero, P. M. Irusta and F. P. Polack (2009). "Lack of antibody affinity maturation due to poor Toll-like receptor stimulation leads to enhanced respiratory syncytial virus disease." Nat Med 15(1): 34-41.
Demeio, J. L. and D. L. Walker (1957). "Demonstration of antigenic relationship between mumps virus and hemagglutinating virus of Japan." J Immunol 78(6): 465-471.
Demicheli, V., A. Rivetti, M. G. Debalini and C. Di Pietrantonj (2012). "Vaccines for measles, mumps and rubella in children." Cochrane Database Syst Rev(2): CD004407.
Department of Health and Human Services, National Institutes of Health, National Institute of Allergy and Infectious Diseases; Notice of Award, Issue Date 05/07/2012; Grant Number 1R01AI097368-01A1
Development and Use of Integral Assays in Clinical Trials, available at http://clincancerres.aacrjournals.org/content/clincanres/18/6/1540.full.pdf.
Dittrich S, Hahné S, van Lier A, Kohl R, Boot H, Koopmans M, van Binnendijk R. "Assessment of serological evidence for mumps virus infection in vaccinated children." Vaccine. 2011 Nov 15;29(49):9271-5. doi: 10.1016/j.vaccine.2011.09.072. Epub 2011 Oct 6.
Drake K., and T. McGuire, "Stock-Price Evidence for Anticompetitive Effects in the Nexium 'Reverse-Payment' Settlement," *Journal of Competition Law & Economics* , 12(4), 2016, pp. 735-747.
Drake K., M. Starr, and T. McGuire, "Do 'Reverse Payment' Settlements Constitute an Anticompetitive Pay-for-Delay?" *International Journal of the Economics of Business,* 22(2), 2015, pp. 173-200.
Early Clinical Trials With Live Biotherapeutic Products, June 2016, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/General/UCM292704.pdf.
Ellebedy, A. H., K. J. Jackson, H. T. Kissick, H. I. Nakaya, C. W. Davis, K. M. Roskin, A. K. McElroy, C. M. Oshansky, R. Elbein, S. Thomas, G. M. Lyon, C. F. Spiropoulou, A. K. Mehta, P. G. Thomas, S. D. Boyd and R. Ahmed (2016). "Defining antigen-specific plasmablast and memory B cell subsets in human blood after viral infection or vaccination." Nat Immunol 17(10): 1226-1234.

Elwenspoek, M. M. C., K. Sias, X. Hengesch, V. K. Schaan, F. A. D. Leenen, P. Adams, S. B. Meriaux, S. Schmitz, F. Bonnemberger, A. Ewen, H. Schachinger, C. Vogele, C. P. Muller and J. D. Turner (2017). "T Cell Immunosenescence after Early Life Adversity: Association with Cytomegalovirus Infection." Front Immunol 8: 1263.
Enzyme-linked immunosorbent assay compared with neutralization tests for evaluation of live mumps vaccines J. Clin. Microbiol.-1984-Sakata-21-5
Eriksen et al, "Seroepidemiology of mumps in Europe (1996-2008): why do outbreaks occur in highly vaccinated populations?" Epidemiol Infect. 2013 Mar;141(3):651-66. doi: 10.1017/S0950268812001136. Epub 2012 Jun 12.
European Commission, Accession to the EU, available at https://ec.europa.eu/neighbourhood-enlargement/policy/glossary/terms/accession-eu_en.
European Commission, Annex I: Summary of Product Characteristics - ProQuad, available at https://ec.europa.eu/health/documents/community-register/2013/20130731126261/anx_126261_en.pdf.
European Medicines Agency, EPAR Summary for the Public: ProQuad, available at http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/000622/WC500044065.pdf.
EUROPEAN MEDICINES AGENCY, PRIORIX -SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET (ANNEX III), available at http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Priorix_30/WC500124199.pdf.
European Medicines Agency, ProQuad, available at http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000622/human_med_000997.jsp&mid=WC0b01ac058001d124.
European Medicines Agency, Scientific Discussion: MMRVAXPRO, available at http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Scientific_Discussion/human/000604/WC500030167.pdf.
Fahlgren, K.: *Two doses of MMR vaccine-sufficient to eradicate measles, mumps and rubella?* , Scand. J. Soc. Med. 16:129-135, (Sept. 1) 1988.
Fairfax, K. A., A. Kallies, S. L. Nutt and D. M. Tarlinton (2008). "Plasma cell development: from B-cell subsets to long-term survival niches." Semin Immunol 20(1): 49-58.
"FDA Approves GlaxoSmithKline (GSK)'s Hib Vaccine, Hiberix(R)," *FierceBiotech* , August 20, 2009, available at http://www.fiercebiotech.com/biotech/fda-approves-glaxosmithkline-gsk-s-hib-vaccine-hiberix-r.
FDA , Guidance for Industry, Q1A(R2) Stability Testing of New Drug Substances and Products, Nov. 2003, available at https://www.fda.gov/downloads/drugs/guidances/ucm073369.pdf.
FDA Guidance for Industry: E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6 (R1), available at https://www.fda.gov/downloads/Drugs/Guidances/UCM464506.pdf.
FDA Guidance for Industry: Early Clinical Trials with Live Biotherapeutic Products: Chemistry, Manufacturing, and Control Information, available at https://www.fda.gov/downloads/Biologi.../UCM292704.pdf.
FDA Guidance for Industry: Investigator Responsibilities - Protecting the Rights, Safety, and Welfare of Study Subjects, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM187772.pdf.
FDA Guidance for industry: Oversight of Clinical Investigations - A Risk-Based Approach to Monitoring, Guidance for Industry, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269919.pdf.

FDA Regulatory Procedures Manual, Section 4-1-1 Warning Letter Procedures, available at https://www.fda.gov/ICECI/ComplianceManuals/RegulatoryProceduresManual/ucm176870.htm.
FDA, "Biologics License Applications (BLA) Process (CBER)," available at https://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/BiologicsLicenseApplicationsBLAProcess/default.htm.
FDA, "Engerix-B," available at https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm110102.htm.
FDA, "February 3, 2006 Approval Letter - RotaTeq," available at http://wayback.archive-it.org/7993/20170723031528/https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm142303.htm.
FDA, "Important Information Regarding Three Lots of Sanofi Pasteur's 2014-2015 Fluzone Quadrivalent (Influenza Vaccine) Supplied in Multidose Vials," Apr. 21, 2015, available at http://wayback.archive-it.org/7993/20170112095755/http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/Recalls/ucm445261.htm.
FDA, "IND Application Procedures: Clinical Hold," available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm362971.htm.
FDA, "Investigational New Drug (IND) Application," available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm.
FDA, "March 17, 1995 Approval Letter - Varivax," available at http://wayback.archive-it.org/7993/20170723031727/https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm142828.htm.
FDA, "Recall: Influenza A (H1N1) 2009 Monovalent Vaccine Live, Intranasal," available at http://wayback.archive-it.org/7993/20170112095910/http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/Recalls/ucm196632.htm.
FDA, "Vaccine Product Approval Process," available at https://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/BiologicsLicenseApplicationsBLAProcess/ucm133096.htm.
FDA, "Vaccines and Related Biological Products Advisory Committee," available at https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/VaccinesandRelatedBiologicalProductsAdvisoryCommittee/default.htm.
FDA, "Warning Letter," Feb. 9, 2001, available at https://web.archive.org/web/20100311061607/http://www.fda.gov/downloads/ICECI/EnforcementActions/WarningLetters/2001/UCM078249.pdf.
FDA, "Non-Inferiority Clinical Trials to Establish Effectiveness: Guidance for Industry," November 2016, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm202140.pdf.
FDA, Application Integrity Policy, available at https://www.fda.gov/downloads/ICECI/EnforcementActions/ApplicationIntegrityPolicy/ucm072631.pdf.
FDA, Article, FDA's Office of Pharmaceutical Quality: One Year In, Apr. 2016, available at https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/UCM494312.pdf.

FDA, Article, New Drug Quality, Sept. 2012, available at https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/UCM319879.pdf.
FDA, Biological Products: Reporting of Biological Product Deviations in Manufacturing, Final Rule, 65 Fed. Reg. 66621 (Nov. 7, 2000) (to be codified as 21 CFR Parts 600 and 606), available at https://www.gpo.gov/fdsys/pkg/FR-2000-11-07/pdf/00-28133.pdf.
FDA, Biological Products; Reporting of Errors and Accidents in Manufacturing, Proposed Rule,62 Fed. Reg. 49642 (proposed Sept. 23, 1997) (to be codified 21 CFR Parts 600 and 606), available at https://www.gpo.gov/fdsys/pkg/FR-1997-09-23/pdf/97-25129.pdf.
FDA, Blog, Continuous Manufacturing Has A Strong Impact on Drug Quality, Apr. 2016, available at https://blogs.fda.gov/fdavoice/index.php/2016/04/continuous-manufacturing-has-a-strong-impact-on-drug-quality/.
FDA, CBER Clinical Review of Studies Submitted in Support of Licensure of ProQuad™, Aug. 26, 2005, available at http://wayback.archive-it.org/7993/20170723150913/https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM123800.pdf.
FDA, Clinical Studies Section of Labeling for Human Prescription Drug and Biological Products - Content and Format, Jan. 2006, available at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm127534.pdf.
FDA, Compliance Policy Guide § 120.100, Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities, available at https://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm073837.htm.
FDA, Determining the Safety and Efficacy of Vaccines to Protect Against Viruses that Infect the Central Nervous System, Biologics Research Projects, https://www.fda.gov/BiologicsBloodVaccines/ScienceResearch/BiologicsResearchAreas/ucm127315.htm
FDA, Draft Guidance for Industry, Biological Product Deviation Reporting for Licensed Manufacturers of Biological Products other than Blood and Blood Components, Aug. 10, 2001, available at 2001 WL 34768160 (F.D.A.).
FDA, Draft Guidance for Industry, Stability Testing of Drug Substances and Drug Products, June 1998, available at https://www.fda.gov/ohrms/dockets/98fr/980362gd.pdf.
FDA, Draft Guidance, Additional Safeguards for Children in Clinical Investigations, Process for Handling Referrals to FDA Under 21 CFR 50.54, Dec. 2006, available at https://www.fda.gov/OHRMS/DOCKETS/98fr/06d-0172-gdl0001.pdf.
FDA, Draft Guidance, Chemistry, Manufacturing, and Controls Changes to an Approved Application: Certain Biological Products, Dec. 2017, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/General/UCM590118.pdf.
FDA, Draft Guidance, Clinical Development Programs for Drugs, Devices, and Biological Products Intended for the Treatment of Osteoarthritis, July 1999, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm071577.pdf.
FDA, Draft Guidance, Clinical Lactation Studies - Study Design, Data Analysis, and Recommendations for Labeling, Feb. 2005, available at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm127505.pdf.

FDA, Draft Guidance, CMC Postapproval Manufacturing Changes for Specified Biological Products To Be Documented in Annual Reports, Aug. 2017, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM570441.pdf.
FDA, Draft Guidance, Comparability Protocols for Human Drugs and Biologics: Chemistry, Manufacturing, and Controls Information Guidance for Industry, Apr. 2016, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM496611.pdf.
FDA, Draft Guidance, Current Good Manufacturing Practice Requirements for Combination Products, Jan. 2017, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126198.htm.
FDA, Draft Guidance, Data Integrity and Compliance With Current Good Manufacturing Practice Guidance for Industry, Apr. 2016, available at https://www.fda.gov/downloads/drugs/guidances/ucm495891.pdf.
FDA, Draft Guidance, Drug Interaction Studies--Study Design, Data Analysis, Implications for Dosing, and Labeling Recommendations, Oct. 2017, available at https://www.fda.gov/downloads/drugs/guidances/ucm292362.pdf.
FDA, Draft Guidance, Drug Products, Including Biological Products, that Contain Nanomaterials, Dec. 2017, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM588857.pdf.
FDA, Draft Guidance, Enrichment Strategies for Clinical Trials to Support Approval of Human Drugs and Biological Products, Dec. 2012, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm332181.pdf.
FDA, Draft Guidance, Established Conditions: Reportable CMC Changes for Approved Drug and Biologic Products Guidance for Industry, May 2015, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm448638.pdf.
FDA, Draft Guidance, Exculpatory Language in Informed Consent, Aug. 2011, available at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm271036.pdf.
FDA, Draft Guidance, Institutional Review Board (IRB) Written Procedures - Draft Guidance for Institutions and IRBs, Aug. 2016, available at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm512761.pdf.
FDA, Draft Guidance, Investigational New Drug Applications (INDs)-Determining Whether Human Research Studies Can Be Conducted Without an IND, Sept. 2013, available at https://www.fda.gov/downloads/drugs/guidances/ucm229175.pdf.
FDA, Draft Guidance, Quality Metrics Technical Conformance Guide, July 2015, available at https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/Manufacturing/UCM508464.pdf.
FDA, Draft Guidance, Revised, Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application, Jan. 2018, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM434176.pdf.
FDA, Draft Guidance, Submission of Quality Metrics Data Guidance for Industry, Nov. 2016, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM455957.pdf.
FDA, Ensuring the Safety of Vaccines in the United States, available at https://www.fda.gov/downloads/biologicsbloodvaccines/safetyavailability/vaccinesafety/ucm298181.pdf.

FDA, FDA Researchers Advance Science for Vaccines to Prevent Mumps and Whooping Cough, https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm488978.htm
FDA, Final Guidance, CGMP for Phase 1 Investigational Drugs, July 2008, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070273.pdf.
FDA, Final Guidance, Contract Manufacturing Arrangements for Drugs: Quality Agreements Guidance for Industry, Nov. 2016, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM353925.pdf.
FDA, Final Guidance, Current Good Manufacturing Practice Requirements for Combination Products, Jan. 2017, available at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm429304.pdf.
FDA, Final Guidance, Formal Dispute Resolution: Scientific and Technical Issues Related to Pharmaceutical CGMP, Jan. 2006, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070279.pdf.
FDA, Final Guidance, Guideline on the Preparation of Investigational New Drug Products (Human and Animal), Nov. 1992, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070315.pdf.
FDA, Final Guidance, Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Production, Oct. 2006, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070287.pdf.
FDA, Final Guidance, PAT - A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance, Sept. 2004, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070305.pdf.
FDA, Final Guidance, Process Validation: General Principles and Practices, Jan. 2011, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070336.pdf.
FDA, Final Guidance, Pyrogen and Endotoxins Testing: Questions and Answers, June 2012, available at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm314718.htm.
FDA, Final Guidance, Quality Systems Approach to Pharmaceutical CGMP Regulations, Sept. 2006, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070337.pdf.
FDA, Final Guidance, Questions and Answers on Current Good Manufacturing Practices for Drugs, Dec. 2011, available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm124740.htm.
FDA, Final Guidance, Sterile Drug Products Produced by Aseptic Processing - Current Good Manufacturing Practice, Sept. 2004, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070342.pdf.
FDA, Final Guideline, Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products, 61 FR 36466-01, July 10, 1996, available at 1996 WL 381691.
FDA, Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities; Final Policy, 56 Fed. Reg. 46191 (notice Sept. 10, 1991), available at https://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/ucm134741.htm.

FDA, Guidance for Industry and FDA Staff, Dear Health Care Provider Letters: Improving Communication of Important Safety Information, Jan. 2014, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM233769.pdf.
FDA, Guidance for Industry on Providing Clinical Evidence of Effectiveness for Human Drugs and Biological Products; Availability, 63 Fed. Reg. 27093 (notice May 15, 1998), available at https://www.gpo.gov/fdsys/pkg/FR-1998-05-15/pdf/98-12901.pdf.
FDA, Guidance for Industry, Biological Product Deviation Reporting for Licensed Manufacturers of Biological Products Other than Blood and Blood Components, Aug. 2001, available at https://www.fda.gov/OHRMS/DOCKETS/98fr/010221gd.pdf.
FDA, Guidance for Industry, Biological Product Deviation Reporting for Licensed Manufacturers of Biological Products Other than Blood and Blood Components, Oct. 2006, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/General/UCM163923.pdf.
FDA, Guidance for Industry, Changes to an Approved Application: Biological Products, July 1997, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/.../UCM170166.pdf.
FDA, Guidance for Industry, Changes to an Approved NDA or ANDA Questions and Answers, Jan. 2001, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm077097.pdf.
FDA, Guidance for Industry, Changes to an Approved NDA or ANDA, Apr. 2004, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm077097.pdf.
FDA, Guidance for Industry, Characterization and Qualification of Cell Substrates and Other Biological Materials Used in the Production of Viral Vaccines for Infectious Disease Indications, Feb. 2010, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/UCM202439.pdf.
FDA, Guidance for Industry, Clinical Studies Section of Labeling for Human Prescription Drug and Biological Products - Content and Format, Jan. 2006, available at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm127534.pdf.
FDA, Guidance for Industry, CMC Postapproval Manufacturing Changes To Be Documented in Annual Reports, Mar. 2014, available at https://www.fda.gov/downloads/Drugs/.../Guidances/UCM217043.pdf.
FDA, Guidance for Industry, Content and Format of Chemistry, Manufacturing and Controls Information and Establishment Description Information for a Vaccine or Related Product, Jan. 1999, available at https://www.fda.gov/downloads/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/vaccines/ucm092272.pdf.
FDA, Guidance for Industry, E6 Good Clinical Practice Consolidated Guidance, Apr. 1996, available at https://clinicalcenter.nih.gov/ccc/clinicalresearch/guidance.pdf.
FDA, Guidance for Industry, FDA Review of Vaccine Labeling Requirements for Warnings, Use Instructions, and Precautionary Information, Sept. 2004, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/UCM092196.pdf.
FDA, Guidance for Industry, For the Evaluation of Combination Vaccines for Preventable Diseases: Production, Testing and Clinical Studies, Apr. 1997, available at https://www.fda.gov/downloads/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/vaccines/ucm175909.pdf.

FDA, Guidance for Industry, General Principles for the Development of Vaccines to Protect Against Global Infectious Diseases, Dec. 2011, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/UCM282995.pdf.
FDA, Guidance for Industry, Integrated Summary of Effectiveness, Oct. 2015, available at https://www.fda.gov/downloads/drugs/guidances/ucm079803.pdf.
FDA, Guidance for Industry, Labeling for Human Prescription Drug and Biological Products - Implementing the PLR Content and Format Requirements, Feb. 2013, available at https://www.fda.gov/downloads/drugs/guidances/ucm075082.pdf.
FDA, Guidance for Industry, Labeling for Human prescription drug and Biological products, Jan. 2006, available at https://www.fda.gov/downloads/drugs/guidances/ucm075082.pdf.
FDA, Guidance for Industry, M4Q: The CTD - Quality, Aug. 2001, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073280.pdf.
FDA, Guidance for Industry, Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products, May 1998, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072008.pdf.
FDA, Guidance for Industry, Q1C Stability Testing for New Dosage Forms, Nov. 1996, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073374.pdf.
FDA, Guidance for Industry, Q1D Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products, Jan. 2003, available at https://www.fda.gov/downloads/Drugs/Guidances/ucm073379.pdf.
FDA, Guidance for Industry, Q1E Evaluation of Stability Data, June 2004, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073380.pdf.
FDA, Guidance for Industry, Q6B Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Aug. 1999, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073488.pdf.
FDA, Guidance for Industry, Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients, Aug. 2001, available at https://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm200364.htm.
FDA, Guidance for Industry, Stability Testing of Drug Substances and Drug Products, June 1998, available at https://www.fda.gov/downloads/drugs/guidances/ucm073369.pdf.
FDA, Guidance, "Off-Label" and Investigational Use Of Marketed Drugs, Biologics, and Medical Devices - Information Sheet, Jan. 1998, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126486.htm.
FDA, Guidance, Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products, July 2015, available at https://www.fda.gov/downloads/drugs/guidances/ucm389069.pdf.
FDA, Guidance, Analytical Procedures and Methods Validation for Drugs and Biologics; Guidance for Industry, Apr. 2015, available at https://www.fda.gov/downloads/drugs/guidances/ucm386366.pdf.
FDA, Guidance, Changes to an Approved Application for Specified Biotechnology and Specified Synthetic Biological Products, July 1997, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm124805.pdf.

FDA, Guidance, Charging for Investigational Drugs Under an IND - Qs & As, June 2016, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351264.pdf.
FDA, Guidance, Charging for Investigational Products - Information Sheet, Jan. 1998, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126427.htm.
FDA, Guidance, Collection of Race and Ethnicity Data in Clinical Trials, Oct. 2016, available at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm126396.pdf.
FDA, Guidance, Completeness Assessments for Type II API DMFs Under GDUFA Guidance for Industry, Oct. 2017, available at https://www.fda.gov/downloads/drugs/guidances/ucm321884.pdf.
FDA, Guidance, Container Closure Systems for Packaging Human Drugs and Biologics -- Questions and Answers, May 2002, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm070553.pdf.
FDA, Guidance, Container Closure Systems for Packaging Human Drugs and Biologics, May 1999, available at https://www.fda.gov/downloads/drugs/guidances/ucm070551.pdf.
FDA, Guidance, Contract Manufacturing Arrangements for Drugs: Quality Agreements, Dec. 2016, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM353925.pdf.
FDA, Guidance, Cooperative Manufacturing Arrangements for Licensed Biologics, Nov. 2008, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/General/ucm069908.pdf.
FDA, Guidance, Cooperative Research - Information Sheet, Jan. 1998, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126422.htm.
FDA, Guidance, Current Good Manufacturing Practice for Phase 1 Investigational Drugs, July 2008, available at https://www.fda.gov/downloads/drugs/guidances/ucm070273.pdf.
FDA, Guidance, Data Retention When Subjects Withdraw from FDA-Regulated Clinical Trials, Oct. 2008, available at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm126489.pdf.
FDA, Guidance, Drug Study Designs - Information Sheet, Jan. 1998, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126501.htm.
FDA, Guidance, Early Clinical Trials With Live Biotherapeutic Products: Chemistry, Manufacturing, and Control Information; Guidance for Industry, June 2016, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/General/UCM292704.pdf.
FDA, Guidance, Emergency Use of an Investigational Drug or Biologic - Information Sheet, Jan. 1998, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126491.htm.
FDA, Guidance, Environmental Assessment of Human Drug and Biologics Applications, Mar. 2016, available at https://www.fda.gov/downloads/Drugs/Guidances/UCM444658.pdf.
FDA, Guidance, Evaluation of Gender Differences in Clinical Investigations - Information Sheet, Jan. 1998, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126552.htm.
FDA, Guidance, Exception from Informed Consent Requirements for Emergency Research, Apr. 2013, available at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm249673.pdf.
FDA, Guidance, Expanded Access to Investigational Drugs for Treatment Use - Questions & Answers, Oct. 2017, available at https://www.fda.gov/downloads/drugs/guidances/ucm351261.pdf.
FDA, Guidance, FDA Guidance Document Concerning Use of Pilot Manufacturing Facilities for the Development and Manufacture of Biological Products, July 1995, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/General/UCM168111.pdf.

FDA, Guidance, Financial Conflicts of Interest: HHS Guidance, May 2004, available at https://www.hhs.gov/ohrp/regulations-and-policy/guidance/financial-conflict-of-interest/index.html.
FDA, Guidance, Financial Disclosure by Clinical Investigators, Industry, and FDA Staff, Feb. 2013, available at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm341008.pdf.
FDA, Guidance, For the Submission of Chemistry, Manufacturing, and Controls Information for a Therapeutic Recombinant DNA-Derived Product or a Monoclonal Antibody Product for In Vivo Use, Aug. 1996, available at https://www.fda.gov/downloads/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/general/ucm173477.pdf.
FDA, Guidance, Foreign Clinical Studies, Acceptance of - Information Sheet, Jan. 1998, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126426.htm.
FDA, Guidance, Formal Dispute Resolution: Scientific and Technical Issues Related to Pharmaceutical CGMP, Jan. 2006, available at https://www.fda.gov/downloads/drugs/guidances/ucm070279.pdf.
FDA, Guidance, Guideline on the Preparation of Investigational New Drug Products (Human and Animal), Mar. 1991, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm070315.pdf.
FDA, Guidance, IND Meetings for Human Drugs and Biologics Chemistry, Manufacturing, and Controls Information, May 2001, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm070568.pdf.
FDA, Guidance, Independent Consultants for Biotechnology Clinical Trial Protocols, Aug. 2004, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm127220.htm.
FDA, Guidance, Informed Consent Information Sheet, Jan. 2016, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm404975.htm.
FDA, Guidance, Informed Consent, A Guide to - Information Sheet, Jan. 1998, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126431.htm.
FDA, Guidance, Institutional Review Boards Frequently Asked Questions - Information Sheet, Jan. 1998, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126420.htm.
FDA, Guidance, Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Production, Oct. 2006, available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070287.pdf.
FDA, Guidance, Investigator Responsibilities - Protecting the Rights, Safety, and Welfare of Study Subjects, Oct. 2009, available at https://www.fda.gov/downloads/Drugs/.../Guidances/UCM187772.pdf.
FDA, Guidance, Manufacturing Biological Intermediates and Biological Drug Substances Using Spore-Forming Microorganisms, Sept. 2007, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/General/UCM190467.pdf.
FDA, Guidance, Monoclonal Antibodies Used as Reagents in Drug Manufacturing, Mar. 2001, available at https://www.fda.gov/downloads/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/blood/ucm080417.pdf.
FDA, Guidance, Nonclinical Studies for the Safety Evaluation of Pharmaceutical Excipients, May 2005, available at https://www.fda.gov/ohrms/dockets/98fr/2002d-0389-gdl0002.pdf.
FDA, Guidance, Non-local IRB Review - Information Sheet, Jan. 1998, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126423.htm.
FDA, Guidance, Oversight of Clinical Investigations - A Risk-Based Approach to Monitoring, Aug. 2013, available at https://www.fda.gov/downloads/Drugs/Guidances/UCM269919.pdf.

FDA, Guidance, Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims, Dec. 2009, available at https://www.fda.gov/downloads/drugs/guidances/ucm193282.pdf.
FDA, Guidance, Payment to Research Subjects - Information Sheet, Jan. 1998, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126429.htm.
FDA, Guidance, Pharmacogenomic Data Submissions, Mar. 2005, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm079849.pdf.
FDA, Guidance, Possible Dioxin/PCB Contamination of Drug and Biological Products, Aug. 1999, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm070310.pdf.
FDA, Guidance, Process Validation: General Principles and Practices, Jan. 2011, available at https://www.fda.gov/downloads/drugs/guidances/ucm070336.pdf.
FDA, Guidance, Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations, Sept. 2006, available at https://www.fda.gov/downloads/Drugs/Guidances/UCM070337.pdf.
FDA, Guidance, Recruiting Study Subjects - Information Sheet, Jan. 1998, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126428.htm.
FDA, Guidance, Screening Tests Prior to Study Enrollment - Information Sheet, Jan. 1998, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126430.htm.
FDA, Guidance, Sponsor - Investigator - IRB Interrelationship - Information Sheet, Jan. 1998, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126425.htm.
FDA, Guidance, Sterile Drug Products Produced by Aseptic Processing - Current Good Manufacturing Practice, Sept. 2004, available at https://www.fda.gov/downloads/Drugs/Guidances/ucm070342.pdf.
FDA, Guidance, Submission Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products, Nov. 1994, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm072171.pdf.
FDA, Guidance, Submission of Documentation in Applications for Parametric Release of Human and Veterinary Drug Products Terminally Sterilized by Moist Heat Processes, Feb. 2010, available at https://www.fda.gov/downloads/Drugs/Guidances/ucm072180.pdf
FDA, Guidance, Submitting and Reviewing Complete Responses to Clinical Holds, Oct. 2000, available at https://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127538.pdf.
FDA, Guidance, The Establishment and Operation of Clinical Trial Data Monitoring Committees, Mar. 2006, available at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm127073.pdf.
FDA, Guidance, Treatment Use of Investigational Drugs - Information Sheet, Jan. 1998, available at https://www.fda.gov/RegulatoryInformation/Guidances/ucm126495.htm.
FDA, Guidances, Pharmaceutial Quality/Manufacturing Standards (CGMP), Oct. 2017, available at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/ucm064971.htm.
FDA, Guideline for Submitting Documentation for the Stability of Human Drugs and Biologics, Feb. 1987, available at 1987 WL 959486.
FDA, Guideline for the Format and Content of the Clinical and Statistical Sections of an Application, July 1998, available at https://www.fda.gov/downloads/Drugs/.../Guidances/UCM071665.pdf.
FDA, ICH Harmonized Tripartite Guideline, Evaluation for Stability Data Q1E, Feb. 2003, available at http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q1E/Step4/Q1E_Guideline.pdf.
FDA, Information Sheet Guidance, Clinical Investigator Administrative Actions - Disqualification - Information Sheet, Mar. 2014, available at https://www.fda.gov/downloads/RegulatoryInformation/guidances/UCM214008.pdf.

FDA, Information Sheet Guidance, FDA Inspections of Clinical Investigators - Information Sheet, June 2010, available at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm126553.pdf.
FDA, Information Sheet Guidance, FDA Institutional Review Board Inspections - Information Sheet, Jan. 2006, available at https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126555.pdf.
FDA, Information Sheet Guidance, Statement of Investigator (Form FDA 1572) - Frequently Asked Questions - Information Sheet, May 2010, available at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm214282.pdf.
FDA, Information Sheet Guidance, Waiver of IRB Requirements for Drug and Biological Product Studies - Information Sheet, Oct. 2017, available at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm126500.pdf.
FDA, Inspection Technical Guides, Expiration Dating and Stability Testing for Human Drug Products, Oct. 18, 1985, available at https://www.fda.gov/ICECI/Inspections/InspectionGuides/InspectionTechnicalGuides/ucm072919.htm.
FDA, International Conference on Harmonisation; Final Guideline on Stability Testing of Biotechnological/ Biological Products; Availability, 61 Fed. Reg. 36466 (notice July 10, 1996), available at https://www.gpo.gov/fdsys/pkg/FR-1996-07-10/pdf/96-17471.pdf.
FDA, International Conference on Harmonisation; Guidance on General Considerations for Clinical Trials, 62 Fed. Reg. 66113 (notice Dec. 17, 1997), available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073132.pdf.
FDA, Manual, 4723.1 Standing Operating Procedures for NDA/ANDA Field Alert Reports (PDF - 15KB), Nov. 1998, available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm090016.htm.
FDA, Manual, CDER Manual of Policies and Procedures (MaPPs), Mar. 2018, available at https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/default.htm.
FDA, Manual, Compliance Policy Programs and Guidelines, Feb. 2018, available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm090016.htm.
FDA, Manual, Compliance Program Guidance Manual, Mar. 2015, available at https://www.fda.gov/ICECI/ComplianceManuals/ComplianceProgramManual/default.htm.
FDA, Manual, Consistent Application of Current Good Manufacturing Practice Determinations, Jan. 2018, available at https://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/default.htm.
FDA, Notice of Guidance, Q6A Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Dec. 29, 2000, available at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm134966.htm.
FDA, Presentation, Application of cGMPs to Drug Product Quality Microbiology Laboratory Tests and Manufacturing Process Validation, Sept. 2016, available at http://sbiaevents.com/redifall2016-files/.
FDA, Presentation, Approaches to GMP inspection, June 2014, available at https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/UCM407991.pdf.
FDA, Presentation, Ensuring Quality over the Product Lifecycle: Risk-based Product Specific Inspections in OPQ, Sept. 2016, available at http://sbiaevents.com/redifall2016-files/.
FDA, Presentation, FDA Drug Quality Regulation, June 2014, available at https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/UCM407992.pdf.

FDA, Presentation, FDA Drug Quality Regulations: Current Topics, Sept. 14, available at https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/UCM441208.pdf.
FDA, Presentation, FDA Small Business Regulatory Education for Industry (REdI) Conference "Focus on CGMPs and FDA Inspections," Summer 2015, available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm456362.htm.
FDA, Presentation, FDA's Pre-Approval Inspection (PAI) Program and How to prepare for a successful outcome, Fall 2015, available at https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/UCM466481.pdf.
FDA, Presentation, Inspection of NDA and BLA Applications, Sept. 2016, available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm514324.htm.
FDA, Presentation, Pet Peeves and Roadblocks in CMC: Improving your Quality Submissions through the Product Lifecycle, Sept. 2014, available at https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/UCM441138.pdf.
FDA, Presentation, Pharmaceutical Quality Symposium, July 2016, available at http://sbiaevents.com/pqs-files-page/.
FDA, Presentation, Risk and Team-based Integrated Quality Assessment in the Office of Pharmaceutical Quality, Sept. 2016, available at http://sbiaevents.com/redifall2016-files/.
FDA, Proposed Rule, Biological Products Reporting of Errors and Accidents in Manufacturing, 62 FR 49642-01, Sept. 23, 1997, available at 1997 WL 582671(F.R.).
FDA, Reference Material, Guide to Inspections of Pharmaceutical Quality Control Laboratories, July 1993, available at https://www.fda.gov/ICECI/Inspections/InspectionGuides/ucm074918.htm#_top.
FDA, Regulatory Procedures Manual, Chapter 4: Advisory Actions, Section 4-1-1, Warning Letter Procedures, Dec. 2017, available at https://www.fda.gov/downloads/ICECI/ComplianceManuals/RegulatoryProceduresManual/UCM074330.pdf.
FDA, Regulatory Procedures Manual, Chapter 5: Administrative Actions, Aug. 2015, available at https://www.fda.gov/downloads/iceci/compliancemanuals/regulatoryproceduresmanual/ucm074324.pdf.
FDA, Regulatory Procedures Manual, Chapter 6: Judicial Actions, Dec. 2017, available at https://www.fda.gov/downloads/iceci/compliancemanuals/regulatoryproceduresmanual/ucm074317.pdf.
FDA, Report, Final Report from the FDA-EMA pilot program for the parallel assessment of quality-by-design elements of marketing applications, Apr. 2017, available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm552716.htm.
FDA, Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products and Draft Guidance and Two Guidance for Industry on the Content and Format of Labeling for Human Prescription Drug and Biological Products; Final Rule and Notices (2006), 71 Fed. Reg. 3922 (Jan. 24, 2006) (to be codified at 21 CFR Parts 201, 314, and 601), available at https://www.fda.gov/OHRMS/DOCKETS/98fr/06-545.pdf.
FDA, Requirements on Content and Format of Labeling for Human Prescription Drugs and Biologics; Requirements for Prescription Drug Product Labels, Proposed Rule, 65 Fed. Reg. 81082 (proposed Dec. 22, 2000) (to be codified at 21 CFR Parts 201), available at https://www.gpo.gov/fdsys/pkg/FR-2000-12-22/pdf/00-32375.pdf.
FDA, Resource, CDER's Quality Initiative, Aug. 2017, available at https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm417014.htm.

FDA, Resource, Integration of FDA Facility Evaluation and Inspection Program for Human Drugs: A Concept of Operations, Sept. 2017, available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm576307.htm.
FDA, Resource, International Council on Harmonisation-Quality, Sept. 2017, available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm576307.htm.
FDA, Resource, Office of Pharmaceutical Quality, Mar. 2018, available at https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm418347.htm.
FDA, Resource, OPS Process Analytical Technology - (PAT) Initiative, Sept. 2015, available at https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm088828.htm.
FDA, Resource, Quality Metrics for Drug Manufacturing, Dec. 2017, available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm526869.htm.
FDA, Resource, Questions and Answers on Current Good Manufacturing Practices (CGMP) for Drugs, Feb. 2018, available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm124740.htm.
FDA, Resource, Report a Product Quality Issue: Identify quality defects in distributed drug products that may present a potential safety threat, June 2017, available at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/ucm529718.htm.
FDA, September 6, 2005 Approval Letter - ProQuad, available at http://wayback.archive-it.org/7993/20170723150912/https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm123799.htm.
FDA, Statement Regarding the Demonstrations of Effectiveness of Human Drug Products and Devices, 60 Fed. Reg. 39180 (notice Aug. 1, 1995), available at https://www.gpo.gov/fdsys/pkg/FR-1995-08-01/pdf/95-18877.pdf.
FDA, Summary Basis for Regulatory Action - ProQuad, Mar. 27, 2015, available at http://wayback.archive-it.org/7993/20170723150902/https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM441486.pdf.
FDA, Supplemental Approval - ProQuad, October 22, 2015, available at http://wayback.archive-it.org/7993/20170723150901/https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM469262.pdf
FDA, Technical Specifications Document, Technical Specifications Document: "Quality Metrics Technical Conformance Guide, Version 1.0", July 2015, available at https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/Manufacturing/UCM508464.pdf.
FDA, Vaccine Product Approval Process, available at https://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/BiologicsLicenseApplicationsBLAProcess/ucm133096.htm.
FDA, Webinar, Postapproval Changes Related to Drug Product Quality, Manufacturing and Controls that may be Documented in Annual Reports, May 2014, available at http://wayback.archive-it.org/7993/20170112023703/available at http:/www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm396083.htm.
FDA, Webinar, Revised Draft Guidance for Industry: Submission of Quality Metrics Data Webinar, Dec. 2016, available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm530313.htm.
FDA, White Paper, FDA Pharmaceutical Quality Oversight, available at https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM442666.pdf.

Fedova, D., J. Novotny and I. Kubinova (1992). "Serological diagnosis of parainfluenza virus infections: verification of the sensitivity and specificity of the haemagglutination-inhibition (HI), complement-fixation (CF), immunofluorescence (IFA) tests and enzyme immunoassay (ELISA)." Acta Virol 36(3): 304-312.
Fiebelkorn et al, VPD Surveillance Manual, 5th Edition, 2012, Mumps: Chapter 9-1 to 9-18.
Fiebelkorn, A. P. et al.: *Mumps Antibody Response in Young Adults After a Third Dose of Measles-Mumps-Rubella Vaccine* , Open Forum Infectious Diseases, 1(3), (Dec.) 2014.
Final Administrative Procedures for CLIA Categorization (2017), available at https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm070889.pdf.
Findlay, J.W. et al., Validation of immunoassays for bioanalysis: a pharmaceutical industry perspective, J Pharm Biomed Anal. 2000 Jan;21(6):1249-73.
Finkelstein A., "Static and Dynamic Effects of Health Policy: Evidence from the Vaccine Industry," *Quarterly Journal of Economics* , 119(2), 2004, pp. 527-564.
FirstCare, "2017 Prescription Drug Formulary," pp. 1-150.
Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Veterinary Medicine (CVM), May 2001, available at https://www.fda.gov/downloads/Drugs/Guidance/ucm070107.pdf.
Fortune, Sanofi and Merck Are Ditching a 22-Year-Old Joint Venture, Mar. 8, 2016, available at http://fortune.com/2016/03/08/sanofi-merck-joint-venture/.
Franz, S., P. Rennert, M. Woznik, J. Grutzke, A. Ludde, E. M. Arriero Pais, T. Finsterbusch, H. Geyer, A. Mankertz and N. Friedrich (2017). "Mumps Virus SH Protein Inhibits NF-kappaB Activation by Interacting with Tumor Necrosis Factor Receptor 1, Interleukin-1 Receptor 1, and Toll-Like Receptor 3 Complexes." J Virol 91(18).
Frasca, D., A. Diaz, M. Romero and B. B. Blomberg (2017). "Ageing and obesity similarly impair antibody responses." Clin Exp Immunol 187(1): 64-70.
Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities; Final Policy, 56 Fed Reg 46191 (Sept. 10, 1991).
Freed G.L., *et al.* , "Variation in Provider Vaccine Purchase Prices and Payer Reimbursement," *Pediatrics* , 122(6), December 2008, pp. 1325-1331.
Friedewald, W. F., E. S. Miller and L. R. Whatley (1947). "The Nature of Non-Specific Inhibition of Virus Hemagglutination." J Exp Med 86(1): 65-75.
Fu et al, "Effectiveness of one dose of mumps vaccine against clinically diagnosed mumps in Guangzhou, China, 2006-2012", Hum Vaccin Immunother. 2013 Dec;9(12):2524-8.
G. Amexis, S. Rubin, V. Chizhikov, F. Pelloquin, K. Carbone, K. Chumakov. Sequence diversity of Jeryl Lynn strain of mumps virus, available at https://core.ac.uk/download/pdf/82001558.pdf.
G. H. Guyatt (2014). "Blinded interpretation of study results can feasibly and effectively diminish interpretation bias." J Clin Epidemiol 67(7): 769-772.
Givens v. Lederle , 556 F.2d 1341 (5th Cir. 1977).
GlaxoSmithKline (2016). Safety and Immunogenicity Study of GlaxoSmithKline (GSK) Biologicals' Measles, Mumps and Rubella (MMR) Vaccine (209762) Compared to Merck & Co., Inc.'s MMR Vaccine in Healthy Children 12 to 15 Months of Age, National Library of Medicine. NCT02184572.
Glazer J., and T.G. McGuire, "A Welfare Measure of 'Offset Effects' in Health Insurance," *Journal of Public Economics,* 96, 2012, pp. 520-523.
Glazer J., H. Huskamp, and T.G. McGuire, "A Prescription for Drug Formulary Evaluation: An Application of Price Indexes," Forum for Health Economics and Policy, 15(2), 2012, Article 3.
Goldman D., and D. Lakdawalla, "Intellectual Property, Information Technology, Biomedical Research, and Marketing of Patented Products," Chapter 13 in M. Pauly, T, McGuire and P. Barros (eds.) *Handbook of Health Economics,* Volume 2, Elsevier Publishing, 2012, pp. 825-872.

Gotzsche, P. C. (1989). "Methodology and overt and hidden bias in reports of 196 double-blind trials of nonsteroidal antiinflammatory drugs in rheumatoid arthritis." Control Clin Trials 10(1): 31-56.
Gotzsche, P. C. (1996). "Blinding during data analysis and writing of manuscripts." Control Clin Trials 17(4): 285-290; discussion 290-283.
Gould, P. S., A. J. Easton and N. J. Dimmock (2017). ""Live Attenuated Influenza Vaccine contains Substantial and Unexpected Amounts of Defective Viral Genomic RNA."." Viruses 9(10).
Gouma S, Hahné SJ, Gijselaar DB, Koopmans MP, van Binnendijk RS. "Severity of mumps disease is related to MMR vaccination status and viral shedding." Vaccine. 2016 Apr 7;34(16):1868-73. doi: 10.1016/j.vaccine.2016.02.070. Epub 2016 Mar 5.
Gouma, S., M. P. Koopmans and R. S. van Binnendijk (2016). "Mumps virus pathogenesis: Insights and knowledge gaps." Hum Vaccin Immunother 12(12): 3110-3112.
Gouma, S., T. M. Schurink-Van't Klooster, H. E. de Melker, J. Kerkhof, G. P. Smits, S. J. Hahne, C. A. van Els, G. J. Boland, A. C. Vossen, P. R. Goswami, M. P. Koopmans and R. S. van Binnendijk (2014). "Mumps serum antibody levels before and after an outbreak to assess infection and immunity in vaccinated students." Open Forum Infect Dis 1(3): ofu101.
Grabowski H.G., and J.M. Vernon, “The Search for New Vaccines: The Effects of the Vaccines for Children Program,” The AEI Press, Washington, D.C., 1997.
Guidance for Industry (Draft), Assay Development and Validation for Immunogenicity Testing of Therapeutic Protein Products. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH). April 2016. Available at https://www.fda.gov/downloads/Drugs/Guidances/UCM192750.pdf.
Guidance for Industry on Chemistry, Manufacturing, and Controls Information; Withdrawal and Revision of Seven Guidances, 71 Fed. Reg. 31194 (June 1, 2006).
Guidance for Industry, Analytical Procedures and Methods Validation for Drugs and Biologics. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), July 2015. Available at https://www.fda.gov/downloads/drugs/guidances/ucm386366.pdf.
Guidance for Industry, Bioanalytical Method Validation (Draft Guidance, Revision 1). U.S. Department of Health and Human Services Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Veterinary Medicine (CVM), September 2013. Available at https://www.fda.gov/downloads/drugs/guidances/ucm368107.pdf.
Guidance on Alternatives to Lot Release for Licensed Biological Products, 58 Fed. Reg 38771 (July, 20 1993).
Guideline for Industry, Text on Validation of Analytical Procedures, ICH-Q2A, March 1995. Available at https://www.fda.gov/downloads/Drugs/.../Guidances/ucm073381.pdf.
Guidelines for good clinical practice (GCP) for trials on pharmaceutical products; WHO Technical Report Series, No. 850, 1995, Annex 3, available at http://apps.who.int/medicinedocs/en/d/Jwhozip13e/.
Guidelines on clinical evaluation of vaccines: regulatory expectations; WHO Technical Report Series, No. 1004, 2017, Annex 9, available at http://www.who.int/biologicals/expert_committee/WHO_TRS_1004_web_Annex_9.pdf.
Guidelines on procedures and data requirements for changes to approved vaccines; WHO Technical Report Series No. 993, 2015, Annex 4, available at http://apps.who.int/medicinedocs/en/m/abstract/Js22021en/.
Gut, J. P., C. Lablache, S. Behr and A. Kirn (1995). "Symptomatic mumps virus reinfections." J Med Virol 45(1): 17-23.
Guzman, M. G. and G. Kouri (2004). "Dengue diagnosis, advances and challenges." Int J Infect Dis 8(2): 69-80.
H.R.5546, National Childhood Vaccine Injury Act of 1986, 99th Congress (1985-1986), available at https://www.congress.gov/bill/99th-congress/house-bill/5546.

Habel, K. (1946). "Preparation of mumps vaccines and immunization of monkeys against experimental mumps infection." Public Health Rep 61(46): 1655-1664.
Hackett L.B., and J.J. Tofflen, "Report on the United States Vaccine Industry," Prepared by Mercer Management Consulting, Commissioned by the Department of Health and Human Services, June 14, 1995, pp. 1-33, available at https://quod.lib.umich.edu/c/cohenaids/5571095.0504.060.
Hamami, D., R. Cameron, K. G. Pollock and C. Shankland (2017). "Waning Immunity Is Associated with Periodic Large Outbreaks of Mumps: A Mathematical Modeling Study of Scottish Data." Front Physiol 8: 233.
Han, W. G., M. E. Emmelot, H. Jaadar, H. I. Ten Hulscher, C. A. van Els and P. Kaaijk (2016). "Development of an IFNgamma ELISPOT for the analysis of the human T cell response against mumps virus." J Immunol Methods 431: 52-59.
Handbook for Good Clinical Research Practice (GCP): Guidance for Implementation, available at http://apps.who.int/medicinedocs/documents/s14084e/s14084e.pdf.
Hanna-Wakim, R., L. L. Yasukawa, P. Sung, A. M. Arvin and H. A. Gans (2008). "Immune responses to mumps vaccine in adults who were vaccinated in childhood." J Infect Dis 197(12): 1669-1675.
Harmsen, T., M. C. Jongerius, C. W. van der Zwan, A. D. Plantinga, C. A. Kraaijeveld and G. A. Berbers (1992). "Comparison of a neutralization enzyme immunoassay and an enzyme-linked immunosorbent assay for evaluation of immune status of children vaccinated for mumps." J Clin Microbiol 30(8): 2139-2144.
Hashimoto, H. et al.: *An office-based prospective study of deafness in mumps* , Pediatric Infectious Disease Journal, 28(3): 173–5, (Mar.) 2009.
Havlíková et al, "Mumps in the Czech Republic in 2013: Clinical Characteristics, Mumps Virus Genotyping, and Epidemiological Links", Cent Eur J Public Health. 2016 Mar;24(1):22-8.
Hawkes, R. A. and K. J. Lafferty (1967). "The enchancement of virus infectivity by antibody." Virology 33(2): 250-261.
Health Resources & Services Administration National Vaccine Injury Compensation Program Fact Sheet (available at https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/faq/vicp-fact-sheet.pdf).
Henderson, F. W. (1987). "Pulmonary infections with respiratory syncytial virus and the parainfluenza viruses." Semin Respir Infect 2(2): 112-121.
Henle, G., S. Harris and W. Henle (1948). "The reactivity of various human sera with mumps complement fixation antigens." J Exp Med 88(1): 133-147.
Hersh, B. S., et al.: *Mumps outbreak in a highly vaccinated population* . J Pediatrics, 119(2): 187-93, (Aug.) 1991.
HHS, National Vaccine Advisory Committee Charter, July 30, 1987.
HHS, National Vaccine Advisory Committee, June 9-10, 1988 Meeting Minutes.
Hilleman, "Combined Measles Mumps and Rubella Vaccines, Combined Vaccines: Development, Clinical Research and Approval" (Humana Press Inc. 1999).
Hilleman, M. R. (1966). "Advances in control of viral infections by nonspecific measures and by vaccines, with special reference to live mumps and rubella virus vaccines." Clin Pharmacol Ther 7(6): 752-762.
Hilleman, M. R. (1992). "Past, present, and future of measles, mumps, and rubella virus vaccines." Pediatrics 90(1 Pt 2): 149-153.
Hilleman, M. R., E. B. Buynak, R. E. Weibel and J. Stokes, Jr. (1968). "Live, attenuated mumps-virus vaccine." N Engl J Med 278(5): 227-232.
Hilleman, M. R., E. B. Buynak, R. E. Weibel, J. Stokes, Jr., J. E. Whitman, Jr. and M. B. Leagus (1968). "Development and evaluation of the Moraten measles virus vaccine." JAMA 206(3): 587-590.
Hilleman, M. R., et al.: *Live Attenuated Mumps Virus Vaccine: 4. Protective Efficacy as Measured in Field Evaluation* , New Eng. J. Med., 276: 252-258, (Feb. 2) 1967.
Homan et al, "Are cases of mumps in vaccinated patients attributable to mismatches in both vaccine T-cell and B-cell epitopes? An immunoinformatic analysis", Hum Vaccin Immunother. 2014;10(2):290-300.
Horvath, S. (1975). "Estimation of hemagglutination-inhibition titers." Arch Virol 49(2-3): 199-205.

House Comm. on Energy and Commerce, 99th Cong., 2nd Sess., Childhood Immunizations, a Report (Comm. Print 99-LL 1986).
House Report No. 99-908, 1986 WL 31971, National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-1 to 300aa-34.
HRSA, National Vaccine Injury Compensation Program, available at https://www.hrsa.gov/vaccine-compensation/index.html.
HRSA, Public Health Service Act, Title XXI - Vaccines, available at https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/about/title-xxi-phs-vaccines-1517.pdf
HRSA, What You Need to Know About the National Vaccine Injury Compensation Program (VICP), Sept. 2016, available at https://www.hrsa.gov/sites/default/files/vaccinecompensation/resources/84521booklet.pdf.
Hsiung, G. D., P. Isacson and G. Tucker (1963). "Studies of Parainfluenza Viruses. Ii. Serologic Interrelationships in Humans." Yale J Biol Med 35: 534-544.
http://www.cdc.gov/osels/ph_surveillance/nndss/phs/files/ProvisionalNationa%20NotifiableDiseasesSurveillanceData20100927.pdf, "National Notifiable Diseases Surveillance System (NNDSS)"
http://www.nvic.org/injury-compensation/origihanlaw.aspx
http://wwwn.cdc.gov/nndss/document/ProvisionalNationaNotifiableDiseasesSurveillanceData20100927.pdf, Provisional National Notifiable Diseases Surveillance Data
https://www.cdc.gov/media/transcripts/t060419.htm, Press Briefing on Mumps Outbreak In the Midwest with Dr. Julie Gerberding, and Dr. Jane Seward
https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5952md.htm?s_cid=mm5952md_w, Morbidity and Mortality Weekly Report (MMWR) Notifiable Diseases and Mortality Tables, Weekly, January 7, 2011
https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6052md.htm?s_cid=mm6052md_w, Morbidity and Mortality Weekly Report (MMWR) Notifiable Diseases and Mortality Tables, Weekly, January 6, 2012
https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6452md.htm?s_cid=mm6452md_w, Morbidity and Mortality Weekly Report (MMWR), Notifiable Diseases and Mortality Tables, Weekly, January 8, 2016
https://www.cdc.gov/mmwr/volumes/64/wr/mm6453a1.htm?s_cid=mm6453a1_w, Morbidity and Mortality Weekly Report (MMWR), Summary of Notifiable Infectious Diseases and Conditions - United States, 2015
https://www.cdc.gov/mmwr/volumes/65/wr/mm6552md.htm?s_cid=mm6552md_w, Morbidity and Mortality Weekly Report (MMWR), Notifiable Diseases and Mortality Tables, Weekly, January 6, 2017
https://www.cdc.gov/mmwr/volumes/66/wr/mm6652md.htm?s_cid=mm6652md_w, Morbidity and Mortality Weekly Report (MMWR), Notifiable Diseases and Mortality Tables Weekly January 5, 2018
https://www.cdc.gov/mumps/outbreaks.html, "Mumps Cases and Outbreaks"
https://www.cdc.gov/nndss/infectious.html, National Notifiable Diseases Surveillance System (NNDSS), "About Notifiable Infectious Diseases and Conditions Data"
https://www.cdc.gov/nndss/infectious-tables.html, National Notifiable Diseases Surveillance System (NNDSS), Notifiable Infectious Diseases and Conditions Tables
https://www.cdc.gov/vaccinesafety/ensuringsafety/history/index.html.
https://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm123796.pdf, Current ProQuad Package Insert
https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073308.pdf, Guidance for Industry Submitting Marketing Applications According to the ICH-CTD Format-General Considerations- Draft Guidance
https://www.hrsa.gov/vaccine-compensation/index.html
https://www.niaid.nih.gov/research/emerging-infectious-diseases-pathogens
https://www.thermofisher.com
https://wwwn.cdc.gov/nndss/document/5yearweeklyaverage.pdf
https_www.fda.gov_BiologicsBloodVaccines_Vaccines_ApprovedProducts_ucm094050_htm

Huang, A. S. et al.: *Risk factors for mumps at a university with a large mumps outbreak* , Public Health Report, 124(3): 419-426, (May-June) 2009.
Hunsaker J., G. Veselovskiy, and J.A. Gazmararian, "Health Insurance Plans and Immunization: Assessment of Practices and Policies, 2005-2008," *Pediatrics* , 124(5), 2009, pp. S532-S539.
Hviid, A., S. Rubin and K. Muhlemann (2008). "Mumps." Lancet 371(9616): 932-944.
Hwang T.J., and A.S. Kesselheim, "Vaccine Pipeline has Grown During the Past Two Decades with More Early-Stage Trials from Small and Medium-Sized Companies," *Health Affairs* , 35(2) 2016, pp. 219-226.
ICH E11, Clinical Investigation of MP in Pediatric Populations, available at http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E11/Step4/E11_Guideline.pdf .
ICH E3, Structure and Content of Clinical Study Reports, available at http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E3/E3_Guideline.pdf.
ICH E6, Good Clinical Practices, available at http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf.
ICH E8, General Considerations for Clinical Trials, http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E8/Step4/E8_Guideline.pdf.
ICH Q1A-F, Stability Testing Guidelines: Stability Testing of New Drug Substances and Products, available at http://www.pharma.gally.ch/ich/q1a038095en.pdf.
ICH Q3A-D, Impurities in New Drug Substances, available at http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q3A_R2/Step4/Q3A_R2__Guideline.pdf.
ICH Q4-Q4B, Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions, available at http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q4B/Step4/Q4B_Guideline.pdf.
ICH Q5A-E, Quality of Biotechnological Products: Viral Safety Evaluation of Biotechnology Products Derived From Cell Lines of Human or Animal Origin, available at http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002801.pdf.
ICH Q6A-B, Specifications: Test Procedures and Acceptable Criteria for New Drug Substances and New Drug Products: Chemical Substances, available at http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q6A/Step4/Q6Astep4.pdf.
ICH Q7, Good Manufacturing Practices Guide for Active Pharmaceutical Ingredients, available at http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q7/Step4/Q7_Guideline.pdf.
ICH VALIDATION OF ANALYTICAL PROCEDURES: Text and Methodology Q2_R1__Guideline, available at http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q2_R1/Step4/Q2_R1__Guideline.pdf.
Immunization Action Coalition, Vaccine Timeline, available at http://www.immunize.org/timeline/.
IMS National Sales Perspectives (NSP) Data, Aged Data Adhoc, Nov. 18, 2016.
IMS National Sales Perspectives (NSP) Data, Current Data Adhoc, Nov. 18, 2016.
Inou, Y., T. Nakayama, N. Yoshida, H. Uejima, K. Yuri, M. Kamada, T. Kumagai, H. Sakiyama, A. Miyata, H. Ochiai, T. Ihara, T. Okafuji, T. Okafuji, T. Nagai, E. Suzuki, K. Shimomura, Y. Ito and C. Miyazaki (2004). "Molecular epidemiology of mumps virus in Japan and proposal of two new genotypes." J Med Virol 73(1): 97-104.

Intercenter Agreement Between CDER and CBER (effective October 31, 1991), available at https://www.fda.gov/CombinationProducts/JurisdictionalInformation/ucm121179.htm.
IOM, “Financing Vaccines in the 21st Century: Assuring Access and Availability,” National Academies Press, Washington DC, 2004.
Irie, T., K. Kiyotani, T. Igarashi, A. Yoshida and T. Sakaguchi (2012). "Inhibition of interferon regulatory factor 3 activation by paramyxovirus V protein." J Virol 86(13): 7136-7145.
J. A. Sterne (2008). "Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study." BMJ 336(7644): 601-605.
J.W.A. Findlay, et al., *Validation of Immunoassays for Bioanalysis: A Pharmaceutical Industry Perspective* , Journal of Pharmaceutical & Biomedical Analysis, 21(2000):1249-1273.
Jackson, K. J., Y. Wang and A. M. Collins (2014). "Human immunoglobulin classes and subclasses show variability in VDJ gene mutation levels." Immunol Cell Biol 92(8): 729-733.
Jarvinen, T. L., R. Sihvonen, M. Bhandari, S. Sprague, A. Malmivaara, M. Paavola, H. J. Schunemann and
Jin, L., B. Rima, D. Brown, C. Orvell, T. Tecle, M. Afzal, K. Uchida, T. Nakayama, J. W. Song, C. Kang, P. A. Rota, W. Xu and D. Featherstone (2005). "Proposal for genetic characterisation of wild-type mumps strains: preliminary standardisation of the nomenclature." Arch Virol 150(9): 1903-1909.
Jin, L., C. Orvell, R. Myers, P. A. Rota, T. Nakayama, D. Forcic, J. Hiebert and K. E. Brown (2015). "Genomic diversity of mumps virus and global distribution of the 12 genotypes." Rev Med Virol 25(2): 85-101.
Johansson, B., T. Tecle and C. Orvell (2002). "Proposed criteria for classification of new genotypes of mumps virus." Scand J Infect Dis 34(5): 355-357.
Johnson, J. B., D. S. Lyles, M. A. Alexander-Miller and G. D. Parks (2012). "Virion-associated complement regulator CD55 is more potent than CD46 in mediating resistance of mumps virus and vesicular stomatitis virus to neutralization." J Virol 86(18): 9929-9940.
Johnson, J. B., K. Grant and G. D. Parks (2009). "The paramyxoviruses simian virus 5 and mumps virus recruit host cell CD46 to evade complement-mediated neutralization." J Virol 83(15): 7602-7611.
Jokinen, S., P. Osterlund, I. Julkunen and I. Davidkin (2007). "Cellular immunity to mumps virus in young adults 21 years after measles-mumps-rubella vaccination." J Infect Dis 196(6): 861-867.
Julkunen, I., P. Vaananen and K. Penttinen (1984). "Antibody responses to mumps virus proteins in natural mumps infection and after vaccination with live and inactivated mumps virus vaccines." J Med Virol 14(3): 209-219.
Kancherla, V. S. et al. *Mumps resurgence in the United States* . J Allergy Clin Immunol. 2006;118(4):938-941. 10.1016/j.jaci.2006.07.033
Kärber, G. (1931). "Beitrag zur kollektiven Behandlung pharmakologischer Reihenversuche." Naunyn-Schmiedebergs Archiv für experimentelle Pathologie und Pharmakologie 162(4): 480-483.
Katz, J. M., K. Hancock and X. Xu (2011). "Serologic assays for influenza surveillance, diagnosis and vaccine evaluation." Expert Rev Anti Infect Ther 9(6): 669-683.
Katzelnick, L. C., L. Gresh, M. E. Halloran, J. C. Mercado, G. Kuan, A. Gordon, A. Balmaseda and E. Harris (2017). "Antibody-dependent enhancement of severe dengue disease in humans." Science 358(6365): 929-932.
Keshavarz, M., A. Shafiee, M. H. Nicknam, P. Khosravani, A. Yousefi and M. Izad (2017). "Immune Response to the Mumps Virus in Iranian Unvaccinated Young Adults." Jpn J Infect Dis 70(2): 127-131.
Kidokoro, M., R. Tuul, K. Komase and P. Nymadawa (2011). "Characterization of mumps viruses circulating in Mongolia: identification of a novel cluster of genotype H." J Clin Microbiol 49(5): 1917-1925.
Killip, M. J., D. F. Young, B. L. Precious, S. Goodbourn and R. E. Randall (2012). "Activation of the beta interferon promoter by paramyxoviruses in the absence of virus protein synthesis." J Gen Virol 93(Pt 2): 299-307.

Kim, H. W., J. G. Canchola, C. D. Brandt, G. Pyles, R. M. Chanock, K. Jensen and R. H. Parrott (1969). "Respiratory syncytial virus disease in infants despite prior administration of antigenic inactivated vaccine." Am J Epidemiol 89(4): 422-434.

Kim-Farley, R et al.: *Clinical Mumps Vaccine Efficacy,* Am J Epidemiology, 121(4): 593-7, (Apr.) 1985.

Kingham, R. K., G; Carver, K.C. (2014). Key Regulatory Guidelines for the Development of Biologics in the United States and Europe. Biological Drug Products: Development and Strategies. W. S. Wang, M, John Wiley & Sons, Inc.: 75-109

Koh H.K., and K.G. Sebelius, "Promoting Prevention through the Affordable Care Act," *New England Journal of Medicine* , 363(14), September 2010, pp. 1296-1299.

Kolli, D., X. Bao and A. Casola (2012). "Human metapneumovirus antagonism of innate immune responses." Viruses 4(12): 3551-3571.

Kontio, M., S. Jokinen, M. Paunio, H. Peltola and I. Davidkin (2012). "Waning antibody levels and avidity: implications for MMR vaccine-induced protection." J Infect Dis 206(10): 1542-1548.

Krasnova, V. P., N. V. Iuminova and V. A. Liashenko (1994). "[An intranasal method of revaccination against mumps]." Vopr Virusol 39(1): 24-26.

Kumakura, S., H. Shibata, T. Isobe, M. Hirose, M. Ohe, N. Nishimura, K. Onoda, A. Nagai and S. Yamaguchi (2013). "Comparison of hemagglutination inhibition assay and enzyme immunoassay for determination of mumps and rubella immune status in health care personnel." J Clin Lab Anal 27(5): 418-421.

Kurosaki, T., K. Kometani and W. Ise (2015). "Memory B cells." Nat Rev Immunol 15(3): 149-159.

Kuter et al, "Safety and Immunogenicity of a Combination: Measles, Mumps, Rubella and Varicella Vaccine (ProQuad®)," Hum Vaccin. 2006 Sep-Oct;2(5):205-14.

Kuter et al, "Safety and Immunogenicity of M-M-RII (Combination Measles-Mumps-Rubella Vaccine) in Clinical Trials of Healthy Children Conducted Between 1988 and 2009" Pediatr Infect Dis J. 2016 Sep;35(9):1011-20.

Kutty, P. K. et al.: *Seroprevalence of Antibody to Mumps Virus in the US Population, 1999-2004* , J. Infectious Diseases, 202(5): 667-74 (Sept. 1) 2010.

Labeling and Prescription Drug Advertising; Content and Format for Labeling for Human Prescription Drugs, 44 Fed. Reg. 37434 (June 26, 1979) (to be codified in 21 CFR pt. 201 and 202).

Latner, D. R. et al. *Estimates of Mumps Seroprevalence May Be Influenced by Antibody Specificity and Serologic Method* . Clin Vaccine Immunol. 2014;21(3):286-97. 10.1128/CVI.00621-13

Latner, D. R. et al.: *Enzyme-Linked Immunospot Assay Detection of Mumps-Specific Antibody-Secreting B cells as an Alternative Method of Laboratory Diagnosis* , Clinical and Vaccine Immunology, 18(1): 35-42, (Jan.) 2011.

Latner, D. R. et al.: *Remembering Mumps* , PLOS Pathog, 11(5): 1-4 (May 7) 2015.

Latner, D. R. et al: *Mumps Virus Nucleoprotein and Hemagglutinin-Specific Antibody Response Following a Third Dose of Measles Mumps Rubella Vaccine* , Open Forum Infectious Diseases, 4(4), (Oct. 1) 2017.

Le P., and M.B. Rothberg, "Cost-effectiveness of the Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults," JAMA Intern Med., February 2018, available at Fhttps://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2666789.

LeBaron, C. W., B. Forghani, C. Beck, C. Brown, D. Bi, C. Cossen and B. J. Sullivan (2009). "Persistence of mumps antibodies after 2 doses of measles-mumps-rubella vaccine." J Infect Dis 199(4): 552-560.

Lebo, E. J. et al.: *Seroprevalence of Measles, Mumps, Rubella and Varicella Antibodies in the United States Population, 2009-2010* , Open Forum Infectious Diseases, 2(1), (Feb. 20) 2015.

Lefrancois, L. (1984). "Protection against lethal viral infection by neutralizing and nonneutralizing monoclonal antibodies: distinct mechanisms of action in vivo." J Virol 51(1): 208-214.

Legal Status of Approved Labeling for Prescription Drugs; Prescribing for Uses Unapproved by the Food and Drug Administration, 37 Fed. Reg. 16503 (proposed August 15, 1972) (to be codified at 21 CFR pt. 130).

Lennette, E. H., F. W. Jensen, R. W. Guenther and R. L. Magoffin (1963). "Serologic responses to para-influenza viruses in patients with mumps virus injection." J Lab Clin Med 61: 780-788.
LENNOX ES. "Transduction of linked genetic characters of the host by bacteriophage P1." Virology. 1955 Jul;1(2):190-206.
Leonardi, "Immunogenicity and Safety of MMRV and PCV-7 Administered Concomitantly in Healthy Children," Pediatrics, 2001 December, 128(6)
Lerner A.P., "The Concept of Monopoly and the Measurement of Monopoly Power," *The Review of Economic Studies* , 1(3), June 1934, pp. 157-175.
Lieberman, "The Safety and Immunogenicity of a Quadrivalent Measles, Mumps, Rubella and Varicella Vaccine in Healthy Children A Study of Manufacturing Consistency and Persistence of Antibody," The Pediatric Infectious Disease Journal, July 2006 25(7)
Lieu T., T.G. McGuire, and A.R. Hinman, "Overcoming Economic Barriers To The Optimal Use Of Vaccines," *Health Affairs,* 24(3), 2005, pp. 666-679.
Lin, R., D. Heeke, H. Liu, E. Rao, J. D. Marshall, V. Chio, F. Cataniag, L. Yu, F. Zuo and M. P. McCarthy (2017). "Development of a robust, higher throughput green fluorescent protein (GFP)-based Epstein-Barr Virus (EBV) micro-neutralization assay." J Virol Methods 247: 15-21.
Linde, G. A., M. Granstrom and C. Orvell (1987). "Immunoglobulin class and immunoglobulin G subclass enzyme-linked immunosorbent assays compared with microneutralization assay for serodiagnosis of mumps infection and determination of immunity." J Clin Microbiol 25(9): 1653-1658.
Lindley M.C., *et al.* , "Financing the Delivery of Vaccines to Children and Adolescents: Challenges to the Current System," *Pediatrics* , 124(5), December 2009, pp. S548-S557.
Livingston, K. A. et al. *Mumps vaccine effectiveness and risk factors for disease in households during an outbreak in New York City* . Vaccine 2014;32:369-374. 10.1016/j.vaccine.2013.11.021
Lo, M. S., R. M. Brazas and M. J. Holtzman (2005). "Respiratory syncytial virus nonstructural proteins NS1 and NS2 mediate inhibition of Stat2 expression and alpha/beta interferon responsiveness." J Virol 79(14): 9315-9319.
Loon, Francesco van et al. "Mumps surveillance--United States, 1988-1993." MMWR. CDC surveillance summaries : Morbidity and mortality weekly report. CDC surveillance summaries 44 3 (1995): 1-14.
Lopez-Perea, N., J. Masa-Calles, M. V. Torres de Mier, A. Fernandez-Garcia, J. E. Echevarria, F. De Ory and M. V. Martinez de Aragon (2017). "Shift within age-groups of mumps incidence, hospitalizations and severe complications in a highly vaccinated population. Spain, 1998-2014." Vaccine 35(34): 4339-4345.
Ma, "Combination Measles-Mumps-Rubella-Varicella Vaccine in Healthy Children," Medicine, 2015 November; 94(44)
Ma, A., and T.G. McGuire (guest editors), "The Industrial Organization of Health Care, III," *Journal of Economics & Management Strategy* , 8(3), Fall 1999.
Ma, A., T.G. McGuire, and M.H. Riordan (guest editors), "The Industrial Organization of Health Care, II" *Journal of Economics & Management Strategy* , 1997.
MacDonald et al, "Mumps is Back: Why is Mumps Eradication Not Working?", Adv Exp Med Biol. 2011;697:197-220.
Maguire Hayden buys vacant Wayne lab building from Merck, THE INQUIRER, Dept. 14, 2016, available at http://www.philly.com/philly/business/real_estate/commercial/maguire-hayden-buys-chester-county-lab-property.html.
Malone K.M., and A.R. Hinman, "Vaccination Mandates: The Public Health Imperative and Individual Rights," Chapter 13 in Law Public Health Practice, edited by R.A. Goodman *et al.* , Oxford University Press: New York, 2003, pp. 262-284.

Marin M., *et al* ., "Use of Combination Measles, Mumps, Rubella, and Varicella Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP)," *Morbidity and Mortality Weekly Report* , 59(RR-3), May 7, 2010, pp. 1-12.
Marin, "Update on Mumps Epidemiology, United States," Presentation to ACIP on October 25, 2017.
Marin, M. et al. *Recommendation of the Advisory Committee on Immunization Practices for Use of a Third Dose of Mumps Virus-Containing Vaccine in Persons at Increased Risk for Mumps During an Outbreak* . MMWR 2018;67(1):33-8. 10.15585/mmwr.mm6701a7
Marin, M., *Current Mumps Vaccination Recommendation and Epidemiology in the United States* , CDC Advisory Committee on Immunization Practices (ACIP), February 23, 2017 Meeting.
Matsubara, K., S. Iwata and T. Nakayama (2012). "Antibodies against mumps virus component proteins." J Infect Chemother 18(4): 466-471.
Mauldin, J., et al. *Mumps Virus-Specific Antibody Titers from Pre-Vaccine Era Sera: Comparison of the Plaque Reduction Neutralization Assay and Enzyme Immunoassays.* J Clin Microbiol. 2005;43(9):4847-4851. 10.1128/JCM.43.9.4847–4851.2005
May, M., C. A. Rieder and R. J. Rowe (2018). "Emergent lineages of mumps virus suggest the need for a polyvalent vaccine." Int J Infect Dis 66: 1-4.
Mazur v. Merck & Co. , 742 F. Supp. 239 (E.D. Pa. 1990).
Mazur v. Merck & Co. , 767 F. Supp. 697 (E.D. Pa. 1991).
Mazur v. Merck & Co. , 964 F 2d 1348 (3rd Cir. 1992).
McGuire T., K. Drake, E. Elhauge, R. Hartman, and M. Starr, "Resolving Reverse-Payment Settlements with the Smoking Gun of Stock Price Movements," *Iowa Law Review* , 101(4), 2016, pp. 1581-1599.
McGuire T.G., "Setting Prices for New Vaccines (in Advance)," *International Journal of Health Care Finance and Economics* , 3, 2003, pp. 207-224.
McGuire, T.G., and M.H. Riordan (guest editors), "The Industrial Organization of Health Care," *Journal of Economics & Management Strategy* , 3(1), 1994.
McGuire, T.G., and S. Bauhoff, "Adoption of a Cost-Saving Innovation: Germany, UK and Simvastatin," in N. Klusen, F. Verheyen, and C. Wagner, eds., *England and Germany in Europe – What Lessons Can We Learn from Each Other?* Baden-Baden, Germany: Nomos, 2011, pp. 11-26.
McLean, H. Q., A. P. Fiebelkorn, J. L. Temte, G. S. Wallace, C. Centers for Disease and Prevention (2013). "Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the Advisory Committee on Immunization Practices (ACIP)." MMWR Recomm Rep 62(RR-04): 1-34.
Measles, Mumps, Rubella (MMR) Vaccine , CDC Advisory Committee on Immunization Practices (ACIP), February 22-23, 2012 Summary Report, 83-102.
Measles-Mumps-Rubella-Varicella Vaccine Safety , CDC Advisory Committee on Immunization Practices (ACIP), June 24-26, 2009 Summary Report, 137-65.
Mercer Management Consulting, "Lessons Learned: New Procurement Strategies for Vaccines, Final Report to the GAVI Board," June 28, 2002.
Merck & Co., Inc., Form 10-K, for the Fiscal Year ended December 31, 2016.
Merck & Co., Inc., Form 10-Q, for the quarterly period ended September 30, 2017.
Merck Manuals, Consumer Version, Overview of Immunization, available at https://www.merckmanuals.com/home/infections/immunization/overview-of-immunization.
Merck, About, available at https://www.merck.com/about/home.html.
Merck, Merck and Serum Institute Announce Collaboration to Develop and Expand Global Access to Pneumococcal Conjugate Vaccine (PCV), Aug. 3, 2011, available at https://www.merck.com/licensing/our-partnership/Serum-collab-pneumococcal-vaccine-partnership.html.

Merck, Merck Joint Venture Relationship with Sanofi Pasteur, Feb. 2009, available at https://s21.q4cdn.com/488056881/files/doc_downloads/ventures/01E51DB9-C6BB-4512-A941-D665F031FED2_merck_sanofi_2009_update.pdf.
Merck, Merck Vaccines Branded Timeline, available at https://www.merck.com/docs/VACC-1213236-0000-Merck-Vaccines-Branded-Timeline-FINAL.pdf.
Merck, M-M-R II Label, Current Production Label.
Merck, M-M-R II Label, May 2007.
Merck, ProQuad Label, Frozen Formulation HSA, Current Production Label.
Merck, ProQuad Label, Frozen Formulation RHA, Current Production Label.
Merck, ProQuad Label, Refrigerator-Stable Formulation, Current Production Label.
Merck, Sinopharm and Merck Sign Statement of Mutual Intent, July 27, 2010, available at https://www.merck.com/licensing/our-partnership/Sinopharm-partnership.html.
Merk. ANNUAL REPORT 2003, available at httph://www.merck.com/finance/annualreport/ar2003/pdf/merck2003ar.pdf.
Meta Data - MRK-CHA00587762
Meta Data - SCHOFIELD_00000315
Method Transfer, Partial Validation, and Cross Validation- Recommendations 12248_2014_Article_9650
Moher, D., S. Hopewell, K. F. Schulz, V. Montori, P. C. Gotzsche, P. J. Devereaux, D. Elbourne, M. Egger, D. G. Altman and G. Consolidated Standards of Reporting Trials (2010). "CONSORT 2010 Explanation and Elaboration: Updated guidelines for reporting parallel group randomised trials." J Clin Epidemiol 63(8): e1-37.
Molecular biology, pathogenesis and pathology of mumps virus. Rubin S, Eckhaus M, Rennick LJ, Bamford CG, Duprex WP. J Pathol. 2015 Jan
Molony, R. D., A. Malawista and R. R. Montgomery (2017). "Reduced dynamic range of antiviral innate immune responses in aging." Exp Gerontol.
Mona Marin, MD. Division of Viral Diseases, CDC. "Update on Mumps Epidemiology, United States." Center for Disease Control and Prevention, October 25, 2017. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2017-10/mumps-02-marin-508.pdf.
Monto, A. S., R. E. Malosh, J. G. Petrie and E. T. Martin (2017). "The Doctrine of Original Antigenic Sin: Separating Good From Evil." J Infect Dis 215(12): 1782-1788.
MSD, MSD Reintegrates Vaccines Division into its Portfolio, Jan. 3, 2017, available at http://www.msd.ch/en/infocenter/meldungen/impfungen.xhtml.
MSD, MSD to Enter a New Era with Our Vaccines Portfolio in Europe, Building on the Heritage of Sanofi Pasteur MSD, available athttp://www.msd.com/about/featured-stories/spmsd/index.html.
Mufson, M. A., C. Diaz, M. Leonardi, C. J. Harrison, S. Grogg, A. Carbayo, S. Carlo-Torres, R. JeanFreau, A.
Muhlemann, K. (2004). "The molecular epidemiology of mumps virus." Infect Genet Evol 4(3): 215-219.
Mumps Cases and Outbreaks , CDC, https://www.cdc.gov/mumps/outbreaks.html (last updated Feb. 9, 2018).
Mumps Disease and Vaccine , CDC Advisory Committee on Immunization Practices (ACIP), February 22-23, 2017 Summary Report, 115-25.
Mumps Disease and Vaccine , CDC Advisory Committee on Immunization Practices (ACIP), June 21-22, 2017 Summary Report, 139-52.
Mumps virus-specific antibody titers from pre-vaccine era sera comparison of the plaque reduction neutralization assay and enzyme immunoassays
Mumps. Hviid A, Rubin S, Mühlemann K. Lancet. 2008 Mar 15
Mumps: Questions and Answers, "Information about the disease and vaccines", Immunization Action Coalition, dated April 28, 2011
Mumps: Questions and Answers, "Information about the disease and vaccines", Immunization Action Coalition, dated August 3, 2012

Mumps: Questions and Answers, "Information about the disease and vaccines", Immunization Action Coalition, dated June 22, 2010
Mumps: Questions and Answers, "Information about the disease and vaccines", Immunization Action Coalition, dated March 30, 2014
Mumps: Questions and Answers, "Information about the disease and vaccines", Immunization Action Coalition, dated March 6, 2008
Naruse, H, "Studies on the adaptation of mumps virus to chick embryo," Medical Microbiology and Immunology, 1986; 174(6):295-304
National Childhood Vaccine Injury Act of 1986; Delegation of Authority; Assistant Secretary for Health, 53 Fed. Reg. 22054 (June 13, 1988).
National Notifiable Infectious Diseases and Conditions: United States, Annual Data for 2016, Table 2j "Meningococcal disease; Mumps; Novel Influenza A virus infections," CDC Wonder website, available at https://wonder.cdc.gov/nndss/static/2016/annual/2016-table2j-H.pdf.
National Notifiable Infectious Diseases: Weekly Tables, Table II (Part 11) "Meningococcal disease; Mumps; Pertussis," CDC Wonder website, available at https://wonder.cdc.gov/nndss/nndss_weekly_tables_menu.asp?mmwr_year=2017&mmwr_week=52.
"National, State, and Urban Area Vaccination Coverage among Children Aged 19-35 Months – United States, 2003," *Morbidity and Mortality Weekly Report* , 53(29), 2004, pp. 658-661.
National Vaccine Advisory Committee, Report of the Subcommittee on Improvement of Existing Vaccines (Wilfert, Sept. 13, 1989), available at http://web.archive.org/web/20161221073322/http://archive.hhs.gov/nvpo/nvac/Improvement%20of%20Existing%20Vaccines%209-13-89.pdf.
National Vaccine Injury Compensation Program, Pub. L. No. 99-660, 100 Stat. 3755 (1986) (codified as amended at 42 U.S.C. §§ 300aa-1 to -34).
NCVIA, H.R. Rep. No. 908, 99th Cong. 2nd Sess. 1986, 1986 U.S.C.C.A.N. 6344, 1986 WL 31971 (Leg. Hist.).
Nelson, G. E. et al.: *Epidemiology of a Mumps Outbreak in a Highly Vaccinated Island Population and Use of a Third Dose of Measles-Mumps-Rubella Vaccine for Outbreak Control—Guam 2009 to 2010* , Pediatric Infectious Disease Journal, 32(4): 374-380, (Apr.) 2013.
Neumann, P. W., J. M. Weber, A. G. Jessamine and M. V. O'Shaughnessy (1985). "Comparison of measles antihemolysin test, enzyme-linked immunosorbent assay, and hemagglutination inhibition test with neutralization test for determination of immune status." J Clin Microbiol 22(2): 296-298.
New Approaches for Immunization and Therapy against Human Metapneumovirus Clin. Vaccine Immunol.-2015-Wen-858-66
New Drug and Antibiotic Regulations, 50 Fed. Reg. 7452 (February 22, 1985) (to be codified in 21 CFR pt. 71, 170, 171, 180, 201, 310, 312, 314, 330, 430, 431, 433, 510, 511, 514, 570, 571, 601, 812, 1003, and 1010).
(NIH Project No. 1R01AI097368-01A1 to Dr. Biao He, University of Georgia, titled Developing a Novel Mumps Vaccine)
NIH, "HHS-Licensed Products Approved by the FDA", available at https://www.ott.nih.gov/reportsstats/hhs-licensed-products-approved-fda .
NIH, Application of Notice of Award for Project Number 1R01AI097368-01A1, Developing a Novel Mumps Vaccine.
NIH, NIAID Emerging Infectious Diseases/Pathogen, available at https://www.niaid.nih.gov/research/emerging-infectious-diseases-pathogens.
NIH, Notice of Award for Project Number 1R01AI097368-01A1, Developing a Novel Mumps Vaccine, 2012 May 7, at p.26.

NIH, Project Information1R01AI097368-01A1, Research Portfolio Online Reporting Tools, https://projectreporter.nih.gov/project_info_description.cfm?aid=8371494&icde=38326202&ddparam=&ddvalue=&ddsub=&cr=14&csb=default&cs=ASC&pball=
Nojd, J., T. Tecle, A. Samuelsson and C. Orvell (2001). "Mumps virus neutralizing antibodies do not protect against reinfection with a heterologous mumps virus genotype." Vaccine 19(13-14): 1727-1731.
Norrby, E., A. A. Salmi, B. Vandvik, B. Hammarskjold and M. Panelius (1972). "The antibody response to different measles virus antigens under various conditions of immunization." Adv Exp Med Biol 31(0): 49-69.
NVIC, The National Childhood Vaccine Injury Act of 1986, available at http://www.nvic.org/injury-compensation/origihanlaw.aspx.
Ogbuanu, I. U. et al.: *Impact of a third dose of measles-mumps-rubella vaccine on a mumps outbreak* , Pediatrics, 130(6): 1567-74, (Dec.) 2012.
Ogra, P. L., Y. Chiba, K. R. Beutner and A. Morag (1976). "Vaccination by non-parenteral routes: characteristics of immune response." Dev Biol Stand 33: 19-26.
Orenstein, W. A., K. L. Herrmann, P. Holmgreen, R. Bernier, K. J. Bart, D. L. Eddins and N. J. Fiumara (1986). "Prevalence of rubella antibodies in Massachusetts schoolchildren." Am J Epidemiol 124(2): 290-298.
Orlíková et al, "Protective effect of vaccination against mumps complications, Czech Republic, 2007-2012." BMC Public Health. 2016 Apr 1;16:293. doi: 10.1186/s12889-016-2958-4.
Orvell, C. (1984). "The reactions of monoclonal antibodies with structural proteins of mumps virus." J Immunol 132(5): 2622-2629.
Örvell, C. (1988). Paramyxoviridae: Mumps Virus. Laboratory Diagnosis of Infectious Diseases Principles and Practice. . New York, NY, Springer: 507-524.
Orvell, C., T. Tecle, B. Johansson, H. Saito and A. Samuelson (2002). "Antigenic relationships between six genotypes of the small hydrophobic protein gene of mumps virus." J Gen Virol 83(Pt 10): 2489-2496.
Package Insert - Havrix, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM224555.pdf.
Package Insert - ProQuad Frozen HAS, available at https://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm123796.pdf.
Palgen, J. L., E. M. Jurgens, A. Moscona, M. Porotto and L. M. Palermo (2015). "Unity in diversity: shared mechanism of entry among paramyxoviruses." Prog Mol Biol Transl Sci 129: 1-32.
Park et al, "Mumps outbreak in a highly vaccinated school population: Assessment of secondary vaccine failure using IgG avidity measurements", Vaccine. 2007 Jun 11;25(24):4665-70. Epub 2007 Apr 24.
Park, M. S., J. I. Kim, S. Park, I. Lee and M. S. Park (2016). "Original Antigenic Sin Response to RNA Viruses and Antiviral Immunity." Immune Netw 16(5): 261-270.
Pawelczyk, M. and M. L. Kowalski (2017). "The Role of Human Parainfluenza Virus Infections in the Immunopathology of the Respiratory Tract." Curr Allergy Asthma Rep 17(3): 16.
Peltola, H. et al.: *Mumps Outbreaks in Canada and the United States* , Mumps Vaccines, Clinical Infectious Diseases, 45: 459-466, (Aug. 15) 2007.
Penttinen, K., V. Tommila and K. Cantell (1955). "The variation in the results of hemagglutination and hemagglutination inhibition tests with influenza and mumps viruses caused by the red cells of different fowls." Ann Med Exp Biol Fenn 33(1-2): 158-168.
Performance Standards Reporting Requirements for Essential Assays in Clinical PACCT_Assay_Standards_Document
Perrett, K. P., C. Jin, E. Clutterbuck, T. M. John, A. P. Winter, E. Kibwana, L. M. Yu, N. Curtis and A. J.
Persistence of mumps antibodies after 2 doses of measles-mumps-rubella vaccine
Peter R. Krause, Minimum Potency Throughout Dating and Lot Release Practices of Other Agencies/Countries, FDA, Apr. 21, 2015, available at http://www.cfsph.iastate.edu/IICAB/meetings/april2015/KrauseP.HumanVaccines.pdf.

Pindyck R., and D. Rubinfeld, *Microeconomics* , 8th Edition, Prentice Hall, 2013, Chapter 12.
Pipkin, P. A., M. A. Afzal, A. B. Heath and P. D. Minor (1999). "Assay of humoral immunity to mumps virus." J Virol Methods 79(2): 219-225.
Plotkin, "Commentary: Mumps vaccines: do we need a new one?" Pediatr Infect Dis J. 2013 Apr;32(4):381-2. doi: 10.1097/INF.0b013e3182809dda.
Plotkin, "History of vaccination", Proc Natl Acad Sci U S A. 2014 Aug 26;111(34):12283-7.
Plotkin, "The History of Rubella and Rubella Vaccination Leading to Elimination," Clinical Infectious Diseases, 2006, 43, Supplement 3, S164–S168.
Plotkin, S. A., D. Cornfeld and T. H. Ingalls (1965). "Studies of immunization with living rubella virus. Trials in children with a strain cultured from an aborted fetus." Am J Dis Child 110(4): 381-389.
Plotkin, S. A., J. Farquhar, M. Katz and T. H. Ingalls (1967). "A new attenuated rubella virus grown in human fibroblasts: evidence for reduced nasopharyngeal excretion." Am J Epidemiol 86(2): 468-477.
Plotkin, S.A. et al. *Nomenclature for Immune Correlates of Protection After Vaccination* . Clin Infect Dis. 2012;54(11):1615-1617. 10.1093/cid/cis238
Plotkin, Stanley A., et al., *Plotkin's Vaccines* (Elsevier, 7th ed. 2017).
Pocock, S. J., M. D. Hughes and R. J. Lee (1987). "Statistical problems in the reporting of clinical trials. A survey of three medical journals." N Engl J Med 317(7): 426-432.
Pollard (2012). "B cell memory to a serogroup C meningococcal conjugate vaccine in childhood and response to booster: little association with serum IgG antibody." J Immunol 189(5): 2673-2681.
Procedures for Review of Safety, Effectiveness, and Labeling, 37 Fed. Reg. 16679 (proposed Aug. 14, 1972) (to be codified at 21 CFR pt. 273).
Quinlisk, P. M. *Mumps Control Today* . J Infect Dis 2010;202(5):655-656. 10.1086/655395
Quintero-Del-Rio, G. Bautista, M. Povey, C. Da Costa, O. Nicholson and B. L. Innis (2015). "Safety and Immunogenicity of Human Serum Albumin-Free MMR Vaccine in US Children Aged 12-15 Months." J Pediatric Infect Dis Soc 4(4): 339-348.
Reisinger "A Combination Measles, Mumps, Rubella, and Varicella Vaccine (ProQuad) Given to 4- to 6-Year- Old Healthy Children Vaccinated Previously With M-M-RII and Varivax," Pediatrics, 2006 February 117(2)
Relationships Between Rhinitis Symptoms, Respiratory Viral Infections and Nasopharyngeal Colonization With Streptococcus pneumoniae, Haemophilus influenzae and Staphylococcus aureus in Children Attending Daycare: ERRATUM, Pediatr Infect Dis J 2013;32(6): 707.
Removal of Review and Reclassification Procedures for Biological Products Licensed Prior to July 1, 1972, 81 Fed. Reg. 7445 (February 12, 2016).
Request for Data and Information Regarding Safety, Effectiveness, and Labeling Review, 39 Fed. Reg 21176 (June 19, 1974).
Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922 (Jan. 24, 2006) (to be codified at 21 CFR pt. 201, 314, and 601).
Requirements on Content and Format of Labeling for Human Prescription Drugs and Biologics; Requirements for Prescription Drug Product Labels, 65 Fed. Reg. 81082 (proposed Dec. 22, 2000) (to be codified at 21 CFR pt. 201).
Review of Warnings, Use Instructions, and Precautionary Information. Pub.L. 99-660, Title III, § 314, Nov. 14, 1986, 100 Stat. 3782.
Revocation of Certain Regulations; Biological Products (Final Rule), 61 Fed. Reg. 40,153 (Aug. 1, 1996).
Revocation of Certain Regulations; Opportunity for Public Comment (Proposed Rules), 60 Fed. Reg. 53,480 (Oct. 13, 1995).
Reyes v. Wyeth Laboratories , 498 F.2d 1264 (5th Cir. 1974).

Rodewald L.E., W.A. Orenstein, D.D. Mason, and S.L. Cochi, "Vaccine Supply Problems: A Perspective of the Centers for Disease Control and Prevention," *Clinical Infectious Diseases* , Supplement Article, Vol. 42, 2006, pp. S104-S110.
Rodriguez et al, "Relationships Between Rhinitis Symptoms, Respiratory Viral Infections and Nasopharyngeal Colonization With Streptococcus pneumoniae, Haemophilus influenzae and Staphylococcus aureus in Children Attending Daycare", Pediatr Infect Dis J 2013;32: 227-232.
Rodriguez, K. R. and C. M. Horvath (2014). "Paramyxovirus V protein interaction with the antiviral sensor LGP2 disrupts MDA5 signaling enhancement but is not relevant to LGP2-mediated RLR signaling inhibition." J Virol 88(14): 8180-8188.
Ross, Christian H. "Stanley Alan Plotkin's Development of a Rubella Vaccine (1969)." Embryo Project Encyclopedia (2017-06-28). Available at https://embryo.asu.edu/pages/stanley-alan-plotkins-development-rubella-vaccine-1969.
Rotarix Package Insert, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM133539.pdf.
RotaTeq Package Insert, available at https://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm142288.
Rubin, "Response-Mumps Vaccines-Do We Need a New One", The Pediatric Infectious Disease Journal: October 2013 - Volume 32 - Issue 10 - p 1156-1157
Rubin, et al, Mumps Virus-Specific Antibody Titers from Pre-Vaccine Era Sera. J. Clin. Microbiol. 2005 Sep; 43(9):4847-51.
Rubin, S. A. et al.: *Recent Mumps Outbreaks in Vaccinated Populations: No Evidence of Immune Escape* , J Virol., 86(1): 615–620, (Jan.) 2012.
Rubin, S. A., L. Qi, S. A. Audet, B. Sullivan, K. M. Carbone, W. J. Bellini, P. A. Rota, L. Sirota and J. Beeler (2008). "Antibody induced by immunization with the Jeryl Lynn mumps vaccine strain effectively neutralizes a heterologous wild-type mumps virus associated with a large outbreak." J Infect Dis 198(4): 508-515.
Rubin, S. et al.: *Emerging Mumps Infection* , The Pediatric Infectious Disease Journal, 35(7): 799-801, (July) 2016.
Rubin, S., M. Eckhaus, L. J. Rennick, C. G. Bamford and W. P. Duprex (2015). "Molecular biology, pathogenesis and pathology of mumps virus." J Pathol 235(2): 242-252.
Sabbe, M. et al.: *The resurgence of mumps and pertussis* , Human Vaccines and Immunotherapeutics, 12(4): 955-9, (Apr. 2) 2016.
Sagonowsky E., "GSK exits U.S. market with its HPV vaccine Cervarix," October 21, 2016, available at https://www.fiercepharma.com/pharma/gsk-exits-u-s-market-its-hpv-vaccine-cervarix.
Sanofi Pasteur, History, available at http://www.sanofipasteur.us/ckfinder/userfiles/files/historyEN.pdf.
Sanofi Pasteur, Sanofi Pasteur and MSD End Joint Vaccines Business in Europe, Jan. 2, 2017, available at https://www.sanofipasteur.com/media/Project/One-Sanofi-Web/sanofipasteur-com/en/media-room/docs/PR_20170102_SanofiPasteurAndMSD_EN.pdf.
Santak, M., M. Markusic, M. L. Balija, S. K. Kopac, R. Jug, C. Orvell, J. Tomac and D. Forcic (2015). "Accumulation of defective interfering viral particles in only a few passages in Vero cells attenuates mumps virus neurovirulence." Microbes Infect 17(3): 228-236.
Santoli J.M., *et al.* , "Insurance Status and Vaccination Coverage among U.S. Preschool Children," *Pediatrics,* 113, no. 6 Supp., 2004 pp. 1959-1964.
Santos, E. M., G. R. Silva e Sa, M. M. Siqueira, M. Martins Rde, L. A. Camacho, R. von Doellinger Vdos and L. Maia Mde (2014). "Immune response to the mumps component of the MMR vaccine in the routine of immunisation services in the Brazilian National Immunisation Program." Mem Inst Oswaldo Cruz 109(3): 335-339.

Sanz, J. C., B. Ramos, A. Fernandez, L. Garcia-Comas, J. E. Echevarria and F. de Ory (2018). "Serological diagnosis of mumps: Value of the titration of specific IgG." Enferm Infecc Microbiol Clin 36(3): 172-174.
Sato, H., P. Albrecht, J. T. Hicks, B. C. Meyer and F. A. Ennis (1978). "Sensitive neutralization test for virus antibody. 1. Mumps antibody." Arch Virol 58(4): 301-311.
Sato, H., P. Albrecht, S. Krugman and F. A. Ennis (1979). "Sensitive neutralization test for rubella antibody." J Clin Microbiol 9(2): 259-265.
Sauder, C. J., K. M. Vandenburgh, R. C. Iskow, T. Malik, K. M. Carbone and S. A. Rubin (2006). "Changes in mumps virus neurovirulence phenotype associated with quasispecies heterogeneity." Virology 350(1): 48-57.
Schlegel, M. et al.: *Comparative efficacy of three mumps vaccines during disease outbreak in eastern Switzerland: cohort study,* British Med J., 319: 352-3, 1999.
Schmidt, M. E. and S. M. Varga (2017). "Modulation of the host immune response by respiratory syncytial virus proteins." J Microbiol 55(3): 161-171.
Schmitt, H. J., M. Just and A. Neiss (1993). "Withdrawal of a mumps vaccine: reasons and impacts." Eur J Pediatr 152(5): 387-388.
Schomacker, H., A. Schaap-Nutt, P. L. Collins and A. C. Schmidt (2012). "Pathogenesis of acute respiratory illness caused by human parainfluenza viruses." Curr Opin Virol 2(3): 294-299.
Schulz, K. F. (1995). "Subverting randomization in controlled trials." JAMA 274(18): 1456-1458.
Schulz, K. F., D. G. Altman, D. Moher and C. Group (2010). "CONSORT 2010 Statement: Updated guidelines for reporting parallel group randomised trials." J Clin Epidemiol 63(8): 834-840.
Schulz, K. F., I. Chalmers, R. J. Hayes and D. G. Altman (1995). "Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials." JAMA 273(5): 408-412.
Schwartz J.L., "The First Rotavirus Vaccine and the Politics of Acceptable Risk," *The Milbank Quarterly* , 90(2), June 2012, pp. 278-310.
Schwarze-Zander, C., R. Draenert, C. Lehmann, M. Stecher, C. Boesecke, S. Sammet, J. C. Wasmuth, U. Seybold, D. Gillor, U. Wieland, T. Kummerle, C. P. Strassburg, A. Mankertz, A. M. Eis-Hubinger, G. Jager, G. Fatkenheuer, J. R. Bogner, J. K. Rockstroh and J. J. Vehreschild (2017). "Measles, mumps, rubella and VZV: importance of serological testing of vaccine-preventable diseases in young adults living with HIV in Germany." Epidemiol Infect 145(2): 236-244.
Sensitive Hemagglutination Inhibition Test for Mumps Antibody, available at http://jcm.asm.org/content/13/5/870.full.pdf.
"Seqirus now shipping its complete portfolio of seasonal influenza vaccines to US market for the 2016-2017 season," available at http://www.seqirus-us.com/news-room/Seqirus-shipping-complete-portfolio-of-seasonal-vaccines-to-US-market.
Shah, V. P., K. K. Midha, S. Dighe, I. J. McGilveray, J. P. Skelly, A. Yacobi, T. Layloff, C. T. Viswanathan, C. E. Cook, R. D. McDowall and et al. (1991). "Analytical methods validation: bioavailability, bioequivalence and pharmacokinetic studies. Conference report." Eur J Drug Metab Pharmacokinet 16(4): 249-255.
Sheerin, D., P. J. Openshaw and A. J. Pollard (2017). "Issues in vaccinology: Present challenges and future directions." Eur J Immunol 47(12): 2017-2025.
Shinefield, "Dose-Response Study of a Quadrivalent Measles, Mumps, Rubella and Varicella Vaccine in Healthy Children," The Pediatric Infectious Disease Journal, 2005 August; 24(8)
Shinefield, "Evaluation of a Quadrivalent Measles, Mumps, Rubella and Varicella Vaccine in Healthy Children," The Pediatric Infectious Disease Journal, 2005 August; 24(8)
"Shingrix approved in the US for prevention of shingles in adults aged 50 and over," October 23, 2017, available at https://www.gsk.com/en-gb/media/press-releases/shingrix-approved-in-the-us-for-prevention-of-shingles-in-adults-aged-50-and-over/.

Shults RA, Williams AF. "Graduated Driver Licensing Night Driving Restrictions and Drivers Aged 16 or 17 Years Involved in Fatal Night Crashes - United States, 2009-2014." MMWR Morb Mortal Wkly Rep 2016;65:725-730. DOI: http://dx.doi.org/10.15585/mmwr.mm6529a1.
Siegrist C-A. Vaccine immunology. In: Plotkin SA, Orenstein WA, Offit PA, editors. Vaccines, sixth edition. Philadelphia (PA): Elsevier Saunders; 2012, Chapter 2.
Singer N., "In Wyeth, Pfizer Sees a Drug Pipeline," *The New York Times* , January 26, 2009 available at http://www.nytimes.com/2009/01/27/business/27wyeth.html.
Soleimanjahi, H., T. Bamdad, F. Fotouhi, M. H. Roustai and S. Faghihzadeh (2005). "Prevalence of HI antibody titer against rubella virus to determine the effect of mass vaccination in Tehran." J Clin Virol 34(2): 153-154.
Spearman, C. (1908). "The Method of "Right and Wrong Cases' (Constant Stimuli) without Gauss's Formulae." British Journal of Psychology 2: 227-242.
Stark, P.B., 2016. The value of P-values, The American Statistician, 70, DOI:10.1080/00031305.2016.1154108
Statement Regarding the Demonstrations of Effectiveness of Human Drug Products and Devices, 60 Fed Reg 39180 (Aug. 1, 1995).
Stokes, J., et al.: *Trivalent Combined Measles-Mumps-Rubella Vaccine, Findings in Clinical-Laboratory Studies* , J. Am. Med. Assoc., 218(1):57-61, (Oct 4) 1971.
Stokes, J., Jr., et al.: *Live Attenuated Mumps Virus Vaccine: 2. Early Clinical Studies* , Pediatrics, 39:363-371, (Mar) 1967.
Subchapter D – Drugs for Human Use: Reorganization and Republication, 39 Fed. Reg. 11680 (Mar. 29, 1974).
Subchapter F – Biologics: Reorganization and Republication, 38 Fed. Reg. 32048 (November 20, 1973).
Sullivan, K. M. et al.: *Effectiveness of Mumps Vaccine in a School Outbreak,* Am J Dis Children, 139(9): 909-12, (Sept.) 1985.
Sullivan, N. J. (2001). "Antibody-mediated enhancement of viral disease." Curr Top Microbiol Immunol 260: 145-169.
SUMMARY BASIS FOR REGULATORY ACTION, Sept. 11, 205, available at https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM462939.pdf.
SUMMARY FOR BASIS OF APPROVAL: ENGERIX-B, available at https://wayback.archive-it.org/7993/20170403230357/https:/www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM110155.pdf.
SUMMARY FOR BASIS OF APPROVAL: HAVRIX, available at http://wayback.archive-it.org/7993/20170723025041/https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM244562.pdf.
Swann, Regulatory considerations for development of bioanalytical assays for biotechnology products (2011)
Swedan, S., J. Andrews, T. Majumdar, A. Musiyenko and S. Barik (2011). "Multiple functional domains and complexes of the two nonstructural proteins of human respiratory syncytial virus contribute to interferon suppression and cellular location." J Virol 85(19): 10090-10100.
The Free Library, Merck & Co., Inc. and Kaketsuken Sign Agreement to Develop and Market Vaccines in Japan, Dec. 1, 1993, available at https://www.thefreelibrary.com/MERCK+%26+CO.%2c+INC.+AND+KAKETSUKEN+SIGN+AGREEMENT+TO+DEVELOP+AND+MARKET...-a014674685.
Thompson, M., et al. Harmonized Guidelines for Single-Laboratory Validation of Methods of Analysis, Pure Appl. Chem., 2002, 74(5):835-855.
Tirado, S. M. and K. J. Yoon (2003). "Antibody-dependent enhancement of virus infection and disease." Viral Immunol 16(1): 69-86.
Title III, National Childhood Vaccine Injury Act of 1986; Delegation of Authority, 53 Fed. Reg. 36127 (Sept. 16, 1988).

Tiwari, G. and R. Tiwari (2010). "Bioanalytical method validation: An updated review." Pharm Methods 1(1): 25-38.
Toscani, L. et al.: *Comparison of the Efficacy of Various Mumps Vaccine Strains: A Study Conducted in Schools,* Soz. Praventivmed, 41: 341-7, 1996.
Trent, D. (2015). The Regulatory Path to Vaccine Licensure. Vaccinology: An Essential Guide. G. B. Milligan, A.D.T: 212-230.
U.S. Department of Justice and the Federal Trade Commission, "Horizontal Merger Guidelines," August 19, 2010, pp. 1-34, available at https://www.ftc.gov/sites/default/files/attachments/merger-review/100819hmg.pdf.
Ubol, S. and S. B. Halstead (2010). "How innate immune mechanisms contribute to antibody-enhanced viral infections." Clin Vaccine Immunol 17(12): 1829-1835.
Ueda, *Development of measles vaccines in Japan* , Vaccine 27(2009): 3230-3231.
United States of America et al. v. Merck & Co. , No. 2:10-cv-04374-CDJ (E.D. Pa.), Amended Complaint for Violations of the Federal False Claims Act, at Dkt. No. 12.
United States vs. Barr Laboratories, Inc. , 812 F. Supp. 458 (D.N.J. 1993).
Update 1-Merck sells vaccine lab to PPD in research deal, REUTERS, Jan 5. 2009, available at https://www.reuters.com/article/ppd-merck/update-1-merck-sells-vaccine-lab-to-ppd-in-research-deal-idUSN0536976420090105.
Update on Mumps Epidemiology in the US for 2017 and Review of Published Studies of 3rd Dose MMR for Mumps Outbreak Control , CDC Advisory Committee on Immunization Practices (ACIP), June 21-22, 2017 Summary Report, 141-45.
Update on the Multi-State Mumps Outbreak in the United States , CDC Advisory Committee on Immunization Practices (ACIP), June 29-30, 2006 Record of the Proceedings, 73-6.
US National Library of Medicine, ClinicalTrials.gov listing identifier NCT00092391
USCFC, Appendix B, Vaccine Rules of the United States Court of Federal Claims, Aug. 1, 2017, available at https://www.uscfc.uscourts.gov/sites/default/files/170801VaccineRules.pdf.
USCFC, Vaccine Claims/Office of Special Masters, available at https://www.uscfc.uscourts.gov/vaccine-programoffice-special-masters.
Usonis, V., V. Bakasenas, A. Kaufhold, K. Chitour and R. Clemens (1999). "Reactogenicity and immunogenicity of a new live attenuated combined measles, mumps and rubella vaccine in healthy children." Pediatr Infect Dis J 18(1): 42-48.
Vaan de Kerk, D. J., M. H. Jansen, I. J. ten Berge, E. M. van Leeuwen and T. W. Kuijpers (2013). "Identification of B cell defects using age-defined reference ranges for in vivo and in vitro B cell differentiation." J Immunol 190(10): 5012-5019.
"Vaccine Timeline: Historic Dates and Events Related to Vaccines and Immunization," Immunization Action Coalition, available at http://www.immunize.org/timeline/.
Vaccines Licensed for Use in the United States, available at https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm093833.htm.
van Zelm, M. C. (2014). "B cells take their time: sequential IgG class switching over the course of an immune response?" Immunol Cell Biol 92(8): 645-646.
Vandermeulen et al, "Mumps outbreaks in highly vaccinated populations: What makes good even better?", Hum Vaccin. 2009 Jul;5(7):494-6.
Vandermeulen, C. et al.: *Detection of mumps virus-specific memory B cells by transfer of peripheral blood mononuclear cells into immune-deficient mice* , Immunology, 131(1): 33-39, (Sept.) 2010.
Vandermeulen, C., G. Leroux-Roels and K. Hoppenbrouwers (2009). "Mumps outbreaks in highly vaccinated populations: What makes good even better?" Hum Vaccin 5(7): 494-496.

Vandermeulen, C., L. Verhoye, S. Vaidya, F. Clement, K. E. Brown, K. Hoppenbrouwers and G. Leroux-Roels (2010). "Detection of mumps virus-specific memory B cells by transfer of peripheral blood mononuclear cells into immune-deficient mice." Immunology 131(1): 33-39.
Vatti, A., D. M. Monsalve, Y. Pacheco, C. Chang, J. M. Anaya and M. E. Gershwin (2017). "Original antigenic sin: A comprehensive review." J Autoimmun 83: 12-21.
Vidarsson, G. et al., *IgG Subclasses and Allotypes: From Structure to Effector Functions* , Front Immunol. 2014;5:520. doi: 10.3389/fimmu.2014.00520
Viral and Rickettsial Vaccines; Implementation of Efficacy Review, 47 Fed. Reg. 24696 (June 8, 1982) (to be codified at 21 CFR pt. 610 and 630).
Virus neutralization by antibodies. Vincent Racaniello. Virology Blog, 24 July 2009.
Vollmers, C., R. V. Sit, J. A. Weinstein, C. L. Dekker and S. R. Quake (2013). "Genetic measurement of memory B-cell recall using antibody repertoire sequencing." Proc Natl Acad Sci U S A 110(33): 13463-13468.
Vygen et al, "Waning immunity against mumps in vaccinated young adults, France 2013." Euro Surveill. 2016;21(10):30156. doi: 10.2807/1560-7917.ES.2016.21.10.30156.
"WAES*NET- Merck's International AE Reporting System," Judith A. Sromovsky, MS, Manager Worldwide Product Safety and Epidemiology, Merck & Co. Drug Information Journal, Vol 26, pp. 544-549, 1992, available at http://journals.sagepub.com/doi/abs/10.1177/009286159202600411?journalCode=dijb.
Walsh B., E. Doherty and C. O'Neill, "Since the Start of the Vaccines for Children Program, Uptake has Increased, and Most Disparities Have Decreased," *Health Affairs* , 35(2), February 2016, pp. 356-364.
Warning Letter from Deborah D. Ralston, Director, FDA Office of Regional Operations, to Dr. Roberta McKee, Vice-President of Vaccine & Sterile Quality Operations, Feb. 9, 2001, available at https://web.archive.org/web/20100311061607/http://www.fda.gov/downloads/ICECI/EnforcementActions/WarningLetters/2001/UCM078249.pdf.
Warning Letter to G.J. Brewer, M. D. University of Michigan Medical School, 14 January 2009, available at http://wayback.archive-it.org/7993/20170112063702/http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2009/ucm152450.htm.
Watson, "Safety and Immunogenicity of a Combined Live Attenuated Measles, Mumps, Rubella, and Varicella Vaccine (MMRIIV) in Healthy Children," The Journal of Infectious Diseases, 1996 March 173
Weibel, R. E. et al.: *Persistence of immunity following monovalent and combined live measles, mumps, and rubella vaccines* , Pediatrics, 51(3):467-475, (Mar) 1973.
Weibel, R. E., et al.: *Clinical and Laboratory Studies of Combined Live Measles, Mumps, and Rubella Vaccines using the RA 27/3 Rubella Virus (40979)* , Proc. Soc. Exp. Biol. Med., 165(2):323-326, 1980.
Weibel, R. E., et al.: *Live Attenuated Mumps Virus Vaccine: 3. Clinical and Serologic Aspects in a Field Evaluation* , New Eng J Med, 276(5):245-251 (Feb 2), 1967.
Weibel, R. E., et al.: *Long term follow-up for immunity after monovalent and combined live measles, mumps, and rubella vaccines* , Pediatrics, 56(3):380-387, (Sept) 1975.
Weibel, R. E., et al.: *Persistence of antibody after administration of monovalent and combined live measles, mumps, and rubella vaccines* , Pediatrics, 61(1):5-11, (Jan. 1) 1978.
Weibel, R. E., J. Stokes, Jr., E. B. Buynak, J. E. Whitman, Jr. and M. R. Hilleman (1967). "Live attenuated mumps-virus vaccine. 3. Clinical and serologic aspects in a field evaluation." N Engl J Med 276(5): 245-251.
Weibel, R. E., J. Stokes, Jr., E. B. Buynak, M. B. Leagus and M. R. Hilleman (1968). "Jeryl Lynn strain live attenuated mumps virus vaccine. Durability of immunity following administration." JAMA 203(1): 14-18.
Weibel, R.E., et al: *Evaluation of Live Attenuated Mumps Virus Vaccine, Strain Jeryl Lynn, First International Conference on Vaccines Against Viral and Rickettsial Diseases of Man, Washington, DC* , Pan American Health Organization Scientific Publication No.147, pp 430-437, (May) 1967.

Wellcare, “Comprehensive Formulary (List of Covered Drugs)” for Signature/Classic Prescription Drug Plans in New York, pp. I-50.
Wellington K., and K.L. Goa, “Measles, Mumps, Rubella Vaccine (Priorix™; GSK-MMR): A Review of its Use in the Prevention of Measles, Mumps and Rubella,” *Drugs* , 63(19), 2003, pp. 2107-2126.
Wen, S. C. and J. V. Williams (2015). "New Approaches for Immunization and Therapy against Human Metapneumovirus." Clin Vaccine Immunol 22(8): 858-866.
Wenner, H. A., A. Monley and M. H. Jenson (1952). "A study of infections caused by mumps and Newcastle disease viruses. II. Some properties of specific and non-specific serum hemagglutination inhibitor components." J Immunol 68(4): 357-368.
Wenner, H. A., M. H. Jenson and A. Monley (1952). "A study of infections caused by mumps and Newcastle disease viruses. I. Specific and non-specific serologic relations." J Immunol 68(4): 343-356.
Wharton, M. et al.: *A Large Outbreak of Mumps in the Postvaccine Era* , J Inf Diseases, 158(6): 1253-60, (Dec.) 1988.
Whelan et al, "Ongoing mumps outbreak in a student population with high vaccination coverage, Netherlands, 2010", Euro Surveill. 2010 Apr 29;15(17):pii=19554
Whitaker, "Measles and mumps outbreaks in the United States: Think globally, vaccinate locally," Vaccine, 2014 Aug 20;32(37):4703-4
Whitman, C. et al.: *Mumps Outbreak in a Highly Vaccinated Population in New York City* , NY State Pediatrician (Newsletter), 1998.
WHO (2007). Mumps virus vaccines, WHO position paper. Weekly Epidemiological Record. Geneva, Switzerland, World Health Organization. No. 7, 2007, 82: 49-60.
WHO (2016). Guidelines on clinical evaluation of vaccines: regulatory expectations. Geneva, Switzerland, World Health Organization. WHO TRS 924.
WHO Expert Committee on biological standardization, available at http://apps.who.int/iris/bitstream/10665/129494/1/TRS_987_eng.pdf?ua=1&ua=1.
WHO, WHO/KFDA Workshop on Stability Evaluation of Vaccines, Seoul, Republic of Korea, Apr. 23-25, 2008, available at http://www.who.int/biologicals/publications/meetings/areas/vaccines/stability/WHO-KFDA%20stability%20WHO-Web-Version%2030%20Mar%2009.pdf?ua=1.
Wiedmann, "M-M-R® II manufactured using recombinant human albumin (rHA) and M-M-R® II manufactured using human serum albumin (HSA) exhibit similar safety and immunogenicity profiles when administered as a 2-dose regimen to healthy children," Vaccine, 2015 March 18; 33
Williams, J. V. (2005). "The clinical presentation and outcomes of children infected with newly identified respiratory tract viruses." Infect Dis Clin North Am 19(3): 569-584.
Wilson, R. L., S. M. Fuentes, P. Wang, E. C. Taddeo, A. Klatt, A. J. Henderson and B. He (2006). "Function of small hydrophobic proteins of paramyxovirus." J Virol 80(4): 1700-1709.
Wood, L., M. Egger, L. L. Gluud, K. F. Schulz, P. Juni, D. G. Altman, C. Gluud, R. M. Martin, A. J. Wood and
World Health Organization, Mumps, http://www.who.int/biologicals/areas/vaccines/mmr/mumps/en/
Wu, H., L. Shi, Q. Wang, L. Cheng, X. Zhao, Q. Chen, Q. Jiang, M. Feng, Q. Li and D. Han (2016). "Mumps virus-induced innate immune responses in mouse Sertoli and Leydig cells." Sci Rep 6: 19507.
Wu, H., X. Zhao, F. Wang, Q. Jiang, L. Shi, M. Gong, W. Liu, B. Gao, C. Song, Q. Li, Y. Chen and D. Han (2017). "Mouse Testicular Cell Type-Specific Antiviral Response against Mumps Virus Replication." Front Immunol 8: 117.
Wyeth v. Levine , 555 US 555 (2009).
Xu, P., Z. Li, D. Sun, Y. Lin, J. Wu, P. A. Rota and B. He (2011). "Rescue of wild-type mumps virus from a strain associated with recent outbreaks helps to define the role of the SH ORF in the pathogenesis of mumps virus." Virology 417(1): 126-136.

Young, M. L., et al.: *Experiences with Jeryl Lynn Strain Live Attenuated Mumps Virus Vaccine in a Pediatric Outpatient Clinic* , Pediatrics, 40(5):798-803, (Nov) 1967.
Yung, C-F. et al.: *Mumps complications and effects of mumps vaccination, England and Wales, 2002-2006* , Emerging Infectious Disease, 17(4): 661-7, (Apr.) 2011.

Appendix D

Issue Timeline

This is not intended to be an exhaustive timeline, nor a full description in detail.
HIGHLY CONFIDENTIAL – ATTORNEYS' EYES ONLY

2/28/97
Merck submitted IND for ProQuad®.
MRK-KRA00145486

7/14/97
[redacted]
GSK-MMR- ND-0047687 at '688; GSK-MMR- ND-000221 at '221-222

12/18/97
[redacted].
GSK-MMR- ND-0047687 at '688; GSK-MMR- ND-0000018 at '166-168; GSK-MMR-IND-0000221 at '221-222; GSK-MMR- ND-0002235 at '236; GSK-MMR-IND-0047707 at '707-708

1997

1998

Potency Issue

ELISA Issue

Efficacy Issue

Merck Mumps Vaccines

MMRII Label Descrip.

MMRII Label Clinical Pharma

Merck INDS (Mumps Related)

BB IND 7068

GSK

Merck Statements

1997
Per CBER request, Merck conducted stability analysis to determine if could meet 4.3 log at end expiry
MRK-KRA01715116 at '128; MRK-KRA00587151

12/5/97
CBER's interpretation of the mumps potency claim in the MMRII label was an end expiry claim
MRK-KRA01972448 at '451

12/16/97
CBER requested a draft clinical protocol to support the end expiry clinical studies.
MRK-KRA00137711 at '713-714

1/23/98
Merck's stability analysis concluded that lots manufactured after 1994 predicted end expiry was 3.9 log, not 4.3 log
MRK-KRA00587151; MRK-KRA01715116

1/23/98
Merck proposed to CBER to lower end expiry claim to 3.7 log to ensure end expiry claim through 24 month shelf life
MRK-KRA00666494 at '525-526

2/3/98
As part of a marketing strategy, Merck initiated a "Head to Head" clinical trial comparing MMRII and Priorix.
MRK-KRA00667054; MRK-KRA00626121 at '122, '127; MRK-KRA00666494 at '559

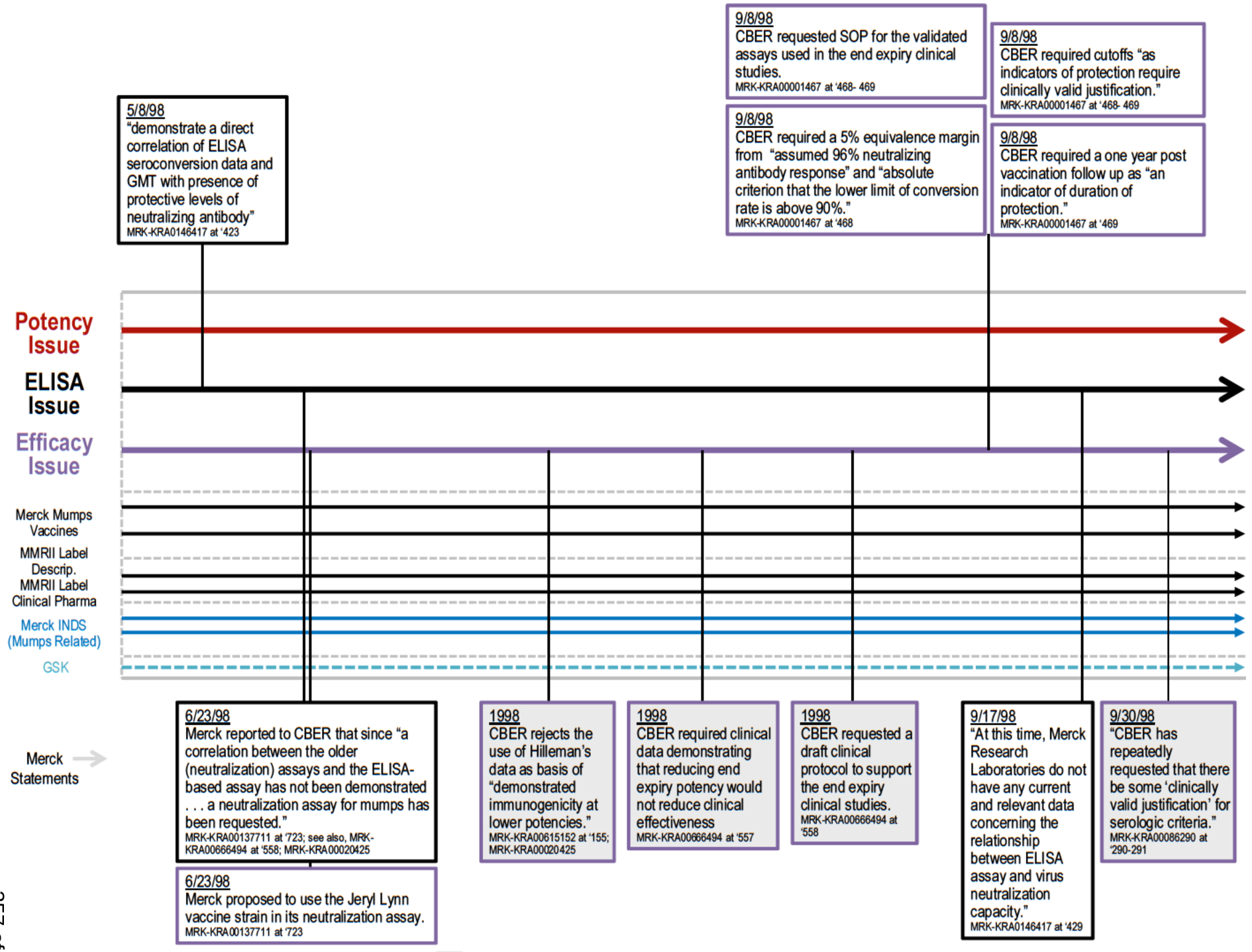
2/3/98
Merck stated: Important to test using neutralization assay because studies shown that ELISA results using vaccine strain may not correlate with results from neutralization assay, a clinically relevant assay.
MRK-KRA00667054 at '056-061

3/6/98
Merck senior management agreed "end expiry study is needed" and "necessary for regulatory purposes."
MRK-KRA00095320

3/6/98
Merck had "only limited clinical data" at 4.3 log and "no data" below 4.1 log.
MRK-KRA00095320

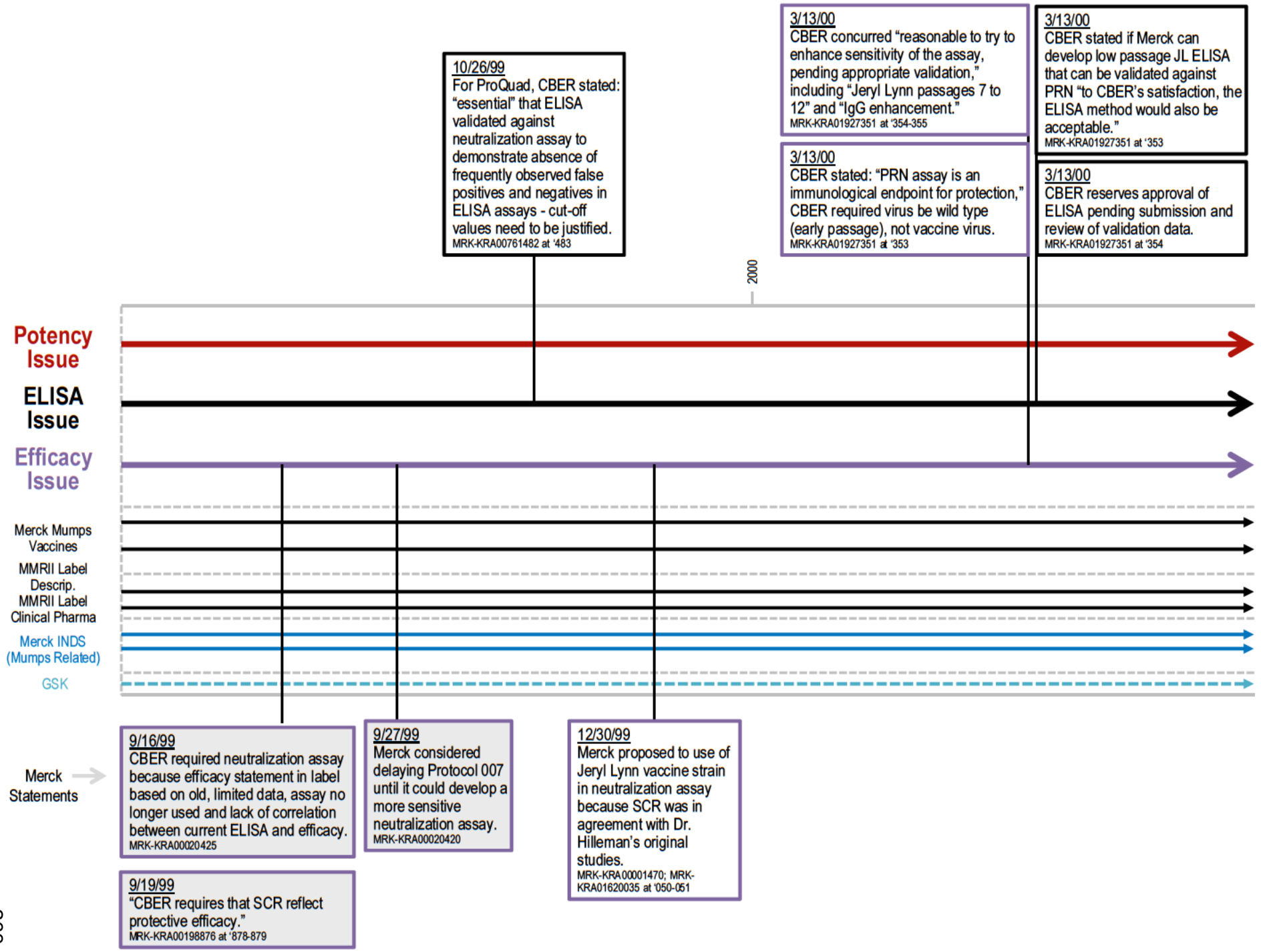
Key: Potency Issue ELISA Issue Efficacy Issue Internal Document

HIGHLY CONFIDENTIAL – ATTORNEYS' EYES ONLY



1/99
PIDJ article comparing immunogenicity between MMRII and Priorix.
GSK-MMR-0029832 at '832, '834
1999
Potency Issue
ELISA Issue
Efficacy Issue
Merck Mumps Vaccines
MMRII Label Descrip.
MMRII Label Clinical Pharma
Merck INDS (Mumps Related)
GSK
Merck Statements
11/18/98
"Neutralization assay necessary due to inability to re-establish clinical correlation."
MRK-KRA01731773 at '778
11/18/98
"Surrogate assay must be highly specific (100%) for WT neutralizing response."
MRK-KRA01731773 at '778
11/18/98
"Interested in protection against wild type, not vaccine strain."
MRK-KRA01731773 at '778
11/18/98
"CBER considers WT neutralizing antibody assay to be 'gold standard.'"
MRK-KRA01731773 at '779
12/10/98
Merck advised CBER that clinical study would evaluate a targeted end expiry titer of 3.7 log.
MRK-KRA00756233 at '235-236
12/10/98
Merck committed that until the clinical study was completed the end-expiry specification was 4.3 log
MRK-KRA00756233 at '235-236
12/10/98
Merck proposed to CBER to overfill mumps to provide "high level of assurance" expiry specification met through expiry.
MRK-KRA00756233 at '235-236; see also, MRK-KRA00018614
12/10/98
Merck represented to CBER overfill was an interim plan and would re-evaluate in "short interval" when clinical study data available.
MRK-KRA00756233 at '235-236; MRK-KRA00095144 at '144-45
Key: Potency Issue ELISA Issue Efficacy Issue Internal Document
HIGHLY CONFIDENTIAL – ATTORNEYS' EYES ONLY

HIGHLY CONFIDENTIAL – ATTORNEYS' EYES ONLY



Potency Issue
ELISA Issue
Efficacy Issue
Merck Mumps Vaccines
MMRII Label Descrip.
MMRII Label Clinical Pharma
Merck INDS (Mumps Related)
GSK
Merck Statements
8/20/00 CBER states avg. log loss 0.55 log plus variability .226 MRK-KRA00018614
10/11/00 Form 483 for failure to report pre-Sept.99 out of specification mumps lots MRK-KRA00071265 at '265-266
8/10/00 CBER: requested retrospective stability data to ensure meet 4.3 end expiry. MRK-KRA01522617
8/10/00 CBER: despite ongoing communications upcoming Team Biologics Inspection was a separate issue. MRK-KRA01522617
8/14/00 Team Biologics Inspections begins MRK-KRA00071265
10/11/00 Team Biologics Inspections ends MRK-KRA00071265
10/24/00 483 Response: Failures "within the expected range" "based on historical trends" and "a unique situation" MRK-KRA00784030 at '031-033
10/24/00 Provides to CBER "Statistical Analysis" ~.8 log loss (LB 95% CI) pre-Sept.99 MRK-KRA00756534 at '535-536
10/24/00 AIGENT objective: Target ≤10% pre-positive rate and ≥95% seroconversions MRK-KRA00026912 at '912, '915
10/26/00 "emergency" declared MRK-KRA00490081 at '472
11/22/00 CBER "expressed concern" re "apparent decline in mumps stability" MRK-KRA01727942 at '942-944
11/22/00 Options considered re stability issues: reduce shelf life; overfill; lower expiry to 3.7 log MRK-KRA01727942 at '942-944; MRK-KRA00562323 at '006
11/22/00 Preferred option lower end expiry based upon PRN preliminary subset analysis MRK-KRA01727942 at '944
11/29/00 CBER approved running preliminary subset analysis using an Anti-IgG if no changes to assay MRK-KRA00001218 at '218-219
Key: Potency Issue ELISA Issue Efficacy Issue Internal Document
HIGHLY CONFIDENTIAL – ATTORNEYS' EYES ONLY

2/9/01
Warning Letter: Products must meet spec. - not historical trend; requested efficacy and stability data for low potency lots.
https://web.archive.org/web/20100311061607/http://www.fda.gov/downloads/ICECI/EnforcementActions/WarningLetters/2001/UCM078249.pdf
2001
BB IND 10076
12/6/00
Krah begins running preliminary subset AIGENT sera
MRK-KRA00052242
12/14/00
"unacceptable risk of current product failure" - potentially culminating in recall or branding
MRK-KRA00590949 at '949-950
12/19/00
"Conclusion: even with new higher mumps target, compliance with labeled mumps potency may not be feasible"
MRK-KRA00562323 at '002
12/21/00
Even with overfill "may not be sufficient to maintain" end expiry specification.
MRK-KRA01727952 at '959-960
1/26/01
AIGENT preliminary subset data finished
MRK-KRA00052242
1/29/01
CBER: requested ELISA cutoff linked to a biologically relevant reference standard - correlate with PRN
MRK-KRA00818776
2/23/01
Warning Letter required "group effort": MMD and MRL to respond
MRK-KRA00549510 at '514
2/23/01
President informed: 223 lots below 4.3 pre Sept.99 - 106 lots considered a compliance issue
MRK-KRA00549510 at '510 –511
2/23/01
President informed: ~1.0 log loss over 24 months since Sept.99
MRK-KRA00549510 at '511–512
2/23/01
Proposed: retesting AIGENT sera with vaccine strain to "be reassured"; surveillance investigation; recall; revaccination large cohorts
MRK-KRA00549510 at '511–515
Potency Issue
ELISA Issue
Efficacy Issue
Merck Mumps Vaccines
MMRII Label Descrip.
MMRII Label Clinical Pharma
Merck INDS (Mumps Related)
GSK
Merck Statements
Key: Potency Issue ELISA Issue Efficacy Issue Internal Document
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Potency Issue
ELISA Issue
Efficacy Issue
Merck Mumps Vaccines
MMRII Label Descrip.
MMRII Label Clinical Pharma
Merck INDS (Mumps Related)
GSK
Merck Statements
2/25/01 AIGENT: "very artificial because of IgG" MRK-KRA00549464 at '471
2/27/01 Draft response to Warning Letter disclosing 223 lots projected ≤4.3 log and 1.0 log loss MRK-KRA00086295
2/27/01 95% confidence that each lot released will be ≥ 4.0 through expiry MRK-KRA01896072 at '072-073
2/28/01 Current product meets 4.0 log not 4.3 log. MRK-KRA01896072 at '072-073
3/2/01 Stability data not support current shelf life claim - must provide clinical data to decrease label claim MRK-KRA00086318
3/5/01 President updated: "optimistic" no action needed - no mass revaccination MRK-KRA00616007
3/5/01 BPDR for mumps lot 0628706: to ensure lots will meet 4.3 at expiry, the minimum specification was revised from 4.3 to 5.0 MRK-KRA00754239
3/6/01 Protocol 007 kids sera retested in PRN without IgG, AIGENT with vaccine strain, WT ELISA MRK-KRA00064825; MRK-KRA00026792; MRK-KRA00068391
3/8/01 Warning Letter response - no disclosure of 223 lots, no disclosure of 1 log loss, no disclosure of secret retesting – "actions taken to date comprehensively address all concerns" "implemented changes ... to ensure compliance" MRK-KRA01537603
3/8/01 Warning Letter Response: submitted preliminary subset data as evidence that MMRII is effective MRK-KRA01537603
Key: Potency Issue ELISA Issue Efficacy Issue Internal Document
HIGHLY CONFIDENTIAL – ATTORNEYS' EYES ONLY

6/01
Relator reports AIGENT issues to FDA
RELATOR00001044
8/6/01
CBER inspected AIGENT lab issued Form 483, including the changing raw data without justification
MRK-KRA01649971
3/12/01
Serial 63 submitted attaching preliminary subset results; correlation analysis; AIGENT validation analysis
MRK-KRA00017036
3/13/01
Current stability analysis projects 12 month shelf life with 4.3 log expiry
MRK-KRA00562218
4/4/01
Stability Issues Meeting with CBER: no disclosure of out of compliance projections, no 223 lots, no 1.0 log loss, no secret testing
MRK-KRA01649955
4/20/01
BPDR 01-005: 4 mumps lots out of specification - AIGENT results used to support no public health risk - Overfilled to ensure future compliance
MRK-KRA00754233
7/5/01
Protocol 007 to lower end expiry spec. "most expeditious and sound alternative"
MRK-KRA01896349
7/23/01
Can't meet 1 of the 2 FDA objectives for our annual program until the expiry spec is lowered to 4.0
MRK-KRA01977383 at '383
8/2/01
Current stability data not support end-expiry claim greater than 4.0 log
MRK-KRA00247149
8/20/01
483 AIGENT Response: committed to providing highest quality info, supported by sound science and well controlled practices and procedures
MRK-KRA00000481
Potency Issue
ELISA Issue
Efficacy Issue
Merck Mumps Vaccines
MMRII Label Descrip.
MMRII Label Clinical Pharma
Merck INDS (Mumps Related)
GSK
Merck Statements
Key: Potency Issue ELISA Issue Efficacy Issue Internal Document
HIGHLY CONFIDENTIAL – ATTORNEYS' EYES ONLY

12/7/01
CBER re AIGENT 483: data unacceptable
MRK-KRA00071082 at 083
12/7/01
Merck: "we would like to salvage the product and get a sense of the data"
MRK-KRA00071082 at 086
10/16/01
CBER OK to correlate WT ELISA and AIGENT data while waiting on 483 determination
MRK-KRA00561452
10/16/01
CBER requested individual titers around cutoff in PRN and ELISA to confirm categorizing in comparable fashion
MRK-KRA00561452
10/16/01
If continued uncertainty about biological/clinical relevance of cutoff, expected CBER to require 4-fold criterion – Merck's choice to use 4-fold criteria or correlate ELISA to PRN
MRK-KRA00561452
10/16/01
CBER requested "additional justification" for ELISA cutoffs - need to relate to protection - compare to PRN
MRK-KRA00561452
10/16/01
CBER: without reference standard for sero-protective level best can do is relate ELISA cutoff to acceptable biologically relevant cutoff-PRN
MRK-KRA00561452
9/28/01
If CBER required a ELISA cutoff 4-fold (<10Ab - ≥40Ab) then SCR range from 80.9%–85.2%
MRK-KRA00561416; MRK-KRA00561418
Potency Issue
ELISA Issue
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Merck INDS (Mumps Related)
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Merck Statements
Key: Potency Issue ELISA Issue Efficacy Issue Internal Document
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2002
Potency Issue
ELISA Issue
Efficacy Issue
Merck Mumps Vaccines
MMRII Label Descrip.
MMRII Label Clinical Pharma
Merck INDS (Mumps Related)
GSK
Merck Statements
1/11/02
CBER: "there is nothing really scientifically wrong" with AIGENT so despite AIGENT 483 willing to use as basis for discussion on ELISA cutoff
MRK-KRA00071388
1/11/02
ELISA cutoff linked to PRN
MRK-KRA00071388
1/18/02
"With some creative math ... the shelf life is about 15-16 months."
MRK-KRA00024008
1/21/02
"current release specification, approx. 7% of the lots are expected to be < 4.3 at expiry"
MRK-KRA00561350
1/22/02
Merck writing ProQuad study reports so "increasingly urgent" to reach closure on ELISA cutoff issue
MRK-KRA00071388
1/22/02
CRRC informed of misbranding concerns due to "product still not compliant with labeled mumps potency"
MRK-KRA00019085 at '004, '010, '014
2/4/02
Serial 80: represented "original" data is reliable and proposed use
MRK-KRA00000410 at '411
3/23/02
CBER accepted AIGENT data to support mumps expiry change
MRK-KRA00064005 at '012
4/8/02
Antonello's correlation analysis WT ELISA & AIGENT
MRK-KRA00544529; MRK-KRA00544540
4/10/02
Team Biologics Inspection of MMD found deficiencies for mumps and measles potency failures - concern with justification not to recall
MRK-KRA00784057
1/31/02
For ProQuad, CBER required justification for the ELISA be linked to a biologically relevant reference standard - requested results correlated to a neutralization assay.
MRK-KRA00818776 at '778
Key: Potency Issue ELISA Issue Efficacy Issue Internal Document
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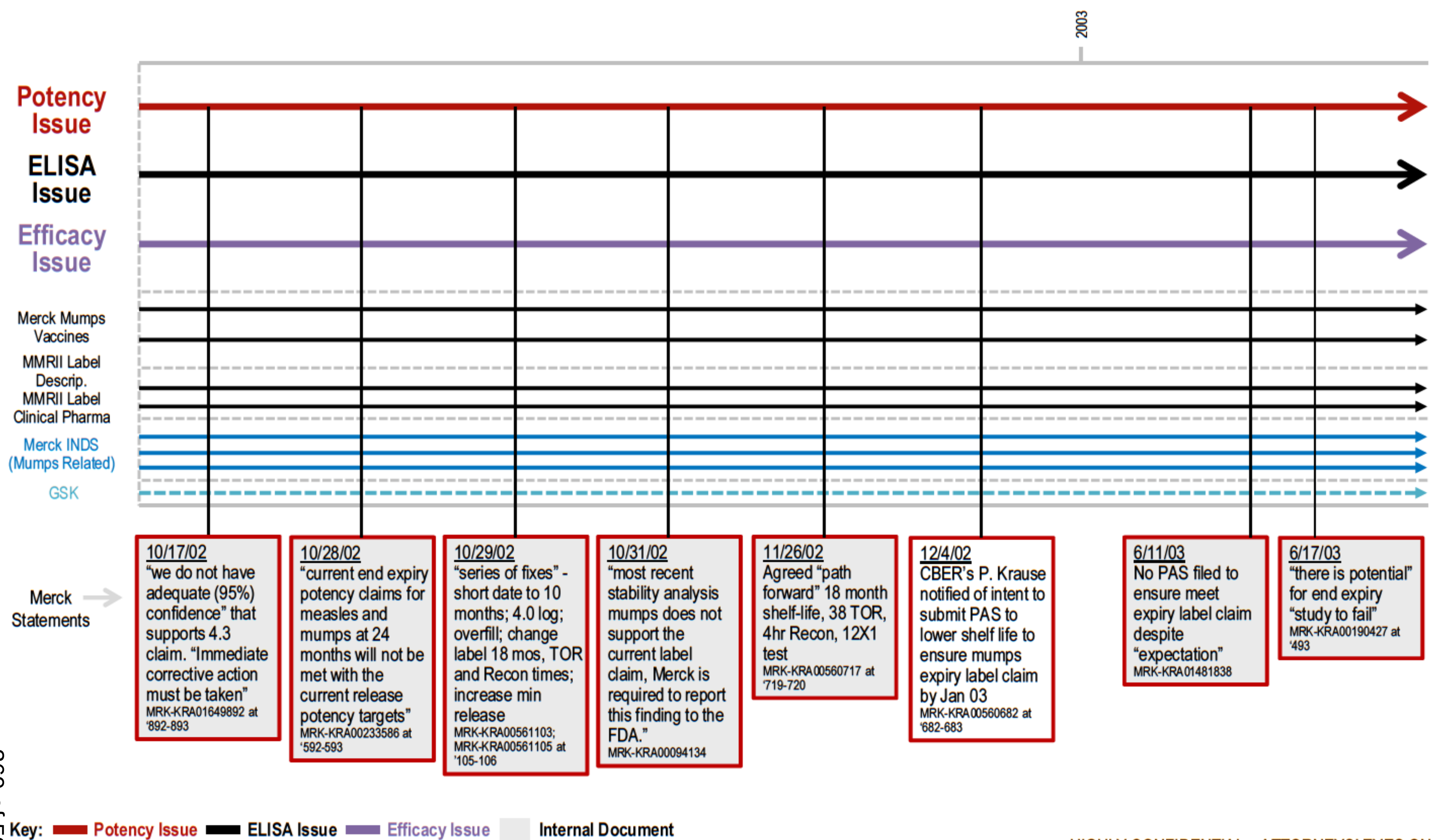
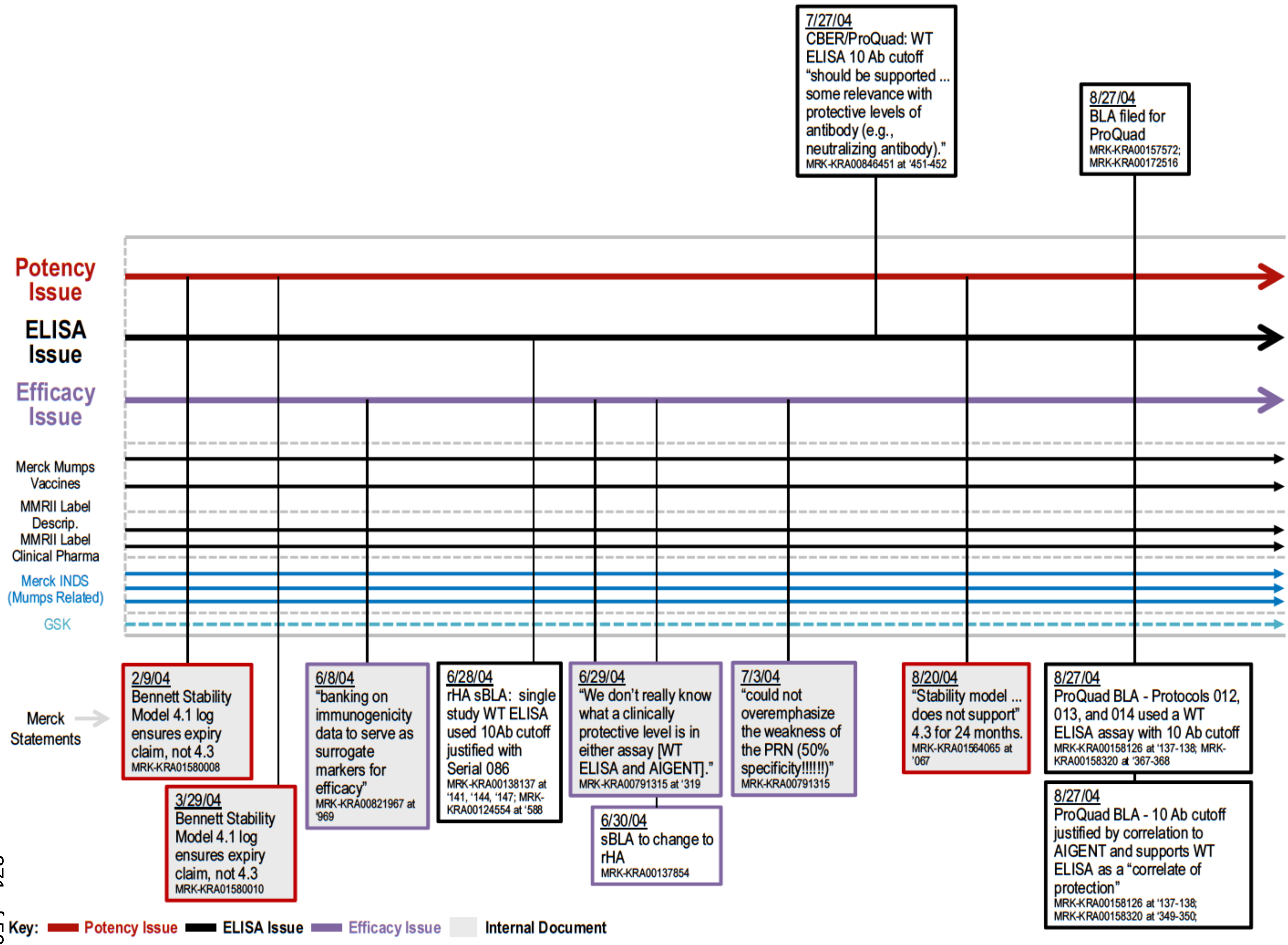
Potency Issue
ELISA Issue
Efficacy Issue
Merck Mumps Vaccines
MMRII Label Descrip.
MMRII Label Clinical Pharma
Merck INDS (Mumps Related)
GSK
Merck Statements
6/11/02
Serial 87: Requested testing for one year persistence and revaccinations be based solely on WT ELISA because "correlates well" to AIGENT
MRK-KRA00126540
7/16/02
"key issue" "current product does not meet expiry specifications"
MRK-KRA00498914 at '917
7/26/02
Proposed new stabilizer to "protect" franchise and "comply better" with specs
MRK-KRA00207690
7/26/02
Short-term stability fixes to maintain product on the market original issues identified in 1996 not fully addressed
MRK-KRA00207690
9/5/02
Maximum shelf life of 12 months – "This is what I was fearful of - 12 month will be unacceptable"
MRK-KRA01562819 at '820
9/5/02
"We have much larger problem … if we can only support 12 month."
MRK-KRA01562819 at '820
9/5/02
Decision to "wait" on follow up on mumps potency or stability issues until "4.0 was approved"
MRK-KRA01562819
9/5/02
Identified risk of new mumps potency failures without adequate corrective action – "We've been lucky" "only a matter of time" can predict "lots will fail"
MRK-KRA01562819
9/17/02
"No product since shelf life estimates reduce to less than 12 month."
MRK-KRA00501762 at '764
10/2/02
Success of end expiry study "at risk"
MRK-KRA00615152 at '155-156
Key: Potency Issue ELISA Issue Efficacy Issue Internal Document
HIGHLY CONFIDENTIAL – ATTORNEYS' EYES ONLY



HIGHLY CONFIDENTIAL – ATTORNEYS' EYES ONLY

HIGHLY CONFIDENTIAL – ATTORNEYS' EYES ONLY



HIGHLY CONFIDENTIAL – ATTORNEYS' EYES ONLY
Potency Issue
ELISA Issue
Efficacy Issue
Merck Mumps Vaccines
MMRII Label Descrip.
MMRII Label Clinical Pharma
Merck INDS (Mumps Related)
GSK
Merck Statements
2005
PROQUAD
3/30/05
CBER requests all run results not "most frequent observed results" regarding sera around WT ELISA cutoff
MRK-KRA00763902
12/3/04
CBER rejects end expiry study
MRK-KRA00000315 at 356-357
9/18/04
"end expiry of 20,000 [4.3] in their labels ... is wrong as we cannot guarantee this potency in our product"
MRK-KRA01574732 at 732-733
10/5/04
CBER requested data to support WT ELISA cutoff for seropositivity, relative to the AIGENT
MRK-KRA00846405
10/19/04
CBER previously requested WT ELISA seropositive cutoff be justified use of known mumps neutralizing and non-neutralizing sera, "was never provided"
MRK-KRA00846460
10/26/04
"PRN is ... correlate of protection.... We need to convince CBER that the ELISA will provide equivalent results to PRN and thus equate (bridge) to protection."
MRK-KRA00781533
11/4/04
Bennett Stability Model 4.1 log ensures expiry claim, not 4.3
MRK-KRA01580012
11/12/04
CBER requested analysis of WT ELISA predictive value in identifying sera tested positive in AIGENT. Merck did not provide new data nor analysis, referred CBER back to Serial 86.
MRK-KRA00155481
4/22/05
In response to CBER's 3/30/05 request: provide no "new" information to CBER
MRK-KRA00798644
4/27/05
Response to 3/30/05 CBER request, refers back to Serial 86.
MRK-KRA00779585 at 585-586
Key: Potency Issue ELISA Issue Efficacy Issue Internal Document

Schedule 1

Summary of MMRII Label Changes

LABEL CHANGES FOR M-M-R II[1]

M-M-R II [MEASLES, MUMPS, & RUBELLA VIRUS VACCINE LIVE]

The M-M-R-II vaccine (Measles, Rumps, & Rubella virus vaccine live) is a combination live virus vaccine for vaccination against measles (rubeola), mumps and rubella (German measles). It was approved by the FDA in 1978.[2] Since that time, there have been numerous labeling revisions to date regarding M-M-R II. A summary of relevant changes is provided below.

Following is a summary of label changes for M-M-R II (Measles, Mumps, & Rubella) beginning with selected relevant language from the earliest available version issued March 1, 1995:

- **March 1, 1995[3]:**
  a) In the DESCRIPTION section, the language, "When reconstituted as directed, the dose for injection is 0.5 mL and contains not less than the equivalent of 1,000 $TCID_{50}$ (tissue culture infectious doses) of the U.S. Reference Measles Virus; 20,000 $TCID_{50}$, of the U.S. Reference Mumps Virus; and 1,000 $TCID_{50}$ of the U.S. Reference Rubella Virus."
  b) In the CLINICAL PHARMACOLOGY section, the paragraph: "Clinical studies of 279 triple seronegative children, 11 months to 7 years of age, demonstrated that M-M-R-II is highly immunogenic and generally well tolerated. In these studies, a single injection of the vaccine induced measles hemagglutination-inhibition (HI) antibodies in 95 percent, mumps neutralizing antibodies in 96 percent, and rubella HI antibodies in 99 percent of susceptible persons."
  c) In the PRECAUTIONS section, the language, "As for any vaccine, vaccination with M-M-R II may not result in seroconversion in 100% of susceptible persons given the vaccine."
  d) In the DOSAGE AND ADMINISTRATION section, the language, "During shipment, to ensure that there is no loss of potency, the vaccine must be maintained at a temperature of 10°C (50°F) or less. Before reconstitution, store M-M-R II at 2 - 8°C (36 - 46°F). *Protect from light*."
  e) In the DOSAGE AND ADMINISTRATION section, the language, "Each dose contains not less than the equivalent of 1,000 $TCID_{50}$ of the U.S. Reference Measles Virus, 20,000 $TCID_{50}$ of the US. Reference Mumps Virus and 1,000 $TCID_{50}$ of the U.S. Reference Rubella Virus."

[1] This is not intended to be an exhaustive history of changes, nor a full description in detail.
[2] U.S. Vaccines & Immunizations, available at https://www.cdc.gov/vaccines/terms/usvaccines.html
[3] March 1, 1995 Label, MRK-KRA00757060

f) In the HOW SUPPLIED section, under the subheading titled *Storage*, "It is recommended that the vaccine be used as soon possible after reconstitution. Protect vaccine from light at all times, since such exposure may inactivate the virus. Store reconstituted vaccine in the vaccine vial in a dark place at 2 - 8°C (36 - 46°F) and discard if not used within 8 hours."

- **April 1, 1999**[4]**:**
  a) In the DESCRIPTION section, there was an addition of language describing the growth medium for measles and mumps, Medium 199.
  b) In the DESCRIPTION section, the addition of a paragraph stating that, "The cells, virus pools, fetal bovine serum, and human albumin are all screened for the absence of adventitious agents. Human albumin is processed using the Cohn cold ethanol fractionation procedure."
  c) In the DESCRIPTION section, the paragraph describing the contents of each dose of the vaccine was modified to specify the amount of sorbitol and hydrolized gelatin in each injection dose, and to include other ingredients that were not listed in the previously approved label.
  d) In the CLINICAL PHARMACOLOGY section, the addition of an introductory paragraph stating that measles, mumps and rubella are three common childhood diseases that may be associated with serious complications and/or death.
  e) In the CLINICAL PHARMACOLOGY section, there was an addition of the statement that a small percentage (1-5%) of vaccines may fail to seroconvert after the primary dose.
  f) In the CLINICAL PHARMACOLOGY section, the addition of a paragraph regarding how efficacy of the vaccine was established.
  g) In the CLINICAL PHARMACOLOGY section, the modification of language regarding antibody persistence.
  h) In the INDICATIONS AND USAGE section, language regarding the recommended vaccination schedule was modified and placed under a new subheading accordingly titled *Recommended Vaccination Schedule*.
  i) In the INDICATIONS AND USAGE section, language regarding the measles component of the vaccine was modified and placed under a new subheading titled *Measles Outbreak Schedule, Infants Between 6-12 Months of Age*.
  j) In the INDICATIONS AND USAGE section, under the subheading *Other Populations*, the addition of language regarding susceptible individuals in high-risk groups.
  k) In the CONTRAINDICATIONS section, a modification was made to the entry for febrile respiratory illness or other active febrile infection.

[4] April 1, 1999 Label, MRK-KRA00757072

l) In the PRECAUTIONS section, there was a change in language from "may not result in seroconversion" to "may not result in protection."
m) The ADVERSE REACTIONS section was reorganized with some modifications to language and there was an addition of new paragraphs under the subheading *Other*.
n) In the ADVERSE REACTIONS section, there was a change to language regarding burning and/or stinging at the injection site. The words "of short duration" were removed. The language was also moved from a single sentence in the opening paragraph of the entire section to a new subheading titled *Skin* near the end of the section.
o) The *Use With Other Vaccines* subsection was rewritten with minor changes and moved from the INDICATIONS AND USAGE section to the DOSAGE AND ADMINISTRATION section.
p) In the HOW SUPPLIED section, under the subheading *Storage*, the addition of language regarding freezing during shipment.

- **October 1, 2000[5]:**
  a) In the WARNINGS section, the addition of language regarding the use of albumin.

- **September 1, 2002[6]:**
  a) In the INDICATIONS AND USAGE section under *Recommended Vaccination Schedule*, there was a change in language regarding revaccination.

- **February 1, 2006[7]:**
  a) In the DESCRIPTION section, there was a change in the composition of the stabilizer used in the growth medium. Human albumin was replaced with recombinant human albumin.
  b) In the CLINICAL PHARMACOLOGY section there was a change in the number of children who participated in clinical studies.
  c) In the INDICATIONS AND USAGE section under *Post-Exposure Vaccination*, the references to "individuals exposed to natural mumps" were replaced with references to "individuals exposed to wild-type mumps."

[5] October 1, 2000 Label, MRK-KRA00757064
[6] September 1, 2002 Label, MRK-KRA00757096
[7] February 1, 2006 Label, MRK-KRA00757081

- **February 1, 2007**[8]**:**
  a) In the ADVERSE REACTIONS section under *Respiratory System*, there was an addition of Pneumonia to the list.

- **December 1, 2007**[9]**:**
  a) In the DESCRIPTION section, the mumps potency claim was reduced with the language changed to indicate that each 0.5 mL dose of the vaccine contains not less than 12,500 $TCID_{50}$ of mumps virus.

- **September 1, 2009**[10]**:**
  a) Format change. The addition of a patient information column printed parallel to the label titled "**Patient Information about M-M-R II (pronounced "em ar too") Generic name: Measles, Mumps, and Rubella Virus Vaccine Live**", containing a summary of information about M-M-R II. This column could be torn off from the label and contained the following subject headings:

     What is M-M-R II and how does it work?
     What do I need to know about measles, mumps, and rubella?
     Who should not get M-M-R II?
     How is M-M-R II given?
     What are the possible side effects of M-M-R II?
     What are the ingredients of M-M-R II?
     What else should I know about M-M-R II?

- **March 1, 2010**[11]**:**
  a) In the HOW SUPPLIED section under the subheading *Storage*, the modification of language regarding avoiding loss of potency.

- **February 1, 2014**[12]**:**
  a) Format change. Removal of the patient information column from previous approved version. Label reverted to the approved format prior to changes that were made in March 2010. "**Patient Information about M-M-R II Generic name: Measles, Mumps, and Rubella Virus Vaccine Live**" now printed as a separate leaflet.

[8] February 1, 2007 Label, MRK-KRA00757104
[9] December 1, 2007 Label, MRK-KRA00757100
[10] September 1, 2009 Label, MRK-KRA01449292
[11] March 1, 2010 Label, MRK-KRA01449276
[12] February 1, 2014 Label, MRK-KRA01449226

Following is a detailed review of selected label changes for M-M-R II (Measles, Mumps, & Rubella:

I. April 1, 1999 Label Changes

1. In the DESCRIPTION section, there was an addition of language describing the growth medium for measles and mumps, Medium 199.

DESCRIPTION	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	The growth medium for measles and mumps is Medium 199 (a buffered salt solution containing vitamins and amino acids and supplemented with fetal bovine serum) containing SPGA (sucrose, phosphate, glutamate, and recombinant human albumin) as stabilizer and neomycin.

2. In the DESCRIPTION section, the addition of a paragraph stating that, "The cells, virus pools, fetal bovine serum, and human albumin are all screened for the absence of adventitious agents. Human albumin is processed using the Cohn cold ethanol fractionation procedure."

DESCRIPTION	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	The cells, virus pools, fetal bovine serum, and human albumin are all screened for the absence of adventitious agents. Human albumin is processed using the Cohn cold ethanol fractionation procedure.

3. In the DESCRIPTION section, the paragraph describing the contents of each dose of the vaccine was modified to specify the amount of sorbitol and hydrolized gelatin in each injection dose, and to include other ingredients that were not listed in the previously approved label.

DESCRIPTION	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
The reconstituted vaccine is for subcutaneous administration. When reconstituted as directed, the dose for injection is 0.5mL and contains not less than the equivalent of 1,000 $TCID_{50}$ (tissue culture infectious doses) of the U.S. Reference Measles Virus; 20,000 $TCID_{50}$ of the U.S. Reference Mumps Virus; and 1,000 $TCID_{50}$ of the U.S. Reference	The reconstituted vaccine is for subcutaneous administration. Each 0.5 mL dose contains not less than 1,000 $TCID_{50}$ (tissue culture infectious doses) of measles virus; 20,000 $TCID_{50}$ of mumps virus; and 1,000 $TCID_{50}$ of rubella virus. Each dose of the vaccine is calculated to contain sorbitol (14.5 mg), sodium phosphate, sucrose (1.9 mg), sodium chloride, hydrolyzed gelatin (14.5 mg), human albumin (0.3 mg), fetal bovine serum (<1 ppm),

Rubella Virus. Each dose contains approximately 25 mcg of neomycin. The product contains no preservative. Sorbitol and hydrolized gelatin are added as stabilizers.	other buffer and media ingredients and approximately 25 mcg of neomycin. The product contains no preservative.

4. In the CLINICAL PHARMACOLOGY section, the addition of an introductory paragraph stating that measles, mumps and rubella are three common childhood diseases that may be associated with serious complications and/or death.

CLINICAL PHARMACOLOGY	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	Measles, mumps, and rubella are three common childhood diseases, caused by measles virus, mumps virus (paramyxoviruses), and rubella virus (togavirus), respectively, that may be associated with serious complications and/or death. For example, pneumonia and encephalitis are caused by measles. Mumps is associated with aseptic meningitis, deafness and orchitis; and rubella during pregnancy may cause congenital rubella syndrome in the infants of infected mothers.

5. In the CLINICAL PHARMACOLOGY section, there was an addition of the statement that a small percentage (1-5%) of vaccines may fail to seroconvert after the primary dose.

CLINICAL PHARMACOLOGY	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Clinical studies of 279 triple seronegative children, 11 months to 7 years of age, demonstrated that M-M-R II is highly immunogenic and generally well tolerated. In these studies, a single injection of the vaccine induced measles hemagglutination-inhibition (HI) antibodies in 95%, mumps neutralizing antibodies in 96%, and rubella HI antibodies in 99% of susceptible persons.	Clinical studies of 279 triple seronegative children, 11 months to 7 years of age, demonstrated that M-M-R II is highly immunogenic and generally well tolerated. In these studies, a single injection of the vaccine induced measles hemagglutination-inhibition (HI) antibodies in 95%, mumps neutralizing antibodies in 96%, and rubella HI antibodies in 99% of susceptible persons. <u>However, a small percentage (1-5%) of vaccinees may fail to seroconvert after the primary dose</u> (see also INDICATIONS AND USAGE, *Recommended Vaccination Schedule*).

6. In the CLINICAL PHARMACOLOGY section, the addition of a paragraph regarding how efficacy of the vaccine was established.

CLINICAL PHARMACOLOGY	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	Efficacy of measles, mumps and rubella vaccine was established in a series of double-blind controlled field trials which demonstrated a high degree of protective efficacy afforded by the individual vaccine components. These studies also established that seroconversion in response to vaccination against measles, mumps and rubella paralleled protection from these diseases.

7. In the CLINICAL PHARMACOLOGY section, the modification of language regarding antibody measurement and persistence.

CLINICAL PHARMACOLOGY	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Vaccine induced antibody levels following administration of M-M -R II have been shown to persist up to 11 years without substantial decline. Continued surveillance will be necessary to determine further duration of antibody persistence.	Following vaccination, antibodies associated with protection can be measured by neutralization assays, HI or ELISA (enzyme linked immunosorbent assay) tests. Neutralizing and ELISA antibodies to measles, mumps and rubella viruses are still detectable in most individuals 11-13 years after primary vaccination.

8. In the INDICATIONS AND USAGE section, language regarding the recommended vaccination schedule was modified and placed under a new subheading accordingly titled *Recommended Vaccination Schedule*.

INDICATIONS AND USAGE	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
M-M-R II is indicated for simultaneous immunization against measles, mumps, and rubella in persons 15 months of age or older. A second dose of M-M-R II or monovalent measles vaccine is recommended (see *Revaccination*).	M-M-R II is indicated for simultaneous vaccination against measles, mumps, and rubella in individuals 12 months of age or older. Individuals first vaccinated at 12 months of age or older should be revaccinated prior to elementary school entry. Revaccination is intended to seroconvert those who do not respond to the first dose. The Advisory Committee on Immunization Practices (ACIP) recommends administration of the first dose of M-M-R II at 12 to 15 months of age and administration of the second dose of M-M-R II at 4 to 6 years of age. In addition, some public health jurisdictions mandate the age for

	revaccination. Consult the complete text of applicable guidelines regarding routine revaccination including that of high-risk adult populations.

9. In the INDICATIONS AND USAGE section, language regarding the measles component of the vaccine was modified and placed under a new subheading titled *Measles Outbreak Schedule, Infants Between 6-12 Months of Age*.

INDICATIONS AND USAGE	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Infants who are less than 15 months of age may fail to respond to the measles component of the vaccine due to presence in the circulation of residual measles antibody of material origin, the younger the infant, the lower the likelihood of seroconversion. In geographically isolated or other relatively inaccessible populations for whom immunization programs are logistically difficult, and in population groups in which natural measles infection may occur in a significant proportion of infants before 15 months of age, it may be desirable to give the vaccine to infants at an earlier age. Infants vaccinated under these conditions at less than 12 months of age should be revaccinated after reaching 15 months of age. There is some evidence to suggest that infants immunized at less than one year of age may not develop sustained antibody levels when later reimmunized. The advantage of early protection must be weighed against the chance for failure to respond adequately on reimmunization.	Local health authorities may recommend measles vaccination of infants between 6 to 12 months of age in outbreak situations. This population may fail to respond to the components of the vaccine. Safety and effectiveness of mumps and rubella vaccine in infants less than 12 months of age have not been established. The younger the infant, the lower the likelihood of seroconversion (see CLINICAL PHARMACOLOGY). Such infants should receive a second dose of M-M-R II between 12 to 15 months of age followed by revaccination at elementary school entry.

10. In the INDICATIONS AND USAGE section, under the subheading *Other Populations*, the addition of language regarding susceptible individuals in high-risk groups.

INDICATIONS AND USAGE	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	Vaccination is recommended for susceptible individuals in high-risk groups such as college students, health-care workers, and military personnel.

11. In the CONTRAINDICATIONS section, a modification was made to the entry for febrile respiratory illness or other active febrile infection.

CONTRAINDICATIONS	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Any febrile respiratory illness or other active febrile infection.	Febrile respiratory illness or other active febrile infection. However, the ACIP has recommended that all vaccines can be administered to persons with minor illnesses such as diarrhea, mild upper respiratory infection with or without low-grade fever, or other low-grade febrile illness.

12. In the PRECAUTIONS section, there was a change in language from "may not result in seroconversion" to "may not result in protection."

PRECAUTIONS	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
As for any vaccine, vaccination with M-M-R II may not result in seroconversion in 100% of susceptible persons given the vaccine.	As for any vaccine, vaccination with M-M-R II may not result in protection in 100% of vaccinees.

13. The ADVERSE REACTIONS section was reorganized with some modifications to language and there was an addition of new paragraphs under the subheading *Other*.

ADVERSE REACTIONS	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	Death from various, and in some cases unknown, causes has been reported rarely following vaccination with measles, mumps, and rubella vaccines; however, a causal relationship has not been established. No deaths or permanent sequelae were reported in a published post-marketing surveillance study in Finland involving 1.5 million children and adults who were vaccinated with M-M-R II during 1982 - 1993. Under the National Childhood Vaccine Injury Act of 1986, health-care providers and manufacturers are required to record and report certain suspected adverse events occurring within specific time periods after vaccination. However, the U.S. Department of Health and Human Services (DHHS) has established a Vaccine Adverse Event Reporting System (VAERS) which will accept all reports of suspected events. A VAERS report form as well as information regarding reporting

	requirements can be obtained by calling VAERS 1-800-822-7967.

14. In the ADVERSE REACTIONS section, there was a change to language regarding burning and/or stinging at the injection site. The words "of short duration" were removed. The language was also moved from a single sentence in the opening paragraph of the entire section to a new subheading titled *Skin* near the end of the section.

ADVERSE REACTIONS	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Burning and/or stinging of short duration at the injection site have been reported.	Stevens-Johnson syndrome; erythema multiforme; urticaria; rash. Local reactions including burning/stinging at injection site; wheal and flare; redness (erythema); swelling; induration; tenderness; vesiculation at injection site.

15. In the HOW SUPPLIED section, under the subheading *Storage*, the addition of language regarding freezing during shipment.

HOW SUPPLIED	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	Freezing during shipment will not affect potency.

II. October 1, 2000 Label Changes

1. In the WARNINGS section, the addition of language regarding the use of albumin.

WARNINGS	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	"This product contains albumin a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases. Although there is a theoretical risk for transmission of Creutzleidt-Jacob disease (CJD), no cases of transmission of CJD or viral disease have ever been identified that were associated with the use of albumin."

III. September 1, 2002 Label Changes

1. In the INDICATIONS AND USAGE section under the subheading *Recommended Vaccination Schedule*, there was a change in language regarding revaccination.

INDICATIONS AND USAGE	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Revaccination may seroconvert primary failures or boost antibody titers of previously vaccinated individuals whose titers have declined.	Revaccination is intended to seroconvert those who do not respond to the first dose.

IV. February 1, 2006 Label Changes

1. In the DESCRIPTION section, there was a change in the composition of the stabilizer used in the growth medium. Human albumin was replaced with recombinant human albumin.

DESCRIPTION	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
The growth medium for measles and mumps is Medium 199 (a buffered salt solution containing vitamins and amino acids and supplemented with fetal bovine serum) containing SPGA (sucrose, phosphate, glutamate, and <u>human albumin</u>) as stabilizer and neomycin.	The growth medium for measles and mumps is Medium 199 (a buffered salt solution containing vitamins and amino acids and supplemented with fetal bovine serum) containing SPGA (sucrose, phosphate, glutamate, and <u>recombinant human albumin</u>) as stabilizer and neomycin.

2. In the CLINICAL PHARMACOLOGY section, there was a change in the number of children participating in clinical studies.

CLINICAL PHARMACOLOGY	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Clinical studies of 279 triple seronegative children, 11 months to 7 years of age, demonstrated that M-M-R II is highly immunogenic and generally well tolerated. In these studies, a single injection of the vaccine induced measles hemagglutination-inhibition (HI) antibodies in 95%, mumps neutralizing antibodies in 96%, and rubella HI antibodies in 99% of susceptible persons. However, a small percentage (1-5%) of vaccinees may fail to seroconvert after the primary dose (see also	Clinical studies of 284 triple seronegative children, 11 months to 7 years of age, demonstrated that M-M-R II is highly immunogenic and generally well tolerated. In these studies, a single injection of the vaccine induced measles hemagglutination-inhibition (HI) antibodies in 95%, mumps neutralizing antibodies in 96%, and rubella HI antibodies in 99% of susceptible persons. However, a small percentage (1-5%) of vaccinees may fail to seroconvert after the primary dose (see also INDICATIONS AND USAGE, *Recommended Vaccination Schedule*).

INDICATIONS AND USAGE, *Recommended Vaccination Schedule*).	

3. In the INDICATIONS AND USAGE section under *Post-Exposure Vaccination*, the references to "individuals exposed to natural mumps" were replaced with references to "individuals exposed to wild-type mumps."

INDICATIONS AND USAGE	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Vaccination of individuals exposed to natural measles may provide some protection if the vaccine can be administered within 72 hours of exposure. If, however, vaccine is given a few days before exposure, substantial protection may be afforded. There is no conclusive evidence that vaccination of individuals recently exposed to natural mumps or natural rubella will provide protection.	Vaccination of individuals exposed to wild-type measles may provide some protection if the vaccine can be administered within 72 hours of exposure. If, however, vaccine is given a few days before exposure, substantial protection may be afforded. There is no conclusive evidence that vaccination of individuals recently exposed to wild-type mumps or wild-type rubella will provide protection.

V. December 1, 2007 Label Changes

1. In the DESCRIPTION section, the mumps potency claim was reduced with the language changed to indicate that each 0.5 mL dose of the vaccine contains not less than 12,500 $TCID_{50}$ of mumps virus.

DESCRIPTION	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
The reconstituted vaccine is for subcutaneous administration. Each 0.5 mL dose contains not less than 1,000 $TCID_{50}$ (tissue culture infectious doses) of measles virus; 20,000 $TCID_{50}$ of mumps virus; and 1,000 $TCID_{50}$ of rubella virus.	The reconstituted vaccine is for subcutaneous administration. Each 0.5 mL dose contains not less than 1,000 $TCID_{50}$ (tissue culture infectious doses) of measles virus; 12,500 $TCID_{50}$ of mumps virus; and 1,000 $TCID_{50}$ of rubella virus.

VI. March 1, 2010 Label Changes

1. In the HOW SUPPLIED section under the subheading *Storage*, the modification of language regarding avoiding loss of potency.

HOW SUPPLIED	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
During shipment, to ensure that there is no loss of potency, the vaccine must be maintained at a temperature of 10°C (50°F) or colder. Freezing during shipment will not affect potency of the vaccine.	To maintain potency, M-M-R II must be stored between -58°F and +46°F (-50°C to +8°C). Use of dry ice may subject M-M-R II to temperatures colder than -58°F (-50°C).

Schedule 2

Summary of ProQuad Label Changes

LABEL CHANGES FOR PROQUAD[1]

ProQuad [Measles, Mumps, Rubella and Varicella (Oka/Merck) Virus Vaccine Live]

ProQuad is the trade name of a combined attenuated live virus vaccine containing measles, mumps, rubella, and varicella viruses. The original formulation of ProQuad provided for frozen storage of the product and was approved by the FDA on September 6, 2005[2]. ProQuad is a sterile lyophilized preparation that consists of the components of two previously licensed vaccines, MMRII and Varicella Virus Vaccine: [3]

- M-M-R II (Measles, Mumps and Rubella Virus Vaccine Live):
  - Measles Virus Vaccine Live, a more attenuated line of measles virus, derived from Enders' attenuated Edmonston strain;
  - Mumps Virus Vaccine Live, the Jeryl Lynn (B level) strain of mumps virus;
  - Rubella Virus Vaccine Live, the Wistar RA 27/3 strain of live attenuated rubella virus

- Varicella Virus Vaccine Live, the Oka/Merck strain of varicella-zoster virus.

ProQuad is for subcutaneous injection and it exists as frozen and refrigerator-stable formulations[4] including a frozen formulation manufactured with human serum albumin (HSA), a frozen formulation manufactured with recombinant human serum albumin (rHA), and a formulation approved for refrigerator storage manufactured with recombinant human serum albumin. [5] The refrigerated formulation is also referred to as "ProQuad 4C." The FDA approved Merck's application for ProQuad 4C on August 4, 2006[6] but confirmation whether this product has been made available for sale in the United States is unavailable.

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[1] This is not intended to be an exhaustive history of changes, nor a full description in detail.
[2] Source: MMWR Weekly, December 2, 2005, 54 (47);1212-1214 available at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5447a4.htm; September 6, 2005 Approval Letter – ProQuad available at http://wayback.archive-it.org/7993/20170723150912/https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm123799.htm
[3] March 27, 2015 Summary Basis for Regulatory Action – ProQuad available at http://wayback.archive-it.org/7993/20170723150902/https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM441486.pdf
[4] *Id*.
[5] October 22, 2015 Approval Letter - PROQUAD available at http://wayback.archive-it.org/7993/20170723150901/https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM469262.pdf
[6] Approval Memo for supplement STN # 125108/102, MRK-KRA00761626

In December 2014, the FDA approved Merck's application to replace HSA with rHA in the preparation of bulks used in the frozen formulation of ProQuad.[7] However it is believed that this change was not implemented and ProQuad is still manufactured with HSA. The quadrivalent vaccine is manufactured at Merck's West Point, PA facility and distributed by Merck of Whitehouse Station, N.J.

Since the original approval there have been a number of ProQuad labeling amendments to date. A summary of relevant changes is provided below.

Following is a summary of label changes for ProQuad [Measles, Mumps, Rubella, and Varicella (Oka/Merck Virus) Vaccine Live] beginning with selected relevant language from the original approved product label issued August 1, 2005:

- **August 1, 2005[8]:**
  a) In the DESCRIPTION section, the language, "Each 0.5-mL dose contains not less than 3.00 log10 $TCID_{50}$ (50% tissue culture infectious dose) of measles virus; 4.30 log10 $TCID_{50}$ of mumps virus; 3.00 log10 $TCID_{50}$ of rubella virus; and a minimum of 3.99 log10 PFU (plaque-forming units) of Oka/Merck varicella virus."
  b) In the CLINICAL PHARMACOLOGY section, the language, "In clinical efficacy studies, seroconversion in response to vaccination against measles, mumps, and rubella paralleled protection from these diseases."
  c) In the CLINICAL PHARMACOLOGY section, the language, "Clinical studies with a single dose of ProQuad have shown that vaccination elicited rates of antibody responses against measles, mumps, and rubella that were similar to those observed after vaccination with a single dose of M-M-RII (see CLINICAL STUDIES) and seroresponse rates for varicella virus were similar to those observed after vaccination with a single dose of VARIVAX (see CLINICAL STUDIES)."
  d) In the CLINICAL PHARMACOLOGY section, under the subheading *Mechanism of action*, the language, "The duration of protection from measles, mumps, rubella, and varicella infections after vaccination with ProQuad is unknown."
  e) In the CLINICAL PHARMACOLOGY section under the subheading *Persistence of Antibody Responses after Vaccination*, the following language:
     i "The persistence of antibody at 1 year after vaccination was evaluated in a subset of 2107 children enrolled in the clinical trials. Antibody was detected in 98.9% (1722/1741) for measles, 96.7% (1676/1733) for mumps, 99.6% (1796/1804) for rubella, and 97.5% (1512/1550) for

[7] Supplemental Approval Letter, MRK-KRA00184876
[8] August 1, 2005 Label, MRK-KRA01448948

varicella (≥5 gpELISA units/mL) of vaccinees following a single dose of ProQuad."

ii "Experience with M-M-RII demonstrates that antibodies to measles, mumps, and rubella viruses are still detectable in most individuals 11 to 13 years after primary vaccination."

f) In the CLINICAL STUDIES section, the following language:

i "Formal studies to evaluate the clinical efficacy of ProQuad have not been performed."

ii "Efficacy of the measles, mumps, rubella and varicella components of ProQuad was previously established in a series of clinical studies with the monovalent vaccines. A high degree of protection from infection was demonstrated in these studies."

iii "The presence of detectable antibody was assessed by an appropriately sensitive enzyme-linked immunosorbent assay (ELISA) for measles, mumps (wild type and vaccine type strains), and rubella, and by gpELISA for varicella."

iv "Children were positive for mumps antibody if the antibody level was ≥10 ELISA units/mL."

v "Following a single dose of ProQuad, the vaccine response rates were 97.4% (95% CI: 96.9, 97.9) for measles, 95.8 (95% CI: 95.1, 96.4) to 98.8% (95% CI: 97.9, 99.4) for mumps, and 98.5% (95% CI: 98.1, 98.8) for rubella. The vaccine response rate was 91.2% (95 % CI: 90.3, 92.0) for varicella. These results were similar to the immune response rates induced by concomitant administration of single doses of M-M-R II and VARIVAX at separate injection sites. Fever and measles-like rashes were the only adverse experiences that occurred more frequently in recipients of a single dose of ProQuad compared with recipients of single doses of M-M-R II and VARIVAX (see ADVERSE REACTIONS)."

vi Under the subheading titled *Children Who Received a Second Dose of ProQuad*, the language, "The proportion of initially seronegative vaccinees with positive serological responses following two doses were 99.4% (95% CI: 98.6, 99.8) for measles, 99.9% (95% CI: 99.4, 100) for mumps, 98.3% (95% CI: 97.2, 99.0) for rubella, and 99.4% (95% CI: 98.7, 99.8) for varicella (≥5 gpELISA units/mL). The geometric mean titers (GMTs) following the second dose of ProQuad increased approximately 2-fold each for measles, mumps, and rubella, and approximately 41-fold for varicella."

vii Under the subheading titled *Children Who Received ProQuad at 4 to 6 Years of Age After Primary Vaccination With M-M-RII and VARIVAX*, the language, "Following the dose of ProQuad, seropositivity rates were 99.2% (95% CI: 97.6, 99.8) for measles, 99.5% (95% CI: 98.0,

99.9) for mumps, 100% (95% CI: 99.0, 100) for rubella, and 98.9% (95% CI: 97.2, 99.7) for varicella (≥5 gpELISA units/mL). Approximate geometric mean fold-rises in antibody titers (pre-vaccination to post-vaccination) for measles, mumps, rubella, and varicella were 1.2, 2.4, 3.0 and 12, respectively. Post-vaccination GMTs for recipients of ProQuad were similar to those following a second dose of M-M-RII and VARIVAX administered concomitantly at separate injection sites. Additionally, GMTs for measles, mumps, and rubella were similar to those following a second dose of M-M-RII given concomitantly with placebo."

viii In the subheading titled *Studies With Other Vaccines*, the language, "In a clinical trial involving 1913 healthy children 12 to 15 months of age, 949 received ProQuad plus Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP) and Haemophilus Influenzae type b Conjugate (Meningococcal Protein Conjugate) and Hepatitis B (Recombinant) Vaccine concomitantly at separate injection sites. Another 485 healthy children received ProQuad at the initial visit followed by DTaP and Haemophilus b Conjugate and Hepatitis B (Recombinant) Vaccine given concomitantly 6 weeks later while 479 children were immunized with M-M-RII and VARIVAX given concomitantly at separate injection sites at the first visit. Seroconversion rates and antibody titers for measles, mumps, rubella, varicella, anti-PRP and hepatitis B were comparable between the 2 groups at approximately 6 weeks post-vaccination indicating the ProQuad and Haemophilus b Conjugate (Meningococcal Protein Conjugate) and Hepatitis B (Recombinant) Vaccine may be administered concomitantly at separate injection sites."

- **August 1, 2006**[9]**:**
  a) In the DESCRIPTION section, language describing the contents of each dose of the vaccine was modified.
  b) In the CLINICAL STUDIES section, the addition of an additional clinical study under the subsection titled *Children who received a single dose of ProQuad at 12 through 23 months of age*.

- **October 1, 2009**[10]**:**
  a) Format change. Label was revised to comply with the Physician's Labeling Rule format and reorganized into two parts with an introductory overview

[9] August 1, 2006 Label, MRK-KRA01448979
[10] October 1, 2009 Label, MRK-KRA01634481

titled HIGHLIGHTS OF PRESCRIBING INFORMATION followed by FULL PRESCRIBING INFORMATION.

b) The INDICATIONS AND USAGE section was modified with new language describing the vaccine and its use in children 15 months to 12 years of age if a second dose of measles, mumps, rubella, and varicella is needed.
c) The WARNINGS and PRECAUTIONS sections were combined and there was an addition of language regarding fever and febrile seizures.
d) The ADVERSE REACTIONS section was restructured and an introductory paragraph was added under a new subheading, *Clinical Trials Experience*.
e) In the ADVERSE REACTIONS section, there was an addition of language under the subheading *Clinical Trials Experience* regarding the potential risk of febrile seizures following ProQuad administration.
f) In the ADVERSE REACTIONS section, the subheading *Post-marketing surveillance* was retitled *Post-Marketing Experience* in bold font and there was a modification of the introductory language.
g) In the CLINICAL PHARMACOLOGY section, there was a modification and addition of language under the subheading *Mechanism of Action* regarding the efficacy of ProQuad and how it has been shown to induce immunity.
h) The HOW SUPPLIED section was retitled HOW SUPPLIED/STORAGE AND HANDLING and there was an addition of language in bold font regarding storage of the vaccine at room temperature. The same language was also added to the DOSAGE AND ADMINISTRATION section.

Following is a detailed review of selected label changes for ProQuad [Measles, Mumps, Rubella, and Varicella (Oka/Merck Virus) Vaccine Live]:

I. August 1, 2006 Label Changes

1. In the DESCRIPTION section, language describing the contents of each dose of the vaccine was modified.

DESCRIPTION	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Each 0.5-mL dose of the vaccine contains no more than 21 mg of sucrose, 11 mg of hydrolyzed gelatin, 2.4 mg of sodium chloride, 1.8 mg of sorbitol, 0.40 mg of monosodium L-glutamate, 0.34 mg of sodium phosphate dibasic, 0.31 mg of human albumin, 0.17 mg of sodium bicarbonate, 72 mcg of potassium phosphate monobasic, 60 mcg of potassium chloride; 36 mcg of potassium phosphate dibasic; residual components of MRC-5 cells including DNA and	Each 0.5-mL dose of the vaccine contains no more than 20 mg of sucrose, 11 mg of hydrolyzed gelatin, 2.5 mg of urea, 2.3 mg of sodium chloride, 16 mg of sorbitol, 0.38 mg of monosodium L-glutamate, 1.4 mg of sodium phosphate, 0.25 mg of human albumin, 0.13 mg of sodium bicarbonate,94 mcg of potassium phosphate, 58 mcg of potassium chloride; residual components of MRC-5 cells including DNA and protein; 5 mcg of neomycin, bovine serum

protein; <16 mcg of neomycin, bovine calf serum (0.5 mcg), and other buffer and media ingredients.	albumin (0.5 mcg), and other buffer and media ingredients."

2. In the CLINICAL STUDIES section, the addition of an additional clinical study under the subsection titled *Children who received a single dose of ProQuad at 12 through 23 months of age*.

CLINICAL STUDIES	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	In an additional clinical study, 1519 children 12 through 23 months of age received either the refrigerator-stable formulation of ProQuad (N=1006) or the frozen formulation of ProQuad (N=513). Subjects enrolled in this trial had a negative clinical history, no known recent exposure, and no vaccination history of measles, mumps, rubella, and varicella. Children were excluded from study participation if they had an immune impairment or had a history of allergy to components of the vaccine. No concomitant vaccines were permitted during the study participation. Following a single dose of the refrigerator-stable formulation of ProQuad, the vaccine response rates were 99.1% (95%CI: 98.2, 99.6) for measles, 97.7% (95% CI: 96.5, 98.6) for mumps, and 99.6% (95% CI: 98.9, 99.9) for rubella. The vaccine response rate was 90.1% (95% CI: 87.9, 92.0) for varicella. The results were similar to the immune response rates induced by the frozen formulation of ProQuad in the same study. The refrigerator-stable formulation of ProQuad was generally well tolerated. The safety profile of the refrigerator-stable formulation of ProQuad was comparable to that of the frozen formulation of ProQuad (see ADVERSE REACTIONS)."

II. October 1, 2009 Label Changes

1. Format change. Label was revised to comply with the Physician's Labeling Rule format and reorganized into two parts with an introductory overview titled HIGHLIGHTS OF PRESCRIBING INFORMATION followed by FULL PRESCRIBING INFORMATION.

2. The INDICATIONS AND USAGE section was modified with new language describing the vaccine and its use in children 15 months to 12 years of age if a second dose of measles, mumps, rubella, and varicella is needed.

INDICATIONS AND USAGE	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
ProQuad is indicated for simultaneous vaccination against measles, mumps, rubella, and varicella in children 12 months to 12 years of age. ProQuad may be used in children 12 months to 2 years of age if a second dose of measles, mumps and rubella vaccine is to be administered.	ProQuad is a vaccine indicated for active immunization for the prevention of measles, mumps, rubella, and varicella in children 12 months through 12 years of age.

3. The WARNINGS and PRECAUTIONS sections were combined and there was an addition of language regarding fever and febrile seizures.

WARNINGS AND PRECAUTIONS	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	Administration of ProQuad (dose 1) to children 12 to 23 months old who have not been previously vaccinated against measles, mumps, rubella, or varicella, nor had a history of the wild-type infections, is associated with higher rates of fever and febrile seizures at 5 to 12 days after vaccination when compared to children vaccinated with M-M-R II and VARIVAX administered separately (see *Adverse Reactions*).

4. The ADVERSE REACTIONS section was restructured and an introductory paragraph was added under a new subheading, *Clinical Trials Experience*.

ADVERSE REACTIONS	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in clinical practice. Vaccine-related adverse reactions reported during clinical trials were assessed by the study investigators to be

	possibly, probably, or definitely vaccine-related and are summarized below.

5. In the ADVERSE REACTIONS section, there was an addition of language under the subheading *Clinical Trials Experience* regarding the potential risk of febrile seizures following ProQuad administration.

ADVERSE REACTIONS	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	These studies were not designed or statistically powered to detect a difference in rates of febrile seizure between recipients of ProQuad as compared to M-M-R II and VARIVAX. The risk of febrile seizure has not been evaluated in a clinical study comparing the incidence rate after ProQuad (dose 2) with the incidence rate after concomitant M-M-R II (dose 2) and VARIVAX (dose 2).

6. In the ADVERSE REACTIONS section, the subheading *Post-marketing surveillance* was retitled *Post-Marketing Experience* in bold font and there was a modification of the introductory language.

ADVERSE REACTIONS	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
The discussion that follows describes adverse reactions which have been identified post-approval for the monovalent components of ProQuad. Because these reactions are described in the literature or reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship.	The following adverse events have been identified during post-approval use of either the components of ProQuad or ProQuad. Because the events are in some cases described in the literature or reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

7. In the CLINICAL PHARMACOLOGY section, there was a modification and addition of language under the subheading *Mechanism of Action* regarding the efficacy of ProQuad and how it has been shown to induce immunity.

CLINICAL PHARMACOLOGY	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
In clinical efficacy studies, seroconversion in response to vaccination against measles, mumps, and rubella paralleled protection from these diseases.	ProQuad has been shown to induce measles-, mumps-, rubella-, and varicella-specific immunity, which is thought to be the mechanism by which it protects against these four childhood diseases. The efficacy of ProQuad was established through the use of immunological correlates for protection against measles, mumps, rubella, and varicella. Results from efficacy studies or field effectiveness studies that were previously conducted for the component vaccines were used to define levels of serum antibodies that correlated with protection against measles, mumps, and rubella.

8. The HOW SUPPLIED section was retitled HOW SUPPLIED/STORAGE AND HANDLING and there was an addition of language in bold font regarding storage of the vaccine at room temperature. The same language was also added to the DOSAGE AND ADMINISTRATION section.

HOW SUPPLIED/STORAGE AND HANDLING *-and-* *DOSAGE AND ADMINISTRATION*	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label, in either of the aforementioned sections.	**IF NOT USED IMMEDIATELY, THE RECONSTITUTED VACCINE MAY BE STORED AT ROOM TEMPERATURE, PROTECTED FROM LIGHT, FOR UP TO 30 MINUTES.**

Schedule 3

Summary of MumpsVax Label Changes

LABEL CHANGES FOR MUMPSVAX[1]

MUMPSVAX [MUMPS VIRUS VACCINE LIVE, MSD] JERYL LYNN STRAIN

MUMPSVAX (Mumps Virus Vaccine Live, MSD) Jeryl Lynn Strain is a live virus vaccine for immunization against mumps. It was approved by the FDA in 1970. Merck stopped manufacturing new lots of MUMPSVAX in 2007[2] and the product is currently listed as a discontinued vaccine on the CDC website.[3] There were numerous labeling revisions to MUMPSVAX over the course of the vaccine's history. A summary is provided below.

Following is a summary of label changes for MUMPSVAX (Mumps Virus Vaccine Live, MSD) beginning with selected relevant language from the earliest available version issued March 1, 1991:

- **March 1, 1991[4]:**
  a) In the DESCRIPTION section, the language, "When reconstituted as directed, the dose for injection is 0.5 mL and contains not less than the equivalent of 20,000 $TCID_{50}$ (tissue culture infectious doses) of the U.S. Reference Mumps Virus."
  b) In the CLINICAL PHARMACOLOGY section, the language, "Extensive clinical trials have demonstrated that MUMPSVAX is highly immunogenic and well tolerated. A single injection of the vaccine has been shown to induce mumps neutralizing antibodies in approximately 97 percent of susceptible children and approximately 93 percent of susceptible adults. . . . Although the antibody level is significantly lower than that following natural infection; it is protective and long lasting. Vaccine-induced antibody levels have been shown to persist for at least 15 years with a rate of decline comparable to that seen in natural infection. If the present pattern continues, it will provide a basis for the expectation that immunity following vaccination will be permanent. However, continued surveillance will be required to demonstrate this point."
  c) In the INDICATIONS AND USAGE section, the language, "Children vaccinated when younger than 12 months of age should be revaccinated. Based on available evidence, there is no reason to routinely revaccinate persons who were vaccinated originally when 12 months of age or older."

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[1] This is not intended to be an exhaustive history of changes, nor a full description in detail.
[2] 2011 Final Stability Annual Review for MUMPSVAX Virus Vaccine, signed and dated March 16, 2011, MRK-KRA01634074
[3] Source: Selected U.S. Discontinued Vaccines, available at https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/b/discontinued_vaccines.pdf
[4] March 1, 1991 Label, MRK-KRA01449133

d) In the PRECAUTIONS section, the statement, "As for any vaccine, vaccination with MUMPSVAX may not result in seroconversion in 100% of susceptible persons given the vaccine."
e) In the DOSAGE AND ADMINISTRATION section, the following statements:
   i "The dosage of vaccine is the same for all persons. Inject the total volume (about 0.5 mL) of reconstituted vaccine subcutaneously, preferably in to the outer aspect of upper arm."
   ii "During shipment, to ensure that there is no loss of potency, the vaccine must be maintained at a temperature of 10°C (50°F) or less."
   iii "Before reconstitution, store MUMPSVAX at 2-8°C (36-46°F). *Protect from light*."
   iv "Each dose of MUMPSVAX contains not less than the equivalent of 20,000 $TCID_{50}$ of the U.S. Reference Mumps Virus."
f) In the HOW SUPPLIED section under the subheading titled *Storage*, "It is recommended that the vaccine be used as soon as possible after reconstitution. Protect vaccine from light at all times, since such exposure may inactivate the virus. Store reconstituted vaccine in the vaccine vial in a dark place at 2-8°C (36-46°F) and discard if not used within 8 hours."

- **April 1, 1999[5]:**
   a) In the DESCRIPTION section, there was an addition of language describing the growth medium for mumps, Medium 199, and a modification of language regarding cell cultures.
   b) In the DESCRIPTION section, the paragraph describing the contents of each dose of the vaccine was modified.
   c) In the CLINICAL PHARMACOLOGY section, there was an addition of the statement that a small percentage (1-5%) of vaccines may fail to seroconvert after the primary dose.
   d) In the CLINICAL PHARMACOLOGY section, the removal and revision of language regarding how efficacy of the vaccine was established and of language discussing antibody measurement and persistence.
   e) In the INDICATIONS AND USAGE section, the removal of a statement regarding natural immunity.
   f) In the INDICATIONS AND USAGE section, a new subheading was added titled *Other Vaccination Considerations, Other Populations* specifically recommending vaccination for high-risk groups.
   g) The addition of a new section titled WARNINGS beginning with a statement regarding temperature elevation.

[5] April 1, 1999 Label, MRK-KRA01449062

h) In the PRECAUTIONS section, there was a change in language from "may not result in seroconversion" to "may not result in protection."
i) In the HOW SUPPLIED section, under the subheading *Storage*, the addition of language regarding freezing during shipment.

- **October 1, 2000**[6]**:**
  a) In the WARNINGS section, the addition of language regarding the use of albumin.

- **September 1, 2002**[7]**:**
  a) The Merck & Co. manufacturing address in the header was changed from West Point, PA to Whitehouse Station, NJ.
  b) In the INDICATIONS AND USAGE section under the subheading Recommended Vaccination Schedule, there was a change in language regarding revaccination.

- **February 1, 2007**[8]**:**
  a) Final approved label before Merck stopped manufacturing new lots of the vaccine. No substantive changes.

Following is a detailed review of selected label changes for MUMPSVAX (Mumps Virus Vaccine Live, MSD) Jeryl Lynn Strain:

I. April 1, 1999 Label Changes

1. In the DESCRIPTION section, there was an addition of language describing the growth medium for mumps, Medium 199, and a modification of language regarding cell cultures.

DESCRIPTION	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
The virus was adapted to and propagated in cell cultures of chick embryo free of avian leukosis virus and other adventitious agents.	The virus was adapted to and propagated in chick embryo cell culture. The growth medium for mumps is Medium 199 (a buffered salt solution containing vitamins and amino acids and supplemented with fetal bovine serum) containing SPGA (sucrose, phosphate, glutamate, and human albumin) as stabilizer and neomycin.

[6] October 1, 2000 Label, MRK-KRA01449090
[7] September 1, 2002 Label, MRK-KRA01448998
[8] February 1, 2007 Label, MRK-KRA01448934

	The cells, virus pools, fetal bovine serum, and human albumin are all screened for the absence of adventitious agents. Human albumin is processed using the Cohn cold ethanol fractionation procedure.

2. In the DESCRIPTION section, language describing the contents of each dose of the vaccine was modified.

DESCRIPTION	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Each dose contains approximately 25mcg of neomycin. The product contains no preservative. Sorbitol and hydrolyzed gelatin are added as stabilizers.	Each dose of the vaccine is calculated to contain sorbitol (14.5 mg), sodium phosphate, sucrose (1.9 mg), sodium chloride, hydrolyzed gelatin (14.5 mg), human albumin (0.3 mg), fetal bovine serum (<1 ppm), other buffer and media ingredients and approximately 25 mcg of neomycin.

3. In the CLINICAL PHARMACOLOGY section, there was an addition of the statement that a small percentage (1-5%) of vaccines may fail to seroconvert after the primary dose.

CLINICAL PHARMACOLOGY	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Although the antibody level is significantly lower than that following natural infection; it is protective and long lasting.	Although the antibody level is significantly lower than that following natural infection; it is protective and long lasting. <u>However, a small percentage (1-5%) of vaccinees may fail to seroconvert after the primary dose</u> (see also INDICATIONS AND USAGE, *Recommended Vaccination Schedule*).

4. In the CLINICAL PHARMACOLOGY section, the removal and revision of language regarding how efficacy of the vaccine was established and of language discussing antibody measurement and persistence.

CLINICAL PHARMACOLOGY	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Vaccine-induced antibody levels have been shown to persist for at least 15 years with a rate of decline comparable to that seen in natural infection. If the present pattern continues, it will provide a basis for the expectation that immunity following vaccination will be permanent.	Efficacy of mumps vaccine was established in a series of double-blind controlled field trials which demonstrated a high degree of protective efficacy. These studies also established that seroconversion in response to mumps vaccination paralleled protection from these

However, continued surveillance will be required to demonstrate this point.	diseases. Following vaccination, antibodies associated with protection can be measured by neutralization assays, hemagglutination-inhibition (HI), or ELISA (enzyme linked immunosorbent assay) tests.

5. In the INDICATIONS AND USAGE section, the removal of a statement regarding natural immunity.

INDICATIONS AND USAGE	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Most adults are likely to have been infected naturally and generally may be considered immune, even if they did not have clinically recognizable disease. A booster is not needed.	*Language in the left column was removed from the April 1, 1999 approval label.*

6. In the INDICATIONS AND USAGE section, a new subheading was added titled *Other Vaccination Considerations-Other Populations* specifically recommending vaccination for high-risk groups.

INDICATIONS AND USAGE	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	Vaccination is recommended for susceptible individuals in high-risk groups such as college students, health-care workers, and military personnel.

7. In the CONTRAINDICATIONS section, a modification was made to the entry for febrile respiratory illness or other active febrile infection.

CONTRAINDICATIONS	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Any febrile respiratory illness or other active febrile infection.	Febrile respiratory illness or other active febrile infection. However, the ACIP has recommended that all vaccines can be administered to persons with minor illnesses such as diarrhea, mild upper respiratory infection with or without low-grade fever, or other low-grade febrile illness.

8. The addition of a new section titled WARNINGS beginning with a statement regarding temperature elevation.

WARNINGS	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	The physician should be alert to the temperature elevation which may occur following vaccination (see ADVERSE REACTIONS).

9. In the PRECAUTIONS section, there was a change in language from "may not result in seroconversion" to "may not result in protection."

PRECAUTIONS	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
As for any vaccine, vaccination with MUMPSVAX may not result in seroconversion in 100% of susceptible persons given the vaccine.	As for any vaccine, vaccination with MUMPSVAX may not result in protection in 100% of vaccinees.

10. In the HOW SUPPLIED section, under the subheading *Storage*, the addition of language regarding freezing during shipment.

HOW SUPPLIED	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	Freezing during shipment will not affect potency.

II. October 1, 2000 Label Changes

1. In the WARNINGS section, the addition of language regarding the use of albumin.

WARNINGS	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Language in the right column did not exist in the previous label.	This product contains albumin a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases. Although there is a theoretical risk for transmission of Creutzleidt-Jacob disease (CJD), no cases of transmission of CJD or viral disease have ever been identified that were associated with the use of albumin.

III. September 1, 2002 Label Changes

1. In the INDICATIONS AND USAGE section under the subheading *Recommended Vaccination Schedule*, there was a change in language regarding revaccination.

INDICATIONS AND USAGE	
PREVIOUS LANGUAGE	*REVISED LANGUAGE*
Revaccination may seroconvert primary failures or boost antibody titers of those individuals whose titers have declined.	Revaccination is intended to seroconvert those who do not respond to the first dose.

Schedule 4

Transcription of MMRV-46-01 Laboratory Notebook Page

MRK-KRA00064825

Project No. V205 **Project Page** MMRV-46-01

Investigator D. Krah **Date** March 6, 2001

Subject Mumps neutralization assay – sera from Protocol 007: Data being generated for information only – Not part of formal testing for Protocol 007

Filed in Book Number/Title MMRV Filer 2001 (A)

Purpose: Measure mumps neutralization titers of selected sera from (DKrah March 6, 2001) M-M-R® II Protocol 007 (low/non-responders from previous testing in the anti-IgG enhanced mumps neutralization assay). Neutralization is being tested here without anti-IgG enhancement, + using Jeryl Lynn™ vaccine virus + JL135 as indicator viruses. Sera are being tested (due to limited amounts available) @ a 1:4 starting initial dilution (1:8 after addition of virus). The assay is being performed following Virus + Cell Biology Res. Proc. #874.3422 ("Mumps plaque reduction neutralization assay")

Note: dates are given in month/day/year format, unless otherwise specified. DKrah March 6, 2001.

Sera:

(1) From Protocol 007 (M-M-R® II): pre + post (42d) sera from cases: (pediatric)

7-2	7-31	7-133	7-166	7-174
7-223	7-678	7-1124	7-1715	7-1716

(2) Adult lab volunteer sera: (from 1/18/01 subaliquotting):

DK

MKY

Prepare duplicate sets of each serum dilution series – one to receive JL135 mumps + the other to receive Jeryl Lynn vaccine virus

See attached "PRN assay help sheet" for serum dilution, reagents + incubation time + temperatures. See attached Box + sample code for inoculation key. David Krah March 6, 2001.

Remove overlays + fix cells with 90% acetone, 10% water as described in Virus + Cell Biology Res. Proc. #874.3488. See attached "Information sheet for immunostaining" for details of the acetone fixing. Hold fixed cells overlaid with RCM063 @ 2-8°C for later immunostaining (as described in Virus + Cell Biology Res. Proc. #874.3488). David Krah March 9, 2001.

[Translation of MRK-KRA00064825]

Schedule 5

Mumps House Standard Adjustment

Date	Document Number	Description
9/16/2002	MRK-KRA01899697 at '698, 703, 713-14 (emphasis added)	Merck submitted a Prior Approval Supplement (PAS) on September 16, 2002 for "Measles Formulation and Potency Assay Format Changes to Support Potency through Twenty Four Months Expiry" that also proposed to "apply house standard calibration to all mumps and rubella potency values….House standard calibration is proposed for all material destined for release to the market and samples placed onto stability." "The proposed changes are required to provide adequate assurances that the manufacturing process produces product that meets its claimed specification through expiry (24 months)."
5/18/2005	MRK-KRA00000315 at '336-37	"The mumps house standard potency was reassigned from 4.2 to 4.3 log10 TCID50/0.1 mL based on 3064 thousand assay runs over about 8 years. The reassigned house standard serves both as an assay control and calibration standard that normalizes unknown potency values to compensate for the assay running high or low on any particular day."
11/10/1998	MRK-KRA01894999 at '5002	"One way to illustrate adjustment to a house standard is to view it as a means to compensate for differential sensitivity among assay runs. Suppose for instance that the assigned potency for the house standard is 3.0 log10 TCID50/0. 1mL …. Now suppose an assay is performed yielding measured potencies of 2.8 and 2.6 log10 TCID50/0.1mLfor the house standard and test material respectively. The difference between the assigned and measured house standard potency, 3.0 -2.8 = 0.2 log10 TCID50/0.1mL, is a reflection of a decrease in sensitivity of that run of the assay; thus we would predict that all materials tested in that run measure 0.2 log10 TCID50/0.1mL lower than the norm. We therefore adjust all potencies to account for the decrease in sensitivity in that run, and the potency of the test material would be adjusted up as follows: 2.6 + 0.2 = 2.8 log10 TCID50/0.1mL."
2/26/2003	MRK-KRA00049385 at '386-87	As a result of house stand calibration and a reassignment of the mumps house standard potency from 4.2 log10 TCID50/dose to 4.3 log10 TCID50/dose.

Date	Document Number	Description
2/26/2003	MRK-KRA00049385 at '392 (emphasis added)	**Consequences of Re-Assigning Mumps Potency from 4.2 to 4.3** • Mumps Expiry Clinical Trial – Expiry potency 4.0 vs. 4.1 (10,000 vs. 12,589) $TCID_{50}$/Dose • ProQuad® – Mumps specifications/measurements will increase 0.1 Log_{10} • Kaketsuken - M-M-R®II – JNDA filed with data calibrated to 4.2 • Stability – Calibrated stability data will increase 0.1 Log_{10}
11/7/2003	MRK-KRA01481321; MRK-KRA01481322 at '334 (emphasis added)	**Table 6. Relationship of specifications to the assignment mumps expiry as 4.0 vs. 4.1 log_{10} $TCID_{50}$/dose.** Mumps Component M-M-R™II / Current / Using 95% UCI / Using Point Estimate Maximum Release Specification: None / 5.5 / 5.5 Target Post-Lyophilization Fill Potency: 5.2 / 5.1 / 5.1 Minimum Release Specification: 5.0 / 4.9 / 4.9 Manufacturing Window: N/A (No max. spec.) / 0.6 / 0.6 Stability Window: 0.7 / **0.8** / **0.9** Expiry Potency: 4.3 / **4.1 (4.08[b])** / **4.0 (4.04[b])** Assay Format (One vial x number of assay runs): 1 x 6 1 x 12 Below 5.0 / 1 x 6 All lots 1 x 12 ≤ 4.9 or ≥ 5.5 / 1 x 6 All lots 1 x 12 ≤ 4.9 or ≥ 5.5 House Standard Calibration: None / Calibrated / Calibrated TOR: 40 hours[a] / **35 hours** / **40 hours[c]** Reconstitute and Store at 2–8°C: 8 hours[a] / 8 hours / 8 hours Expiry Dating Period: 24 Months[a] / 24 Months / 24 Months [a] Currently reported values are not supported by stability model. [b] Calculated potency and calibrated to mumps house standard using potency assignment of 4.3 log_{10} $TCID_{50}$/0.1 mL [c] Calculated TOR exceeds 40 h but limited by measles component.
2/26/2003	MRK-KRA00049385 at '392	"Calibrated stability data will increase 0.1 log10"
5/18/2005	MRK-KRA00000315	Merck calibrated the potency results of the mumps component of MMRII

Date	Document Number	Description
	at '336-37	tested in the Protocol 007 clinical studies, the potency of the three groups tested in Protocol 007 clinical studies were adjusted by raising each assigned potency by 0.1 log10 TCID50/dose.
2/26/2003	MRK-KRA00049385 at '392	The 4.0 log10 TCID50/dose group tested in Protocol 007 was reassigned to a potency of 4.1 log10 TCID50/dose. "Expiry potency 4.0 vs. 4.1 (10,000 vs. 12,589) TCID50/dose."
5/18/2005	MRK-KRA01971196; MRK-KRA00000315 at '336-37	CBER approved the PAS.

Schedule 6

Epidemiological Studies Relating to Mumps

Citation[1]	Bates (if applicable)
Kim-Farley, R et al.: *Clinical Mumps Vaccine Efficacy,* Am J Epidemiology, 121(4): 593-7, (Apr.) 1985.	MRK-KRA01620084-88
Sullivan, K. M. et al.: *Effectiveness of Mumps Vaccine in a School Outbreak,* Am J Dis Children, 139(9): 909-12, (Sept.) 1985.	MRK-KRA01620090-093
Chaiken, B. P. et al.: *The Effect of a School Entry Law on Mumps Activity in a School District*, JAMA, 257(18): 2455-58, (May 8) 1987.	MRK-KRA00622684 at '714-717
Wharton, M. et al.: *A Large Outbreak of Mumps in the Postvaccine Era*, J Inf Diseases, 158(6): 1253-60, (Dec.) 1988.	MRK-KRA01620100-107
Hersh, B. S., et al.: *Mumps outbreak in a highly vaccinated population*. J Pediatrics, 119(2): 187-93, (Aug.) 1991.	MRK-KRA00622684 at '728-734
Toscani, L. et al.: *Comparison of the Efficacy of Various Mumps Vaccine Strains: A Study Conducted in Schools,* Soz. Praventivmed, 41: 341-7, 1996.	MRK-KRA00622684 at '736-745
Schlegel, M. et al.: *Comparative efficacy of three mumps vaccines during disease outbreak in eastern Switzerland: cohort study,* British Med J., 319: 352-3, 1999.	MRK-KRA00622684 at '747-748
Whitman, C. et al.: *Mumps Outbreak in a Highly Vaccinated Population in New York City*, NY State Pediatrician (Newsletter), 1998.	MRK-KRA00622684 at '750-751
Fiebelkorn, A. P. et al.: *Mumps Antibody Response in Young Adults After a Third Dose of Measles-Mumps-Rubella Vaccine*, Open Forum Infectious Diseases, 1(3), (Dec.) 2014.	
Cardemil, C. V. et al.: *Effectiveness of a Third Dose of MMR Vaccine for Mumps Outbreak Control*, New Eng J Med., 377(10): 947-956, (Sept. 7) 2017.	Pallansch Ex. 12
Lebo, E. J. et al.: *Seroprevalence of Measles, Mumps, Rubella and Varicella Antibodies in the United States Population, 2009-2010*, Open Forum Infectious Diseases, 2(1), (Feb. 20) 2015.	
Kutty, P. K. et al.: *Seroprevalence of Antibody to Mumps Virus in the US Population, 1999-2004*, J. Infectious Diseases, 202(5): 667-74 (Sept. 1) 2010.	MRK-KRA00210533-540

[1] This is not intended to be an exhaustive list, nor a full description in detail.

Citation[1]	Bates (if applicable)
CDC, *Summary of Notifiable Infectious Diseases and Conditions – United States, 2015*, MMWR, 64(53): 1-143, (Aug. 11) 2017.	Kuter Ex. 7
Latner, D. R. et al: *Mumps Virus Nucleoprotein and Hemagglutinin-Specific Antibody Response Following a Third Dose of Measles Mumps Rubella Vaccine*, Open Forum Infectious Diseases, 4(4), (Oct. 1) 2017.	
Latner, D. R. et al.: *Enzyme-Linked Immunospot Assay Detection of Mumps-Specific Antibody-Secreting B cells as an Alternative Method of Laboratory Diagnosis*, Clinical and Vaccine Immunology, 18(1): 35-42, (Jan.) 2011.	
Vandermeulen, C. et al.: *Detection of mumps virus-specific memory B cells by transfer of peripheral blood mononuclear cells into immune-deficient mice*, Immunology, 131(1): 33-39, (Sept.) 2010.	
Kancherla, V. S. et al.: *Mumps resurgence in the United States*, J Allergy Clin Immunol, 11(4): 938-41, (Oct.) 2006.	MRK-KRA00120141-144
Peltola, H. et al.: *Mumps Outbreaks in Canada and the United States*, Mumps Vaccines, Clinical Infectious Diseases, 45: 459-466, (Aug. 15) 2007.	MRK-KRA01532703-710
Dayan, G. H. et al.: *Mumps Outbreaks in Vaccinated Populations: Are Available Mumps Vaccines Effective Enough to Prevent Outbreaks?*, Clinical Infectious Diseases, 47: 1458-467, (Dec. 1) 2008.	MRK-KRA01301361-370
Dayan, G. H. et al.: *Recent Resurgence of Mumps in the United States*, New England J Med., 358(15): 1580-1589, (Apr. 10) 2008.	MRK-KRA01532949-958
Barskey, A. E. et al.: *Mumps resurgences in the United States A historical perspective*, Vaccine, 27: 6186-6195, 2009.	MRK-KRA01532914-923
Huang, A. S. et al.: *Risk factors for mumps at a university with a large mumps outbreak*, Public Health Report, 124(3): 419-426, (May-June) 2009.	MRK-KRA01038877-885
Quinlisk, M. P.: *Mumps Control Today*, J Infect Dis., 202(5): 655-656, (Sept. 1) 2010.	MRK-KRA00027898-899
Rubin, S. A. et al.: *Recent Mumps Outbreaks in Vaccinated Populations: No Evidence of Immune Escape*, J Virol., 86(1): 615–620, (Jan.) 2012.	

Citation[1]	Bates (if applicable)
Barskey, A. E. et al.: *Mumps Outbreak in Orthodox Jewish communities in the United States*, New England Journal of Medicine, 367(18): 1704-13, (Nov. 1) 2012.	
Nelson, G. E. et al.: *Epidemiology of a Mumps Outbreak in a Highly Vaccinated Island Population and Use of a Third Dose of Measles-Mumps-Rubella Vaccine for Outbreak Control—Guam 2009 to 2010*, Pediatric Infectious Disease Journal, 32(4): 374-380, (Apr.) 2013.	
Cortese, M.M. et al.: *Mumps Vaccine Performance among University Students during a Mumps Outbreak*, Clinical Infectious Diseases, 46(8): 1172-80, (Apr. 15) 2008.	
Date, A. A. et al.: *Long-Term Persistence of Mumps Antibody after Receipt of 2 Measles-Mumps-Rubella (MMR) Vaccinations and Antibody Response after a Third MMR Vaccination among a University Population*, Journal of Infectious Diseases, 197(12): 1662-68, (June 15) 2008.	CDC0000284 at '341-347
Yung, C-F. et al.: *Mumps complications and effects of mumps vaccination, England and Wales, 2002-2006*, Emerging Infectious Disease, 17(4): 661-7, (Apr.) 2011.	
Hashimoto, H. et al.: *An office-based prospective study of deafness in mumps*, Pediatric Infectious Disease Journal, 28(3): 173–5, (Mar.) 2009.	MRK-KRA00860221-223
Rubin, S. et al.: *Emerging Mumps Infection*, The Pediatric Infectious Disease Journal, 35(7): 799-801, (July) 2016.	
Latner, D. R. et al.: *Remembering Mumps*, PLOS Pathog, 11(5): 1-4 (May 7) 2015.	
Sabbe, M. et al.: *The resurgence of mumps and pertussis*, Human Vaccines and Immunotherapeutics, 12(4): 955-9, (Apr. 2) 2016.	
Livingston, K. A. et al.: *Mumps vaccine effectiveness and risk factors for disease in households during an outbreak in New York City*, Vaccine, 32(3): 369-74, (Jan. 9) 2014.	
Ogbuanu, I. U. et al.: *Impact of a third dose of measles-mumps-rubella vaccine on a mumps outbreak*, Pediatrics, 130(6): 1567-74, (Dec.) 2012.	CDC0000001 at '008-017

Citation[1]	Bates (if applicable)
Albertson, J. P. et al.: *Mumps outbreak at a university and recommendation for a third dose of measles-mumps-rubella vaccine—Illinois, 2015–2016*, MMWR, 65(29): 731–734, (July 29) 2016.	MRK-KRA02102732-35

Schedule 7

Studies on Mumps Efficacy

Type of Study	Citation[1]	Bates (if applicable)
Monovalent Mumps (pre-licensure)	Weibel, R.E., et al: *Evaluation of Live Attenuated Mumps Virus Vaccine, Strain Jeryl Lynn, First International Conference on Vaccines Against Viral and Rickettsial Diseases of Man, Washington, DC*, Pan American Health Organization Scientific Publication No.147, pp 430-437, (May) 1967. Also cited as: Weibel, R.E., et al: *Evaluation Of Live Attenuated Mumps Virus Vaccine, Strain Jeryl Lynn, First International Conference on Vaccines Against Viral and Rickettsial Diseases of Man*, World Health Organization, 147, (May) 1967.	
Monovalent Mumps (pre-licensure)	Hilleman, M. R., et al.: *Live Attenuated Mumps Virus Vaccine: 4. Protective Efficacy as Measured in Field Evaluation*, New Eng. J. Med., 276: 252-258, (Feb. 2) 1967.	
Monovalent Mumps (pre-licensure)	Buynak, E. B., et al.: *Live Attenuated Mumps Virus Vaccine: 1. Vaccine Development*, Proc Soc Exp Biol Med, 123:768-775 (Dec), 1966.	
Monovalent Mumps	Buynak, E.B., et al.: *Jeryl Lynn Strain Live Attenuated Mumps Virus Vaccine*, J. Am. Med. Assoc., 203(1):63-67 (Jan 1), 1968.	
Monovalent Mumps (pre-licensure)	Stokes, J., Jr., et al.: *Live Attenuated Mumps Virus Vaccine: 2. Early Clinical Studies*, Pediatrics, 39:363-371, (Mar) 1967.	
Monovalent Mumps (pre-licensure)	Weibel, R. E., et al.: *Live Attenuated Mumps Virus Vaccine: 3. Clinical and Serologic Aspects in a Field Evaluation*, New Eng J Med, 276(5):245-251 (Feb 2), 1967.	
Monovalent Mumps	Young, M. L., et al.: *Experiences with Jeryl Lynn Strain Live Attenuated Mumps Virus Vaccine in a Pediatric Outpatient Clinic*, Pediatrics, 40(5):798-803, (Nov) 1967.	

[1] This is not intended to be an exhaustive list, nor a full description in detail.

Type of Study	Citation[1]	Bates (if applicable)
MMR Trivalent (pre-licensure)	Stokes, J., et al.: *Trivalent Combined Measles-Mumps-Rubella Vaccine, Findings in Clinical-Laboratory Studies*, J. Am. Med. Assoc., 218(1):57-61, (Oct 4) 1971.	MRK-KRA01954958 at '244-248; *see also* MRK-KRA01955502.
MMR Trivalent (pre-licensure)	Buynak, E. B., et al.: *Combined Live Measles, Mumps, Rubella Vaccine*, J. Am. Med. Assoc., 207:2259-2262, (Mar. 24) 1969.	MRK-KRA01954958 at '250-253; *see also* MRK-KRA01955502.
MMR Trivalent (persistence)	Weibel, R. E. et al.: *Persistence of immunity following monovalent and combined live measles, mumps, and rubella vaccines*, Pediatrics, 51(3):467-475, (Mar) 1973.	MRK-KRA01954958 at '255-263; *see also* MRK-KRA01955502.
MMR Trivalent (persistence)	Weibel, R. E., et al.: *Long term follow-up for immunity after monovalent and combined live measles, mumps, and rubella vaccines*, Pediatrics, 56(3):380-387, (Sept) 1975.	MRK-KRA01954958 at '265-272; *see also* MRK-KRA01955502.
MMR Trivalent (persistence)	Weibel, R. E., et al.: *Persistence of antibody after administration of monovalent and combined live measles, mumps, and rubella vaccines*, Pediatrics, 61(1):5-11, (Jan. 1) 1978.	MRK-KRA01954958 at '274-280; *see also* MRK-KRA01955502.
MMRII Trivalent (pre-licensure)	Weibel, R. E., et al.: *Clinical and Laboratory Studies of Combined Live Measles, Mumps, and Rubella Vaccines using the RA 27/3 Rubella Virus (40979)*, Proc. Soc. Exp. Biol. Med., 165(2):323-326, 1980.	MRK-KRA01954958 at '309-312. *See* MRK-KRA01955502 at '749-897 (Data and clinical documentation summarized in Study Summaries 1 through 7, section D), Reference 15; *see also* MRK-KRA00018678.
MMRII Trivalent (post-licensure)	Fahlgren, K.: *Two doses of MMR vaccine-sufficient to eradicate measles, mumps and rubella?*, Scand. J. Soc. Med. 16:129-135, (Sept. 1) 1988.	MRK-KRA01955502 at 726, Reference 17. MRK-KRA01954958 at '320-326.

Schedule 8

ACIP Schedule of Recommended Vaccines

Date[i]	ACIP Recommendation
1967	ACIP suggests mumps vaccine be considered for children approaching puberty, for adolescents, and for adults.[ii]
1968	ACIP suggests that mumps vaccine may be used at any age from 12 months.[iii]
1972	ACIP suggests that mumps vaccine is of particular value in children approaching puberty, adolescents, and adults, especially males.[iv]
1977	ACIP recommends routine vaccination with one dose of mumps vaccine for all children at any age after 12 months.[v]
1980	ACIP recommends vaccination of susceptible children, adolescents, and adults, unless such vaccination is contraindicated.[vi]
1989	ACIP recommends that a second dose of measles-containing vaccine be administered to children 4 to 6 years of age (at time of entry to kindergarten or first grade), and designated MMRII as the vaccine of choice.[vii]
1998	ACIP changes the recommended age for routine vaccination to 12 to 15 months for the first dose of MMR, and to 4 to 6 years for the second dose of MMR.[viii]
2006	ACIP formally recommends two doses of a live mumps virus-containing vaccine for school-aged children (grades K to 12) and adults in high risk groups. ACIP also recommended that a second dose of mumps vaccine should be considered in outbreak settings for children aged 1 to 4 years and adults who have received 1 dose of vaccine, depending on the epidemiology of the outbreak.[ix]
2010	ACIP makes the following recommendations: For the first dose of measles, mumps, rubella, and varicella vaccines at age 12 to 47 months, either measles, mumps, and rubella (MMR) vaccine and varicella vaccine or MMRV vaccine may be used. Providers who are considering administering MMRV vaccine should discuss the benefits and risks of both vaccination options with the parents or caregivers. Unless the parent or caregiver expresses a preference for MMRV vaccine, CDC recommends that MMR vaccine and varicella vaccine should be administered for the first dose in this age group. For the second dose of measles, mumps, rubella, and varicella vaccines at any age (15 months to 12 years) and for the first dose at age ≥48 months, use of MMRV vaccine generally is preferred over separate injections of its equivalent component vaccines (*i.e.*, MMR vaccine and varicella vaccine). Considerations should include provider assessment, patient preference, and the potential for adverse events.[x]

2018	ACIP recommends that persons previously vaccinated with two doses of a mumps virus-containing vaccine who are identified by public health authorities as being part of a group or population at increased risk for acquiring mumps because of an outbreak should receive a third dose of a mumps virus-containing vaccine.[xi]
Current Schedule	ACIP recommends routine administration of two doses of mumps vaccine. It recommends either MMR or MMRV for the first dose, which should be administered at 12 to 15 months. It recommends MMRV for the second dose, which should be administered at 4 to 6 years old. The second dose may be given as early as four weeks after the first dose. For catch-up vaccinations, ACIP recommends two doses at least 4 weeks apart. For international travel, ACIP recommends that infants 6 to 11 months received one dose before departure and two doses at 12 to 15 months (12 months in high risk areas). The second dose can be given as early as 4 weeks after the first dose. For children over 12 months, ACIP recommends two doses at least 4 weeks apart before departure. During a mumps outbreak, persons older than 12 months who have previously received two or less doses and are identified by public health authorities to be at increased risk during an outbreak should receive one dose.[xii]

[i] This is not intended to be an exhaustive list, nor a full description in detail.

[ii] CDC, Recommendation of the Public Health Service Advisory Committee on Immunization Practices: mumps vaccine. MMWR 1967; 16:430-1.

[iii] CDC, Recommendation of the Public Health Service Advisory Committee on Immunization Practices: mumps vaccine. MMWR 1968; 17:419.

[iv] CDC, Mumps Surveillance: January 1972-June 1974. Atlanta, GA: U.S. Department of Health, Education, and Welfare, Public Health Service, 1974.

[v] CDC, Recommendation of the Public Health Service Advisory Committee on Immunization Practices: mumps vaccine. MMWR 1977; 26:393-4.

[vi] CDC, Recommendation of the Immunization Practices Advisory Committee (ACIP): mumps vaccine. MMWR 1980; 29:87-8,93-4.

[vii] CDC, Measles prevention: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 1989; 38(No. S-9):1-18.

[viii] CDC, Measles, Mumps, and Rubella – Vaccine Use and Strategies for Elimination of Measles, Rubella, and Congenital Rubella Syndrome and Control of Mumps: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 1998; 47(RR-8); 1-57.

[ix] CDC, Notice to Readers: Updated Recommendations of the Advisory Committee on Immunization Practices (ACIP) for the Control and Elimination of Mumps. MMWR 2006; 55(22):629-30.

[x] CDC. Use of Combination Measles, Mumps, Rubella, and Varicella Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2010; 59(RR03); 1-12.

[xi] CDC, Recommendation of the Advisory Committee on Immunization Practices for Use of a Third Dose of Mumps Virus – Containing Vaccine in Persons at Increased Risk for Mumps During an Outbreak. MMWR 2018; 67(1); 33-38.

[xii] CDC, Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger, UNITED STATES, 2018 (Jan. 1, 2018).

Schedule 9

Statistics on Outbreaks of Mumps Disease

Year	Reported Mumps Cases
1986	7,790[i]
1987	12,848
1988	4,866
1989	5,712
1990	5,292
1991	4,264
1992	2,572
1993	1,692
1994	1,537
1995	906
1996	751
1997	683
1998	666
1999	387
2000	338
2001	266

Year	Reported Mumps Cases
2002	270
2003	231
2004	258
2005	314
2006	6,584
2007	800
2008	454
2009	1991
2010	2,612
2011	404
2012	229
2013	584
2014	1,223[ii]
2015	1,329[iii]
2016	6,369[iv]
2017	5,629[v]

[i] Annual data from 1986 through 2013 comes from the 13th Edition of the Centers for Disease Control and Preventions textbook *Epidemiology and Prevention of Vaccine-Preventable Diseases* (Pinkbook), Appendix E.

[ii] Centers for Disease Control, MMWR, *Summary of Notifiable Infectious Diseases and Conditions – United States, 2014*, 63(54), 20 (2016).

[iii] Centers for Disease Control, MMWR, *Summary of Notifiable Infectious Diseases and Conditions – United States, 2015*, 64(53), 22 (2017).

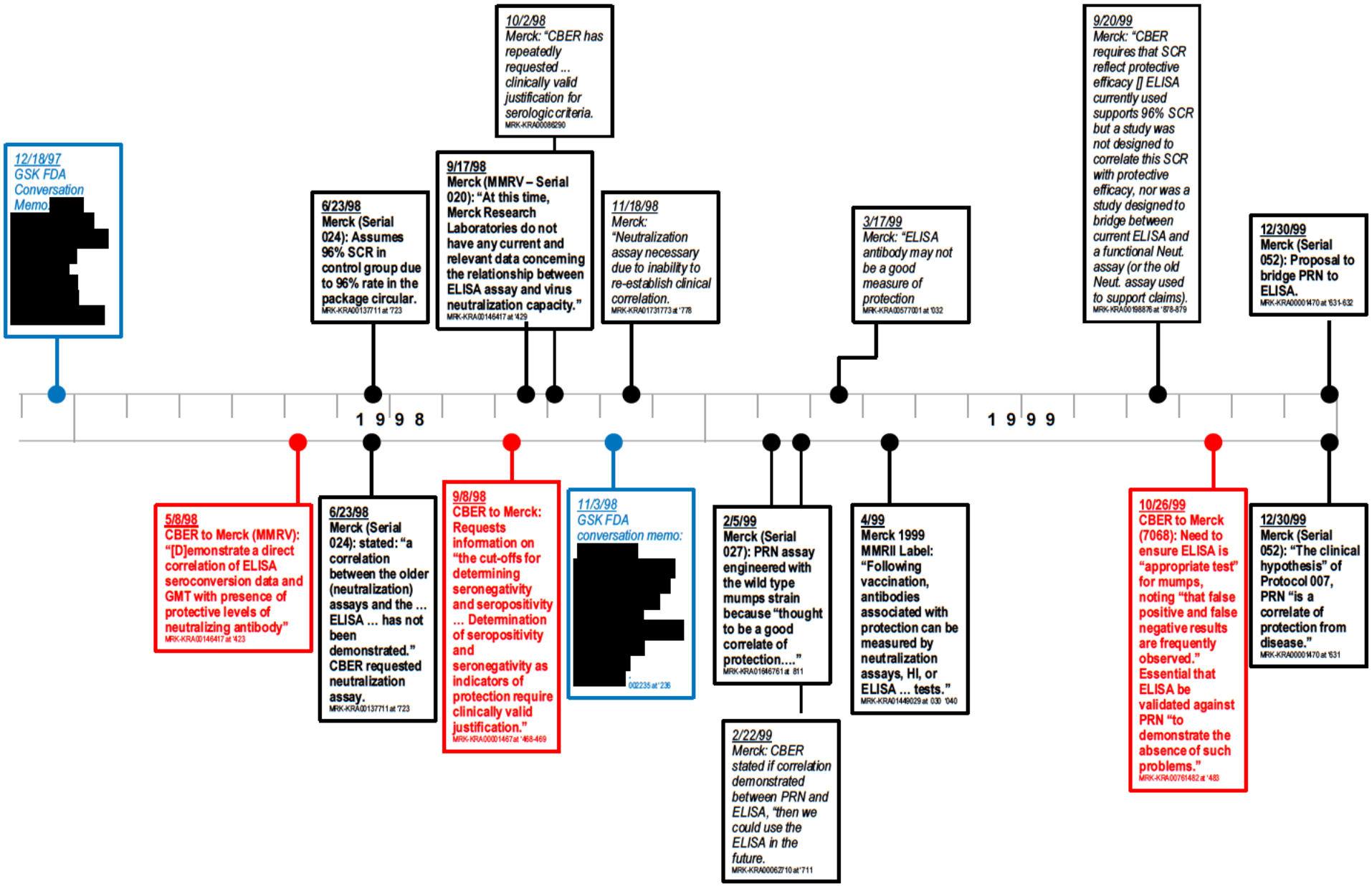
[iv] National Notifiable Infectious Diseases and Conditions: United States, Annual Data for 2016, Table 2j "Meningococcal disease; Mumps; Novel Influenza A virus infections," CDC Wonder website, available at https://wonder.cdc.gov/nndss/static/2016/annual/2016-table2j-H.pdf.

[v] National Notifiable Infectious Diseases: Weekly Tables, Table II (Part 11) "Meningococcal disease; Mumps; Pertussis," CDC Wonder website, available at https://wonder.cdc.gov/nndss/nndss_weekly_tables_menu.asp?mmwr_year=2017&mmwr_week=52.

Schedule 10

Correlates of Protection Statement Timeline

Correlates of Protection Statement Timeline

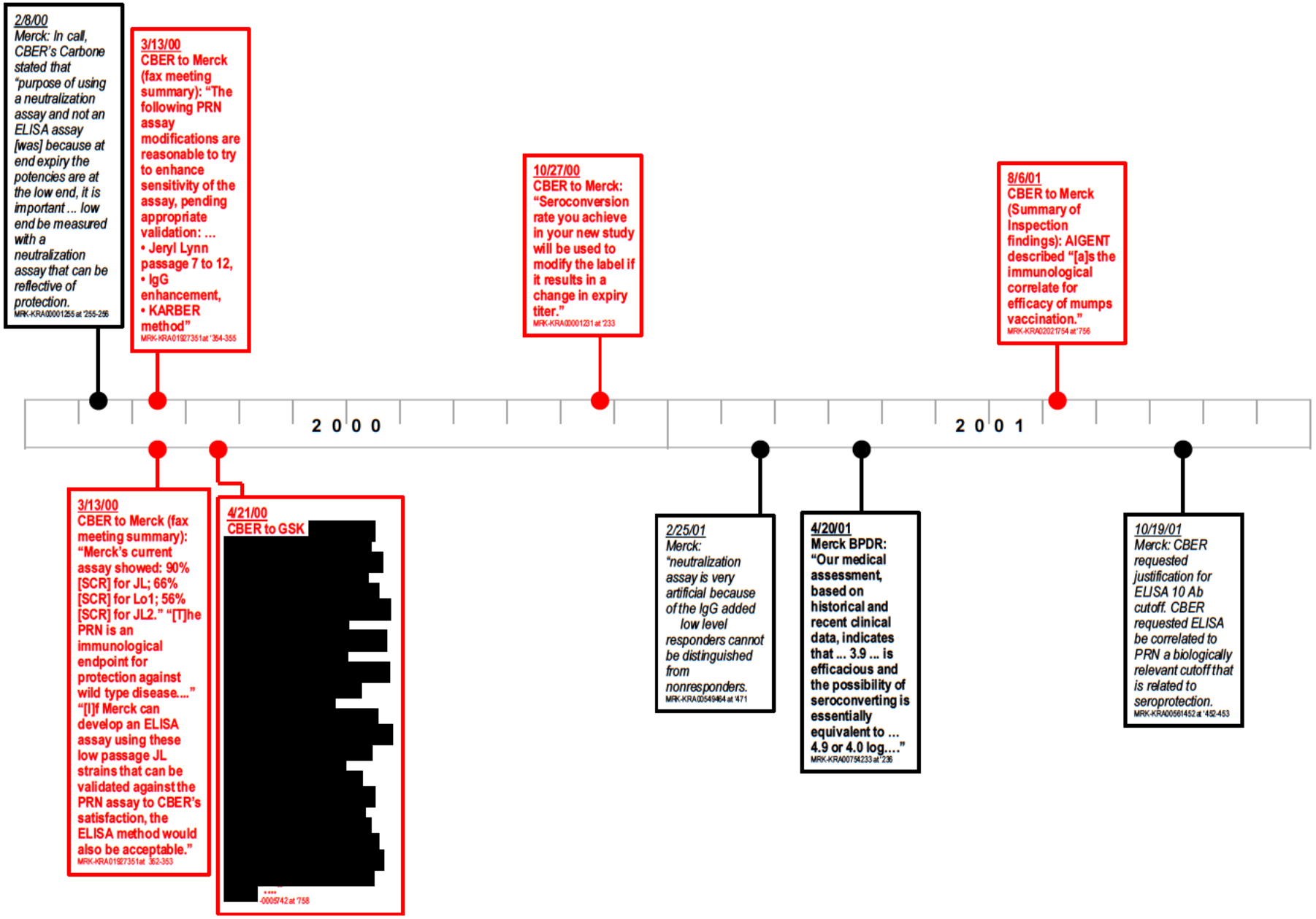


Appx1329

KEY: Formal Merck to CBER; *Merck internal*; **Formal CBER to Merck/GSK;** *GSK internal*

This is not intended to be an exhaustive timeline, nor a full description in detail.

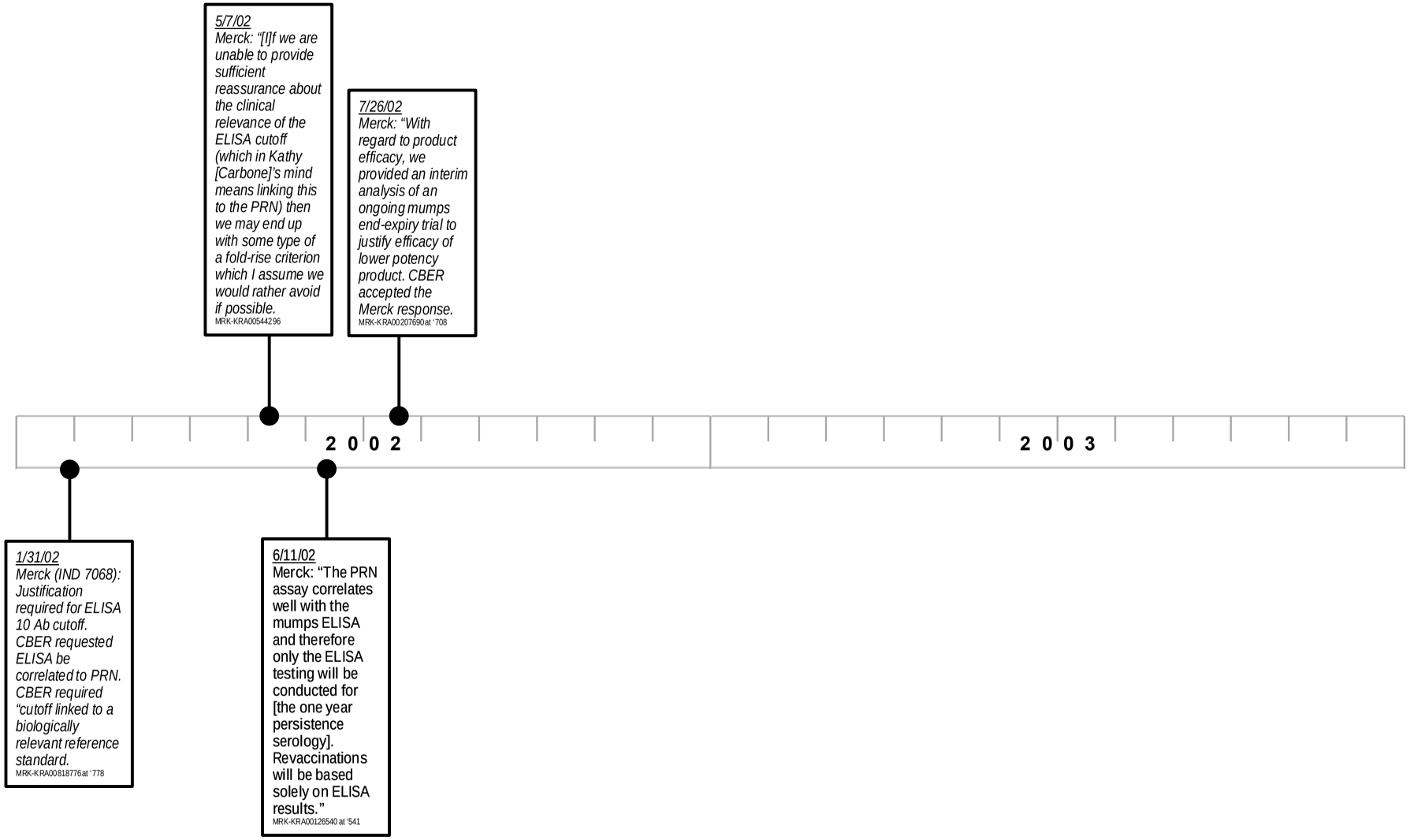
Correlates of Protection Statement Timeline



KEY: Formal Merck to CBER; *Merck* internal; Formal CBER to Merck/GSK; GSK internal

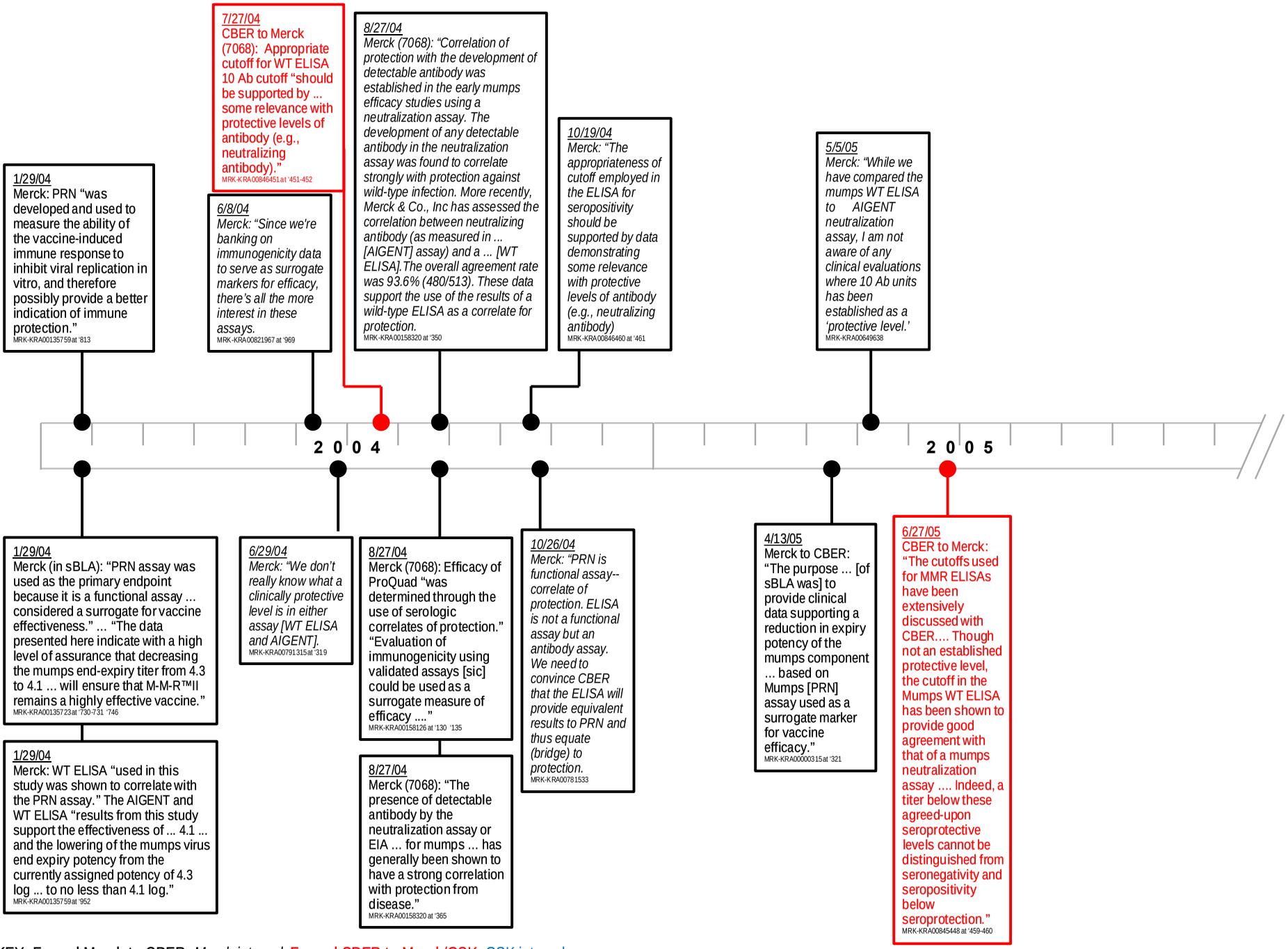
Appx1330

Correlates of Protection Statement Timeline



KEY: Formal Merck to CBER; *Merck internal*; Formal CBER to Merck/GSK; GSK internal

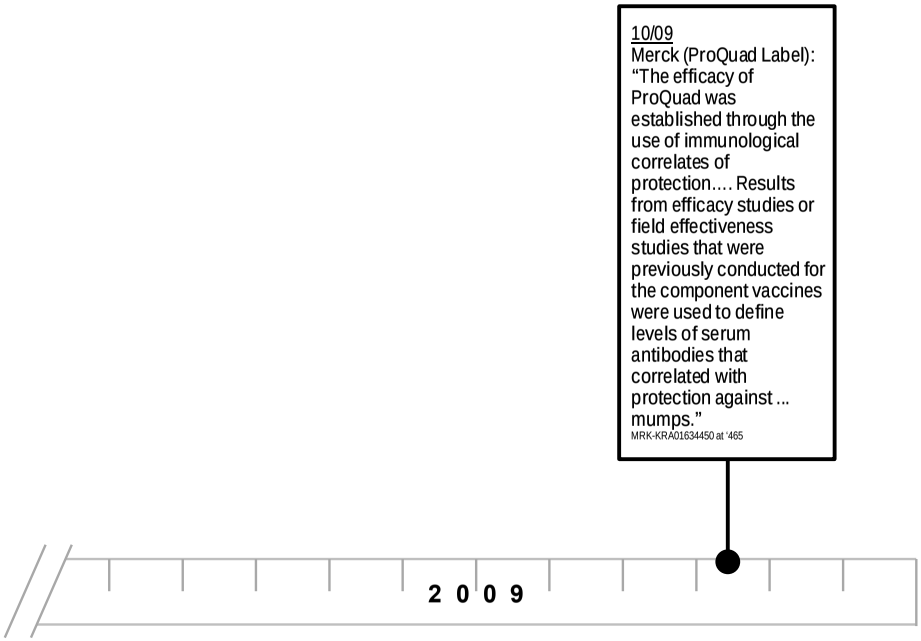
Correlates of Protection Statement Timeline



KEY: Formal Merck to CBER; *Merck internal*; Formal CBER to Merck/GSK; GSK internal

Appx1332

Correlates of Protection Statement Timeline



Appx1333

KEY: Formal Merck to CBER; *Merck internal*; Formal CBER to Merck/GSK; GSK internal

Schedule 11

MMRII – Regulatory History

MMRII – Regulatory History[1]

Date	Event
June 30, 1967	Merck submitted an Initial Investigation New Drug (IND) Application for a combined measles, mumps, and rubella vaccine ("MMR").[2]
April 22, 1971	NIH's Division of Biologics Standards (DBS)[3] approved the IND for MMR.[4]
September 5, 1975	Merck submitted an IND for "MMRII."[5] This IND was designated BB-IND 1016. MMRII included the RA 27/3 (human diploid fibroblast) strain of rubella vaccine instead of other strains.[6] Clinical testing of MMRII and the RA27/3 strain of rubella vaccine started in January 1976.[7] The RA 27/3 strain replaced previous strains HPV-77 and Cendehill because it induced a higher and more persistent antibody response and was associated with fewer adverse events.[8]
September 15, 1978	FDA approved the IND for MMRII and licensed the combined measles, mumps, and rubella vaccine that included RA27/3.[9]
1977-1980	Merck submitted seven post-marketing studies it performed from 1975 to 1978 to support the original licensure of MMRII.[10]
January 1979	FDA approved[11] the RA 27/3 (human diploid fibroblast) strain of rubella vaccine (Meruvax II); all other strains were discontinued.[12]
February 1996	FDA initiated a Section 314 review of the MMRII label.[13] From this it was determined that an end expiry study needed to be done.[14]
November 5, 1997	Meeting between FDA's CBER and Merck involved a discussion concerning the requirement to state in the label end of shelf-life titer for

[1] This is not intended to be an exhaustive history, nor a full description in detail.
[2] MRK-KRA00283308.
[3] Testing vaccines was regulated by NIH's Division of Biologics Standards until 1972 when this function was transferred to the Food and Drug Administration.
https://www fda.gov/AboutFDA/WhatWeDo/History/ucm064476.htm.
[4] http://www.immunize.org/timeline/ (BLA 101069); *see also, e.g.*, MRK-KRA00153450; MRK-KRA01538727.
[5] MRK-KRA00283308.
[6] The RA 27/3 strain was first isolated by Dr. Stanley Plotkin in the late 1960's. *See, e.g.*, Ross, Christian H. "Stanley Alan Plotkin's Development of a Rubella Vaccine (1969)." Embryo Project Encyclopedia (2017-06-28). Available at https://embryo.asu.edu/pages/stanley-alan-plotkins-development-rubella-vaccine-1969. *See also* Plotkin, "The History of Rubella and Rubella Vaccination Leading to Elimination," Clinical Infectious Diseases, 2006, 43, Supplement 3, S164-S168.
[7] *See, e.g.*, MRK-KRA01383134 at '4008-146.
[8] AAP-0001315 at '325; GSK-MMR-0177368 at '383.
[9] MRK-KRA00019685 at '698; MRK-KRA00019109 at '111.
[10] MRK-KRA00792125 at '134. Reports on these studies appear to have been submitted to the FDA between 1977 and 1980 (MRK-KRA01383134 at '4003-146).
[11] "The U. S. Food and Drug Administration (FDA) must license (approve) a vaccine before it can be used in the United States."
https://www fda.gov/downloads/biologicsbloodvaccines/safetyavailability/vaccinesafety/ucm298181.pdf.
[12] http://www.immunize.org/timeline/; Plotkin, "The History of Rubella and Rubella Vaccination Leading to Elimination," Clinical Infectious Diseases, 2006, 43, Supplement 3, S164–S168.
[13] MRK-KRA00095142; MRK-KRA01972735 at '737; MRK-KRA00625250.
[14] *See* MRK-KRA01972735.

Date	Event
	mumps,[15] and the determination that Merck's label was interpreted to state an end-expiry mumps specification.[16]
December 16, 1997	In response to FDA questions, Merck presented a proposal for a clinical trial to investigate mumps immunogenicity at vaccine end expiry (Protocol 007).[17] The study was designed to determine if children vaccinated with MMRII at mumps virus end-expiry potency below 4.3 log10 TCID50 would achieve similar seroconversion rates as children receiving MMRII at the targeted mumps release potency (~4.9 log10 TCID50).[18]
1998-1999	Merck submitted additional information related to the clinical trial to investigate mumps immunogenicity at vaccine expiry (Protocol 007) at least from January 28, 1998 through August 20, 1999.[19]
January 28, 1998	Merck submitted a description of the stability analyses performed by Merck using a mixed effect statistical model, which is supposed to acknowledge variability among lots.[20] This was part of information submitted concerning the clinical trial investigating the mumps immunogenicity at vaccine expiry.
June 23, 1998	Merck submitted a detailed proposal describing the clinical trial protocol for evaluating the immunogenicity of the expiry potency of the mumps component in the trivalent vaccine.[21] This was part of information submitted concerning the clinical trial investigating the mumps immunogenicity at vaccine expiry.
February 5, 1999	Merck submitted additional information regarding the approach to assigning the potency of the aged vaccine lots used in clinical trial to investigate mumps immunogenicity at vaccine expiry.[22]
April 9, 1999	Merck submitted a request to supplement the Biologics License Application (BLA) for MMRII to use Grifols as an alternate vendor of human serum albumin (HSA) due to an uncertainty of supply from the currently approved vendors of HSA, Centeon, and Michigan Biologics Products Institute.[23]
June 18, 1999	Merck submitted a letter to CBER noting that the label expiry claim would be reevaluated once the clinical trial was complete. Merck further proposed an increase in the release titer for mumps-containing vaccines and changes to the assay format for potency testing.[24] This was part of information submitted concerning the clinical trial investigating the mumps immunogenicity at vaccine expiry.

[15] MRK-KRA01972448 at '451.
[16] MRK-KRA01972448 at '451.
[17] MRK-KRA00000315 at '320.
[18] MRK-KRA00001222; MRK-KRA00001270; MRK-KRA00018536.
[19] MRK-KRA00018536.
[20] MRK-KRA00049100.
[21] MRK-KRA00137711.
[22] MRK-KRA00137638.
[23] MRK-KRA00262316 at '318; MRK-KRA01972602 at '603; MRK-KRA01968029.
[24] MRK-KRA00018608.

Date	Event
August 1999	Several conversations took place between Merck and FDA regarding increasing the minimum release titer for the mumps component of mumps-containing vaccines to 5.0 log10 TCID50.[25]
October 20, 1999	Merck submitted a prior approval supplement to the BLA for MMRII to increase the target mumps potency from 4.9 to 5.2 log10 TCID50 with minimum release potency specification of 5.0 log10 TCID50.[26]
September 28, 1999	FDA approved Merck's Supplemental Biologics License Application (sBLA) for MMRII to include Grifols as an alternate vendor of HSA.[27]
February 11, 2000	FDA approved Merck's prior approval supplement for MMRII to increase the target mumps potency from 4.9 to 5.2 log10 TCID50 with minimum release potency specification of 5.0 log10 TCID50.[28]
2000-2001	Merck submitted additional information related to the comparison of low and high mumps titer lots at least from February 24, 2000 through March 20, 2001.[29]
February 24, 2000	Merck submitted a proposal for monitoring and analyzing spontaneously reported adverse events for mumps containing vaccines that include the increased minimum release titer of 5.0 log10 TCID50 for the mumps component.[30]
March 13, 2000	Merck and CBER personnel held an in-person meeting to discuss, among other things, Merck's proposed changes to the neutralization assay to be used in Protocol 007.[31] At the conclusion of the meeting, Merck and CBER prepared summaries of the discussion.[32] CBER stated that it was reasonable to try certain methods to enhance the sensitivity of the assay, pending appropriate validation, including the use of the Jeryl Lynn passage 7 to 12 antigen, an IgG enhancement, and the KARBER method. CBER also requested validation data for the neutralization assay to be submitted for their review and concurrence with protocol. It was also recommended that a reference serum be included in all assays to assess assay-to-assay variability.[33]
April 3, 2000	Merck submitted a request to supplement the BLA for MMRII to include a culture medium re-feed for the mumps harvested virus fluids manufacturing process on day 2 of the 4-day infection cycle.[34]

[25] MRK-KRA00018629.
[26] MRK-KRA00040705; MRK-KRA00018536 at '537; MRK-KRA01622093.
[27] MRK-KRA01968026.
[28] MRK-KRA00018536 at '537; MRK-KRA00049174 at '175; MRK-KRA01622070.
[29] MRK-KRA00025183; MRK-KRA00019634; MRK-KRA00019636; MRK-KRA00019638; MRK-KRA00019647; MRK-KRA00024594; MRK-KRA01899087 at '088; MRK-KRA00625182 at '184; MRK-KRA01622067; MRK-KRA01630295; MRK-KRA01623322.
[30] MRK-KRA00025183; MRK-KRA01622067; MRK-KRA01622068.
[31] MRK-KRA01927351; MRK-KRA00001262.
[32] MRK-KRA01927351; MRK-KRA00001262.
[33] MRK-KRA01927351; MRK-KRA00001262.
[34] MRK-KRA01965392.

Date	Event
June 30, 2000	Merck submitted an annual report that included review of the potency assay variability in the mumps reference standard after 6 months of experience.[35]
October 6, 2000	Merck submitted a report summarizing reported adverse events for MMRII lots manufactured with high mumps potency target compared with historical lots.[36]
February 2, 2001	Merck submitted a validation report to the FDA for the mumps wild type ELISA where the serostatus cutoff was set at 10 Ab units/mL.[37]
2001-2002	Merck submitted additional information to the FDA regarding the 10 Ab cutoff for the wild type ELISA at least from March 12, 2001 through June 10, 2002.[38]
March 12, 2001	Merck submitted a summary of the validation of the anti-IgG enhanced mumps wild-type plaque-reduction assay as well as a proposal to validate the wild-type mumps ELISA assay to support use of the wild-type mumps ELISA in the mumps end-expiry study.[39]
March 20, 2001	Merck submitted a report comparing reported adverse events and adverse events reporting rates associated with low and high fill mumps titer lots of MMRII.[40]
August 7, 2001	Merck's sBLA to include a culture medium re-feed for the mumps harvested virus fluids manufacturing process on day 2 of the 4-day infection cycle was approved.[41]
October 10, 2001	Merck submitted information from a bridging study on mumps wild type ELISA and legacy mumps ELISA.[42]
October 12, 2001	Merck submitted an IND for Combined Live Measles-Mumps-Rubella (RA27/3) Virus Vaccine (with Recombinant Human Albumin – rHA) to be able to investigate the bioequivalence of MMRII manufactured with recombinant human albumin (rHA) as compared to MMRII manufactured with HSA.[43]
January 26, 2001	FDA agreed to the clinical evaluation of MMRII manufactured with rHA compared to HSA to be used in support of licensure of MMRII with rHA. This sBLA was a manufacturing supplement to the existing MMRII license (STN 101069).[44]

[35] MRK-KRA01630295.
[36] MRK-KRA00625182.
[37] MRK-KRA00154997.
[38] MRK-KRA00545051; MRK-KRA00761628 at '629; MRK-KRA00017036 at '038.
[39] MRK-KRA00017036 at '038.
[40] MRK-KRA01623322.
[41] MRK-KRA01624008.
[42] MRK-KRA00761628 at '629.
[43] MRK-KRA00196728 ("M-M-R®II (STN 101069) is currently manufactured using serum-derived Human Albumin as a component of the viral growth media in the bulk manufacturing process. To address use of material derived from blood or blood products, Merck plans to substitute Recombumin™ 20% [recombinant human albumin (rHA)] for human serum albumin (HSA) in the manufacturing process for M-M-R®II."); *see also id.* at '730 (noting that the IND is being submitted "[a]t CBER's request.").
[44] MRK-KRA00196728.

Date	Event
June 10, 2002	Merck submitted Serial 086 seeking to justify the 10 Ab cutoff chosen for the mumps wild type ELISA, providing clarification regarding reference sera used in the mumps wild type ELISA as they related to the AIGENT (Anti-IgG Mumps Plaque Reduction Neutralization) Assay and providing certain data of titers in relative range around cutoffs of both assays in order to confirm that both assays are categorizing sera in a comparable fashion.[45]
September 16, 2002	Merck submitted a request to supplement the BLA for MMRII to include a measles product formulation change and product potency assay format changes, including incorporating house standard calibration of measles, mumps, and rubella potency to all potency results, including release and stability testing.[46] Additional information was submitted at least on October 1, 2003.[47]
June 26, 2003	Merck submitted a request to supplement the BLA for MMRII to request an exemption from general safety testing as a release test for MMRII.[48] Additional information was submitted on at least September 26, 2003.[49]
August 18, 2003	Merck submitted information related to use of a new measles stock seed in the MMRII vaccine due to limited volume of the original 1967 measles stock seed.[50]
October 24, 2003	FDA approved Merck's request for exemption from general safety testing as a release test for MMRII.[51]
January 29, 2004	Merck submitted a request to supplement the BLA for MMRII to reduce the quantity of mumps virus included in MMRII from 20,000 $TCID_{50}$ per vaccine dose to 12,500 $TCID_{50}$ per vaccine dose.[52] Additional information related to this was submitted at least from December 3, 2004 to April 13, 2005,[53] and this sBLA was resubmitted on April 18, 2005.[54] Additional information was submitted at least from July 13, 2005 to June 5, 2007.[55]
February 27, 2004	Merck submitted a request to supplement the BLA for MMRII for approval of the use of white leghorn chicken (WG) eggs as an alternate source of primary chick embryo cells in the manufacture of measles and mumps vaccines.[56] Additional information was submitted on at least June 1, 2004 through July 26, 2004.[57]

[45] MRK-KRA00126468
[46] MRK-KRA01926583 at '584.
[47] MRK-KRA01899087
[48] MRK-KRA01624340.
[49] MRK-KRA01967402.
[50] MRK-KRA00020789.
[51] MRK-KRA01971295.
[52] MRK-KRA00000032.
[53] MRK-KRA00018817; MRK-KRA00000302; MRK-KRA00000315.
[54] MRK-KRA00000301.
[55] MRK-KRA00141789; MRK-KRA00000387; MRK-KRA00000393; MRK-KRA00000554; MRK-KRA00000368.
[56] MRK-KRA01971489.
[57] MRK-KRA01971339; MRK-KRA01971329; MRK-KRA01971327; MRK-KRA01971325; MRK-KRA01971324.

Date	Event
June 30, 2004	Merck submitted a request to supplement the BLA for MMRII and replace the currently used HSA with rHA (STN 101069/5068) (Protocol 009).[58]
October 19, 2004	FDA approved Merck's sBLA for MMRII to use of white leghorn chicken (WG) eggs as an alternate source of primary chick embryo cells in the manufacture of measles and mumps vaccines.[59]
December 13, 2004	Merck submitted a request to supplement the BLA for MMRII to propose a specification change to the rubella component and propose product potency format assay changes for the mumps and rubella components. This included changing the minimum release specification for the rubella component from 3.2 to 3.4 log TCID50 of dose as well as employing a two-tiered potency testing scheme using expanded testing in the assignment of release and stability potencies for mumps and rubella, with measured initial results that are at or below the release specifications. This two-tiered testing format was previously approved for the measles component on May 18, 2004.[60]
May 24, 2005	FDA approved Merck's sBLA for MMRII proposing mumps potency format assay changes.[61]
August 31, 2005	FDA approved Merck's sBLA to replace HSA with rHA in MMRII.[62] Launch of the rHA formulation did not occur until September 2006.[63]
July 28, 2006	FDA approved the licensure of MMRII manufactured from 2003 Measles Stock Seed manufactured with rHA (STN 101069/5105).[64]
October 31, 2007	Merck submitted a request to supplement the BLA for MMRII to request approval of the use of Sterile Diluent manufactured by DSM Laboratories in reconstitution of MMRII.[65]
December 6, 2007	FDA approved Merck's sBLA for MMRII to reduce the quantity of mumps virus included in MMRII from 20,000 $TCID_{50}$ per vaccine dose to 12,500 $TCID_{50}$ per vaccine dose.[66]
June 23, 2008	Merck submitted a request to supplement the BLA for MMRII to remove sterility, characteristics, total solids, specific gravity, and general safety testing on the 25% v/v gelatin solution used as an excipient in the vaccine formulation.[67]
December 23, 2008	FDA approved Merck's sBLA for MMRII to remove sterility, characteristics, total solids, specific gravity, and general safety testing on the 25% v/v gelatin solution used as an excipient in the vaccine formulation.[68]

[58] MRK-KRA00000226 at '231; MRK-KRA00792125 at '134.
[59] MRK-KRA01971321.
[60] MRK-KRA01926377 at '379.
[61] MRK-KRA01971196.
[62] MRK-KRA00388445; *see also* MRK-KRA00618143; MRK-KRA00000226 at '231.
[63] MRK-KRA00000226 at '231.
[64] MRK-KRA00618143.
[65] MRK-KRA01968956.
[66] MRK-KRA00000383.
[67] MRK-KRA01969891.
[68] MRK-KRA01969886.

Date	Event
January 16, 2009	FDA approved Merck's sBLA for use of Sterile Diluent manufactured by DSM Laboratories in reconstitution of MMRII.[69]
April 29, 2009	Merck submitted a trans-BLA for MMRII for approval for the extension of measles and mumps bulk expiries to nine and twelve years respectively.[70]
July 22, 2009	FDA approved Merck's trans-BLA for MMRII for the extension of measles and mumps bulk expiries to nine and twelve years respectively.[71]
December 17, 2009	Merck submitted a trans-BLA for approval of the use of vaporous hydrogen peroxide (VHP) to replace paraformaldehyde for decontamination of the measles, mumps, and rubella manufacturing units between harvest product changeovers.[72]
July 30, 2010	FDA approved Merck's trans-BLA for the use of VHP to replace paraformaldehyde for decontamination of the measles, mumps, and rubella manufacturing units between harvest product changeovers.[73]
July 20, 2011	Merck submitted a request to supplement the BLA to implement two new reference standards for use in the mumps and rubella potency assays used in the manufacture of ProQuad® and MMRII.[74]
December 20, 2011	FDA approved Merck's sBLA to implement two new reference standards for use in the mumps and rubella potency assays used in the manufacture of ProQuad® and MMRII.[75]
March 21, 2014	Merck submitted a request to supplement the BLA for MMRII to include removal of the lower specification for neomycin potency for MMRII Final Formulated Bulk (FFB).[76]
April 28, 2014	FDA approved Merck's sBLA to include removal of the lower specification for neomycin potency for MMRII FFB.[77]

[69] MRK-KRA01314418.
[70] MRK-KRA01968981.
[71] MRK-KRA01968978.
[72] MRK-KRA01968792.
[73] MRK-KRA00124041.
[74] MRK-KRA00134105.
[75] MRK-KRA02143436; MRK-KRA01968415.
[76] MRK-KRA01968074.
[77] MRK-KRA00142086.

Schedule 12

ProQuad – Regulatory History

ProQuad – Regulatory History[1]

Date	Event
February 28, 1997	Merck submitted an Initial Investigation New Drug Application (IND) for a measles-mumps-rubella-varicella vaccine ("ProQuad®") to the Food and Drug Administration (FDA).[2]
March 15, 2000	Merck submitted additional information to clarify the indication for the measles-mumps-rubella-varicella vaccine.[3]
November 17, 2000	Merck submitted background documents for BB-IND 7068 to describe chemistry, manufacturing and control ("CMC") for ProQuad® as the Biologics License Application (BLA) was being prepared.[4] A Type B meeting with the FDA was held on December 18, 2000.[5] Follow up information was submitted on at least March 12, 2002.[6]
September 10, 2003	Merck submitted a clinical study report describing a randomized multicenter study of the safety, tolerability, and immunogenicity of frozen ProQuad® given concomitantly with other vaccines to healthy children 12 to 15 months of age.[7]
2004-2005	Extensive discussion between the FDA and Merck about the assay validation protocols for the measles, mumps, and rubella ELISA assays.[8] A validation report in Serial 086 for the mumps WT ELISA where the serostatus cutoff is 10 Ab units/mL was submitted to the FDA on June 14, 2004. This protocol was previously submitted to the FDA under the IND for MMRII.[9]
August 27, 2004	Merck submitted original BLA 125108 for ProQuad® to the FDA. ProQuad® was indicated for simultaneous vaccination against measles, mumps, rubella, and varicella in individuals 12 months to 12 years of age.[10]
July 21, 2005	Merck submitted information describing plans to conduct four post-licensure studies with ProQuad®.[11]
August 26, 2005	Clinical review of studies submitted in support of the licensure of ProQuad® was completed.[12]
September 6, 2005	FDA approved BLA 125108 for ProQuad® for the vaccination against measles, mumps, rubella, and varicella in children 12 months to 12 years of

[1] This is not intended to be an exhaustive history, nor a full description in detail.
[2] MRK-KRA00145486.
[3] MRK-KRA00019837; MRK-KRA00020378; MRK-KRA00025188.
[4] MRK-KRA01974364.
[5] MRK-KRA00149924; MRK-KRA00152955.
[6] MRK-KRA00152955.
[7] MRK-KRA00164918.
[8] MRK-KRA00155481; MRK-KRA00782807; MRK-KRA00620408; MRK-KRA00846076; MRK-KRA00846451; MRK-KRA00819969; MRK-KRA00846087.
[9] MRK-KRA00154997.
[10] MRK-KRA00157572; MRK-KRA00158320.
[11] MRK-KRA00176666.
[12] GSK-MMR-0147041; *see also* http://wayback.archive-it.org/7993/20170723150913/https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM123800.pdf.

Date	Event
	age.[13] Approval was for ProQuad® vaccine stored at ≤ -15°C.[14] The FDA approved Merck's ProQuad® based on five pivotal studies: Protocol 009, Protocol 010, Protocol 012, Protocol 013, and Protocol 014, which enrolled subjects and were conducted between March 1998 and May 2002.[15]
September 28, 2005	Merck submitted a request to supplement the ProQuad® BLA to include an algorithm for determining the stability of the vaccine when stored at temperatures higher than -15°C.[16] Additional information related to this was submitted from at least December 20, 2005 to October 12, 2006.[17]
December 2005	Merck proposed a revision of the minimum shelf life for ProQuad® to be 8 months, instead of the 12 months minimum shelf life requested by the CDC.[18] Merck represented to the CDC that this was related to later than anticipated licensure and was expected to be a short term situation.
March 15, 2006	Merck submitted a request to supplement the ProQuad® BLA to include intermediate storage of the vaccine at ≤ -20° C for a maximum of 12 months.[19]
April 5, 2006	Merck submitted a request to supplement the ProQuad® BLA to include a refrigerator-stable formulation.[20] Additional information related to this supplement was submitted on at least August 2, 2006.[21]
June 9, 2006	Merck submitted a request to supplement the ProQuad® BLA to include a comparability protocol for the manufacturing and certification of new stock seeds and working cell banks.[22]
July 6, 2006	FDA approved Merck's sBLA for ProQuad® to include an algorithm for determining the stability of the vaccine when stored at temperatures higher than -15°C.[23]
July 2007	Supplies of ProQuad® were temporarily unavailable as a result of manufacturing constraints. The constraints were the result of lower-than-expected yields of bulk varicella-zoster virus in production lots.[24] Orders for ProQuad® were largely suspended in June 2007.[25]

[13] MRK-KRA00761865; MRK-KRA00184615; http://www.immunize.org/timeline/; *see also* http://wayback.archive-it.org/7993/20170723150912/https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm123799 htm.
[14] MRK-KRA00184615.
[15] MRK-KRA00158320 at '366-368.
[16] MRK-KRA00176712; MRK-KRA00176714.
[17] MRK-KRA00176725; MRK-KRA00176727; MRK-KRA00176736; MRK-KRA00176737; MRK-KRA00177264; MRK-KRA00177266.
[18] MRK-KRA00941941 at '942-943; MRK-KRA00942185; MRK-KRA00942187.
[19] MRK-KRA00176854; MRK-KRA00176856.
[20] MRK-KRA00184644.
[21] MRK-KRA00177218.
[22] MRK-KRA01973733.
[23] MRK-KRA00184664.
[24] https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5903a1.htm.
[25] GSK-MMR-0110008 at '106.

Date	Event
April 23, 2007	Merck submitted a request to supplement the BLA for ProQuad® to request approval for the use of Sterile Diluent manufactured by Hollister-Stier Laboratories in reconstitution of ProQuad®.[26]
October 24, 2007	FDA approved Merck's sBLA for ProQuad® for the use of Sterile Diluent manufactured by Hollister-Stier Laboratories in reconstitution of ProQuad®.[27]
November 9, 2007	Merck submitted a request to supplement the BLA for ProQuad® to request approval of the use of Sterile Diluent manufactured by DSM Laboratories in reconstitution of ProQuad®.[28]
June 23, 2008	Merck submitted a request to supplement the BLA for ProQuad® to remove sterility, characteristics, total solids, specific gravity, and general safety testing on the 25% v/v gelatin solution used as an excipient in the vaccine formulation.[29]
August 22, 2008	Merck provided a preliminary report on Febrile Convulsion based on the Large-Scale Post-Licensure Study of the Short-Term Safety of ProQuad®. This study was initiated in 2006.[30] The Final Study Report associated with this study was submitted on December 19, 2008.[31] Additional information was submitted on at least May 18, 2009 and September 14, 2009.[32]
September 25, 2008	Merck submitted a request to supplement the BLA for ProQuad® to cover concomitant use of ProQuad® with hepatitis A vaccine and pneumococcal conjugate vaccine. Merck also submitted safety data to support vaccination with ProQuad® as a second dose in the second year of a child's life.[33] Initial review of this application was completed on January 12, 2009.[34] Additional information related to the sBLA was submitted at least from May 14, 2009 to August 28, 2009.[35]
December 23, 2008	FDA approved Merck's sBLA for ProQuad® to remove sterility, characteristics, total solids, specific gravity, and general safety testing on the 25% v/v gelatin solution used as an excipient in the vaccine formulation.[36]
January 16, 2009	FDA approved Merck's sBLA for use of Sterile Diluent manufactured by DSM Laboratories in reconstitution of ProQuad®.[37]

[26] MRK-KRA01973293.
[27] MRK-KRA01973290.
[28] MRK-KRA01969955.
[29] MRK-KRA01969891.
[30] MRK-KRA00178644.
[31] MRK-KRA00178878.
[32] MRK-KRA00180787; MRK-KRA00181054.
[33] MRK-KRA00172584.
[34] MRK-KRA00184714.
[35] MRK-KRA00179435; MRK-KRA00180806; MRK-KRA00180974; MRK-KRA00180979; MRK-KRA00181047.
[36] MRK-KRA01969886.
[37] MRK-KRA01314418.

Date	Event
April 29, 2009	Merck submitted a trans-BLA for ProQuad® for approval for the extension of measles and mumps bulk expiries to nine and twelve years respectively.[38]
July 22, 2009	FDA approved Merck's trans-BLA for the extension of measles and mumps bulk expiries to nine and twelve years respectively.[39]
October 29, 2009	FDA approved Merck's sBLA for ProQuad® to cover concomitant use of ProQuad® with hepatitis A vaccine and pneumococcal conjugate vaccine.[40]
December 17, 2009	Merck submitted a trans-BLA for approval of the use of vaporous hydrogen peroxide (VHP) to replace paraformaldehyde for decontamination of the measles, mumps and rubella manufacturing units between harvest product changeovers.[41]
2010	Merck re-launched limited quantities of ProQuad® after the suspension of orders in 2007.[42]
July 30, 2010	FDA approved Merck's trans-BLA for ProQuad® for the use of vaporous hydrogen peroxide (VHP) to replace paraformaldehyde for decontamination of the measles, mumps and rubella manufacturing units between harvest product changeovers.[43]
February 2011	ProQuad® was unavailable again due to manufacturing issues.[44]
Early 2011	Merck requested a meeting with the FDA to discuss a proposed manufacturing change to increase the cells/dose limit for ProQuad®. On April 7, 2011, a briefing document describing a two-dose clinical study of ProQuad® in children was submitted. On May 10, 2011, a Type C meeting took place with the FDA.[45]
July 20, 2011	Merck submitted a request to implement two new reference standards for use in the mumps and rubella potency assays used in the manufacture of ProQuad® and MMRII.[46]
October 3, 2011	Merck submitted a formal request to the FDA for a Type C meeting to obtain FDA concurrence regarding the proposed clinical data package to support the licensure of the replacement of HSA with rHA in ProQuad®.[47] The Type C meeting took place on June 26, 2012.[48] Additional information related to this request was submitted at least from December 14, 2011 to May 10, 2013.[49]

[38] MRK-KRA01968981.
[39] MRK-KRA01968978.
[40] MRK-KRA00184723.
[41] MRK-KRA01968792.
[42] MRK-KRA00089585; MRK-KRA00013982 at '986; MRK-KRA01071459; MRK-KRA00013966 at '968.
[43] MRK-KRA00124041.
[44] MRK-KRA00013982 at '986.
[45] MRK-KRA00286041 at '041-042.
[46] MRK-KRA00134105.
[47] MRK-KRA00182213.
[48] MRK-KRA00184797.
[49] MRK-KRA00182213; MRK-KRA00182219; MRK-KRA00182226; MRK-KRA00143054; MRK-KRA00182837.

Date	Event
December 20, 2011	FDA approved Merck's sBLA to implement two new reference standards for use in the mumps and rubella potency assays used in the manufacture of ProQuad® and MMRII.[50]
Late 2012	ProQuad® was fully available for order.[51] Currently, ProQuad is the only measles, mumps, rubella, and varicella (MMRV) vaccine approved for use in the United States.[52]
February 21, 2014	FDA approved Merck's sBLA to replace HSA with rHA in the manufacture of measles, mumps, and rubella bulks used in the refrigerator-stable formulation of ProQuad®.[53]
December 17, 2014	FDA approved Merck's sBLA replace HSA with rHA in the manufacture of measles, mumps, and rubella bulks used in the frozen formulation of ProQuad®.[54]

[50] MRK-KRA02143436 at '437; MRK-KRA01968415.
[51] MRK-KRA00013982 at '986.
[52] https://www.cdc.gov/vaccinesafety/vaccines/mmrv-vaccine.html.
[53] MRK-KRA00184903.
[54] MRK-KRA00184876.

Schedule 13

Mumpsvax – Regulatory History

Mumpsvax – Regulatory History[1]

Date	Event
May 28, 1963	Merck submitted an Initial Investigation New Drug (IND) Application for a live mumps virus vaccine ("Mumpsvax") to the Food and Drug Administration (FDA).[2]
December 28, 1967	FDA approved the IND for Mumpsvax (BLA 101072).[3]
April 3, 2000	Merck submitted a request to supplement the Biologics License Application (BLA) for Mumpsvax to include a culture medium re-feed for the mumps harvested virus fluids manufacturing process on day 2 of the 4-day infection cycle.[4]
August 7, 2001	FDA approved Merck's Supplemental Biologics License Application (sBLA) to include a culture medium re-feed for the mumps harvested virus fluids manufacturing process on day 2 of the 4-day infection cycle.[5]
December 13, 2004	Merck submitted a request to supplement the BLA for Mumpsvax to propose product potency format assay changes for the mumps and rubella components. This included employing a two-tiered potency testing scheme using expanded testing in the assignment of release and stability potencies for mumps, with measured initial results that are at or below the release specifications. This two-tiered testing format was previously approved for the measles component on May 18, 2004.[6] Additional information related to this supplement was submitted on January 19, 2005.[7]
October 21, 2009	Merck announced that the company would discontinue production of monovalent measles, mumps, and rubella vaccines.[8]
May 27, 2013	Merck requested voluntary revocation of the biologics license for Mumpsvax.[9]
October 3, 2013	Biologics license for Mumpsvax was revoked by the FDA.[10]

[1] This is not intended to be an exhaustive history, nor a full description in detail.
[2] MRK-KRA00283308.
[3] http://www.immunize.org/timeline/; *see also, e.g.*, MRK-KRA01962790.
[4] MRK-KRA01965392.
[5] MRK-KRA01965382.
[6] MRK-KRA01926377 at '379.
[7] MRK-KRA01926962.
[8] http://www.immunize.org/timeline/.
[9] MRK-KRA02143656.
[10] MRK-KRA02143656.

Schedule 14

Summary of Relevant Manufacturing Changes to MMRII and ProQuad

DATE	DOCUMENT	DESCRIPTION
1978	Hilleman, "Combined Measles Mumps and Rubella Vaccines, Combined Vaccines: Development, Clinical Research and Approval" (Humana Press Inc. 1999)	FDA licenses MMRII (the HPV-77 DE strain of live attenuated rubella strain in MMR was replaced with the Wistar RA 27/3 strain).
1990 - 1991	MRK-KRA00542860; MRK-KRA00018611	Merck changed the minimum potency specification on the U.S. label for MMRII from 5,000 TCID50/dose to 20,000 TCID50/dose. Merck switches from using BS-C-1 cell to Vero cells. According to Merck, potency did not change, but the potency testing assay became more sensitive: a lot of vaccines assayed at 5,000 TCID50 in BS-C-1 cells measured a four-fold increase in TCID50 when assayed in Vero cells. No clinical testing conducted associated with this label change.
1993	MRK-KRA00351593	Merck increases the amount of chick embryo trimmed tissue added to the plant bottle used to transfer cell suspension into each Unipro Tank (vaccine bulk manufacturing vessel) from 110 grams to 115 grams for mumps harvested bulk production. A Merck summary of this change from 2006 notes: "This change was in effect through the 1993 mumps campaign. This change was rescinded prior to the next campaign in 1996 after review of potency data from the 1993, 1990, and 1991 campaign showed an association between the lower plant weight and higher potency. This change would not be expected to affect either bulk or final product. The potency of the bulk product produced in 1993 was consistent with the potency obtained in previous mumps campaigns."
11-16-1998	MRK-KRA00783728	Merck changes the passage level of Vero cells used for potency determination of measles and mumps products. Merck states that the purpose of the change is to maintain the sensitivity of the potency assay for measles within historic ranges and for consistency with the acceptable level for potency testing.

DATE	DOCUMENT	DESCRIPTION
02-11-2000	MRK-KRA00095144; MRK-KRA01897091; MRK-KRA01965291; MRK-KRA01625225	Merck begins releasing to market MMRII and MumpsVax with double the potency. Merck increased the minimum release potency for MMRII and MumpsVax to 5.0 log to ensure that it could meet the end expiry label claim of 4.3 log at 24 months. To change minimum release potency to 5.0 log, Merck increased manufacturing target from 4.9 log to 5.2 log for lots filled on or after September 13, 1999. This overfill was supposed to be a temporary measure to last only until Merck could demonstrate through its Protocol 007 end-expiry study that the mumps component of MMRII had sufficient immunogenicity to match the 96% claim on the package insert at potencies below the existing 4.3 log end-expiry specification. The potency assay was also changed from a 3x1 to a 1x6 format for release testing, to reduce the assay variability associated with potency testing.
08-07-2001	MRK-KRA00351593	FDA approves Merck's request to add a culture medium refeed step to the mumps manufacturing process. This refeed step was a replacement of the culture medium volume in the Unipro Tank between the virus seeding of the tank with mumps seed and the harvesting of the virus fluids; no change was made to the type of culture medium used.
10-24-2003	February 9, 2018 30(b)(6) Deposition of Amy Keegan, Exhibit 9	FDA approves Merck's request for an exemption from General Safety Testing requirements for MMRII based on (1) historical General Safety Testing data demonstrating the vaccine is free of undue toxicity; (2) documents in-process safety controls; and (3) extensive adventitious agent testing.
05-18-2004	February 9, 2018 30(b)(6) Deposition of Amy Keegan, Exhibit 9	FDA approves Merck's application that included "house standard calibration of measles, mumps, and rubella potency results" in its $TCID_{50}$ assay used to measure the potency of its mumps-containing vaccines for all tests, including release and stability testing. FDA also approves changes to the potency to add resting in a 1x12 format for all lots with potencies at or below 5.0 $\log_{10}$ $TCID_{50}$/dose. Previously Merck only used this expanded testing for lots that were below the 5.0 $\log_{10}$ $TCID_{50}$/dose minimum release potency.
10-19-2004	MRK-KRA00351593	FDA approved Merck's request to use a second chicken flock (WG Chicken Flock) as an alternate flock for use in measles and mumps bulk manufacturing (Merck requested the change in 1998 because a number of its chickens from its original flock were infected with Chicken Anemia Virus and they could no longer use them).

DATE	DOCUMENT	DESCRIPTION
08-31-2005	MRK-KRA0141909	FDA approves Merck's application to replace HSA with rHA in MMRII. Merck implements this change.
09-06-2005	MRK-KRA00761865	FDA approves Merck's application for ProQuad Frozen.
08-04-2006	MRK-KRA00842361; MRK-KRA00761626	FDA approves Merck's application for ProQuad 4C. The formulation changes supporting the approval include: "1) the addition of urea … and 2) an increase in minimum release packaged container potency of … mumps virus from 4.55 log to 4.74 log 10 PFU/0.5 mL dose." This change was to address the significant potency and stability problems Merck was having with ProQuad 4C. "The newly formulated vaccine will have an expiry shelf life of 18 months when stored at 2-8 C after removal from intermediate storage at ≤ 20C for a maximum of 12 months."
12-06-2007	MRK-KRA01519087	FDA approves label change to decrease the end expiry potency specification from 20,000 TCID50 (4.3 log10 Tcid50)/dose to 12,500 TCID50 (4.1 log10 TCID)/dose (calibrated to house standard) for the mumps component of MMRII.
2010	Q&As about Monovalent M-M-R Vaccines, https://www.cdc.gov/vaccines/hcp/clinical-resources/mmr-faq-12-17-08.html	Merck discontinues sale of its monovalent, Mumpsvax. The only source of mumps vaccine in the United States is MMRII or ProQuad.
08-04-2011	MRK-KRA01285975	FDA approves a change to formulate ProQuad with the varicella Harvest Virus Fluids concentration process (HVFc ProQuad).
01-24-2012	February 9, 2018 30(b)(6) Deposition of Amy Keegan, Exhibit 9	FDA approves Merck's request to implement a new reference standard (house standard) for mumps. The reference standard is used to verify the validity of each potency test and provide a calibration tool. This reference standard is used in the manufacture of MMRII and ProQuad and used to determine potency for MMRII filled container vaccine product samples.
02-21-2014	MRK-KRA00184876; February 9, 2018 30(b)(6) Deposition of Amy Keegan, Exhibit 9	FDA approves Merck's application to replace HSA with rHA in ProQuad.

Schedule 15

Other Mumps Vaccines

Strain	Manufacturer (Vaccine Name)	Cell Substrate[a]	Main Area of Use
Jeryl Lynn or Jeryl Lynn-derived	Merck/Aventis Pasteur MSD (MMR-II in U.S., MMR-Vax in EU; ProQuad)	CWE	Worldwide
	GlaxoSmithKline (RIT-4385, Priorix, Priorix-Tetra)	CWE	Worldwide
	Netherlands Vaccine Institute (BMR vaccin)	CWE	Netherlands
	Sevapharma Inc. (Pavivac; Trivivac)	CK	Czech and Slovak Republics
	S79	CWE	China
Urabe Am9	Sanofi-Pasteur (Trimovax, Imovax mumps)	EHE	Worldwide
	GlaxoSmithKline (Pariorix, Pluserix, Trivirix)[b]	CEF	Europe, Canada
	Novartis Vaccines and Diagnostics (Vaxipar, Morupar)[b]	CEF	Italy, South America
	Biken[b]	CEF	Japan
Leningrad-Zagreb	Institute of Immunology of Zagreb	CEF	India, South America, Eastern Europe
	Serum Institute of India (Tresivac)	CEF	
Leningrad-3	Moscow State Facility of Bacterial Preparations	JQE	Russia, Eastern Europe
Rubini	Berna Biotech (Triviraten)[b]	HDC	Europe
Hoshino	Kitasato Institute (trivalent MPR)	CEF	Japan, Korea
Torii	Takeda Chemicals	CEF	Japan
NK-M46	Chiba Serum Institute	CEF	Japan
S-12	Razi State Serum & Vaccine Institute	HDC	Iran
Sofia-6	Center for Infectious and Parasitic Diseases[b]	GPK	Bulgaria

Source: Plotkin, Stanley A. et al., Plotkin's Vaccines, Table 40.3 "Mumps Vaccine Strains," p. 669 (Elsevier, 7th ed. 2017).

[a] Vaccine Production Level.
[b] No Longer Produced.
CEF, chick embryo fibroblast; CK, canine kidney cells; CWE, chick whole embryo; EHE, embryonated hen's eggs; GPK, guinea-pig kidney; HDC, human diploid cells; JQE, Japanese quail embryo.

Schedule 16

CDC Contracting Under the Vaccines for Children and 317 Programs

There are two programs under which the Centers for Disease Control and Prevention ("CDC") purchases vaccines for children: the Vaccines for Children Program ("VFC") and the Section 317 Program ("317 Program").

Program	Description[1, 2]
Vaccines for Children Program	The VFC program is a federally funded entitlement program that provides vaccines at no cost to eligible children. Most publicly funded funding comes from the VFC program. VFC became operational October 1, 1994. Known as section 1928 of the Social Security Act, the VFC program is an entitlement program (a right granted by law) for eligible children, age 18 and younger. Funding for the VFC program is approved by the Office of Management and Budget and allocated through the Centers for Medicare & Medicaid Services (CMS) to the CDC. The CDC administers and manages key elements of the program. The CDC buys vaccines at a discount and distributes them to state health departments and certain local and territorial public health agencies which in turn distribute them at no charge to private physicians' offices and public health clinics registered as VFC providers. Children are eligible for vaccines under the VFC program if they are on Medicaid, uninsured, underinsured (e.g., their private insurance does not cover vaccines or does not cover certain vaccines), or American Indian or Alaskan Native. The VFC Program helps ensure that all children have a better chance of getting their recommended vaccinations on schedule. Vaccines available through the VFC Program are those recommended by the Advisory Committee on Immunization Practices (ACIP).
317 Program	Section 317 of the Public Health Service Act authorizes the federal purchase of vaccines to vaccinate children, adolescents, and adults under the 317 Program. Over its 50 year history, Section 317 purchased vaccines have been directed towards meeting the needs of priority populations. Most recently this has included underinsured children not eligible for VFC, as well as uninsured adults. Section 317 fills critical public health needs, such as providing routine vaccination for those with no insurance and responding to outbreaks

[1] This is not intended to be exhaustive, nor a full description in detail.

[2] General Sources:
https://www.cdc.gov/vaccines/imz-managers/guides-pubs/qa-317-funds html.
https://www.cdc.gov/vaccines/programs/vfc/index.html.
U.S. House of Representatives, Committee on Energy and Commerce, Subcommittee on Health and the Environment, Childhood Immunizations, September 1986, Committee Print 99-LL.
Deposition of Alan Sims, October 12, 2017, pgs. 19-22, 45-51, 156.
Deposition of Mark Pallansch, October 13, 2017, pgs. 97-98.

Program	Description[1, 2]
	of vaccine-preventable diseases. The 317 Program fills in vaccine coverage for those ineligible for vaccines under the VFC Program.
CDC Purchasing under VFC and 317 Programs	In order for the CDC to purchase a vaccine under these programs, the vaccine needs to be licensed and a part of the recommended vaccination schedule. In those cases, the CDC typically puts out an open bid to vaccine suppliers on a yearly basis, even where there is only one supplier of a particular vaccine. The CDC typically makes vaccine contract awards to all qualified suppliers, taking several considerations into mind: technical capability, meaning whether the manufacturer is licensed and can meet the specific contract terms (e.g., the 12 month shelf life requirement or compliance with Current Good Manufacturing Practices (cGMP)); past performance, which includes consideration of whether company has engaged in fraud; and the price.
Stockpile	The CDC also purchases vaccines for its Strategic National Stockpile. The CDC began stockpiling vaccines in 1983 to account for outbreak situations or other situations in which extra vaccines are needed to cover demand. Typically, the CDC purchases enough vaccines for its stockpile to last 6 months and purchases these vaccines from the same manufacturers it contracts with for the VFC Program. The CDC enters separate stockpile contracts with vaccine manufacturers for doses purchased for its stockpile.

Schedule 17

Possible Confounders for Mumps Outbreaks

Possible Confounder[1]	Source
Failure to vaccinate	Centers for Disease Control and Prevention. *Current Trends Mumps – United States, 1985-1988*. MMWR 1989;38(7):101-05. Centers for Disease Control and Prevention. *Epidemiologic Notes and Reports Mumps in the Workplace – Chicago*. MMWR 1988;37(35):533-38. Centers for Disease Control and Prevention. *Mumps Surveillance – United States, 1988-1993*. MMWR 1995;44(SS-3):1-14. Centers for Disease Control and Prevention. *Update: Multistate Outbreak of Mumps – United States, January 1-May 2, 2006*. MMWR 2006;55(20):559-63.
Population immunity that is below the herd immunity threshold	Livingston, K. A. et al. *Mumps vaccine effectiveness and risk factors for disease in households during an outbreak in New York City*. Vaccine 2014;32:369-374. 10.1016/j.vaccine.2013.11.021 Quinlisk, P. M. *Mumps Control Today*. J Infect Dis 2010;202(5):655-656. 10.1086/655395
Accumulation of susceptible individuals	*Measles, Mumps, Rubella (MMR) Vaccine*, CDC Advisory Committee on Immunization Practices (ACIP), February 22-23, 2012 Summary Report, 83-102. Centers for Disease Control and Prevention. *Update: Multistate Outbreak of Mumps – United States, January 1-May 2, 2006*. MMWR 2006;55(20):559-63. *Mumps Cases and Outbreaks*, CDC, https://www.cdc.gov/mumps/outbreaks.html (last updated Feb. 9, 2018). *Update on the Multi-State Mumps Outbreak in the United States*, CDC Advisory Committee on Immunization Practices (ACIP), June 29-30, 2006 Record of the Proceedings, 73-6. *Mumps Disease and Vaccine*, CDC Advisory

[1] This is not intended to be an exhaustive list, nor a full description in detail.

Possible Confounder[1]	Source
	Committee on Immunization Practices (ACIP), February 22-23, 2017 Summary Report, 115-25. Cardemil, C. V. et al. *Effectiveness of a Third Dose of MMR Vaccine for Mumps Outbreak Control*. N Engl J Med 2017;377:947-56. 10.1056/NEJMoa1703309
Vaccine failure	Centers for Disease Control and Prevention. *Mumps Surveillance – United States, 1988-1993*. MMWR 1995;44(SS-3):1-14. *Measles, Mumps, Rubella (MMR) Vaccine*, CDC Advisory Committee on Immunization Practices (ACIP), February 22-23, 2012 Summary Report, 83-102.
Vaccine effectiveness	Centers for Disease Control and Prevention. *Update: Multistate Outbreak of Mumps – United States, January 1-May 2, 2006*. MMWR 2006;55(20):559-63. Marin, M., *Current Mumps Vaccination Recommendation and Epidemiology in the United States*, CDC Advisory Committee on Immunization Practices (ACIP), February 23, 2017 Meeting. *Mumps Disease and Vaccine*, CDC Advisory Committee on Immunization Practices (ACIP), February 22-23, 2017 Summary Report, 115-25. *Mumps Disease and Vaccine*, CDC Advisory Committee on Immunization Practices (ACIP), June 21-22, 2017 Summary Report, 139-52. *Mumps Cases and Outbreaks*, CDC, https://www.cdc.gov/mumps/outbreaks.html (last updated Feb. 9, 2018). Cardemil, C. V. et al. *Effectiveness of a Third Dose of MMR Vaccine for Mumps Outbreak Control*. N Engl J Med 2017;377:947-56. 10.1056/NEJMoa1703309 Centers for Disease Control and Prevention. *Update: Mumps Outbreak – New York and New Jersey, June 2009-January 2010*. MMWR 2010;59(5):125-50.

Possible Confounder[1]	Source
	Quinlisk, P. M. *Mumps Control Today*. J Infect Dis 2010;202(5):655-656. 10.1086/655395
Vaccine is more effective at preventing asymptomatic infection or atypical mumps than parotitis	Centers for Disease Control and Prevention. *Update: Multistate Outbreak of Mumps – United States, January 1-May 2, 2006*. MMWR 2006;55(20):559-63.
Waning immunity	*Measles, Mumps, Rubella (MMR) Vaccine*, CDC Advisory Committee on Immunization Practices (ACIP), February 22-23, 2012 Summary Report, 83-102. Centers for Disease Control and Prevention. *Update: Multistate Outbreak of Mumps – United States, January 1-May 2, 2006*. MMWR 2006;55(20):559-63. Marin, M., *Current Mumps Vaccination Recommendation and Epidemiology in the United States*, CDC Advisory Committee on Immunization Practices (ACIP), February 23, 2017 Meeting. *Mumps Disease and Vaccine*, CDC Advisory Committee on Immunization Practices (ACIP), June 21-22, 2017 Summary Report, 139-52. Cardemil, C. V. et al. *Effectiveness of a Third Dose of MMR Vaccine for Mumps Outbreak Control*. N Engl J Med 2017;377:947-56. 10.1056/NEJMoa1703309 *Mumps Cases and Outbreaks*, CDC, https://www.cdc.gov/mumps/outbreaks.html (last updated Feb. 9, 2018). *Update on the Multi-State Mumps Outbreak in the United States*, CDC Advisory Committee on Immunization Practices (ACIP), June 29-30, 2006 Record of the Proceedings, at 73-6. *Measles, Mumps, Rubella (MMR) Vaccine*, CDC Advisory Committee on Immunization Practices (ACIP), February 22-23, 2012 Summary Report, 83-102.

Possible Confounder[1]	Source
	Livingston, K. A. et al. *Mumps vaccine effectiveness and risk factors for disease in households during an outbreak in New York City*. Vaccine 2014;32:369-74. 10.1016/j.vaccine.2013.11.021 *Mumps Disease and Vaccine*, CDC Advisory Committee on Immunization Practices (ACIP), February 22-23, 2017 Summary Report, 115-25. Marin, M. et al. *Recommendation of the Advisory Committee on Immunization Practices for Use of a Third Dose of Mumps Virus-Containing Vaccine in Persons at Increased Risk for Mumps During an Outbreak*. MMWR 2018;67(1):33-8. 10.15585/mmwr.mm6701a7
Close contact/crowded environment/conditions that foster frequent high intensity exposure	*Mumps Cases and Outbreaks*, CDC, https://www.cdc.gov/mumps/outbreaks.html (last updated Feb. 9, 2018). Centers for Disease Control and Prevention. *Epidemiologic Notes and Reports Mumps in the Workplace – Chicago*. MMWR 1988;37(35):533-38. Centers for Disease Control and Prevention. *Update: Multistate Outbreak of Mumps – United States, January 1-May 2, 2006*. MMWR 2006;55(20):559-63. *Update on Mumps Epidemiology in the US for 2017 and Review of Published Studies of 3rd Dose MMR for Mumps Outbreak Control*, CDC Advisory Committee on Immunization Practices (ACIP), June 21-22, 2017 Summary Report, 141-45. *Update on the Multi-State Mumps Outbreak in the United States*, CDC Advisory Committee on Immunization Practices (ACIP), June 29-30, 2006 Record of the Proceedings, 73-6. *Measles-Mumps-Rubella-Varicella Vaccine Safety*, CDC Advisory Committee on Immunization Practices (ACIP), June 24-26, 2009 Summary Report, 137-65. Livingston, K. A. et al. *Mumps vaccine effectiveness*

Possible Confounder[1]	Source
	and risk factors for disease in households during an outbreak in New York City. Vaccine 2014;32:369-374. 10.1016/j.vaccine.2013.11.021 Latner, D. R. et al. *Estimates of Mumps Seroprevalence May Be Influenced by Antibody Specificity and Serologic Method*. Clin Vaccine Immunol. 2014;21(3):286-97. 10.1128/CVI.00621-13 Latner, D. R. et al. *Remembering Mumps*. PLoS Pathog 2015;11(5):e1004791. 10.1371/journal.ppat.1004791 Cardemil, C. V. et al. *Effectiveness of a Third Dose of MMR Vaccine for Mumps Outbreak Control*. N Engl J Med 2017;377:947-56. 10.1056/NEJMoa1703309 Centers for Disease Control and Prevention. *Update: Mumps Outbreak – New York and New Jersey, June 2009-January 2010*. MMWR 2010;59(5):125-50. *Measles, Mumps, Rubella (MMR) Vaccine*, CDC Advisory Committee on Immunization Practices (ACIP), February 22-23, 2012 Summary Report, 83-102. Dayan, G. H. et al. *Recent Resurgence of Mumps in the United States*. N Engl J Med 2008;358:1580-9. 10.1056/NEJMoa0706589
Differences between the mumps vaccine strain and the circulating mumps wild strain	*Measles, Mumps, Rubella (MMR) Vaccine*, CDC Advisory Committee on Immunization Practices (ACIP), February 22-23, 2012 Summary Report, 83-102. Latner, D. R. et al. *Estimates of Mumps Seroprevalence May Be Influenced by Antibody Specificity and Serologic Method*. Clin Vaccine Immunol. 2014;21(3):286-97. 10.1128/CVI.00621-13 Livingston, K. A. et al. *Mumps vaccine effectiveness and risk factors for disease in households during an outbreak in New York City*. Vaccine 2014;32:369-374. 10.1016/j.vaccine.2013.11.021 *Mumps Disease and Vaccine*, CDC Advisory

Possible Confounder[1]	Source
	Committee on Immunization Practices (ACIP), February 22-23, 2017 Summary Report, 115-25. *Mumps Disease and Vaccine*, CDC Advisory Committee on Immunization Practices (ACIP), June 21-22, 2017 Summary Report, 139-52. Quinlisk, P. M. *Mumps Control Today*. J Infect Dis 2010;202(5):655-656. 10.1086/655395
Delayed recognition and diagnosis	Centers for Disease Control and Prevention. *Update: Multistate Outbreak of Mumps – United States, January 1-May 2, 2006*. MMWR 2006;55(20):559-63. *Update on the Multi-State Mumps Outbreak in the United States*, CDC Advisory Committee on Immunization Practices (ACIP), June 29-30, 2006 Record of the Proceedings, 73-6. Kancherla, V. S. et al. *Mumps resurgence in the United States*. J Allergy Clin Immunol. 2006;118(4):938-941. 10.1016/j.jaci.2006.07.033
Failure to follow dosing guidelines	Kancherla, V. S. et al. *Mumps resurgence in the United States*. J Allergy Clin Immunol. 2006;118(4):938-941. 10.1016/j.jaci.2006.07.033
Inappropriate storage and handling of vaccine	Kancherla, V. S. et al. *Mumps resurgence in the United States*. J Allergy Clin Immunol. 2006;118(4):938-941. 10.1016/j.jaci.2006.07.033
Unrecognized importation of mumps	*Update on the Multi-State Mumps Outbreak in the United States*, CDC Advisory Committee on Immunization Practices (ACIP), June 29-30, 2006 Record of the Proceedings, 73-6.
Lack of asymptomatic natural boosting due to substantially reduced endemic disease	Latner, D. R. et al. *Estimates of Mumps Seroprevalence May Be Influenced by Antibody Specificity and Serologic Method*. Clin Vaccine Immunol. 2014;21(3):286-97. 10.1128/CVI.00621-13 Latner, D. R. et al. *Remembering Mumps*. PLoS Pathog 2015;11(5):e1004791. 10.1371/journal.ppat.1004791

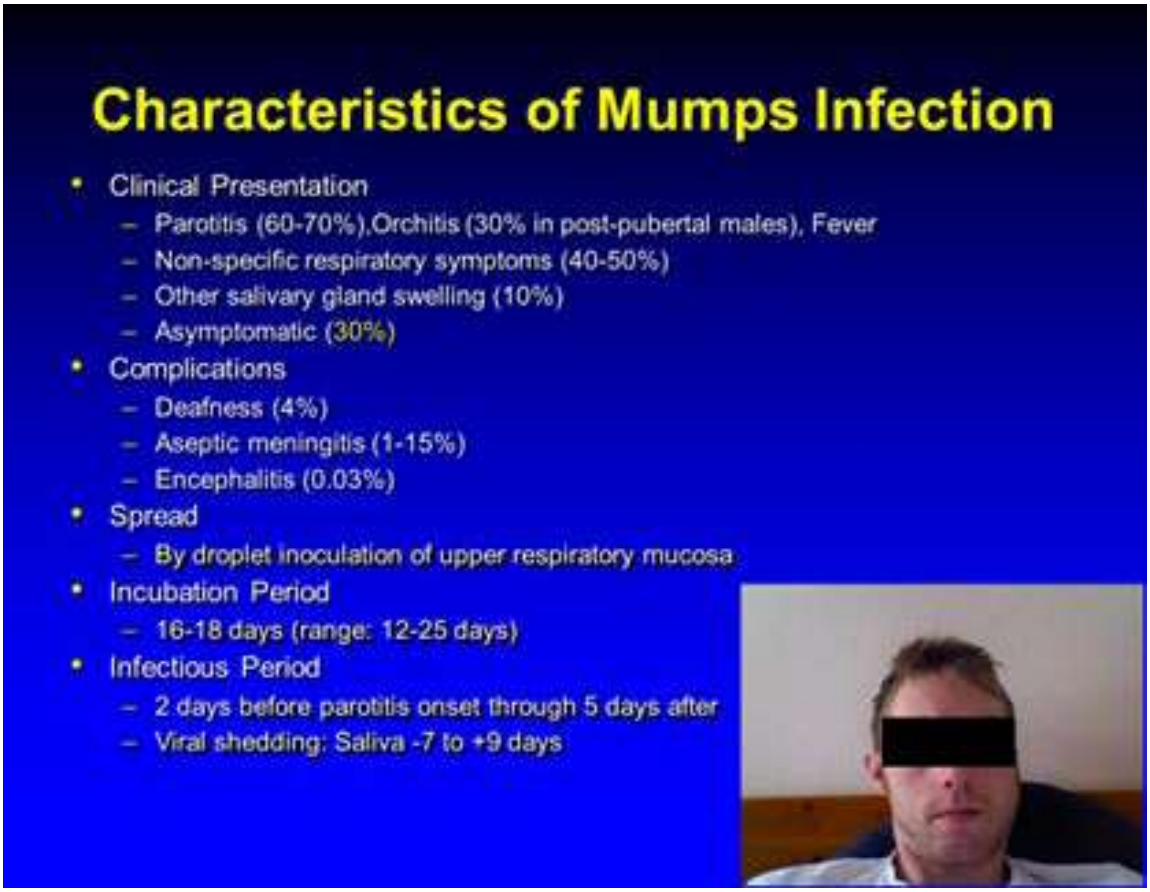
Possible Confounder[1]	Source
	Mumps Disease and Vaccine, CDC Advisory Committee on Immunization Practices (ACIP), February 22-23, 2017 Summary Report, 115-25. *Mumps Disease and Vaccine*, CDC Advisory Committee on Immunization Practices (ACIP), June 21-22, 2017 Summary Report, 139-52.

Schedule 18

Mumps Disease

Mumps is an acute, viral illness that frequently presents with parotitis, other salivary gland swelling, orchitis, aseptic meningitis, or non-specific respiratory symptoms. In addition, it is estimated that more than 30% of infections are asymptomatic, leading to potential for under-reporting. Complications include deafness, aseptic meningitis, and encephalitis, though these are rare. Some complications of mumps are known to occur more frequently among adults than children. In recent U.S. mumps outbreaks, orchitis occurred in 3.3 to 10% of adolescent and adult males.[1]

Mumps is spread by droplet infection, with an incubation period of 16 to 18 days. The infectious period is 2 days before up to 5 days after parotitis onset, with viral shedding from 7 days before up to 9 days after parotitis onset. Mumps typically causes pain, tenderness, and swelling in one or both cheeks or jaw area. Swelling of the lower part of the ear typically occurs first, then it moves downward and forward with fluid building up in the soft tissue and skin of the neck and face. Swelling usually peaks in 1 to 3 days and then subsides in the following week.[2]



See MRK-KRA00027892; MRK-KRA00040971; MRK-KRA00330661; MRK-KRA00041711.

[1] https://www.cdc.gov/mumps/hcp.html#complications
[2] https://www.cdc.gov/mumps/hcp.html#clinical

Schedule 19

Conversion Charts

LOG SCALE CONVERSION

The logarithmic scale is a commonly used nonlinear scale that allows individuals to represent a wide range of values. A logarithmic scale with a basis of 10 means that each 1.0 $\log_{10}$ increase or decrease represents a ten-fold increase or decrease, respectively, in the value. For example, 2.0 $\log_{10}$ = (10x10) = 100.0; 3.0 $\log_{10}$ = (10x10x10) = 1,000.0; 4.0 $\log_{10}$ = (10x10x10x10) = 10,000.0; 5.0 $\log_{10}$ = (10x10x10x10x10) = 100,000.0; and 6.0 $\log_{10}$ = (10x10x10x10x10x10) = 1,000,000.0.

The conversion for values between these values is as follows:

3.0 $\log_{10}$ = 1,000.0
3.1 $\log_{10}$ = 1,258.9
3.2 $\log_{10}$ = 1,584.9
3.3 $\log_{10}$ = 1,995.3
3.4 $\log_{10}$ = 2,511.9
3.5 $\log_{10}$ = 3,162.3
3.6 $\log_{10}$ = 3,981.1
3.7 $\log_{10}$ = 5,011.9
3.8 $\log_{10}$ = 6,309.6
3.9 $\log_{10}$ = 7,943.3
4.0 $\log_{10}$ = 10,000.0
4.1 $\log_{10}$ = 12,589.3
4.2 $\log_{10}$ = 15,848.9
4.3 $\log_{10}$ = 19,952.6
4.4 $\log_{10}$ = 25,118.9
4.5 $\log_{10}$ = 31,622.8
4.6 $\log_{10}$ = 39,810.7
4.7 $\log_{10}$ = 50,118.7
4.8 $\log_{10}$ = 63,095.7
4.9 $\log_{10}$ = 79,432.8
5.0 $\log_{10}$ = 100,000.0
5.1 $\log_{10}$ = 125,892.5
5.2 $\log_{10}$ = 158,489.3
5.3 $\log_{10}$ = 199,526.2
5.4 $\log_{10}$ = 251,188.6
5.5 $\log_{10}$ = 316,227.8
5.6 $\log_{10}$ = 398,107.2
5.7 $\log_{10}$ = 501,187.2
5.8 $\log_{10}$ = 630,957.3
5.9 $\log_{10}$ = 794,328.2
6.0 $\log_{10}$ = 1,000,000.0

AGE PROJECTION CHART

Birth Year	Projected Year for First Dose per ACIP[1]	Projected Year for Second Dose per ACIP[2]	Age in 2018
1995	1996	1999-2001	23
1996	1997	2000-2002	22
1997	1998	2001-2003	21
1998	1999	2002-2004	20
1999	2000	2003-2005	19
2000	2001	2004-2006	18
2001	2002	2005-2007	17
2002	2003	2006-2008	16
2003	2004	2007-2009	15
2004	2005	2008-2010	14
2005	2006	2009-2011	13
2006	2007	2010-2012	12
2007	2008	2011-2013	11
2008	2009	2012-2014	10
2009	2010	2013-2015	9
2010	2011	2014-2016	8
2011	2012	2015-2017	7
2012	2013	2016-2018	6
2013	2014	N/A	5
2014	2015	N/A	4
2015	2016	N/A	3
2016	2017	N/A	2
2017	2018	N/A	1

[1] ACIP recommends vaccination at 12-15 months. https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6204a1.htm.
[2] ACIP recommends vaccination at 4-6 years. *Id.*

TCID CONVERSION

- Merck manufactures mumps vaccine in bulk using a TCID/50 measurement of 0.1 mL.[3]
- The dose administered subcutaneously is 0.5 mL TCID/50.[4]
- To convert the potency measure from the 0.1 mL manufacturing measurement to the 0.5 mL per dose measurement, add 0.7 log to the 0.1 measurement.[5]
- For example, a measurement of 3.6 log10 (0.1mL) is 4.3 log10 (0.5 mL).

A summary of the measurements relevant in this case are set forth in the following chart:

0.1 mL Measurement	0.5 mL Measurement
2.4 Log10 TCID/50	3.1 Log10 TCID/50
2.5 Log10 TCID/50	3.2 Log10 TCID/50
2.6 Log10 TCID/50	3.3 Log10 TCID/50
2.7 Log10 TCID/50	3.4 Log10 TCID/50
2.8 Log10 TCID/50	3.5 Log10 TCID/50
2.9 Log10 TCID/50	3.6 Log10 TCID/50
3.0 Log10 TCID/50	3.7 Log10 TCID/50
3.1 Log10 TCID/50	3.8 Log10 TCID/50
3.2 Log10 TCID/50	3.9 Log10 TCID/50
3.3 Log10 TCID/50	4.0 Log10 TCID/50
3.4 Log10 TCID/50	4.1 Log10 TCID/50
3.5 Log10 TCID/50	4.2 Log10 TCID/50
3.6 Log10 TCID/50	4.3 Log10 TCID/50
3.7 Log10 TCID/50	4.4 Log10 TCID/50
3.8 Log10 TCID/50	4.5 Log10 TCID/50
3.9 Log10 TCID/50	4.6 Log10 TCID/50
4.0 Log10 TCID/50	4.7 Log10 TCID/50
4.1 Log10 TCID/50	4.8 Log10 TCID/50
4.2 Log10 TCID/50	4.9 Log10 TCID/50
4.3 Log10 TCID/50	5.0 Log10 TCID/50
4.4 Log10 TCID/50	5.1 Log10 TCID/50
4.5 Log10 TCID/50	5.2 Log10 TCID/50
4.6 Log10 TCID/50	5.3 Log10 TCID/50
4.7 Log10 TCID/50	5.4 Log10 TCID/50
4.8 Log10 TCID/50	5.5 Log10 TCID/50
4.9 Log10 TCID/50	5.6 Log10 TCID/50
5.0 Log10 TCID/50	5.7 Log10 TCID/50

[3] MRK-KRA00625923; MRK-KRA00333482; MRK-KRA01552314.
[4] MRK-KRA00133294 at '306.
[5] MRK-KRA02101841.

Schedule 20

Known Mumps Viruses

Virus[1]	Type	Applications
Wild-Type Jeryl Lynn™	Wild-Type	Strain evaluated for Protocol 007 and used in competitive trials (Protocol 006) of MMRII and Priorix.[2]
London 1 (Lo-1)	Wild-Type	Strain evaluated for Protocol 007 and used in competitive trials (Protocol 006) of MMRII and Priorix.[3]
Barnes	Wild-Type	Strain evaluated for Protocol 007 and used in competitive trials (Protocol 006) of MMRII and Priorix.[4]
Tennessee	Wild-Type	Strain evaluated for Protocol 007 and used in competitive trials (Protocol 006) of MMRII and Priorix.[5]
Iowa	Wild-Type	Strain isolated in 2006 outbreaks.[6]
Swiss Isolates	Wild-Type	Strain evaluated for Protocol 007.[7]
Enders	Wild-Type	Strain evaluated for Protocol 007.[8]
NY	Wild-Type	Strain evaluated for Protocol 007.[9]
Jones	Wild-Type	Strain evaluated for Protocol 007.[10]
SBL	Wild-Type	
SBL-1	Wild-Type	Strain evaluated for Protocol 007.[11]
JL-135	Low Passage (8) Attenuated	Used in AIGENT.[12]
JL-2	Attenuated	Part of the Jeryl Lynn™ strain and evaluated separately in development of Protocol 007.[13]
JL-5	Attenuated	Used in vaccine made by GSK (RIT-4385) Priorix, that uses part of the Jeryl Lynn™ strain.[14]
Jeryl Lynn™	Attenuated	A mixture of the JL-2 and JL-5 substrains. Licensed for vaccine use by Merck in the U.S. since 1967. Used in

[1] This is not intended to be an exhaustive list, nor a full description in detail.
[2] MRK-KRA00031541 at '545; MRK-KRA00026469
[3] MRK-KRA00031541 at '545; MRK-KRA00026469
[4] MRK-KRA00031541 at '545; MRK-KRA00026469
[5] MRK-KRA00026469
[6] MRK-KRA00292789
[7] MRK-KRA00031541 at '545; MRK-KRA00026469
[8] MRK-KRA00026469
[9] MRK-KRA00026469
[10] MRK-KRA00026469
[11] MRK-KRA00026469
[12] MRK-KRA00056756; MRK-KRA00223634; *see also* Krah Dep. 587:2-588:8
[13] MRK-KRA00031541 at '545; MRK-KRA00667054 at '058; MRK-KRA00026469
[14] MRK-KRA00031541 at '545; MRK-KRA00667054 at '058

Virus[1]	Type	Applications
		MumpsVax, MMRII, ProQuad, and MMRVaxPro.[15] Strain also used in competitive trials (Protocol 006) of MMRII and Priorix.[16]
Urabe Am9	Attenuated	Used for live mumps vaccine first licensed in Japan and then in Belgium, France, and Italy.[17] Used in the Morupar vaccine made by Chiron and the Trimovax vaccine made by Pasteur-Merieux Serums and Vaccines.[18]
Leningrad-3	Attenuated	Used in mumps vaccine made by the Moscow State Facility for Bacterial Preparations, which was used in the former Soviet Union national immunization program starting in 1980.[19]
Leningrad-Zagreb	Attenuated	Further attenuation of Leningrad-3. Used in mumps vaccine made by the Institute of Immunology of Zagreb in Croatia[20] and in the Tresivac vaccine made by Serum Institute of India.[21]
Rubini	Attenuated	Used in the Triviraten vaccine made by Berna Biotech, formerly known as Swiss Serum and Vaccine Institute, which was first licensed in Switzerland in 1985.[22]
Hoshino	Attenuated	Used in mumps vaccine made by the Kitasato Institute in Japan.[23]
Torii	Attenuated	Used in mumps vaccine made by Takeda Chemicals in Japan.[24]
NK-M46	Attenuated	Used in mumps vaccine made by Chiba Serum Institute in Japan.[25]
S-12	Attenuated	Used in mumps vaccine made Razi State Serum & Vaccine Institute in Iran.[26]
Sofia-6	Attenuated	Used in mumps vaccine made by the Center for Infectious and Parasitic

[15] MRK-KRA00123078 at '083; MRK-KRA00031541 at '545; GSK-MMR-0189468 at '473
[16] MRK-KRA00031541 at '545
[17] MRK-KRA00123078 at '084
[18] GSK-MMR-0160936 at '940; GSK-MMR-0189468 at '473
[19] MRK-KRA00264101 at '109; MRK-KRA00123078 at '084
[20] MRK-KRA00264101 at '109; MRK-KRA00123078 at '084
[21] MRK-KRA00264101 at '109; MRK-KRA00123078 at '084; GSK-MMR-0189468 at '473
[22] MRK-KRA00123078 at '084; MRK-KRA01389563.
[23] MRK-KRA00028303; MRK-KRA00264101 at '109
[24] MRK-KRA00028303; MRK-KRA00264101 at '109
[25] MRK-KRA00028303; MRK-KRA00264101 at '109
[26] MRK-KRA00028303; MRK-KRA00264101 at '109

Virus[1]	Type	Applications
		Diseases in Bulgaria, which was introduced into the Bulgarian national vaccination program in 1977.[27]
Miyahara	Attenuated	Used in the mumps vaccine made by the Chem-Sero Therapeutic Research Institute Strain in Japan.[28]
RIT 4385 (or JL-1)	Attenuated	Derived from JL-5. Used in the Priorix vaccine made by GSK since 1997.[29]
S79	Attenuated	Used in MMR vaccine made by the Shanghai Institute of Biological Products in China.[30]

[27] MRK-KRA00028303; MRK-KRA00264101 at '109
[28] MRK-KRA00028303; MRK-KRA00264101 at '109
[29] MRK-KRA00123078 at '084; GSK-MMR-0000162; MRK-KRA00031541 at '545
[30] MRK-KRA00123078 at '085; GSK-MMR-0189468 at '473

Schedule 21

Commonly Used Acronyms

ACRONYM[1]	DEFINITION	DESCRIPTION
317	Reference to Section 317 of the Public Health Services Act	The 317 Program is a discretionary federal program that provides grants to state and local health departments to support mass immunization campaigns. 42 U.S.C. § 247b (Section 317 Public Health Services Act as amended) authorizes the 317 program. The program provides vaccinations for underinsured children who are not eligible for the Vaccines for Children program.
482	FDA Form 482	A notice of inspection provided when a FDA investigator arrives for a site inspection.
483	FDA Form 483	A FDA Form 483 is issued to a firm at the conclusion of an inspection when an investigator has observed conditions that may constitute violations of the Food Drug and Cosmetic Act (FDCA) and related Acts. Merck was issued several 483s, including but not limited, ones on October 11, 2000, August 6, 2001 and May 3, 2002. *See also,* Schedule 24 for list.
ACIP	Advisory Committee on Immunization Practices	The ACIP is a federally chartered, scientific advisory committee of outside experts with the goals of providing the Centers for Disease Control and Prevention (CDC) with advice on decreasing disease through the use of vaccines and other biological products, and on improving the safety of their use.
AERT	Adverse Event Review Team	An internal Merck committee to review adverse event data for a given vaccine. *See* Eric Metzger Deposition Exhibit 5.
AIGENT	Anti-IgG Enhanced Neutralization Assay	Merck's plaque reduction neutralization assay that utilized an anti-human IgG step to increase neutralization used in Protocol 007 to lower the mumps end expiry potency claim in the label.
ASH	Assistant Secretary of Health	The ASH directs the National Vaccine Program (NVP).
BLA	Biologics License Application	Application submitted to Food and Drug Administration (FDA) seeking review and approval for a biologic, which includes vaccines. The application must provide the multidisciplinary FDA reviewer team with sufficient evidence of the efficacy and safety of the proposed product for the FDA to decide whether to approve the vaccine for manufacture

[1] This is not intended to be an exhaustive list, nor a full description in detail.

ACRONYM[1]	DEFINITION	DESCRIPTION
		and sale.
BPC	Biological Process Council	An internal Merck committee. *See* Eric Metzger Deposition Exhibit 5; *see also* MRK-KRA00343384.
BSC **BSEC**	Biologics Specifications Committee Biologics Specifications Executive Committee	A two-tiered internal Merck committee responsible for specifications of biologics. The lower tier of the committee is the BSC, while the BSEC provides a higher level of review with more senior executives. *See* MRK-KRA00249044 at '046; MRK-KRA341216; Alison Fisher Deposition at 32-3, 37, 61, 67, 81.
BSS	Biologics Specifications Subcommittee	A subcommittee of the BPC. *See* MRK-KRA00281062.
CAS/CAST	Clinical Assay Subteam	An internal Merck committee to oversee the operation and throughput of assays and address any clinical, regulatory or lab issues related to the assays. According to David Krah, the CAS was responsible for development of clinical assays. *See* Eric Metzger Deposition Exhibit 5 at 7; Florian Schodel Deposition at 233-4; David Krah Deposition at 266-267.
CBER	Center for Biologics Evaluation and Research	CBER is one of the centers in the FDA that regulates biological and related products including blood, vaccines, allergenics, tissues, and cellular and gene therapies. The Center for Drug Evaluation and Research (CDER) is the other such center.
CCHMC	Cincinnati Children's Hospital Medical Center	The entity that housed Dr. Ward's laboratory and where Merck contemplated outsourcing much of the Protocol 007 assay. *See* MRK-KRA01612678, MRK-KRA00017839.
CDC	Centers for Disease Control and Prevention	A part of the United States Department of Health and Human Services, the CDC purchases and dispenses vaccines for the federal government as part of the country's vaccination programs. The CDC is also responsible for monitoring outbreaks of diseases.
CDOC	Clinical Development Oversight Committee	An internal Merck governance committee responsible for overseeing the clinical and regulatory aspects of product development. CDOC was succeeded by CRRC, which fulfilled essentially the same role as CDOC had previously. *See* Eric Metzger Deposition Exhibit 5 at 11; Joyce Bramble Deposition at 14; Keith Chirgwin Deposition at 142-3.

ACRONYM[1]	DEFINITION	DESCRIPTION
CDTF	Competitive Defense Task Force	An internal Merck committee. *See* Eric Metzger Deposition Exhibit 5 at 15.
CHMP	Committee for Medicinal Products for Human Use	The Committee for Medicinal Products for Human Use (CHMP), formerly known as the Committee for Proprietary Medicinal Products (CPMP), is the European Medicines Agency's committee responsible for elaborating the agency's opinions on all issues regarding medicinal products for human use.
CIA	Corporate Integrity Agreement	An agreement entered into between the government and a government contractor to assure compliance with the statutes, regulations, and written directives in interactions with the government.
CII	Childhood Immunization Initiative	The CII established the goal of increasing vaccination coverage levels among children aged 2 years to greater than 90% by 1996 for the most critical doses of each vaccine routinely recommended for children. It was launched in 1993, after several measles outbreaks. *See* MRK-KRA00260859.
CMC	Chemistry, Manufacturing, and Controls	A category of FDA oversight in which guidance is offered. The category was renamed to Pharmaceutical Quality/CMC.
CMS	Centers for Medicare and Medicaid services	A part of the United States Department of Health and Human Services, CMS administers Medicare, Medicaid, and the children's health insurance program. Some vaccines are administered and paid for through state Medicaid programs.
CP	Control Procedure	An internal Merck document prescribing the use of a laboratory method. *See, e.g.*, MRK-KRA01977772; MRK-KRA01977803 (CP 9110.676 is the Control Procedure for the "INFECTIVITY TEST FOR THE DETERMINATION OF MEASLES, MUMPS, AND RUBELLA VACCINE POTENCY.").
CPE	Cytopathic Effect	An alternative type of assay to PRN is based on CPE, which refers to structural changes in the host cells that are caused by viral invasion.
CPMP	Committee for Proprietary Medicinal Products	A scientific advisory group of the EMEA (European Medicines Evaluation Agency).
CRC	Commitment Review Committee	An internal Merck committee. *See, e.g.*, MRK-KRA01629756.

ACRONYM[1]	DEFINITION	DESCRIPTION
CRRC	Clinical and Regulatory Review Committee	An internal Merck governance committee responsible for overseeing the clinical and regulatory aspects of product development. The CRRC fulfilled essentially the same role as CDOC had previously. *See* Eric Metzger Deposition Exhibit 5 at 6; Joyce Bramble Deposition at 14; Keith Chirgwin Deposition at 142-3.
CSR	Clinical Study Report	An FDA requirement. An "integrated" full report of an individual study of any therapeutic, prophylactic, or diagnostic agent (referred to herein as drug or treatment) conducted in patients. *See, e.g.*, MRK-KRA00135759.
CST	Commercialization Subteam (circa 1998-2004) Clinical Subteam (circa 2014)	An internal Merck committee. *See* Eric Metzger Deposition Exhibit 5 at 12-13.
CTD	Clinical Trial Directive (EU) Common Technical Document (USA)	The CTD acronym can have a different meaning whether in the EU or US. The essence of both uses are similar and both are applicable to Merck's activities. The Clinical Trial Directive in Europe governs clinical trial protocols and are submitted in an application for marketing authorization in the EU. The Common Technical Document in the U.S. is for the Registration of Pharmaceuticals for Human Use (including biotechnology-derived products). The CTD is submitted with new drug applications and marketing applications. The US CTD was designed to be used in the US, EU, and Japan.
CTF	Competitive Task Force	An internal Merck committee. *See* Eric Metzger Deposition Exhibit 5 at 17.
DAP	Data Analysis Plan	*See, e.g.*, MRK-KRA00126567.
DBS	Department of Biologics Standard	DBS was a predecessor to the modern FDA. At the time the mumps vaccine was approved in 1967, DBS (a department of the National Institute of Health) was responsible for approving a manufacturer's license to manufacture and sell vaccines.

ACRONYM[1]	DEFINITION	DESCRIPTION
DMC	Development Management Committee	An internal Merck committee. *See* MRK-KRA01727904.
DMT	Data Management Team	An internal Merck review function. *See* MRK-KRA00802542.
DOD	Department of Defense	The DOD has liaison members in the National Vaccine Advisory Committee. The DOD's interests in issues relating to vaccines include guarding against biologic warfare and assuring the health of all active service members and their families.
DTP	Diphtheria, Tetanus, and Pertussis	Another commonly administered trivalent vaccine to protect against three serious diseases caused by bacteria. Diphtheria and pertussis (whooping cough) are spread from person to person. Tetanus enters the body through cuts or wounds. The DTP vaccine is administered to children in a series of five doses at various ages. Also seen as DPT, DTwP (to designate the old formulation with whole cell pertussis antigen), or DTaP (to designate the current formulation with acellular pertussis antigen).
EDQM	European Directorate for the Quality of Medicines & HealthCare	The EDQM plays an essential role in the complex regulatory framework in place for medicines in Europe. Its aims are to protect public health by enabling the development, supporting the implementation, and monitoring the application of quality standards for safe medicines and their safe use.
EIA or ELIA	Enzyme Immunoassay or Enzyme-Linked Immunosorbent Assay	Commonly used assay to test immunogenicity in a controlled laboratory environment. This assay uses the addition of certain enzymes to measure the presence of virus-specific antibodies.
EMA or EMEA	European Medicines Agency	A decentralized agency of the European Union (EU), located in London, England. This agency is responsible for the scientific evaluation of medicines developed by pharmaceutical companies for use in the European Union. It serves roughly the equivalent role as the FDA in the United States.
FDA	United States Food and Drug Administration	Federal agency responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, United States food supply, cosmetics, and products that emit radiation.

ACRONYM[1]	DEFINITION	DESCRIPTION
FDCA	Federal Food, Drug, and Cosmetics Act	21 U.S.C. § 301 et. seq. The FDA enforces the FDCA. The Act is intended to ensure food safety as well as drug, medical device, and cosmetics safety and effectiveness.
QPA	Quantitative Precipitin Assay	PCR based viral DNA amplification assay. Measures reduction in percentage of virus infection post incubation in serum from vaccinee relative to control potency.
GOS	GOS Stabilizer	GOS formulation stabilizer (a vaccine component) containing gelatin, medium O, and sorbitol. *See* MRK-KRA00020881.
GMP/CGMP	Good Manufacturing Practices or Current Good Manufacturing Practices	System designed to ensure that products are consistently manufactured and controlled according to quality standards and the practices required in order to conform to the guidelines recommended by agencies that control authorization and licensing for manufacture and sale of food, drug products, and active pharmaceutical products. *See* MRK-KRA00255145.
GMT	Geometric Mean Titer (*aka* "Titre")	In a population seronegative before vaccination, the post-vaccination geometric mean titer (post-GMT) is an immunological parameter that expresses antibody response after vaccination. It is the simple arithmetic mean of the logarithms of the last positive dilution of each serum. *See* MRK-KRA00027878.
GRSRC	Global Regulatory Strategic Review Committee	An internal Merck committee. See MRK-KRA01349418; MRK-KRA00040705.
GSK	GlaxoSmithKline	A global health care company. Manufacturer of Priorix, an MMR vaccine sold in Europe and elsewhere in the world (but not in the United States).
HHS	Health and Human Services	A cabinet level department of the United States federal government. Its goal is to protect the health of all Americans and provides essential human services.
HSA	Human Serum Albumin	A component used in the manufacture of MMRII until replaced with rHA.
IAC	Immunization Action Coalition	This coalition works to increase immunization rates and prevent disease by creating and distributing education materials for health professionals and the public. IAC works with and is financially supported by the CDC. IAC

ACRONYM[1]	DEFINITION	DESCRIPTION
		also receives funding from Merck for its work in facilitating communication about the safety, efficacy, and use of vaccines within the broad immunization community.
ICH	International Conference on Harmonization	Launched in 1990, ICH is a unique undertaking that brings together the drug regulatory authorities and the pharmaceutical industry of Europe, Japan, and the United States to reach common standards and guidelines that are adopted by regulatory bodies
IDSA	Infectious Diseases Society of America	The Infectious Diseases Society of America (IDSA) represents physicians, scientists, and other health care professionals who specialize in infectious diseases.
IgG	Immunoglobulin Class G Isotype	Antibodies have a constant region and a variable region. There are five different classes of constant region. IgG is one class of antibody constant region. IgG antibodies comprise 70% of circulating antibodies in humans and have a major role in immune function and disease prevention. *See generally* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4202688/.
IND	Investigational New Drug	Seen in the context of an IND Application. A sponsor who wishes to begin clinical trials with a vaccine must submit an IND to the FDA. The IND describes the vaccine, the method of its manufacture, and quality control tests for release.
IOM	Institute of Medicine	An independent, nonprofit organization that works to provide health and health care advice to decision makers and the public.
IPLT	Integrated Product Leadership Team	An internal Merck committee. *See* Eric Metzger Deposition Exhibit 5 at 19.
ITFDE	International Task Force for Disease Eradication	A task force created after the worldwide elimination of small pox to identify other preventable diseases that could be targeted for eradication.
JL (*see also, e.g.*, JL-1, JL-2, JL-5)	Jeryl Lynn	The strain of the mumps virus originally isolated by Dr. Maurice Hilleman in the 1960s. The JL strain is the basis for the mumps vaccine Merck has used continuously since vaccine approval in 1967.
JVDMC	Joint Venture Development	Committee made up of Merck and Sanofi Pasteur (SPMSD) personnel. *See* MRK-

ACRONYM[1]	DEFINITION	DESCRIPTION
	Management Committee	KRA00663137.
JW	Joan Wlochowski	Relator in False Claims Act case.
LDRC	Late Development Review Committee	An internal Merck committee. *See* Eric Metzger Deposition Exhibit 5 at 20; MRK-KRA01736573.
LEAD	Label Evaluation and Development	An internal Merck committee, circa 2004-2005. Appears to have superseded the work of the earlier WPCRC committee. *See* Eric Metzger Deposition Exhibit 5 at 43-47; MRK-KRA01734446 at '509.
LIMS	Laboratory Information Management System	A software-based laboratory and information management system with features that support a modern laboratory's operations. Merck stores potency, stability and other testing data in a LIMS database.
Lo1	London 1	A wild-type mumps strain.
MeV	Measles Virus	Measles virus abbreviation. *See* MRK-KRA00389693.
MMD	Merck Manufacturing Division	Division of Merck that manufactures and packages product, *e.g.*, vaccines. *See* MRK-KRA00032621.
MMR **M-M-R**	Measles – Mumps – Rubella Vaccine	Combination measles, mumps, and rubella vaccine.
MMRII **MMR II** **M-M-R II**	Measles – Mumps – Rubella II Vaccine	Merck's replacement for MMR containing a different strain of the rubella virus that is still primary vaccine used in US today.
MMRV	Measles –Mumps – Rubella – Varicella Vaccine	A quadrivalent vaccine that combines measles, mumps, rubella and varicella antigens. Merck's quadrivalent is marketed under the name "ProQuad." *See, e.g.*, MRK-KRA00279043.
MMRVAXPRO	Measles – Mumps – Rubella Vaccine	Brand name for Merck's MMRII vaccine developed and approved for sale in Europe. Sold pursuant to a joint venture between Merck and Sanofi Pasteur.
MMWR	Morbidity and Mortality Weekly Report	A weekly report published by the CDC. It is considered the agency's primary vehicle for scientific publication of public health information and recommendations. It includes information about vaccine use and disease outbreaks.
MNVT or MNV	Monkey Neurovirulence Test	Safety test of vaccine performed on monkey brains. *See* MRK-KRA00643909.
MRL	Merck Research Laboratories	The division of Merck in which Protocol 007 took place. *See* MRK-KRA00001270.

ACRONYM[1]	DEFINITION	DESCRIPTION
MuV	Mumps Virus	Mumps virus abbreviation. *See* MRK-KRA00389693.
MVD	Merck Vaccine Division	*See* MRK-KRA00084900.
MVX	Merck Voice Mail	A Merck voice mail message; messages were sometimes transcribed by recipients. *See* Henrietta Ukwu Deposition Exhibit 12; MRK-KRA00343223.
NIH	National Institutes of Health	An agency of the United States Department of Health and Human Services. It is the primary agency of the United States government responsible for biomedical and health-related research.
NIS	National Immunization Survey	The National Immunization Survey is conducted each year by the HHS, through the CDC, to collect data from every state to measure immunization rates.
NVAC	National Vaccine Advisory Committee	The committee advises and makes recommendations to the ASH (Assistant Secretary of Health) regarding the work of the National Vaccine Program and assures input from a broad range of stakeholders (including federal, state and local health agencies, vaccine manufacturers and distributors, health care providers, and consumers, among others).
NVICP	National Vaccine Injury Compensation Program	The NVICP is a no-fault alternative to the traditional tort system for resolving vaccine injury claims that provides compensation to people found to be injured by certain vaccines. The NVICP also incorporates vaccine labeling requirements.
NVP	National Vaccine Program	The program was created as part of the National Childhood Vaccine Injury Act of 1986 (P.L. 99-660), which directs it to coordinate and provide direction to all federal activities related to vaccines and immunization programs.
NVPO	National Vaccine Program Office	The office manages the National Vaccine Program on behalf of the ASH.
OGOS	Optimized GOS	An "optimized" reformulation of GOS that Merck hoped would improve thermal stability of their vaccine product. *See* MRK-KRA00199236.
OMB	Office of Management and Budget	The OMB's role in vaccines is to approve funding for programs like the Vaccines for Children program.
OPAR	Office of Promotional	An internal Merck committee. *See* Eric Metzger

ACRONYM[1]	DEFINITION	DESCRIPTION
	and Advertising Review	Deposition Exhibit 5 at 22.
OSTIC	Office of Scientific and Technical Information Clearance	The OSTIC is one option to review any scientific result or information that is based on work conducted at Merck before it is released. The other option is a divisional vice president. *See* MRK-KRA00582424.
PAS	Prior Approval Supplement	A filing with the FDA to gain approval of a major change that has a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.
PDT	Product Development Team	An internal Merck committee. *See* Eric Metzger Deposition Exhibit 5 at 28-33.
PEI	Paul Ehrlich Institute	The Paul Ehrlich Institute is a German research institution and medical regulatory body, and is the German federal institute for vaccines and biomedicines. It is a federal agency and subordinate to the Federal Ministry of Health. *See* MRK-KRA00095349.
PHSA	Public Health Service Act	42 U.S.C. Chapt. 6A, specifically 42 U.S.C. § 262 provides regulation for biological products, such as biologics license, recall of product presenting imminent hazard, and penalty for offenses.
PHAC	Public Health Agency of Canada	A Canadian regulatory body.
PRIORIX	Measles-Mumps-Rubella Vaccine	A competing trivalent vaccine manufactured and sold by GSK in certain markets outside the United States.
PRN	Plaque Reduction Neutralization	A PRN test measures the ability of an antibody to neutralize an antigen in vitro. PRN test is considered a biologically relevant standard or the "gold standard" for testing mumps.
PRT	Promotional Review Team	An internal Merck committee. *See* Eric Metzger Deposition Exhibit 5 at 34.
PVP	Pharmacovigilence Plan	*See* MRK-KRA00012248.
QA	Quality Assurance	A department responsible for auditing laboratories and procedures for compliance. *See* MRK-KRA00010596.
QPA	Quantitative Precipitin Assay	A simple technique that is routinely used in the analysis of antibody and antigen interactions and for the estimation of the antibody or antigen content in a sample. The technique is based on the interaction of antibody and antigen to form a

ACRONYM[1]	DEFINITION	DESCRIPTION
		large protein complex that in certain solutions (buffer) will result in precipitation. Merck contemplated the use of a modified fnQPA (functional QPA) as an alternative to a PRN Assay.
rHA	Recombinant Human Albumin	A component tested for use in the manufacture of MMRII.
RIVM	Rijksinstituut voor Volksgezondheid en Milieu (Netherlands National Institute for Public Health and the Environment)	The RIVM is a Dutch research institute that is an independent agency of the Dutch Ministry of Health, Welfare and Sport. RIVM supports support the Dutch government in formulating its policy.
RMST	Risk Management Safety Team	An internal Merck committee. *See, e.g.*, MMR II RMST. *See* Eric Metzger Deposition Exhibit 5 at 35.
SBLA	Supplemental Biologics License Application	A supplemental filing to an existing BLA.
SK	Stephen Krahling	Relator in False Claims Act case.
SOHCO	Single Overriding Health Communication Objective	Messaging tool employed by CDC. A SOHCO usually consists of one sentence that sums up the most important aspect of what is being communicated followed by several statements that support or qualify that sentence.
SOP	Standard Operating Procedure	An SOP is a formal, written, approved procedure for laboratory work that must be followed.
STN	Submission Tracking Number	Identifying number assigned by CBER to a given submission. This is also referred to as a Serial.
TARC	Therapeutic Area Review Committee	*See* MRK-KRA00379038; MRK-KRA00251829.
TCID	Tissue Culture Infectious Doses	A unit quantifying the amount of cytopathogenic agents to cause cytopathic effect in 50% of inoculated cell cultures. A measure of how potent a vaccine is. An assay used by Merck to test potency of its mumps vaccine.
TPAC	Tactical Product Approval Committee	A senior Merck management committee. Per Joye Bramble, TPAC is the highest level governance committee that a PDT reported to. *See* Eric Metzger Deposition Exhibit 5 at 36; Abraham Deposition at 205; Bramble Deposition at 207-8.
TTT	Tech Transfer Team	*See* MRK-KRA00195720.
USAID	United States Agency	A federal agency with liaison members in the

ACRONYM[1]	DEFINITION	DESCRIPTION
	for International Development	National Vaccine Advisory Committee. They coordinate U.S. efforts to promote vaccination in other parts of the world, including developing countries.
VA	Veterans Administration	A federal agency with liaison members in the National Vaccine Advisory Committee. They coordinate efforts to provide vaccinations to adults eligible for VA health benefits.
VAC	Vaccine Assay Committee	An internal Merck committee. The objective of the VAC is to provide a forum for the in-depth review of all data used to support clinical assays and approve proposals/plans for these analytical assays to support clinical endpoint evaluations. Per Keith Chirgwin, the VAC reviewed issues related to serological assay protocols. *See* MRK-KRA00279983; Eric Metzger Deposition Exhibit 5 at 37; Keith Chirgwin Deposition at 311-2.
VAERS	Vaccine Adverse Event Reporting System	A post-marketing safety surveillance program sponsored jointly by CDC and FDA, VAERS provides a nationwide mechanism by which adverse events following immunization may be reported, analyzed, and made available to the public.
VARIVAX	Varicella Vaccine	Merck's branded monovalent vaccine against the Varicella (chickenpox) virus.
VCBIO	Virus and Cell Biology Research	Merck department that includes the vaccine research division where Protocol 007 research and clinical studies were conducted. *See* MRK-KRA00002339.
VDMS	Vaccine Data Management System	Official Merck database to manage clinical data. *See* MRK-KRA00063483.
VFC	Vaccines for Children	Federally funded program enacted by Congress to help meet the immunization goals identified by Childhood Immunization Initiative. It is the primary mechanism through which the federal government purchases childhood vaccines. The VFC program provides vaccines at no cost to children who might not otherwise be vaccinated because of inability to pay.
VMC	Vaccine Marketing Committee	An internal Merck committee. The objectives of the Vaccine Marketing Committee (VMC) are to ensure that the marketing plans are supported by MVD senior management and are appropriately integrated into development and manufacturing

ACRONYM[1]	DEFINITION	DESCRIPTION
		strategies. *See* MRK-KRA00626226; Eric Metzger Deposition Exhibit 5 at 39.
VPAC	Vaccine Product Approval Committee	An internal Merck committee. *See* Eric Metzger Deposition Exhibit 5 at 40.
VRBPAC	Vaccines and Related Biological Products Advisory Committee	A non-FDA expert committee (scientists, physicians, biostatisticians, and a consumer representative) that provides advice to the Food and Drug Administration regarding the safety and efficacy of a vaccine for a proposed indication. VRBPAC review follows FDA's own review of a license application for a new indication.
VRC	Vaccine Report Card	An assessment of safety by the blinded investigator in a clinical trial, which includes a record of local and systemic adverse events. *See* MRK-KRA00220377.
VTE	Vaccine Technology & Engineering	A part of MMD. Represented at the BSEC by Barry Garfinkle as of 2003. *See* MRK-KRA00094106.
VZV	Varicella Zoster Virus	The virus which causes chicken pox and herpes zoster. Merck manufactures a vaccine, VARIVAX, which is also a component of ProQuad.
WAES	Worldwide Adverse Experience System	Database of voluntary reports to Merck of adverse experiences after use of a Merck product. Includes reports regardless of outcome or likelihood of causal association. *See* MRK-KRA00338463.
WCS	Worldwide Clinical Summary	*See* MRK-KRA00012828.
WGMPQA	Worldwide GMP Quality Assurance	A quality assurance department of Merck that audits GMP compliance. *See* MRK-KRA00066258.
WPCRC	Worldwide Product Circular Review Committee	An internal Merck committee, circa 1998-2000. Appears to have been superseded by LEAD committee circa 2004-2005. *See* Eric Metzger Deposition Exhibit 5 at 43-47.
WRAPS	Worldwide Regional Annual Product Strategy	*See* MRK-KRA00209480.
WT	Wild Type	A wild type virus is a strain of the virus as it exists in nature and might be encountered by a person in the real world.

Schedule 22

Merck Key Employees

Name[1]	Role or Title
Kati (Katalin) Abraham	April 1989 – May 1990 MMD, Developmental Biologist, BioQC Tech Services June 1990 – February 1992 MMD, Lead Laboratory Supervisor March 1992 – June 1994 MMD, Senior Scientist, Bioanalytical Development June 1994 – May 2001 MMD, Regulatory Administrator May 2001 – December 2006 MRL, Associate Director, Regulatory Compliance Management October 2015 – January 2017 MRL, Director, Regulatory Affairs International
Michael Angelo, Ph.D.	November 1987 – June 1990 MMD, Director, Technical Operations July 1990 – June 1993 MMD, Senior Director, Technical Operations July 1993 – June 1996 MMD, Vice President, Safety and Environment July 1996 – June 1997 MMD, Vice President, Chemical Technology & Engineering July 1997 – June 2010 MMD, Senior Vice President, Global Quality June 2010 – December 2012 MMD, Senior Vice President, Regulatory Integration
Joseph Antonello, Ph.D.	1984 – MRL, Statistician MRL, Senior Statistician 1997 – MRL, Biometrician MRL, Senior Biometrician ~2001 – ~December 2005 MRL, Associate Director, Vaccine Biometrics Research MRL, Director, Vaccine Biometrics Research

[1] This is not intended to be an exhaustive list, nor a full description in detail.

Name[1]	Role or Title
	Prior to 2015 – Present MRL, Senior Principal Scientist, GXP Systems Merck Vaccines
Deitra Arena	1987 – 2013 MRL, Director, Project Management
Ercem Atillasoy, M.D.	2001 – 2003 MMD, Director, Regulatory Affairs 2003 – 2007 MMD, Senior Director, Regulatory Affairs 2007 – 2012 MMD, Executive Director, Regulatory Affairs 2012 – Present MMD, Vice President, Global Regulatory Affairs
Linda Banion	MRL, Executive Administrator
Robert Barber, Ph.D.	June 1997 – April 2001 MMD, Manufacturing Supervisor April 2001 – October 2003 MVD, Regulatory Writer, Worldwide Product Labeling
Susan Behrens, Ph.D.	August 1990 – October 1994 MMD, Section Head/Sr. Engineer, Technical Operations November 1994 – January 1997 MMD, Research Fellow, Pharm R&D January 1997 – May 2001 MMD, Director, Process Engineering May 2001 – November 2005 MMD, Sr. Director, Sterile Process Technology & Engineering, Regulatory & Analytical Sciences November 2005 – March 2012 MMD, Sr. Director, Biological Sciences & Strategy, Vaccine & Sterile Operations
Patrice Benner	April 1999 – April 2012 MRL, Project Manager/Key Data Coordinator
Philip Bennett	1998 – ~December 2012 2001 – 2004 (MRL, Statistician)

Name[1]	Role or Title
	MRL, Biometrician/Statistician, BARDS
David Blois, Ph.D.	~1981 – ~1993 – MRL, Executive Director, Regulatory Affairs ~2003 – MRL, Senior Vice President, Global Regulatory Policy
Gary Bolino	~January 2001 – January 2002 MRL, Manager, Worldwide Regulatory Coordination, Vaccines ~October 2002 – December 2007 MRL, Associate Director, Worldwide Regulatory Coordination (Vaccines) Secretary, Global Regulatory Strategic Review Committee
John Boslego, M.D.	October 1995 – January 2006 MRL, Executive Director, Biologics – Clinical Research
Joye Bramble, Ph.D.	1990 – 1999 MMD, Technology Group Lead April 1999 – April 2002 MRL, Senior Director, Project Planning and Management/Vaccine Integration April 2002 – November 2003 MMD, Senior Director, Bioprocess R&D, Biologics Pilot Plant April 2005 – February 2006 MMD, Executive Director, Transformation Task Force November 2003 – June 2007 MMD, Executive Director, Bioprocess R&D, Bioprocess Clinical Manufacturing and Technology August 2006 – December 2007 MVD, Senior Leader, Therapeutic Protein Commercialization June 2007 – April 2010 MRL, Executive Director, Research Planning and Integration
Patrick Brill-Edwards, M.D.	September 2001 – ~July 2016

Name[1]	Role or Title
	MRL, Associate Director, Worldwide Regulatory Affairs
Kim Bruhin	2000 – 2005 MMD, Manager GMP Compliance 2009 – April 2012 MMD, Senior Coordinator, RAS-Biologics
William Buckland	MRL, Process Research
Kelly Buckley	~2000 – 2002 MRL, Clinical Assay Research and Development (performed ELISA assays for Krah's lab)
Carl Burke, Ph.D.	July 1990 – January 2002 – MRL, Senior Research Fellow, Vaccine Pharmaceutical Research and Development 2003 – 2008 MRL, Senior Director, PR&D Vaccine siRNA Group
Pam Burke	June 2003 – January 2015 MRL, Clinical Assay R&D MRL, Executive Director, Licensing
Vera Byrnes, M.D.	~February 1998 – June 2004 MRL, Project Planning and Management
Isabelle Claxton	
Robert Capen	~1999 – 2001 MRL, Biometrician/Statistician 2001 – MRL, Senior Biometrician/Statistician 2008 – MRL, Associate Director, Scientific Staff
Peggy Carson	July 1999 – November 2003 Marketing/Manufacturing liaison, Planning and Logistics Manager November 2003 – January 2007 Marketing/Manufacturing liaison Planning and Logistics Sr. Analyst January 2007 – Present

Name[1]	Role or Title
	Marketing/Manufacturing liaison Production Planning Business Process Lead
Ivan Chan, Ph.D.	June 1995 – June 2016 MRL, Executive Director, Late Developmental Statistics
Lisa Chiacchierini-Lupinacci	~February 1998 – August 2007 MRL, District Scientist, Clinical Research
Keith Chirgwin, M.D.	1997 – 2000 MRL, Director, Worldwide Regulatory Affairs, 2000 – 2002 MRL, Senior Director, Worldwide Regulatory Affairs, 2002 – 2007 MRL, Executive Director, Worldwide Regulatory Affairs, 2008 – 2012 MRL, Vice President, Worldwide Regulatory Affairs, 2012 – 2013 MRL, Vice President, Vaccines Pipeline and Project Leader
Narendra Chirmule, Ph.D.	2000 – 2007 MRL, Director
Jeff Chodakewitz, M.D.	2002 – 2006 MRL, Vice President, Infectious Disease and Vaccine Clinical Research 2006 – 2008 MRL, Vice President, Clinical Pharmacology 2009 – January 2010 MRL, Vice President, Early Development Group Leader January 2010 – March 2011 MRL, Vice President, Late Stage Development Group Leader March 2011 – July 2012 MRL, Vice President, Late Stage Development May 2012 – January 2013 MRL, Senior Vice President, Late Stage Development

Name[1]	Role or Title
	January 2013 – August 2013 MRL, Senior Vice President, Global Scientific Strategy, Franchise Head, Infectious Disease, Respiratory and Immunology (interim) August 2013 – December 2013 MRL, Therapeutic Area Head, Infectious Diseases and Vaccine
Jim Clair, Ph.D.	1988 MRL, Senior Biometrician / Biostatistician / Senior Research Scientist June 2001 – MRL, Associate Director, Vaccine and Biometrics Research – 2013
Bill Collingwood	August 2009 – March 2013 MMD, Executive Director, Global Supply Chain Planning April 2013 – December 2014 MMD, Executive Director, Global Supply Chain Development December 2014 – August 2016 MMD, World Class Supplier Champion
Paul Coplan, Sc.D.	January 1995 – August 2002 MRL, Associate Director, Epidemiology June 2002 – December 2003 MRL, Associate Director, Global Strategic Regulatory Affairs
Michael Dekleva, Ph.D.	1989 – 1996 MMD, Microbiologist, Vaccine Technology & Engineering 1996 – 2000 MMD, Director, Vaccine Technology & Engineering 2000 – 2004 MMD, Director, Biological/Sterile Validation 2004 – 2008 MMD, Director, Regulatory Affairs Vaccines/Biologics June 2008 – 2012 MMD, Senior Director, Regulatory Affairs 2012 – Present

Name[1]	Role or Title
	MMD, Executive Director, Regulatory Affairs – Vaccines/Biologics
Kimberly Dezura	December 1995 – April 2003 MMD, Senior/Process Engineer April 2003 – November 2006 MMD, Director, Viral Vaccine Technology & Engineering November 2006 – October 2011 MMD, Senior Director, Viral Vaccine Technology & Engineering October 2011 – October 2013 MMD, Executive Director, Technology Integration October 2012 – January 2015 MMD, Executive Director, Biologics Technical Operations October 2014 – January 2016 MMD, IPT Lead, Biotech Operations May 2016 – Present MMD, General Manager, Animal Health Operations
Robert Dolan	1979 – 1995 – 2008 MMD, Vice President, Vaccine and Sterile Operations
Emilio Emini, Ph.D.	2000 – 2001 MRL, Vice President, Vaccine & Biologics Research
Peggy Fahnestock, Ph.D.	1993 – 1994 MMD, Senior Project Biologist 1994 – 1998 MRL, Research Fellow 1998 – 2005 MRL, Senior Research Fellow
Gary Feiler	November 1986 – MRL, Associate Director January 2004 MRL, Sr. Regulatory Coordinator (Vaccines) April 2005

Name[1]	Role or Title
	MRL, Associate Manager, Worldwide Regulatory Coordination (Vaccines) – August 2013
Jeffrey Feldman	1998 – 2002 MRL, Capacity Planning & Management Analyst
Catharina Fujii	1998 – 2002
Alison Fisher, Ph.D.	1984 – 1988 MRL, Staff Chemist, Department of Drug Metabolism (Merck) 1988 – 1990 MRL, Research Biochemist, Department of Drug Metabolism January 2001 – January 2002 MRL, Research Fellow, Department of Drug Metabolism (to support Merck Clinical Studies) July 2002 – February 2004 MRL, Project Manager, Pediatric Combination Vaccine Program March 2004 – Present MRL, Director Worldwide Regulatory Affairs, Vaccines, Worldwide Regulatory Liaison
Mark Galinski, Ph.D.	1996 – 1999 MMD, Senior Scientist, Vaccine Technology & Engineering 1999 – 2002 MMD, Director, Vaccine Technology & Engineering 2002 – 2005 MMD, Director, Vaccine Regulatory & Analytical Sciences 2005 – 2006 MRL, Distinguished Senior Investigator, Vaccine Biologics & Research
Emily Gallagher	2001 – 2005 MVD, Senior Contract Analyst 2005 – July 2010 MVD, Manager, Government Pricing August 2010 – November 2015

Name[1]	Role or Title
	MVD, Associate Director, Global Market Access Pricing
Susan Gallagher	Administrative Assistant
Barry Garfinkle, Ph.D.	January 1994 – December 1998 MMD, Vice President, Vaccine Quality Operations January 1998 – June 2006 MMD, Vice President, Vaccine Technology & Engineering June 2006 – Present MMD, Vice President, Biological Sciences & Strategy
Mario Gorziglia, Ph.D.	Oct 2010 – April 2011 MMD, Scientific Contributor, Global Vaccine Technology & Engineering – Viral Vaccine Technology & Engineering MMD, Principal Scientist, VTE Virology
Douglas Greene, M.D.	February 2001 – April 2002 MRL, Senior Vice President, Clinical & Regulatory Development
Harry Guess, M.D., Ph.D.	March 1998 – Apr 2002 MRL, Manager, Epidemiology
Donna Gulbinski	1985 – 1992 MRL, Staff Biochemist 1992 – 1993 MRL, Laboratory Supervisor, Biological Testing 1993 – 1997 Biotrainer / Sr. Biotrainer, Biological Quality Assurance 1997 – 1999 Biotrainer Coordinator, Biological Quality Assurance 1999 – 2001 Manager, Performance Improvement 2001 Associate Director, Process Change Control and Procedures 2001 – 2004

Name[1]	Role or Title
	Director, Vaccine and Sterile GMP Compliance
T. David Hansen	1988 – 2003 Quality Franchise Leader
Jonathan Hartzel, Ph.D.	2003 MRL, Biometrician, BARDS MRL, Associate Medical Program Clinical Specialist MRL, Senior Biometrician, BARDS ~January 2016 – Present MRL, Director, Biostatistics, BARDS
Jeff Hastings	September 1999 – May 2000 MRL, Clinical Monitor, Vaccines Infectious Diseases
Jill Heimbach	June 1986 – September 1991 Research Biochemist October 1991 – February 2000 Manager / Production Supervisor February 2000 – February 2005 Procurement Manager
Karen Hencken	1981 – 2008 MMD, Lab Technician, Vaccine Production Biologist (Pathology), Quality Assurance MMD, Associate Director, Quality Assurance March 2011 – Present MMD, Manager, Global GLP Quality
John Hennessey, Ph.D.	July 1989 – May 2008 MRL, Senior Director, Bioprocess and Bioanalytical Research
Joseph Heyse, Ph.D.	1997 – ~April 2002 MRL, Senior Director, Health & Economic Statistics 2002 – MRL, Executive Director, BARDS Vaccines February 2010 – MRL, BARDS Area Lead, BARDS – Present

Name[1]	Role or Title
	MRL, Scientific Assistant Vice President, Biostatistics, Methodology Research
Karen Hinckley	March 1990 – May 1992 Associate/Senior Director, Economic Affairs June 1992 – October 1994 Senior Director, Marketing Planning November 1994 – April 1998 Senior Business Director, Pennsylvania Region May 1998 – October 1998 Executive Director, Sales Strategic Planning October 1998 – December 2001 Vice President Sales, Northeast Business Group January 2001 – December 2006 Vice President, Specialty Sales
Lori Hirsch, Esq.	1993 – 1996 Senior Attorney 1996 – 1999 Assistant Counsel 1999 – Present Managing Counsel
Angela Howard Stofflet	1992 – 2004 MRL, Director, Global Regulatory Affairs 2004 – Present MRL, Director, Worldwide Regulatory Liaison
Heather Joseph	January 2001 – April 2004 MRL, Research Microbiologist April 2004 – August 2007 MRL, Associate Project Manager August 2007 – October 2009 MVD, Project Manager November 2009 – September 2011 MRL, Project Manager
Karen Kaplan, M.D.	February 1999 – April 2004 MRL, Associate Director, Scientific Staff MRL, Director, Scientific Staff March 2012 – January 2015 MRL, Clinical Safety and Risk Management Physician January 2015 – Present

Name[1]	Role or Title
	MRL, Executive Director, Clinical Safety and Risk Management
Amy Romanowski Keegan	March 1996 – March 1997 MRL, Chemist, Bioprocess & Bioanalytical Development March 1997 – April 1998 MMD, Scientist, Bioanalytical Development April 1998 – July 2002 MMD, Project Scientist, Bioanalytical Development/Laboratory Technical Support July 2002 – November 2005 MMD, Senior Project Scientist, Laboratory Technical Support November 2005 – September 2009 MMD, Manager, GVTE-Bioanalytical (formerly RAS-BAS) September 2009 – November 2015 CMC, Associate Director, Vaccines November 2015 – Present CMC, Director, Global Regulatory Affairs Vaccines CMC
Robyne Keleman, Ph.D.	April 1996 – December 2001 MRL, Senior Project Scientist, Biological Stability Unit
Paul Keller	~1998 – 2005 MRL, Scientist May 2003 MRL, Senior Scientific Director, Virus and Cell Biology 2004 MRL, Senior Investigator/Manager
Bernard Kelley	1993 – 2003 MMD, President
Michael King, Ph.D.	1989 – 1991 MRL, Executive Director, Process Development 1991 – 1994 MMD, Vice President, US Manufacturing Operations 1994 – 1995

Name[1]	Role or Title
	MMD, VP Regulatory Compliance, Manufacturing Division 1995 – 2007 MMD/MVD, Sr. Vice President, Science and Technology May 2005 – August 2007 MVD, Senior Vice President, Science and Advisor to CEO
Peter S. Kim, Ph.D.	March 2001 MRL, Executive Vice President for Research and Development December 2002 – 2013 MRL, President
Stephanie Olson Klopfer, Ph.D.	March 2013 – Present MRL, Senior Principal Scientist MRL, Associate Director, Scientific Staff
Roe Kowalski	
Peter Kniskern	Sep 1998 – March 2000 MRL, Scientist, Developmental Human Vaccine Serology
David Krah, Ph.D.	1988 – 1991 MRL, Senior Research Virologist, Virus and Cell Biology/Cellular and Molecular Biology 1991 – 1995 MRL, Research Fellow, Virus and Cell Biology 1995 – January 1998 MRL, Senior Research Fellow, Virus and Cell Biology January 1998 – MRL, Senior Investigator, Vaccine Basic Research
Barbara Kuter, Ph.D.	January 1979 – May 1985 MRL, Associate Biologics Program Coordinator, Virus & Cell Biology Research/Clinical Research June 1985 – June 1989 MRL, Medical Program Coordinator, Clinical Research July 1989 – May 1992

Name[1]	Role or Title
	MRL, Senior Medical Program Coordinator, Clinical Research June 1992 – January 1997 MRL, Clinical Associate/Clinical Monitor, Clinical Research February 1997 – 2005 MRL, Director, Clinical Research 2005 – Present MRL, Executive Director of Vaccine Affairs, Medical Affairs
Luc Kuykens, M.D.	1997 – 2001 MRL, Director, Regulatory Affairs, Vaccines
James Laser	October 1973 – February 2002 MMD, Vice President, Vaccine Manufacturing
Carl Levin	
Krista Liotta	Manager, Product Complaints Associate Director, Global Quality
Jeanne Liptock	
Vladimir Liska, Ph.D.	December 1999 – July 2005 MRL, R&D Group Leader / Manager – Virology / Live Virus Vaccines August 2005 – June 2010 MRL, Clinical Research Manager – Virology / Vaccines
Mike Lombardo	~2002 – ~2014 MVD, Senior Director, Marketing, Pediatric Franchise MVD, Executive Director, Marketing and Planning, Pediatric Franchise MVD, Global Brand Franchise Leader, Infant Vaccines
Bill Long	Late 1990s MRL, Clinical Assay Group, Assay Development
Mary Macchi	October 1999 – MMD, Quality Assurance, Biological Stability Unit, Bioanalytical Development 2005

Name[1]	Role or Title
	MMD, Regulatory Coordinator – August 2007 MMD, Senior Regulatory Coordinator
Phil Maher	1998 – 2002 MVD, Senior Manager, Customer Segment Marketing Vaccines 2002 – 2005 MVD, Associate Director, Product Marketing Vaccines 2005 – 2008 MVD, Director, National Account Sales Vaccines & Infectious Diseases 2008 – 2010 MVD, Regional Account Executive 2010 – Present MVD, Customer Team Leader
Susan Manoff, M.D.	2001 – 2015 MRL, Physician, Clinical Research
Rocio Marchese, Ph.D.	July 1999 – November 2003 MRL, Senior Research Immunologist December 2003 – December 2004 MRL, Senior Research Associate January 2005 – July 2007 MRL, Senior Research Fellow October 2008 – Present MRL, Director, Clinical Research
Dorothy Margolskee, M.D.	1987 – 1989 MRL, Associate Director, Clinical Pharmacology 1989 – 1993 MRL, Director, Clinical Pharmacology 1993 – 1996 MRL, Executive Director, Project Planning and Development 1996 – 1999 MRL, Vice President, Project & Vaccine Integration 1999 – 2001 MRL, Senior Vice President, Project & Vaccine Integration

Name[1]	Role or Title
Donna Marron	November 1994 – December 2002 Associate Director, Worldwide Product Labeling November 2002 – November 2007 Associate Director, Adverse Experience Reporting November 2007 – February 2010 MRL, Director, Business Standards and Compliance March 2010 – July 2017 MRL, Head, Business Practices & Payments Compliance August 2017 – Present MRL, Director, Compliance Officer
Holly Matthews, Ph.D.	
Peggy McGeehan	July 2009 – 2017 Administrative Assistant
Martin McGuire	
Roberta McKee, Ph.D.	1987 – 1990 MRL, Post-Doctoral Fellow/Sr. Research Biochemist 1990 – 1998 MRL, Director, Biological Testing & Bioanalytical Development 1998 – 2004 MRL, Vice President, Vaccine & Sterile Quality Operations
Maureen McNamara	May 1992 – December 1994 MRL, Clinical Research Operations January 1995 – June 2004 MRL, Associate Director/Sr. Project Manager/Project Manager June 2004 – December 2005 MRL, Director, Project Management February 2010 – June 2013 MVD, Executive Director, Project Management and Global Scientific Strategy Integration June 2011 – February 2017 MVD, Executive Director, Global Project and Alliance Management

Name[1]	Role or Title
Donald Meade	
Cynthia Morrisey	May 1998 – July 1999 MRL, Stability Coordinator, Bioprocess and Bioanalytical Research July 1999 – November 2004 MRL, Manager, Vaccine Regulatory and Analytical Sciences November 2004 – February 2007 MRL, Manager, Vaccine and Sterile Quality Operations
Manal Morsy, M.D., Ph.D.	1995 – 1997 MRL, Research Fellow, Virus and Cell Biology 1997 – 1999 MRL, Associate Director, Virus and Cell Biology 1999 – 2002 MRL, Associate Director, Worldwide Regulatory Affairs, Vaccines and Biologics 2002 – 2004 MRL, Director, Worldwide Regulatory Affairs, Vaccines and Biologics
Lily Mo	1996 – 2000 MRL, Scientist, Biological Stability Unit
William Mullin	March 2001 – March 2004 MMD, Executive Director, North American Pharmaceutical Quality Operations April 2004 – June 2004 MMD, Vice President, Quality Assurance July 2004 – September 2008 MMD, Vice President, West Point Quality Operations October 2008 – February 2011 MMD, Vice President, Global Vaccine and Sterile Quality Operations February 2011 – December 2013 MMD, Vice President, Sterile Quality Assurance & COE
Luwy Musey, M.D.	Prior to June 2012 MRL, Sr. Principal Scientist June 2012 –

Name[1]	Role or Title
	MRL, Director Clinical Research – Present MRL, Medical Director
Raj Nalavade	Present MMD, Product Leader, Supply Chain Management
David Nalin, M.D.	1983 – 2002 MRL, Director, Clinical Research International MVD, Director, Vaccine Scientific Affairs
Alan Nies, M.D.	1992 – 2002 MRL, Senior Vice President, Clinical Sciences
Tim Obara	September 1996 – October 1998 MVD, Marketing & Strategic Planning Director: Holland October 1998 – December 2000 MVD, International Marketing Director: MMR and Varivax January 2001 – October 2003 MVD, US Marketing Director: Varivax November 2003 – April 2004 MVD, International Marketing Director: Rotateq
Charles Osborn	December 1979 – 1984 MMD, In-process analytical lab Supervisor February 1984 – January 1995 MMD, Analytical Lab Supervisor January 1995 – November 2003 MMD, QA Inspector Supervisor
Chris Petroski	~August 2000 – May 2005 MMD, VRAS – Present MMD, Executive Director, West Point Quality Operations
Roseanne Przasnyski	2005 – 2011 Administrative Assistant.
Beverly Rich	1999 – 2003

Name[1]	Role or Title
	MRL, Research Associate, Clinical Assay Research & Development
Taryn Rogalski-Salter, Ph.D.	~August 2000 – September 2005 MMD, Director, Global Regulatory Policy
Mark Rosolowsky, Ph.D.	1991 – 2006 Senior Director, Regulatory & Analytical Sciences
David Ross	1988 – 1991 MVD, Senior Director, Specialty Products July 1991 – March 1994 MVD, Executive Director, Field Administration, April 1994 – July 1997 MVD, Managing Director, New Zealand July 1997 – July 1999 MVD, Vice President, Worldwide Marketing Specialty Products July 1999 – March 2004 MVD, Vice President, Vaccines Worldwide Marketing
Leonard Rubinstein	1990 – Present MRL, Director, Clinical Research
Carlo Russo, M.D.	1997 – 2003 MRL, Executive Director, Global Strategic Regulatory Development
Jerald Sadoff, M.D.	April 1995 – July 2003 MRL, Executive Director, Clinical Vaccines (Head of Clinical Vaccine Development)
Kellee Salber	
Ronald Salerno, Ph.D.	1973 – January 1990 – December 1993 MLR, Associate Director, Regulatory Liaison, Biologics and Vaccines June 1994 – December 1995 MRL, Director, Europe, Regulatory Liaison, Biologics and Vaccines January 1996 – February 1997

Name[1]	Role or Title
	MRL, Director, Regulatory Liaison Biologics and Vaccines February 1997 – June 2001 MMD, Director, Biologics Licensing
Wendy Santoro	Executive Assistant
Linda Schaffer, D.V.M.	July 1987 – May 1993 MRL, Research Fellow, Pharmacology May 1993 – November 1996 MRL, Project Manager/Senior Project Manager November 1996 – April 1997 MRL, Associate Director, Regulatory Affairs International April 1997 – May 2003 MRL, Director/Senior Director, Project Management 2003 – 2009 MRL, Executive Director / Vice President, Scientific Integration 2009 – 2013 MRL, Senior Vice President, Project Leadership and Management
Florian Schodel, M.D.	November 1996 – November 1998 MRL, Director, Clinical Vaccine Research, Europe November 2000 – March 2002 MRL, Executive Director, Vaccine Integration March 2002 – December 2007 MRL, Executive Director, Biologics/Vaccines Clinical Research January 2008 – April 2010 MRL, Vice President, Clinical Research
Timothy Schofield	November 1976 – November 1978 MRL, Assistant Biologics Program Coordinator December 1978 – May 1981 MRL, Associate Biologics Program Coordinator June 1981 – November 1987 MRL, Biometrician December 1987 – September 1993

Name[1]	Role or Title
	MRL, Senior Biometrician October 1993 – June 1999 MRL, Associate Director July 1999 – April 2005 MRL, Director May 2005 – December 2008 MRL, Senior Director
Edward Scolnick, M.D.	1982 – 2003 MRL, Executive Director, Virus & Cell Biology MRL, Executive Vice President, Science and Technology MRL, Vice President, Virus & Cell Biology MRL, President MRL, Senior Vice President, Basic Research
Maureen Scott	1989 – 1999 MMD, Biologist / Trainer, Environmental Monitoring 1999 – 2004 MMD, Senior Trainer / Associate Manager, BioTraining Department 2005 – 2013 MMD, Learning Lead / Senior Specialist, Training & Development
Alan Shaw, Ph.D.	1990 – MRL, Executive Director, Virus & Cell Biology February 2004 – December 2005 MRL, Senior Director, Adult Vaccine/Medical Affairs
Eric Shaw	February 1996 – February 2008 MRL, Research Fellow
Charlotte Shay	
Daniel Sikkema, Ph.D.	February 2005 – September 2008 MRL, Senior Director, Vaccines and Biologics
Keiko Simon, Ph.D.	November 1993 – November 1996 MRL, Postdoctoral Fellow – Bone Biology 1996 – 2001 MRL, Project Management

Name[1]	Role or Title
	2004 – 2011 MRL, Portfolio Director February 2011 – July 2013 MRL, Vaccines R&D Chief of Staff
Rahul Singhvi, Sc.D.	February 1994 – April 2004 MMD, Director, Vaccine Technology and Engineering
Heather Sinsel	April 2002 – October 2006 MRL, Senior Administrative Assistant October 2006 – November 2013 MRL or MVD, Senior Consular Liaison February 2013 – November 2013 MRL or MVD, Senior Specialist – SDL
Eve Slater, M.D.	1982 – 2002 MRL, Senior Vice President
Keith Soper, Ph.D.	2003 – Present MLR, Senior Director, Biostatistics
Nick Spring	December 1981 – June 1993 MVD, Director of Marketing, UK & Ireland July 1993 – October 1998 MVD, Senior Director, USA November 1997 – December 1998 (non-Merck) January 1999 – January 2002 MVD, Senior Director Global Marketing January 2002 – October 2004 MVD, Executive Director US Operations
Mark Stannard	February 1984 August 2000 Director, Control Monitoring August 2011 – June 2013 Quality Lead, Merck VVM West July 2013 – February 2017 Executive Director, Quality Operations
Bonnie Stankunas	January 1995 – August 2012 MMD, Franchise Lead, Vaccines & Biologics, Global Regulatory Affairs August 2012 – Present

Name[1]	Role or Title
	MMD, Director, Regulatory Liaison, Vaccines & Biologics, Global Regulatory Affairs
Ryan Starr	Quality
Joan Staub	August 1965 – May 1992 June 1992 – May 1996 MRL, Senior Research Associate June 1996 – May 2003 MRL, Project Manager (management of vaccine and pharmaceutical projects) May 2003 – June 2007 MRL, Director, Project Management
Ted Staub	MRL, Pharmaceutical Development
Kenneth Surowitz, Ph.D.	March 2004 – 2006 MRL, Senior Director, Regulatory Affairs, Vaccines/Biologics 2006 – 2008 MBV (Merck BioVentures), Therapeutic Area Lead, Adult Vaccine Franchise 2008 – July 2010 MBV, Therapeutic Area Lead, Biosimilars
Colleen Taddeo	~2000 – 2002 MVD, International Health Education Coordinator
Scott Thaler, M.D.	January 1999 – Jan 2002 MRL, Clinical Monitor, Vaccines Infectious Diseases
Sean Thomas	
Barbara Thompson	
Mark Twyman	1988 – 2006 MVD, Pharmaceutical Drug Representative, Market Research Analyst, Cardiovascular MVD, Promotion Manager, Cardiovascular Product Manager – Hepatitis B Vaccines MVD, Director, Sales and Marketing Operations, Vaccines MVD, National Account Executive, Vaccines MVD, Senior Director, National Payer Accounts, Vaccines

Name[1]	Role or Title
	MVD, Senior Director, US Marketing Pediatric Vaccines MVD, Vice President, International Vaccine Marketing MVD, Vice President, Global Pediatric Vaccine Marketing (last position held)
Henrietta Ukwu, M.D.	September 1992 – July 1996 MRL, Director, Regulatory Affairs, Pharmaceuticals and Vaccines July 1996 – November 1998 MRL, Senior Director, Worldwide Regulatory Affairs, Biologics and Vaccines November 1998 – July 2002 MRL, Vice President, Worldwide Regulatory Affairs, Biologics and Vaccines August 2002 – April 2004 MRL, Vice President, Global Regulatory Policy
Robert Verdugo	1989 – 1993 MVD, Manager, Communications Planning 1993 – 1996 MVD, Product Manager, Companion Animal Products 1996 – 1997 MVD, Group Product Manager, Livestock Pharmaceuticals 2001 – 2004 MVD, Senior Director, International Sales, Marketing & Operations
Tom Vernon, M.D.	2002 Vice President, Policy, Public Health, and Medical Affairs, Vaccines
Cathy Wadsworth	October 1979 – December 2011 MMD, Associate Director, Research and Commercialization Quality
William Wang, Ph.D.	January 2001 – May 2003 MRL, Biometrician, BARDS February 2010 MRL, BARDS area Lead, BARDS China (Shanghai)

Name[1]	Role or Title
	– Present MRL, Executive Director, Biostatistics CSRM Statistics
Michael Washabaugh, Ph.D.	July 1996 – April 2010 MRL, Senior Director, Bioprocess Development
Julie Waterbury, Ph.D.	1989 – 1992 MRL, Research Biochemist 2001 – 2006 MRL, Project Manager Director, Licensing Scientific Liaison, Vaccines 2012 – July 2014 Executive Director, Strategic Licensing & Acquisitions Lead, Vaccines July 2014 – Present Executive Director, Global Vaccine Strategy and Innovation
Ken Wesner	June 1977 – Present Senior Regulatory Analyst
George Williams, Ph.D.	1991 – December 2001 MRL, Senior Vice President, Biostatistics and Research Data Systems, BARDS (last position held at Merck)
Kenneth Wilson	January 1997 – September 1998 Customer Marketing Manager September 1998 – December 2000 MVD, Senior Product Manager January 2001 – June 2002 MVD, Director of Marketing June 2002 – March 2004 MVD, Director of Sales and Marketing
Helen Winterbottom	
Maria Wirths	Director Quality Assurance, Solid Dosage
A Wise	
Robin Wolchko	
Sally Wolfgang	September 2007 – July 2017 Comparator Manager

Name[1]	Role or Title
Sally Wong	Stability Manager
David Wonnacott, Ph.D.	1995 – 2000 MMD, Director, Biologics Licensing (1996)
Bridget Wright	
Mary Yagodich	March 1992 – August 1993 MRL, Virologist August 1993 – December 1994 MRL, Virologist December 1994 – December 1998 MRL, Staff Virologist December 1998 – December 2005 MRL, Research Virologist December 2005 – December 2013 Senior Research Virologist
Beverly Zaber	1980 – 2004 MMD, Senior Director, WW GMP QA and Quality Engineering
Donna Zacholski	2003 Senior Regulatory Manager February 2014 Director, Worldwide Regulatory Affairs
Jinglin Zhong, Ph.D.	Statistician

Schedule 23

Merck Collaborations

Merck Collaborations in Europe

Date	Event
1994	Joint venture Sanofi Pasteur MSD ("SPMSD") formed by Sanofi Pasteur and Merck Sharp & Dohme ("MSD").[1, 2] Sanofi Pasteur MSD, equally owned by Sanofi Pasteur and MSD, was created to develop and commercialize vaccines originating from both companies' pipelines to improve and promote public health in 19 European countries.[3] The joint venture included numerous vaccines including Merck's HPV shot Gardasil, flu vaccines used in Europe, and other inoculations for infections ranging from rabies to pneumonia to hepatitis A and B.[4] Sanofi Pasteur MSD was known as Pasteur Mérieux MSD when the joint venture was first formed.[5] SPMSD headquarters were located in Lyon, France. The joint venture territory included the following countries and certain of their territories and possessions: Austria; Belgium; Denmark; Finland; France; Germany; Greece; Iceland; Ireland; Italy; Liechtenstein; Luxemburg; Netherlands; Norway; Portugal; Spain; Sweden; Switzerland; and United Kingdom.[6] Several European "Accession Countries"[7] were not covered by the joint venture and were still considered Merck only territories.[8] SPMSD was viewed as a stand-alone company responsible for marketing and selling vaccines in Europe.[9] Merck and Sanofi Pasteur each supplied the joint venture with R&D and manufacturing functions.[10] While Merck continued to work closely with SPMSD to apprise them of any changes to vaccines or regulatory filings in the U.S.,[11] SPMSD was responsible for regulatory filings in Europe.[12] SPMSD also coordinated some of the

[1] http://fortune.com/2016/03/08/sanofi-merck-joint-venture/; http://www.msd.com/about/featured-stories/spmsd/index.html.
[2] Merck is known as MSD or Merck Sharp & Dohme outside of the United States and Canada. *See* https://www.merck.com/about/home.html.
[3] https://www.businesswire.com/news/home/20160308005897/en/Sanofi-Pasteur-Merck-MSD-United-States-Canada; http://www msd.com/about/featured-stories/spmsd/index html.
[4] https://www.businesswire.com/news/home/20160308005897/en/Sanofi-Pasteur-Merck-MSD-United-States-Canada.
[5] http://www.sanofipasteur.us/ckfinder/userfiles/files/historyEN.pdf.
[6] https://s21.q4cdn.com/488056881/files/doc_downloads/ventures/01E51DB9-C6BB-4512-A941-D665F031FED2_merck_sanofi_2009_update.pdf.
[7] An "accession country" or "acceding country" is a country that has applied to become a member state of the European Union and has signed the treaty of accession, but has not yet become a member of the EU. *See, e.g.*, https://ec.europa.eu/neighbourhood-enlargement/policy/glossary/terms/accession-eu_en.
[8] MRK-KRA00094351; MRK-KRA00511311.
[9] MRK-KRA00098926; MRK-KRA00020709.
[10] MRK-KRA00098926.
[11] *See, e.g.*, MRK-KRA00542289; MRK-KRA00506469; MRK-KRA00542508; MRK-KRA00042289; MRK-KRA00511311; MRK-KRA00543845; MRK-KRA00564768.
[12] MRK-KRA01732996; MRK-KRA00094351; MRK-KRA00012817; MRK-KRA00527182; MRK-KRA00813336; http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-

Date	Event
	clinical studies and testing in Europe[13] and, at times, co-sponsored those clinical studies with Merck.[14]
1999	Pasteur Mérieux Connaught changed its name to Aventis Pasteur.[15] Pasteur Mérieux MSD changed its name to Aventis Pasteur MSD.[16]
2004	Sanofi-Synthélabo and Aventis merged and became the Sanofi-Aventis Group.[17] The vaccines division of the Group was renamed Sanofi Pasteur,[18] and Aventis Pasteur MSD was renamed Sanofi Pasteur MSD.[19] SPMSD (then Aventis Pasteur MSD) took responsibility for the regulatory filings in Europe for approval of MMRVAXPRO—essentially a version of the MMRII vaccine that employed recombinant human albumin ("rHA") in place of human serum albumin ("HSA") in the manufacturing of measles, mumps, and rubella viral bulks.[20] The marketing authorization application for MMRVAXPRO included Merck's original seven pre-licensure studies for MMRII, Protocol 009 to support the rHA manufacturing update, and Protocol 007 to support the reduction in mumps end expiry.[21] The application also included proposed labeling indicating "not less than 12,500 TCID50" of live attenuated mumps virus (Jeryl Lynn™ [Level B] strain).[22]
2006	The European Medicines Agency recommended marketing authorization[23] for MMRVAXPRO.[24] SPMSD also handled regulatory filings in Europe for ProQuad®, which received marketing authorization from the European

_Scientific_Discussion/human/000604/WC500030167.pdf; MRK-KRA00011758; MRK-KRA00813411; MRK-KRA01350442.

[13] MRK-KRA00810530; MRK-KRA00804080; MRK-KRA00813336; MRK-KRA01888578.

[14] MRK-KRA00042123.

[15] http://www.sanofipasteur.us/ckfinder/userfiles/files/historyEN.pdf.

[16] MRK-KRA00074565.

[17] http://www.sanofipasteur.us/ckfinder/userfiles/files/historyEN.pdf.

[18] http://www.sanofipasteur.us/ckfinder/userfiles/files/historyEN.pdf.

[19] MRK-KRA00074565.

[20] MRK-KRA00011758; MRK-KRA00043293; MRK-KRA00046143.

[21] MRK-KRA00100480.

[22] MRK-KRA01956089 at '134.

[23] The European Medicines Association defines "marketing authorization" as "The approval to market a medicine in one, several or all European Union Member States." *See* http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000622/human_med_000997.jsp&mid=WC0b01ac058001d124.

[24] http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Scientific_Discussion/human/000604/WC500030167.pdf.

Date	Event
	Medicines Agency around the same time as MMRVAXPRO.[25] (MMRII had been marketed in Europe since 1978.[26])
2009	SPMSD was supplying 45 vaccines in Europe to protect infants and children, adolescents, adults, and the elderly from 20 infectious diseases.[27] Primary infant vaccines, human papillomavirus ("HPV") vaccine, flu vaccines, and booster vaccines accounted for ~80% of SPMSD end market sales.[28] Vaccines supplied by SPMSD included vaccines for HPV, rotavirus, shingles, flu, MMR, varicella, and various "booster" vaccines.[29] SPMSD had the right to all vaccine post-Phase II developments originating from both Merck and Sanofi Pasteur.[30] SPMSD shared in the development expenses of vaccines from both Merck and Sanofi Pasteur, while Merck and Sanofi Pasteur could each receive royalty income for certain contributed products.[31]
2011	After a long period of growth for SPMSD, sales began to fall. Some of the drop in the sales was attributed to diminishing sales of Gardasil in certain European countries.[32] Sales were also affected by price wars affecting flu vaccines[33] and a mild flu season.[34]
March 2016	Merck and Sanofi Pasteur announced that the joint venture would end.[35] In a joint statement, the companies said that managing their vaccine portfolios independently would put them both in a better position to drive growth.[36]

[25] http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/000622/WC500044065.pdf; https://ec.europa.eu/health/documents/community-register/2013/20130731126261/anx_126261_en.pdf.
[26] http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Scientific_Discussion/human/000604/WC500030167.pdf at 14; http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Scientific_Discussion/human/000622/WC500044067.pdf at 29.
[27] https://s21.q4cdn.com/488056881/files/doc_downloads/ventures/01E51DB9-C6BB-4512-A941-D665F031FED2_merck_sanofi_2009_update.pdf.
[28] https://s21.q4cdn.com/488056881/files/doc_downloads/ventures/01E51DB9-C6BB-4512-A941-D665F031FED2_merck_sanofi_2009_update.pdf.
[29] MRK-KRA00074565; MRK-KRA00094351.
[30] https://s21.q4cdn.com/488056881/files/doc_downloads/ventures/01E51DB9-C6BB-4512-A941-D665F031FED2_merck_sanofi_2009_update.pdf.
[31] https://s21.q4cdn.com/488056881/files/doc_downloads/ventures/01E51DB9-C6BB-4512-A941-D665F031FED2_merck_sanofi_2009_update.pdf.
[32] MRK-KRA00074565.
[33] MRK-KRA00074565.
[34] MRK-KRA00072165.
[35] http://fortune.com/2016/03/08/sanofi-merck-joint-venture/.
[36] http://fortune.com/2016/03/08/sanofi-merck-joint-venture/.

Date	Event
Dec. 31, 2016	Official closing date of the vaccine joint venture, SPMSD, following clearances granted by the European Commission.[37]
Jan. 1, 2017	Sanofi Pasteur and Merck announce plans to pursue their own vaccine strategies in Europe.[38]

[37] http://www.msd.com/about/featured-stories/spmsd/index.html; https://www.sanofipasteur.com/media/Project/One-Sanofi-Web/sanofipasteur-com/en/media-room/docs/PR_20170102_SanofiPasteurAndMSD_EN.pdf.
[38] http://www.msd.ch/en/infocenter/meldungen/impfungen.xhtml; https://www.sanofipasteur.com/media/Project/One-Sanofi-Web/sanofipasteur-com/en/media-room/docs/PR_20170102_SanofiPasteurAndMSD_EN.pdf.

Merck Collaborations in Japan

Date	Event
1993	Merck and Kaketsuken (the Chemo-Sero-Therapeutic Research Institute in Japan) signed a Letter of Understanding to establish a collaboration by the two companies in the development and marketing of a variety of vaccine products in Japan.[39]
2002	Merck and Kaketsuken continued work to register MMRII in Japan with the goal of expanding the MMRII market.[40] Kaketsuken assisted Merck with the Japanese New Drug Application ("JNDA") for MMRII.[41] The intent was to submit the Japanese New Drug Application ("JNDA") to the Pharmaceutical and Medical Devices Agency in September 2002, but there were complications in completing the JNDA as a result of an end expiry clinical study that was not finished in time for this deadline.[42] Kaketsuken was concerned about this delay because Biken was expected to file for approval of its measles-rubella vaccine by the end of 2002.[43] A delayed filing by Merck would increase the chances of Biken's measles-rubella vaccine being recommended and adopted into the Japanese vaccination schedule, which would have an impact on revenue potential for Merck from mumps vaccines, including MMRII.[44]
February 2003	Merck's JNDA for MMRII was filed.[45] Kaketsuken coordinated the original filing of the JNDA as well as responses to questions concerning the filing with ongoing input from Merck.[46]
2005	Biken's measles-rubella vaccine was licensed.[47]
2012	Merck explored partnering with Biken to develop a different MMR vaccine for Japan.[48] Merck's JNDA with Kaketsuken was still pending.[49]

[39] Merck & Co., Inc. and Kaketsuken Sign Agreement To Develop And Market Vaccines. PR Newswire Association LLC. Dec. 1, 1993. https://www.thefreelibrary.com/MERCK+%26+CO.%2c+INC.+AND+KAKETSUKEN+SIGN+AGREEMENT+TO+DEVELOP+AND+MARKET...-a014674685.
[40] MRK-KRA00330509.
[41] *Id.*
[42] *Id.*
[43] *Id.*
[44] *Id.*
[45] MRK-KRA00040973; MRK-KRA00526677.
[46] MRK-KRA00121120; MRK-KRA00121124; MRK-KRA00190817; MRK-KRA00191280.
[47] Ueda, "Development of measles vaccines in Japan," Vaccine, 2009, 27, 24, 3230-1.
[48] MRK-KRA00456815.
[49] MRK-KRA00456815.

Merck Collaborations Outside of Europe and Japan

Date	Event
2009-2015	Merck explored additional partnerships in at least China, Russia, and India to manufacture, market, and sell certain vaccines those countries.[50]
2010	Merck and Sinopharm (the China National Pharmaceutical Group) signed a "statement of mutual intent" to cooperate on an HPV vaccine and other mutually-selected vaccine products in China and to evaluate a future joint venture potential for promoting and marketing Merck's pharmaceutical products in China.[51] Sinopharm already had its own MMR vaccine, but was interested in both Merck's Jeryl Lynn strain mumps vaccine and its MMRV product.[52]
2011	Russian Technologies (the State Corporation to Facilitate Development, Production, and Export of Hi-Tech Industrial Products) proposed a joint venture with Merck in Russia.[53] The partnership was designed as an equal ownership joint venture where Merck would maintain operational control and Russian Technologies would provide administrative support. The partnership would satisfy local manufacturing mandates and provide market access in Russia to Merck.[54] Merck entered a joint venture with Sun Pharmaceutical Industries Ltd. ("Sun Pharma") in India to develop, manufacture, and sell new formulations of branded generics.[55] Sun Pharma further proposed a vaccine development, manufacturing, and marketing joint venture.[56] Around the same time, Merck agreed to collaborate with the Serum Institute of India ("Serum Institute") to develop and commercialize a pneumococcal conjugate vaccine ("PCV").[57] Merck also explored working with the Serum Institute to develop and commercialize a new MMR vaccine.[58]
2015	Merck was again researching Chinese companies to find a local manufacturing partner and to boost Merck's vaccine business in China.[59]

[50] *See, e.g.*, MRK-KRA00071741; https://www.merck.com/licensing/our-partnership/Sinopharm-partnership.html; MRK-KRA00071784; MRK-KRA0071952; MRK-KRA00077214; https://www merck.com/licensing/our-partnership/Serum-collab-pneumococcal-vaccine-partnership html; MRK-KRA00078487; MRK-KRA01052876; MRK-KRA00455889; MRK-KRA00637900; MRK-KRA01342092; MRK-KRA02069595.
[51] https://www.merck.com/licensing/our-partnership/Sinopharm-partnership html; MRK-KRA00961894 at '902; MRK-KRA01342092.
[52] MRK-KRA00455889; MRK-KRA01342092.
[53] MRK-KRA00071784; MRK-KRA00071952.
[54] MRK-KRA00071784; MRK-KRA00071952.
[55] MRK-KRA00077214.
[56] MRK-KRA00077214.
[57] https://www.merck.com/licensing/our-partnership/Serum-collab-pneumococcal-vaccine-partnership html.
[58] MRK-KRA00078487.
[59] MRK-KRA00637900.

Date	Event
	MMRV was considered a priority for development, but a local partner was considered necessary to handle regulatory issues.[60]

[60] MRK-KRA00637900.

Schedule 24

Chronology of all Biological Process Deviation Reports (BPDR), Form FDA 483, and Warning Letters Regarding Mumps Vaccines (2000-2006)

DATE	INTERACTION	DESCRIPTION
2000-10-11	**Form FDA 483**	Merck was issued a Form FDA 483, containing 24 observations. Four observations are summarized as follows: 1) CBER was not notified of a change in the passage level of Vero cells used for potency determination of measles and mumps products; 2) Merck did not adhere to the commitment made pursuant to the approval of the license supplement regarding increasing the minimum release titer of the mumps component of mumps containing vaccines (Merck committed to tracking adverse events for each lot of the higher titer mumps containing vaccines for the same month of production the previous year, to be performed monthly for the first six months) and to change to a 1x6 assay format; 3) Error and Accident Reports were not submitted to CBER for 13 product stability failures, eleven of them solely for mumps potency failures and two for measles and mumps potency failures; and 4) There was no assurance that procedures and specifications were current and accurate (one of the examples referenced is that of Merck not updating preparation of Vero cells used in the assays for measles and mumps until April, 2000 when modification was in November, 1998).[i]
2001-01-31	**BPDR**	Merck filed Biological Product Deviation Report Form, number BPD 01-002, to the Food and Drug Administration (FDA) for a Biological Product Deviation discovered on December 20, 2000, as a result of an investigation initiated into a recent out-of-specification measles potency result for 10-dose vials of M-M-R II Lot # 0627419, at the 18 month stability interval. An average measles potency value of 2.8 logTCID50/dose was observed, versus the expiry specification of 3.0 logTCID50/dose. M-M-R II Lot # 0627419 was packaged into Lot # 0507J and Lot # 1827H, which had expiry dates of 3/18/01 and 11/21/00, respectively. Distribution of this material was limited to Honduras through Merck & Co., Inc.'s corporate contribution program.[ii]
2001-02-09	**Warning Letter**	Merck received a Warning Letter from the Center for Biologics Evaluation and Research (CBER) regarding the Form FDA 483 that was issued to Merck on October 11, 2000, stemming from the FDA's inspection of Merck's West Point facility from August 14 to October 11, 2000. With regards to M-M-R II, CBER discussed Merck's response to Form FDA 483 Observation 3 (Failure to submit Error and Accident Reports for mumps and measles stability failures): "Regarding the Mumps Virus Vaccine Live stability data, your response indicated the stability profile of each lot was within the expected range based on historical trends. Products must meet their specifications, not the historical trend

		throughout the labeled expiry period." CBER noted that their investigators reported finding that a number of Mumps Vaccine stability samples, representative of lots manufactured before the February 2000 formulation change (overfill), failed to meet the minimum potency specification. Subsequently, CBER requested: "Please submit an analysis of Mumps stability data describing the range of potencies you would expect the various Mumps Vaccine products to reach at the two-year expiration date. For the analysis, assume the initial potency is the minimum release potency specification that was in effect before February 2000. Please summarize the available data regarding product efficacy at the lower end of this potency range." CBER also discussed another deficiency on the part of Merck's stability test failure investigation. Merck failed to include analyses of reserve samples of additional batches. "When the designated stability batch fails to meet its specification, the investigation should include examination of reserve samples of other batches to quickly determine whether the out of specification result represents an anomaly or serious problem." Wrapping up its letter, CBER stated that "Neither this letter nor the list of inspectional observations (Form FDA 483) is meant to be an all-inclusive list of deviations. It is your responsibility to ensure that your facility is in compliance with the provisions of the Federal Food, Drug, and Cosmetic Act and all applicable regulations. Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so that they may take this information into account when considering the award of contracts."[iii]
2001-03-05	**BPDR**	Merck filed a Biological Product Deviation Report Form, number BPD 01-003, to the Food and Drug Administration (FDA) for a Biological Product Deviation discovered on January 4 and 16, 2001. The report stated: "An investigation was initiated into a recent out-of-specification result for single-dose vials of M-M-R II Lot # 0628706 at the 24-month stability interval for potency of measles and mumps at the 4-hour and 8-hour reconstitute and store intervals, respectively. . . . An average mumps potency value of 4.2 logTCID50/dose was observed, versus the expiry specification of 4.3 logTCID50/dose. M-M-R II Lot 0628706 was packaged into Lot # 1540H. This lot was distributed domestically and expired on 10/03/00." "Active Stability Monitoring indicates that the performance of this lot is consistent with the historical performance of previous lots of this product. . . . Our medical assessment determined that clinical studies have

		shown that the minimum dose required to immunize a seronegative child has been found to be as low as … 3.1 logTCID50/dose for mumps. Therefore, for a child who might receive a sub-optimal dose of vaccine in the range of … 4.2 logTCID50/dose for mumps, as measured in the stability study, the possibility of not seroconverting, potentially leading to a lack of immunity, would not be expected….To ensure that lots will meet the mumps potency specification of 4.3 TCID50/dose at expiry, the minimum specification was revised from 4.3 to 5.0 logTCID50/dose at release. Merck concluded its report by saying "Based on the fact that potency values in the range of 2.8 logTCID50/dose for measles and 4.2 logTCID50/dose for mumps would not be expected to lead to a lack of immunity Merck & Co., Inc. believes that no further action is warranted for Lot # 1540H."[iv]
2001-04-20	**BPDR**	Merck filed a Biological Product Deviation Report Form, number BPD 01-005, to the Food and Drug Administration (FDA) for a Biological Product Deviation discovered on March 6, 2001. As part of Merck's interim analysis of seroconversion rates of one-third of the sera from the end-expiry clinical trial (preliminary subset analysis), retention samples of specific M-M-R II lots were evaluated for mumps potency. Lots were selected for testing if their expiry potencies were predicted, based on recent stability analyses, to be below 3.7 log TCID50/dose, the lowest evaluated dose in the clinical trial. The predicted worst-case expiry potencies were calculated based on the measured release potency and applying the lower 95% confidence limit of the loss rate. Using that criteria, five domestically distributed lots were analyzed. Four of the five lots tested yielded results below the label claim of 4.3 log TCID50/dose, but higher than the projected worst-case values of less than 3.7 logTCID50/dose. Two lots had a result of 3.9 logTCID50/dose; one lot was 4.0 logTCID50/dose and the other result was 4.2 logTCID50/dose. The last lot met the current expiry specification. Merck stated: "There were no atypical events that would result in lower than expected potencies associated with the manufacture of these lots." Merck further stated that, based on historical and recent clinical data, their medical assessment was that the mumps component of M-M-R II at a potency of 3.9 logTCID50/dose was efficacious and the chance of a child seroconverting at 3.9 logTCID50/dose was essentially equivalent to those who received a 4.0 or 4.9 logTCID50/dose. Merck further stated: "Our medical assessment, based on both historical and recent clinical data, indicates that the mumps component of MMRII at a potency of 3.9 logTCID50/dose is efficacious and the possibility

		of seroconverting is essentially equivalent to that of a child who receives a dose at 4.9 or 4.0 logTCID/dose." Merck also stated: "On 2/11/00, a Prior Approval Supplement was approved that included an increase in the mumps release potency specification from 4.3 to 5.0 log TCID50/dose….These changes were implemented to ensure that, in the future, potency of lots at expiry would meet the current specification of 4.3 logTCID50/dose." Finally, Merck claimed that potency values in the range of 3.9 logTCID50/dose or above would not be likely to lead to a lack of immunity against mumps.[v]
2001-08-06	**Form FDA 483**	Merck was issued a Form FDA 483 by investigators Kathryn Carbone and Debra Bennett after inspecting the lab that ran the AIGENT assay of Protocol 007. Four observations were listed for Merck's IND 1016: 1) Raw data is being changed with no justification; 2) There is no procedure in place to determine when a Research Lab is assessed to assure suitability for clinical testing prior to startup. For example: Bldg. 16 Rooms 203 and 213 has not been evaluated for testing IND 1016 samples; 3) Spreadsheets used to determine questionable results and retesting of clinical samples for IND-1016 has not been validated; and 4) Notebooks do not identify each technician performing each task.[vi]
2002-05-03	**Form FDA 483**	Merck was issued a Form FDA 483 pursuant to a Team Biologics Inspection on the following dates: April 9-12; 15-18; 29-30 and May 1-3, 2002. Observation number five documented: "Several Stability failure investigations (STI) STI100-S026 dated 12/19/00 (MMR II lot 0627419 – 18 months measles potency), STI00-S041 dated 1/24/01 (MMR II lot 0628706 – 24 months measles potency), STI01-S028/STI01-S037 dated 6/15/01 . . . and STI01-S040 dated 5/24/01 . . . were incomplete as they did not include a documented assessment of potential impact of other lots manufactured that were representative of the stability lots. Lot 0627419 was placed on stability to represent the manufacture MMR II ten-dose lots manufactured in 1999, lot 0628706 represented MMR II single-dose lots manufactured in 1998. . . . At the time of the 18 month stability failure of lot 0627419, two MMR II ten-dose lots filled in 1999 remained in inventory (0631367 and 0631456). These lots were subsequently packaged as lots 1832K, 1833K and 1834K on 1/4/00 & 1/5/00 and released on 1/24/01." Additionally, observation number nine noted that "SOP 223-308X, 'Qualification of ATTENUVAX, MUMPSVAX, or MERUVAX Lot for Use as a House Standard

		in Live Virus Vaccine Potency Testing' requires monthly analyses of the house standard, however there was no documented criteria for the evaluation."[vii]
2002-07-26	**BPDR**	Merck filed a Biological Product Deviation Report, number BPD 02-005, to the Food and Drug Administration (FDA) for a Biological Product Deviation discovered on June 11, 2002 (M-M-R II) and June 17, 2002 (M-M-VAX). The report detailed M-M-R II and M-M-VAX lots that were observed as having out-of-specification measles potency values. The first lot, M-M-R II lot 0633815, was one of three lots placed on a special stability monitoring study to evaluate the 1999 process change to increase the mumps titer. An average measles potency result of 2.9 log10 TCID50/dose for the eight hour "reconstitute and store" sample was observed versus the expiry specification of ≥3.0 log10 TCID50/dose. The second lot, M-M-VAX lot 0634993, was selected for the 1999 M-M-VAX single-dose annual stability study. An average measles potency value of 2.9 log10 TCID50/dose was observed for the eight hour "reconstitute and store" sample, versus the expiry specification of ≥3.0 log10 TCID50/dose.[viii]
2002-10-18	**BPDR**	Merck filed a Biological Product Deviation Report Form, number BPD 02-007, to the Food and Drug Administration (FDA) for a Biological Product Deviation discovered on September 4, 2002. As part of its ongoing stability program, Merck initiated an investigation into a recent 24-month out-of-specification measles potency and measles reconstitute and store potency results obtained during testing of M-M-R II Lot # 0636850 at the 24-month stability interval. M-M-R II Lot # 0636850 was placed on a special stability monitoring study as one of three lots to evaluate the use of a new source of albumin, Instituto Grifols, S.A., used in the diluent for the manufacture of M-M-R II. The average measles potency result (reconstituted, but not stored) for the 24-month interval, was 2.9 log10 TCID50/dose, versus a specification of ≥3.0 log10TCID50/dose. In addition, an average measles potency result of 2.9 log10 TCID50/dose for the eight-hour reconstitute and store sample was observed versus the specification of ≥3.0 logioTCID30/dose. Furthermore, while discussing its manufacturing documentation concerning lot 0636850, Merck noted that M-M-R II Lot # 0636850 had an out of trend, but within specification, high mumps titer of 5.7 log10 TCID50 /dose. Merck asserted that the high mumps titer had no effect on the measles stability results. Finally, Merck reviewed its measles stability profile, which was based on principles developed in 1999 with CBER for the M-M-R II family Mumps

		stability profile. It concluded that a higher minimum release specification would be required to ensure with 95% confidence that the potencies of measles-containing products are ≥3.0 log10TCID50/dose at expiry. To address this, Merck filed a Prior Approval Supplement (PAS) with the FDA on September 16, 2002, containing proposed changes to the measles filling target, release specifications and assay testing scheme.[ix]
2006-05-26	**BPDR**	Merck filed a Biological Product Deviation Report Form, number 06-004, to the Food and Drug Administration (FDA) for a Biological Product Deviation discovered on April 13, 2006, but occurring on December 2001. The BPDR discussed missed or invalid stability intervals discovered following a comprehensive internal assessment of Merck's stability data that was completed in April 2006. This assessment was committed to by Merck in one of its responses to a 2006 Team Biologics Inspection. As a result of the assessment and the re-assessment of Merck's BPDR reporting procedures, five (5) additional missed / invalid stability intervals were discovered. In its summary, Merck noted that all of the instances reviewed within the report occurred prior to the reorganization of Merck's West Point Quality Operations in November 2004, and the implementation of improvements to Merck's quality systems in late 2004 and 2005. The missed/invalid test interval related to M-M-R II was an invalid test interval resulting from a Mumps 6-month potency test that occurred in December 2001 on an M-M-R II Lot. The lot was tested during Study 0734L that was initiated in August 2001 to support the annual requirement for M-M-R II. The Mumps Potency testing was performed in December 2001, but the test data entry for the average value was not performed until March 2002 due to an ongoing investigation. At that time, it was determined that the range criteria were exceeded for the 6-month interval, and the high/low results were invalidated. A third replicate was invalidated due to expired anti-sera, resulting in only three remaining valid test replicates versus the six valid test replicates required for the test. There were no remaining representative samples available to perform additional replicate testing, resulting in an invalid result for the 6-month time point. All subsequent Mumps Potency time points for the study were satisfactory.[x]

[i] October 24, 2000 Merck responses to the Team Biologics inspection Form FDA 483 observations, found at MRK-KRA01897017 and MRK-KRA00783728 AEO; and an October 11, 2000 Memorandum from Christopher Petroski re: "Team Biologics Close Out – Form FDA 483," containing the list of communicated observations from Inspectors Loren and Schofield, found at MRK-KRA00071265.

[ii] Biological Product Deviation Report Form, number BPD 01-002, reported January 31, 2001, found at MRK-KRA00754221.

[iii] February 9, 2001 Warning Letter from the FDA to Roberta McKee found at PUBLIC0000666 (public version), or MRK-KRA00209399 AEO with redactions.

[iv] Biological Product Deviation Report Form, number BPD 01-003, reported March 5, 2001, found at MRK-KRA00754239.

[v] Biological Product Deviation Report Form, number BPD 01-005, reported April 20, 2001, found at MRK-KRA00754233.

[vi] August 6, 2001 Form FDA 483 issued to Alan Shaw from investigators Kathryn Carbone and Debra Bennett, found at MRK-KRA00000547; and August 20, 2001 letter to Dr. Steven Masiello of CBER from Emilio Emini attaching Merck's response to the observations made by Investigators Carbone and Bennett, found at MRK-KRA00000481.

[vii] May 20, 2002 Merck responses to Form FDA 483 observations, resulting from a Team Biologics Inspection occurring on April 9-12, 15-18, 29-30 and May 1-3, found at MRK-KRA00783949 AEO (parent email MRK-KRA00783945 indicates that this was the 'final' version sent to the FDA); see also MRK-KRA02023386 AEO (contains far fewer redactions regarding the Stability failure investigations observation, but it is not the 'final' version).

[viii] Biological Product Deviation Report Form, number BPD 02-005, reported July 26, 2002, found at MRK-KRA00754245.

[ix] October 18, 2002 letter from Roberta McKee to the Food and Drug Administration (FDA), Center for Biologics Evaluation and Research (CBER) attaching a Biological Product Deviation Report Form, number BPD 02-007, Reported October 18, 2002, found at MRK-KRA00754322.

[x] May 26, 2006 Letter from William J. Mullin to Ms. Mary Anne Malarkey, Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research (CBER) attaching a Biological Product Deviation Report Form, number BPD 06-004, reported May 26, 2006, found at MRK-KRA00754392.

Schedule 25

Low Potency Lots Identified in 2001

MMD "Lots in Question"[1]

Fill	Mumps Potency	Per Dose	Est titer End-expiry	DOM	Fill Release	Expiry	QC Release	Packaged Doses
0629591	4.3	5	4	11/2/1998	1/5/1999	11/2/2001	1/22/1999	116,415
0630084	4.5	5.2	4.2	11/9/1998	1/4/1999	11/9/2001	1/22/1999	118,080
0629532	4.1	4.8	3.8	10/8/1998	1/26/1999	10/8/2001	2/12/1999	100,890
0629573	4.4	5.1	4.1	10/21/1998	1/28/1999	10/21/2001	2/12/1999	119,229
0630087	4.2	4.9	3.9	11/12/1998	1/14/1999	11/12/2001	2/12/1999	114,160
0630090	4.2	4.9	3.9	11/16/1998		11/16/2001	2/12/1999	116,196
0630085	4.6	5.3	4.3	11/10/1998	2/9/1999	11/10/2001	2/22/1999	114,390
0630088	4.5	5.2	4.2	11/13/1998	1/25/1999	11/13/2001	2/23/1999	116,220
0629572	4.5	5.2	4.2	10/29/1998	2/11/1999	10/29/2001	2/24/1999	118,020
0629592	4.3	5	4	11/4/1998	2/10/1999	11/4/2001	2/24/1999	118,080
0630089	4.5	5.2	4.2	11/14/1998	2/12/1999	11/14/2001	2/24/1999	118,190
0629574	4.2	4.9	3.9	10/25/1998	2/17/1999	10/25/2001	3/8/1999	113,730
0630092	4.6	5.3	4.3	11/17/1998	2/9/1999	11/17/2001	3/8/1999	111,530
0628889	4.2	4.9	3.9	1/4/1999	3/4/1999	1/4/2002	3/23/1999	115,295
0628890	4.3	5	4	1/5/1999	3/4/1999	1/5/2002	3/23/1999	114,080
0630091	4.3	5	4	11/15/1998	3/15/1999	11/15/2001	3/26/1999	115,208
0630093	4.5	5.2	4.2	12/4/1998	3/15/1999	12/4/2001	3/26/1999	119,140
0630095	4.2	4.9	3.9	11/29/1998	3/26/1999	11/29/2001	3/26/1999	118,898
0630254	4.6	5.3	4.3	12/10/1998	3/15/1999	12/10/2001	3/26/1999	118,815
0630260	4.4	5.1	4.1	12/11/1998	3/15/1999	12/11/2001	3/26/1999	117,975
0630232	4.6	5.3	4.3	11/23/1998	3/2/1999	11/23/2001	4/5/1999	115,710
0630086	4.5	5.2	4.2	11/11/1998	3/23/1999	11/11/2001	4/7/1999	111,809
0630094	4.2	4.9	3.9	11/28/1998	3/31/1999	11/28/2001	4/14/1999	114,829
0630255	4.4	5.1	4.1	1/7/1999	3/26/1999	1/7/2002	4/14/1999	114,385
0630632	4.5	5.2	4.2	1/30/1999	3/26/1999	1/30/2002	4/14/1999	110,400
0630235	4.6	5.3	4.3	11/24/1998	3/1/1999	11/24/2001	4/22/1999	117,380
0630608	4.1	4.8	3.8	1/11/1999	4/8/1999	1/11/2002	4/29/1999	115,310
0630635	4.2	4.9	3.9	1/25/1999	4/14/1999	1/25/2002	4/29/1999	113,848
0630636	4.3	5	4	1/22/1999	4/13/1999	1/22/2002	4/29/1999	115,740
0630628	4.4	5.1	4.1	1/15/1999	4/13/1999	1/15/2002	5/5/1999	116,480
0631041	4.2	4.9	3.9	2/4/1999	4/21/1999	2/4/2002	5/5/1999	117,300
0631042	4.3	5	4	2/5/1999	4/21/1999	2/5/2002	5/5/1999	115,400
0631045	4.1	4.8	3.8	2/11/1999	4/26/1999	2/11/2002	5/19/1999	112,240
0631037	4.4	5.1	4.1	2/21/1999	5/13/1999	2/21/2002	5/27/1999	113,902
0631043	4.2	4.9	3.9	2/7/1999	5/6/1999	2/7/2002	6/1/1999	116,882
0631044	4.3	5	4	2/13/1999	5/10/1999	2/13/2002	6/1/1999	117,554
0630262	4.3	5	4	1/17/1999	5/20/1999	1/17/2002	6/3/1999	114,660
0631370	4.5	5.2	4.2	2/26/1999	5/17/1999	2/26/2002	6/3/1999	118,470

[1] Referenced in MRK-KRA0549510; MRK-KRA00549518.

Fill	Mumps Potency	Per Dose	Est titer End-expiry	DOM	Fill Release	Expiry	QC Release	Packaged Doses
0631372	4.3	5	4	3/1/1999	5/24/1999	3/1/2002	6/3/1999	111,710
0631875	4.3	5	4	3/30/1999	5/14/1999	3/30/2002	6/4/1999	118,650
0631371	4.3	5	4	2/26/1999	5/14/1999	2/26/2002	6/15/1999	112,500
0631447	4.4	5.1	4.1	3/4/1999	6/7/1999	3/4/2002	6/15/1999	118,420
0631446	4.2	4.9	3.9	3/2/1999	6/2/1999	3/2/2002	6/22/1999	115,554
0631485	4.3	5	4	2/23/1999	6/14/1999	2/23/2002	6/29/1999	101,660
0631654	4.4	5.1	4.1	3/20/1999	6/14/1999	3/20/2002	6/29/1999	116,505
0631881	4.2	4.9	3.9	4/7/1999	6/11/1999	4/7/2002	6/29/1999	117,760
0631885	4.4	5.1	4.1	4/9/1999	6/15/1999	4/9/2002	6/29/1999	118,620
0631878	4.5	5.2	4.2	4/3/1999	6/14/1999	4/3/2002	6/30/1999	119,140
0631657	4.3	5	4	3/26/1999	6/16/1999	3/26/2002	7/1/1999	117,020
0631658	4.2	4.9	3.9	4/13/1999	6/17/1999	4/13/2002	7/1/1999	114,540
0631659	4.2	4.9	3.9	4/30/1999	6/17/1999	4/30/2002	7/1/1999	115,300
0631877	4.1	4.8	3.8	4/2/1999	6/24/1999	4/2/2002	7/7/1999	118,350
0631882	4.1	4.8	3.8	4/16/1999	6/22/1999	4/16/2002	7/7/1999	117,300
0631873	4.1	4.8	3.8	3/30/1999	6/16/1999	3/30/2002	7/15/1999	116,908
0632229	4.2	4.9	3.9	4/22/1999	7/1/1999	4/22/2002	7/15/1999	117,851
0632238	4.4	5.1	4.1	4/26/1999	7/6/1999	4/26/2002	7/21/1999	116,290
0631884	4.1	4.8	3.8	5/1/1999	7/7/1999	5/1/2002	7/23/1999	119,390
0632346	4.2	4.9	3.9	5/8/1999	7/7/1999	5/8/2002	7/23/1999	118,520
0632348	4.2	4.9	3.9	5/14/1999	7/7/1999	5/14/2002	7/23/1999	115,546
0632227	4.1	4.8	3.8	4/19/1999	6/22/1999	4/19/2002	7/26/1999	117,460
0631883	4.1	4.8	3.8	4/15/1999	7/15/1999	4/15/2002	7/29/1999	118,056
0632237	4	4.7	3.7	4/24/1999	7/19/1999	4/24/2002	7/29/1999	116,840
0631653	3.9	4.6	3.6	3/19/1999	7/1/1999	3/19/2002	8/6/1999	115,400
0631871	4.3	5	4	3/25/1999	6/14/1999	3/25/2002	8/16/1999	118,475
0631872	4.4	5.1	4.1	3/27/1999	7/15/1999	3/27/2002	8/16/1999	118,635
0631040	4.4	5.1	4.1	2/2/1999	8/12/1999	2/2/2002	8/24/1999	111,390
0632345	4.4	5.1	4.1	5/7/1999	8/12/1999	5/7/2002	8/24/1999	118,220
0632228	4.4	5.1	4.1	4/23/1999	8/2/1999	4/23/2002	8/31/1999	110,650
0632356	4.3	5	4	4/29/1999	8/16/1999	4/29/2002	8/31/1999	117,824
0632998	4.3	5	4	6/25/1999	8/16/1999	6/25/2002	9/1/1999	117,760
0631038	4.3	5	4	2/19/1999	8/16/1999	2/19/2002	9/2/1999	115,621
0632526	4.3	5	4	6/16/1999	8/16/1999	6/16/2002	9/2/1999	118,220
0632768	4.3	5	4	6/20/1999	9/1/1999	6/20/2002	9/2/1999	118,680
0632999	4.3	5	4	6/26/1999	8/16/1999	6/26/2002	9/2/1999	118,140
0633000	4.2	4.9	3.9	6/27/1999	8/17/1999	6/27/2002	9/2/1999	117,300
0633007	4.3	5	4	6/29/1999	8/19/1999	6/29/2002	9/2/1999	117,230
0633009	4.3	5	4	7/1/1999	8/19/1999	7/1/2002	9/2/1999	114,080
0633088	4.3	5	4	7/10/1999	8/17/1999	7/10/2002	9/2/1999	116,325
0633010	4.2	4.9	3.9	6/29/1999	8/20/1999	6/29/2002	9/7/1999	105,200
0632988	4.2	4.9	3.9	6/24/1999	8/16/1999	6/24/2002	9/14/1999	116,730

Fill	Mumps Potency	Per Dose	Est titer End-expiry	DOM	Fill Release	Expiry	QC Release	Packaged Doses
0633008	4.6	5.3	4.3	6/30/1999	9/20/1999	6/30/2002	9/23/1999	117,975
0633087	4.3	5	4	7/11/1999	9/28/1999	7/11/2002	9/28/1999	114,965
0633089	4.2	4.9	3.9	7/11/1999	9/28/1999	7/11/2002	9/28/1999	118,680
0631039	4.3	5	4	2/25/1999	10/25/1999	2/25/2002	10/25/1999	115,520
0631876	4.3	5	4	4/1/1999	10/25/1999	4/1/2002	10/25/1999	119,140
0632767	4.2	4.9	3.9	6/14/1999	10/25/1999	6/14/2002	10/25/1999	113,573
0633090	4.2	4.9	3.9	7/12/1999	10/25/1999	7/12/2002	10/25/1999	117,485
0628891	4.2	4.9	3.9	1/7/1999	10/25/1999	1/7/2002	10/26/1999	112,700
0630234	4.7	5.4	4.4	11/22/1998	10/26/1999	11/22/2001	10/26/1999	115,700
0632772	4.3	5	4	6/13/1999	8/24/1999	6/13/2002	10/26/1999	118,680
0633001	4.3	5	4	6/25/1999	10/25/1999	6/25/2002	10/26/1999	112,240
0633602	4.2	4.9	3.9	8/27/1999	11/30/1999	8/27/2002	10/26/1999	110,885
0633601	4.2	4.9	3.9	8/26/1999	10/21/1999	8/26/2002	11/2/1999	112,030
0633091	4.3	5	4	7/31/1999	10/25/1999	7/31/2002	11/3/1999	117,040
0633444	4.4	5.1	4.1	8/13/1999	10/25/1999	8/13/2002	11/3/1999	110,400
0632765	4	4.7	3.7	6/9/1999	11/2/2000	6/9/2002	11/4/1999	118,085
0632347	4.2	4.9	3.9	5/22/1999	11/12/1999	5/22/2002	11/15/1999	116,680
0633440	4.3	5	4	8/10/1999	11/12/1999	8/10/2002	11/15/1999	115,920
0633453	4.3	5	4	8/18/1999	11/12/1999	8/18/2002	11/15/1999	115,380
0633454	4.3	5	4	8/19/1999	10/25/1999	8/19/2002	11/24/1999	111,917
0633600	4.2	4.9	3.9	8/25/1999	2/1/2000	8/25/2002	11/24/1999	117,160
0632769	4.4	5.1	4.1	6/21/1999	10/25/1999	6/21/2002	2/3/2000	118,220
0631655	4.1	4.8	3.8	4/9/1999	2/18/2000	4/9/2002	2/18/2000	115,100
0631656	4	4.7	3.7	4/11/1999	2/23/2000	4/11/2002	2/23/2000	116,285
0632464	4.1	4.8	3.8	5/6/1999	2/22/2000	5/6/2002	2/23/2000	118,870
0631879	4.4	5.1	4.1	4/2/1999	11/30/1999	4/2/2002	4/6/2000	118,220
0631880	4.1	4.8	3.8	4/6/1999	11/30/1999	4/6/2002	4/20/2000	115,920
0633452	4.3	5	4	9/8/1999	10/26/1999	9/8/2002	7/12/2000	117,442
0632770	4.3	5	4	6/12/1999	8/12/1999	9/1/2001	9/21/1999	118,385
0632773	4.2	4.9	3.9	6/18/1999	8/24/1999	9/1/2001	9/21/1999	118,930
0630103	4.2	4.9	3.9	12/14/1998	3/3/1999	2/25/2001	3/12/1999	114720
0627382	3.8	4.5	3.5	3/28/1998	6/8/1998	3/26/2001	4/21/1999	117970
0627426	4.3	5	4	4/16/1998	6/2/1998	3/26/2001	4/22/1999	117910
0627385	3.8	4.5	3.5	4/1/1998	6/8/1998	3/26/2001	5/4/1999	115320
0628286	4.1	4.8	3.8	1/18/1999	3/30/1999	2/25/2001	5/5/1999	113930
0630623	4.3	5	4	1/11/1999	4/21/1999	2/25/2001	5/5/1999	116250
0630625	4.4	5.1	4.1	1/23/1999	4/26/1999	2/25/2001	5/5/1999	117370
0630626	4.5	5.2	4.2	1/20/1999	4/21/1999	2/25/2001	5/5/1999	57940
0630627	4.1	4.8	3.8	1/20/1999	4/21/1999	2/25/2001	5/5/1999	57530
0630629	4.3	5	4	1/21/1999	4/21/1999	2/25/2001	5/5/1999	110870
0630630	4.5	5.2	4.2	1/24/1999	4/21/1999	3/26/2001	5/5/1999	57600
0630631	4.5	5.2	4.2	1/24/1999	4/21/1999	3/26/2001	5/5/1999	56850

Fill	Mumps Potency	Per Dose	Est titer End-expiry	DOM	Fill Release	Expiry	QC Release	Packaged Doses
0631052	4.6	5.3	4.3	2/8/1999	4/26/1999	3/25/2001	5/5/1999	57310
0631053	4.3	5	4	2/8/1999	4/26/1999	2/27/2001	5/5/1999	48050
0631084	4	4.7	3.7	2/5/1999	4/21/1999	2/27/2001	5/5/1999	57150
0627187	4.1	4.8	3.8	4/22/1998	6/19/1998	3/26/2001	5/7/1999	116100
0627425	4.2	4.9	3.9	4/17/1998	6/1/1998	3/26/2001	5/7/1999	117480
0631051	4.5	5.2	4.2	2/4/1999	4/21/1999	3/25/2001	5/10/1999	56170
0630624	4.3	5	4	1/17/1999	4/26/1999	3/26/2001	5/25/1999	114800
0631054	4.3	5	4	2/12/1999	5/10/1999	2/27/2001	5/28/1999	59070
0631055	4.3	5	4	2/12/1999	5/10/1999	2/27/2001	5/28/1999	59560
0631056	4.2	4.9	3.9	2/15/1999	5/12/1999	3/25/2001	5/28/1999	57640
0631057	4.2	4.9	3.9	2/15/1999	5/12/1999	2/27/2001	5/28/1999	57700
0631046	4.1	4.8	3.8	2/14/1999	5/12/1999	3/26/2001	6/3/1999	116480
0631047	4.5	5.2	4.2	2/16/1999	5/12/1999	3/26/2001	6/3/1999	116160
0631049	4.3	5	4	2/18/1999	5/12/1999	3/26/2001	6/3/1999	117740
0631448	4.1	4.8	3.8	3/4/1999	5/14/1999	3/27/2001	6/3/1999	119270
0631451	4.4	5.1	4.1	3/11/1999	5/17/1999	3/27/2001	6/3/1999	118570
0631452	4.3	5	4	3/8/1999	5/14/1999	3/27/2001	6/3/1999	115530
0631645	4.4	5.1	4.1	3/14/1999	6/7/1999	5/27/2001	6/24/1999	57700
0631646	4.1	4.8	3.8	3/14/1999	6/8/1999	5/28/2001	6/24/1999	55070
0631643	4.3	5	4	3/21/1999	6/10/1999	5/27/2001	6/25/1999	58740
0631644	4.2	4.9	3.9	3/21/1999	6/10/1999	5/27/2001	6/25/1999	56860
0630639	4.4	5.1	4.1	4/5/1999	6/8/1999	5/27/2001	7/9/1999	55820
0631640	4.3	5	4	3/23/1999	6/7/1999	5/27/2001	7/9/1999	112650
0631642	4.2	4.9	3.9	3/17/1999	5/24/1999	5/27/2001	7/9/1999	118800
0631886	4.2	4.9	3.9	3/25/1999	6/24/1999	5/28/2001	7/9/1999	58190
0631888	4.3	5	4	3/28/1999	6/17/1999	5/28/2001	7/9/1999	57130
0631889	4.4	5.1	4.1	3/28/1999	6/17/1999	5/28/2001	7/9/1999	58020
0631887	4.1	4.8	3.8	3/25/1999	6/24/1999	5/28/2001	7/13/1999	56930
0632236	4	4.7	3.7	4/23/1999	6/29/1999	5/28/2001	7/15/1999	118250
0632326	4.3	5	4	4/29/1999	6/29/1999	5/28/2001	7/15/1999	58000
0631649	4	4.7	3.7	4/8/1999	6/21/1999	5/28/2001	7/23/1999	57760
0631650	3.9	4.6	3.6	4/8/1999	6/21/1999	5/28/2001	7/23/1999	57720
0631890	4.5	5.2	4.2	3/31/1999	6/16/1999	5/28/2001	7/23/1999	57810
0631891	4.3	5	4	4/1/1999	6/16/1999	5/28/2001	7/23/1999	58040
0631651	4.1	4.8	3.8	4/15/1999	7/19/1999	5/28/2001	7/29/1999	74320
0631652	4.2	4.9	3.9	4/15/1999	7/19/1999	5/28/2001	7/29/1999	57550
0632232	4.2	4.9	3.9	4/18/1999	7/14/1999	5/28/2001	7/29/1999	57760
0632233	4	4.7	3.7	4/18/1999	7/14/1999	5/28/2001	7/29/1999	58660
0632341	4.5	5.2	4.2	5/2/1999	6/30/1999	6/25/2001	8/4/1999	61560
0632400	4.2	4.9	3.9	5/16/1999	7/15/1999	6/25/2001	8/4/1999	115200
0627835	3.8	4.5	3.5	5/18/1998	6/24/1998	5/18/2001	8/5/1999	117550
0627839	3.7	4.4	3.4	5/15/1998	7/23/1998	5/15/2001	8/5/1999	118040

Fill	Mumps Potency	Per Dose	Est titer End-expiry	DOM	Fill Release	Expiry	QC Release	Packaged Doses
0632230	4.1	4.8	3.8	4/16/1999	7/19/1999	6/24/2001	8/5/1999	179370
0632325	4.2	4.9	3.9	4/29/1999	6/29/1999	5/28/2001	8/5/1999	58390
0632340	4.5	5.2	4.2	5/4/1999	7/19/1999	6/25/2001	8/5/1999	225920
0632342	4.4	5.1	4.1	5/3/1999	6/30/1999	6/25/2001	8/5/1999	90780
0632343	4.3	5	4	5/10/1999		6/25/2001	8/5/1999	127760
0631641	4.3	5	4	3/18/1999	7/15/1999	5/27/2001	8/17/1999	118800
0632457	4.3	5	4	5/19/1999	8/12/1999	6/25/2001	8/17/1999	118090
0632530	4.4	5.1	4.1	6/6/1999	8/12/1999	6/25/2001	8/19/1999	117920
0632766	4.2	4.9	3.9	6/10/1999	8/12/1999	6/25/2001	8/24/1999	116950
0631454	4.3	5	4	3/10/1999	8/12/1999	5/27/2001	8/30/1999	58390
0631455	4.4	5.1	4.1	3/11/1999	8/12/1999	3/27/2001	8/30/1999	57540
0632339	4.1	4.8	3.8	5/7/1999	8/16/1999	6/25/2001	8/30/1999	114680
0632531	4.2	4.9	3.9	6/7/1999	8/16/1999	6/25/2001	8/30/1999	117160
0632529	4.5	5.2	4.2	6/23/1999	8/12/1999	8/4/2001	9/9/1999	118210
0632533	4.5	5.2	4.2	6/17/1999	8/18/1999	8/4/2001	9/9/1999	118630
0632535	4.3	5	4	6/10/1999	7/16/1999	8/3/2001	9/9/1999	111130
0632771	4.2	4.9	3.9	6/14/1999	8/12/1999	8/4/2001	9/9/1999	118100
0632858	4.2	4.9	3.9	6/22/1999	8/18/1999	8/4/2001	9/9/1999	118830
0633011	4.1	4.8	3.8	7/2/1999	8/19/1999	8/4/2001	9/9/1999	117900
0633012	4.5	5.2	4.2	7/3/1999	8/24/1999	8/4/2001	9/9/1999	118120
0632532	4.3	5	4	6/21/1999	9/20/1999	8/4/2001	9/20/1999	114,550
0632455	4.3	5	4	5/17/1999	9/28/1999	6/25/2001	9/28/1999	114,870
0629640	4.3	5	4	11/6/1998	10/26/1999	9/21/2001	10/26/1999	85,100
0632344	4.4	5.1	4.1	5/11/1999	7/29/1999	6/25/2001	10/26/1999	117,720
0632552	4.6	5.3	4.3	7/5/1999	10/25/1999	8/4/2001	10/26/1999	51,530
0632764	4.1	4.8	3.8	6/9/1999	9/27/1999	8/4/2001	10/26/1999	107,200
0633013	4.3	5	4	7/5/1999	9/23/1999	8/4/2001	10/26/1999	118,400
0633014	4.3	5	4	7/7/1999	9/22/1999	8/4/2001	10/26/1999	102,680
0633015	4.2	4.9	3.9	7/4/1999	8/19/1999	8/4/2001	10/26/1999	104,760
0633016	4.2	4.9	3.9	7/6/1999	8/24/1999	8/4/2001	10/26/1999	118,600
0633017	4.4	5.1	4.1	7/7/1999	11/30/1999	8/4/2001	10/26/1999	117,900
0633018	4.5	5.2	4.2	7/9/1999	9/29/1999	8/4/2001	10/26/1999	118,520
0633086	4.2	4.9	3.9	7/9/1999	9/28/1999	8/4/2001	10/26/1999	53,760
0633603	4.2	4.9	3.9	8/28/1999	11/30/1999	9/21/2001	10/26/1999	56,640
0633599	4	4.7	3.7	8/24/1999	11/12/1999	9/21/2001	11/15/1999	116,540
0633707	4.4	5.1	4.1	9/4/1999	11/12/1999	10/16/2001	12/1/1999	55,100
0633595	4.2	4.9	3.9	8/29/1999	11/12/1999	10/16/2001	12/14/1999	111,820
0633598	4.1	4.8	3.8	8/22/1999	10/26/1999	10/16/2001	12/14/1999	86,290
0633705	4.2	4.9	3.9	8/31/1999	11/12/1999	10/16/2001	12/14/1999	56,980
0633513	4.2	4.9	3.9	8/11/1999	10/25/1999	10/16/2001	1/27/2000	57,960
0633570	4.2	4.9	3.9	8/15/1999	10/25/1999	10/16/2001	1/27/2000	48,840
0633597	4.1	4.8	3.8	8/21/1999	10/25/1999	10/16/2001	1/27/2000	108,420

Fill	Mumps Potency	Per Dose	Est titer End-expiry	DOM	Fill Release	Expiry	QC Release	Packaged Doses
0629284	4.3	5	4	11/7/1998	10/25/1999	11/7/2001	2/16/2000	45,470
0630385	4.1	4.8	3.8	2/1/1999	10/25/1999	1/8/2002	2/16/2000	56,790
0630633	4.2	4.9	3.9	1/27/1999	10/25/1999	1/14/2002	2/16/2000	56,700
0630634	4.2	4.9	3.9	1/28/1999	10/25/1999	1/14/2002	2/16/2000	56,710
0630638	4.4	5.1	4.1	3/7/1999	10/25/1999	1/14/2002	2/16/2000	52,730
0631050	4.3	5	4	3/12/1999	10/25/1999	1/14/2002	2/16/2000	117,090
0631449	4.3	5	4	3/6/1999	10/25/1999	1/14/2002	2/16/2000	102,110
0628907	4.1	4.8	3.8	1/31/1999	10/25/1999	1/14/2002	2/23/2000	54,660
0630637	4.6	5.3	4.3	2/20/1999	10/25/1999	1/21/2002	2/24/2000	57,500
0631450	4.1	4.8	3.8	3/9/1999	10/25/1999	1/14/2002	2/24/2000	112,330
0631639	4.1	4.8	3.8	3/16/1999	10/25/1999	1/14/2002	2/24/2000	112,090
0632456	4.1	4.8	3.8	5/21/1999	11/12/1999	1/27/2002	2/24/2000	113,600
0632706	4.3	5	4	7/1/1999	11/18/1999	1/27/2002	2/24/2000	57,210
0632459	4.2	4.9	3.9	5/20/1999	11/12/1999	1/21/2002	2/25/2000	118,230
0633092	4.4	5.1	4.1	7/30/1999	10/25/1999	1/27/2002	2/25/2000	112,570
0633093	4.2	4.9	3.9	8/2/1999	10/25/1999	1/27/2002	2/25/2000	114,780
0633094	4.2	4.9	3.9	8/3/1999	10/25/1999	1/27/2002	2/25/2000	114,070
0633095	4.1	4.8	3.8	8/6/1999	10/25/1999	2/9/2002	3/9/2000	110,290
0633098	4.4	5.1	4.1	8/9/1999	10/25/1999	2/9/2002	3/9/2000	117,180
0633433	4.1	4.8	3.8	8/5/1999	10/25/1999	2/9/2002	3/9/2000	56,220
0633434	4.3	5	4	8/7/1999	10/25/1999	2/9/2002	3/9/2000	57,550
0633100	4.2	4.9	3.9	8/8/1999	10/25/1999	2/9/2002	3/17/2000	118,100
0633097	4.3	5	4	8/7/1999	3/8/2000	2/9/2002	3/30/2000	115,590
0633387	4.3	5	4	8/11/1999	10/25/1999	6/21/2002	7/17/2000	57,670
0633593	4.1	4.8	3.8	9/7/1999	11/12/1999	6/21/2002	7/19/2000	116,000
0633450	4.2	4.9	3.9	8/15/1999	10/25/1999	6/21/2002	9/12/2000	57,020
0631048	4.2	4.9	3.9	2/19/1999	10/25/1999	1/14/2002	9/20/2000	116,310
0629284	4.3	5	4	11/6/1998	10/26/1999	3/4/2001	4/5/1999	20400
0629640	4.3	5	4	11/7/1998	10/25/1999	10/21/2001	12/14/1999	48,575

13 Lots Observed in October 2000 Form FDA 483 for MMD[2]

Product	Fill	Observed Stability Failures
Mumpsvax	1187E	Failed potency at: - 9 months - 12 months - 18 months - 24 months - 30 months Also failed reconstitute and store potency at 24 months.
Mumpsvax	0616798	Failed potency at: - 12 months - 18 months - 24 months - 30 months
MMRII	0627847	Failed mumps potency at: - 6 months - 9 months - 12 months - 18 months - 24 months Also failed measles potency at 18 months. Also failed mumps and measles reconstitute and store potency at 24 months.
MMRII	0624918	Failed measles and mumps potency at: - 24 months Also failed measles and mumps reconstitute and store potency at 24 months.
MMRII	0628001	Failed mumps reconstitute and store potency at 24 months.
MMRII	0067H	Failed mumps reconstitute and store potency at 24 months.

[2] Referenced in MRK-KRA00783728.

Product	Fill	Observed Stability Failures
MMRII	1315B	Failed mumps potency at: - 6 months - 12 months - 17 months - 18 months - 24 months - 30 months
MMRII	1006D	Failed mumps potency at: - 18 months - 24 months - 30 months
MMRII	1348D	Failed mumps potency at: - 6 months - 12 months - 18 months - 24 months - 30 months
MMRII	0624E	Failed mumps potency at: - 24 months
MMRII	0621727	Failed mumps potency at: - 24 months - 30 months
MMRII	0621999	Failed mumps and measles potency at: - 24 months - 30 months
MMVax	0616340	Failed mumps potency at: - 9 months - 24 months - 30 months

Schedule 26

Number of Lots of MMRII Distributed Worldwide

Year	Number of M-M-R™II Doses Distributed* Worldwide[1]
1978	N/A**
1979	N/A**
1980	N/A**
1981	N/A**
1982	202,849
1983	7,167,421
1984	7,915,457
1985	6,852,436
1986	7,262,013
1987	8,357,023
1988	8,609,142
1989	11,905,755
1990	17,283,698
1991	20,014,958
1992	17,489,360
1993	23,420,124
1994	38,830,662
1995	29,644,626
1996	31,010,147
1997	27,925,314
1998	28,701,096
1999	27,204,285
2000	23,258,384
2001	21,748,565
2002	18,124,244
2003	22,176,934
2004	18,497,542
2005	4,977,271
TOTAL	**428,579,306**

**Yearly M-M-R™II dose distribution data not available prior to 1982.

[1] MRK-KRA00174588 at '591.

Schedule 27

Excerpts From Mumps Related MMWRs

DATE[1]	TITLE
1967-12-23	"A live attenuated mumps virus vaccine has recently become available for general use. . . . Live mumps vaccine may be considered for use in children approaching puberty, in adolescents, and in adults, especially males, if they have not had mumps."[2]
1968-11-09	"Live mumps vaccine may be used at any age from 12 months. . . . Since the Committee's initial statement on live, attenuated mumps vaccine in 1967, further experience with the vaccine has been accumulated. In view of evidence showing continued vaccine efficacy and safety, the Committee has modified its recommendation for limited vaccination of young children and now suggests that consideration be given to immunizing all susceptible children over 1 year of age. The Committee reaffirms its position, however, that mumps vaccination programs should not be allowed to take priority over essential ongoing health activities."[3]
1969-10-25	Same as above.[4]
1973-06-02	"Between March 2 and April 30, 1973, 121 cases of mumps (infectious parotitis) occurred among 899 children in the kindergarten through 3rd grades of an Orange County, New York, elementary school (Figure 1). . . . Vaccine efficacy was calculated to be 79%. . . . The reported vaccine efficacy of 79% is lower than the 90% or greater figured usually reported in epidemics of . . . mumps (3) after use of live virus vaccines. In this outbreak the number of children who developed mumps after vaccination is small, and any change in this number would produce relatively large changes in calculated vaccine efficacy. In particular, children developing mumps after killed mumps vaccine, which provides only temporary immunity, would lower the calculated vaccine efficacy if included in the 'vaccinated' group. Although these data suggest a lower vaccine efficacy for live mumps vaccine than that reported previously and than that achieved with other live virus vaccines, more information is needed in epidemic situations to confirm these differences."[5]
1974-12-14	"In 1973, a total of 69,087 cases of mumps were reported in the United States, 37% below the average reported for the 5-year period 1968-1972. The disease incidence, 32.8

[1] This is not intended to be an exhaustive list, nor a full description in detail.
[2] Centers for Disease Control and Prevention (formerly National Communicable Disease Center). *Immunization Practices – Mumps Vaccine.* MMWR 1967;16(51): 430-35.
[3] Centers for Disease Control and Prevention (formerly National Communicable Disease Center). *Recommendation of the Public Health Service Advisory Committee on Immunization Practices – Mumps Vaccine.* MMWR 1968;17(45): 419-23.
[4] Centers for Disease Control and Prevention (formerly National Communicable Disease Center). *Collected Recommendations of the Public Health Service Advisory Committee on Immunization Practices – Mumps Vaccine.* MMWR SUPPLEMENT 1969;18(43): 12-13.
[5] Center for Disease Control. *Epidemiologic Notes and Reports – Mumps in an Elementary School – New York.* MMWR 1973;22(22): 185-90.

DATE[1]	TITLE
	cases per 100,000 population, has reached the lowest point in the history of mumps surveillance."[6]
1977-12-02	"Mumps vaccination programs should not take priority over more essential ongoing community health activities; however, the large-scale production and use of combination live virus vaccines containing the measles, mumps, and rubella antigens have made mumps vaccination a practical component of routine immunization activities."[7]
1980-02-29	"Susceptible children, adolescents, and adults should be vaccinated against mumps, unless vaccination is contraindicated. Persons can be considered susceptible to mumps unless they have documentation of 1) physician-diagnosed mumps or laboratory evidence of immunity, or 2) adequate immunization with live mumps virus vaccine when 12 or more months of age. Persons born before 1957 are likely to have been infected naturally and generally may be considered immune."[8]
1983-10-28	"In 1982, 5,270 cases of mumps were reported to CDC, for an incidence rate of 2.3 cases per 100,000 population (Figure 1). This is 7% higher than the 1981 total of 4,941 cases, the lowest reported incidence since mumps became a nationally notifiable disease in 1968. The small increase in 1982 was principally due to increased mumps disease in Ohio, which does not require mumps vaccination for school attendance. Ohio had almost three times as many cases in 1982 (1,775 cases) as in 1981 (687). The number of reported cases in other states decreased 17.8% between 1981 and 1982."[9]
1984-07-27	"From October 19, through December 14, 1983, 63 cases of mumps were reported from six schools in a school district in Atlantic County, New Jersey."[10]
1984-09-28	"During the first 37 weeks of 1984, a provisional total of 2,112 mumps cases was reported to CDC; this is a 13.5% decline from the 2,443 cases reported during the same period in 1983. To date, two states and the District of Columbia have reported no mumps cases. In 1983, a total of 3,355 mumps cases was reported to CDC, for a reported incidence rate of 1.4 cases per 100,000 population (Table 1). This is 36% lower than the 1982 total of 5,270 cases and is the lowest reported incidence rate since mumps became a nationally

[6] Center for Disease Control. *Surveillance Summary – Mumps Surveillance 1973 – the United States.* MMWR 1974;23(50): 431-32.
[7] Center for Disease Control. *Recommendation of the Public Health Service Advisory Committee on Immunization Practices – Mumps Vaccine.* MMWR 1977;26(48): 393-94.
[8] Center for Disease Control. *Recommendation of the Immunization Practices Advisory Committee (ACIP) – Mumps Vaccine.* MMWR 1980;29(8): 87-93.
[9] Centers for Disease Control and Prevention. *Current Trends Mumps – United States, 1980-1983.* MMWR 1983;32(42): 545-7.
[10] Centers for Disease Control and Prevention. *Mumps Outbreak – New Jersey*. MMWR 1984;33(29): 421-2, 427-30.

DATE[1]	TITLE
	notifiable disease in 1968 (Figure 1). It represents a 98% decrease from 1968, the year after mumps vaccine licensure."[11]
1986-04-04	"For 1985, a provisional total of 2,886 mumps cases (1.2 cases/100,000 population) was reported in the United States . . . . Because the potential for outbreaks will continue in unvaccinated cohorts, considerable medical and economic savings can be realized by including immunization with MMR vaccine as part of compliance with state school-immunization laws. Current data indicate that vaccine-induced immunity persists for at least 19 years and will likely be lifelong. Appropriate administration of mumps vaccine to susceptible adolescents and young adults should be emphasized. In 1984, 305 (11.5%) persons of known age with mumps were 20 years of age or older. Older individuals are at higher risk for mumps complications. Although mumps is generally a self-limited disease, meningeal signs may appear in up to 15% of cases. Adult males are particularly at risk of orchitis, which occurs in up to 20% of clinical cases in postpubertal males . . . . MMR is the vaccine of choice for persons likely to be susceptible to measles and/or rubella, as well as to mumps."[12]
1987-03-20	"In 1985, 2,982 cases of mumps were reported in the United States, representing an annual incidence rate of 1.2 cases/100,000 population (Table 6). . . . Before the routine use of measles-mumps-rubella (MMR) vaccine in recent years, mumps immunization levels were considerably lower than measles or rubella immunization levels. This was partly because of the relatively high cost of mumps vaccine compared with the cost of either measles or rubella vaccines. In addition, mumps has never been given the same priority as measles or rubella in the public or medical community, despite the morbidity due to mumps and the fact that mumps virus was a leading cause of acquired deafness in the prevaccine era and the leading cause of viral encephalitis of known etiology in the United States until 1975 (1). Mumps vaccine was not recommended for routine use in all susceptible children until December 1977 (9). Nevertheless, mumps vaccine has been consistently shown to be highly cost-beneficial (10,11) and to be safe and effective, with reported clinical efficacy in the range of 75%-90% (2,12,13)."[13]

[11] Centers for Disease Control and Prevention. *Mumps – United States, 1983-1984.* MMWR 1984;33(38): 533-5.
[12] Centers for Disease Control and Prevention. *Current Trends Mumps – United States, 1984-1985.* MMWR 1986;35(13): 216-9.
[13] Centers for Disease Control and Prevention. *Epidemiologic Notes and Reports Mumps – United States, 1985-1986.* MMWR 1987;36(10): 151-5.

DATE[1]	TITLE
1987-08-07	"A total of 480 cases of mumps (epidemic parotitis) were reported among students attending 16 universities and colleges in three states where active surveillance was undertaken during the 1986-87 academic year."[14]
1988-09-09	"Between August 18 and December 25, 1987, 116 employees at three futures exchanges in Chicago developed clinically diagnosed mumps (Figure 1). Three cases subsequently occurred in household contacts of affected exchange employees. Twenty-one persons developed complications; nine were hospitalized."[15]
1989-01-13	"To improve immunity levels in high-risk children less than 15 months of age, the ACIP recommends that a routine two-dose vaccination schedule for preschoolers be implemented in areas with recurrent measles transmission (i.e., counties with more than five reported cases among preschool-aged children during each of the last 5 years)."[16]
1989-02-24	"After the introduction of live mumps virus vaccine in 1967 and the recommendation for its routine use in 1977, the incidence rate of reported mumps cases in the United States decreased steadily. In 1985, a record low of 2982 cases occurred, representing a 98.0% decline from the 152,000 cases reported in 1968 (Figure 1). However, from 1985 to 1987, mumps increased; 7790 and 12,848 cases were reported in 1986 and 1987, respectively. During this time, the annual reported incidence rate rose almost fivefold, from 1.1 cases/100,000 population to 5.2 cases/100,000 population (Table 1). However, in 1988, a provisional total of 4730 cases was reported, representing a 63.2% decrease from 1987. In 1987, of the 48 areas (47 states plus the District of Columbia) that routinely reported mumps cases, at least one mumps case was reported from all but three (Delaware, Rhode Island, and Wyoming) of the reporting areas. Similarly, in 1988, all except Maine, North Dakota, and Rhode Island have provisionally reported mumps cases. In 1985, seven states (Illinois, Tennessee, Michigan, Wisconsin, Indiana, Louisiana, and Minnesota) reported more than 500 cases each (case range: 810-2737, incidence range: 18.1-37.7 cases/100,000 population). In addition, in 1985, 680 (22.8%) of the 2982 counties in the 48 reporting areas reported at least one case, compared with 889 (28.3%) of 3138 in 1987. During 1987, 31 (64.6%) of the 48 reporting areas noted more mumps cases than in 1986. . . .

[14] Centers for Disease Control and Prevention. *Mumps Outbreaks on University Campuses – Illinois, Wisconsin, South Dakota*. MMWR 1987;36(30): 496-8, 503-5.
[15] Centers for Disease Control and Prevention. *Epidemiologic Notes and Reports Mumps in the Workplace – Chicago.* MMWR 1988;37(35): 533-8.
[16] Centers for Disease Control and Prevention. *Recommendations of the Immunization Practices Advisory Committee Measles Prevention: Supplementary Statement.* MMWR 1989;38(1): 11-14.

DATE[1]	TITLE
	Ensuring immunity for adolescents and young adults is especially important, given the recent shift in risk of disease to these age groups. . . . The evidence that the shift in risk to older persons through 1987 is limited to states without comprehensive mumps immunization school laws provides further evidence that the relative resurgence of mumps in the United States is not due to vaccine failure but to a failure to vaccinate. . . . The adoption and enforcement of universal comprehensive vaccination requirements for school attendance are likely to reduce mumps incidence substantially. . . . More aggressive outbreak control, including exclusion of susceptibles from school, is also helpful in eliminating transmission in mumps epidemics."[17]
1989-06-09	"Susceptible children, adolescents, and adults should be vaccinated against mumps, unless vaccination is contraindicated. Mumps vaccine is of particular value for children approaching puberty and for adolescents and adults who have not had mumps. MMR vaccine is the vaccine of choice for routine administration and should be used in all situations where recipients are also likely to be susceptible to measles and/or rubella. The favorable benefit-cost ratio for routine mumps immunization is more marked when vaccine is administered as MMR (17). Persons should be considered susceptible to mumps unless they have documentation of 1) physician-diagnosed mumps, 2) adequate immunization with live mumps virus vaccine on or after their first birthday, or 3) laboratory evidence of immunity. Because live mumps vaccine was not used routinely before 1977 and because the peak age-specific incidence was in 5-9-year-olds before the vaccine was introduced, most persons born before 1957 are likely to have been infected naturally between 1957 and 1977. Therefore, they generally may be considered to be immune, even if they may not have had clinically recognizable mumps disease. However, this cutoff date for susceptibility is arbitrary. Although outbreak-control efforts should be focused on persons born after 1956, these recommendations do not preclude vaccination of possibly susceptible persons born before 1957 who may be exposed in outbreak settings."[18]
1995-08-11	"Except for a minimal increase in 1989, the incidence of mumps continued to decline during 1988-1993, from 2.0 per 100,000 population in 1988 to 0.7 per 100,000 population in 1993 (Figure 1). Only 1,692 mumps cases were reported for 1993; this

[17] Centers for Disease Control and Prevention. *Current Trends Mumps – United States, 1985-1988.* MMWR 1989;38(7): 101-5.

[18] Centers for Disease Control and Prevention. *Recommendations of the Immunization Practices Advisory Committee Mumps Prevention.* MMWR 1989;38(22): 388-92, 397-400.

DATE[1]	TITLE
	was the lowest number ever reported to NNDSS and a 99% reduction from the 152,209 cases reported for 1968."[19]
1998-05-22	"The principal strategy to prevent mumps is to achieve and maintain high immunization levels by routinely vaccinating all children with two doses of MMR. . . . Two doses of MMR vaccine separated by at least 1 month (i.e., a minimum of 28 days) and administered on or after the first birthday are recommended for all children and for certain high-risk groups of adolescents and adults. . . . MMR is the vaccine of choice when protection against any of these three diseases is required on or after the first birthday, unless any of its component vaccines is contraindicated. . . . Mumps can occur in highly vaccinated populations; in these outbreaks, substantial numbers of cases have occurred among persons who had previously received a single dose of mumps-containing vaccine (33, 81). . . . Transmission of mumps has occurred in medical settings (122). Therefore, immunity to mumps is highly desirable for all health-care workers (Table 1). Adequate mumps vaccination for health-care workers born during or after 1957 consists of one dose of live mumps-containing vaccine."[20]
2005-12-02	"On September 6, 2005, the Food and Drug Administration licensed a combined live attenuated measles, mumps, rubella, and varicella (MMRV) vaccine (ProQuad®, Merck & Co., Inc., Whitehouse Station, New Jersey) for use in children aged 12 months--12 years. The attenuated measles, mumps, and rubella vaccine viruses in ProQuad are identical and of equal titer to those in the measles, mumps, and rubella (MMR) vaccine, MMRII® (Merck). . . . Advisory Committee on Immunization Practices (ACIP) current recommendations are that children aged 12 months--12 years receive 2 doses of MMR vaccine at least 1 month apart and 1 dose of varicella vaccine (1). MMRV vaccine can decrease the number of injections received by children when all of the component antigens are indicated for administration. One dose of MMRV vaccine should be administered on or after the first birthday, preferably as soon as the child becomes eligible for vaccination (2). . . . MMRV vaccine is indicated for simultaneous vaccination against measles, mumps, rubella, and varicella among children aged 12 months--12 years; MMRV is not indicated for persons outside of this age group. Use of licensed combination vaccines, such as MMRV vaccine, is preferred over separate injection of equivalent component vaccines (6)."[21]

[19] Centers for Disease Control and Prevention. *Mumps Surveillance – United States, 1988-1993*. MMWR 1995;44(SS-3): 1-14.
[20] Centers for Disease Control and Prevention. *Measles, Mumps, and Rubella -- Vaccine Use and Strategies for Elimination of Measles, Rubella, and Congenital Rubella Syndrome and Control of Mumps: Recommendations of the Advisory Committee on Immunization Practices (ACIP)*. MMWR 1998;47(RR-8): 1-57.
[21] Centers for Disease Control and Prevention. *Notice to Readers: Licensure of a Combined Live Attenuated Measles, Mumps, Rubella, and Varicella Vaccine*. MMWR 2005;54(47): 1212-1214.

DATE[1]	TITLE
2006-02-24	"During 2004--2005, the United Kingdom (UK) experienced a nationwide epidemic of mumps, which peaked during 2005 when 56,390 notified cases were reported in England and Wales. The majority of confirmed cases during 2004--2005 were in persons aged 15--24 years, most of whom had not been eligible for routine mumps vaccination. . . . The UK epidemic illustrates the susceptibility of certain cohorts who have not been vaccinated and have not developed immunity through exposure to mumps because of a decrease in mumps circulation after implementation of a childhood immunization program. The epidemic also underscores the importance of ensuring high levels of mumps immunity among adolescents and young adults when vaccination with mumps-containing vaccine is introduced into the routine immunization schedule for children."[22]
2006-02-24	"On July 26, 2005, the Sullivan County Health Department (SCHD) and the New York State Department of Health (NYSDOH) were notified of a cluster of cases of parotitis among campers and staff members at a summer camp. An investigation conducted by NYSDOH identified 31 cases of mumps, likely introduced by a camp counselor who had traveled from the United Kingdom (UK) and had not been vaccinated for mumps. . . . The outbreak described in this report likely resulted from a combination of delay in diagnosis of mumps and failure to report the cluster of illnesses in a timely manner, in addition to close contact and social mixing among camp participants. Controlling the outbreak resulted in a substantial burden on the camp and its staff, including cancellation of activities and likely loss of revenue. Previous mumps outbreaks also have carried substantial burden, particularly with respect to costs associated with school absenteeism (9). To prevent large outbreaks of mumps in their communities, U.S. health-care providers should suspect mumps independent of vaccination history, diagnose mumps by using laboratory testing, and report mumps immediately to local health authorities."[23]
2006-04-07	"In the United States, since 2001, an average of 265 mumps cases (range: 231--293 cases) have been reported each year, and in Iowa, an average of five cases have been reported annually since 1996. However, in 2006, by March 28, a total of 219 mumps cases had been reported in Iowa (Figure 1), and an additional 14 persons with clinically compatible symptoms were being investigated in three neighboring states (11 in Illinois, two in Nebraska, and one in Minnesota) in what has become the largest epidemic of mumps in the United States since 1988 (1). . . . Despite control efforts and a highly vaccinated population, this epidemic has spread across Iowa and potentially to neighboring states. Ongoing investigations will focus on identifying actual vaccine

[22] Centers for Disease Control and Prevention. *Mumps Epidemic – United Kingdom, 2004-2005*. MMWR 2006;55(7): 173-5.
[23] Centers for Disease Control and Prevention. *Mumps Outbreak at a Summer Camp – New York, 2005*. MMWR 2006;55(7): 175-7.

DATE[1]	TITLE
	coverage on college campuses, potential modes of mumps transmission, and the effectiveness of 1 or 2 doses of MMR."[24]
2006-04-14	"The state of Iowa has been experiencing a large mumps outbreak that began in December 2005 (1). As of April 10, 2006, a total of 515 possible mumps cases have been reported to the Iowa Department of Public Health (IDPH) during 2006 (2). This outbreak has spread across Iowa, and mumps activity, possibly linked to the Iowa outbreak, is under investigation in six neighboring states, including Illinois (n = four), Kansas (n = 33), Minnesota (n = one), Missouri (n = four), Nebraska (n = 43), and Wisconsin (n = four) (CDC, unpublished data, April 10, 2006). The reasons for this outbreak are under investigation."[25]
2006-05-26	"CDC and state and local health departments continue to investigate an outbreak of mumps that began in Iowa in December 2005 (1) and involved at least 10 additional states as of May 2, 2006."[26]
2006-06-09	"Evidence of immunity through documentation of adequate vaccination is now defined as 1 dose of a live mumps virus vaccine for preschool-aged children and adults not at high risk and 2 doses for school-aged children (i.e., grades K--12) and for adults at high risk (i.e., health-care workers, international travelers, and students at post--high school educational institutions). . . . Adequate mumps vaccination for health-care workers born during or after 1957 consists of 2 doses of a live mumps virus vaccine. Health-care workers with no history of mumps vaccination and no other evidence of immunity should receive 2 doses (at a minimum interval of 28 days between doses). Health-care workers who have received only 1 dose previously should receive a second dose. Because birth before 1957 is only presumptive evidence of immunity, health-care facilities should consider recommending 1 dose of a live mumps virus vaccine for unvaccinated workers born before 1957 who do not have a history of physician-diagnosed mumps or laboratory evidence of mumps immunity. . . . Depending on the epidemiology of the outbreak (e.g., the age groups and/or institutions involved), a second dose of mumps vaccine should be considered for children aged 1--4 years and adults who have received 1 dose. . . . During an outbreak, health-care facilities should strongly consider recommending 2 doses of a live mumps virus vaccine to

[24] Centers for Disease Control and Prevention. *Mumps Epidemic – Iowa, 2006.* MMWR 2006;55(13): 366-8.
[25] Centers for Disease Control and Prevention. *Exposure to Mumps During Air Travel – United States, April 2006.* MMWR 2006;55(14): 401-2.
[26] Centers for Disease Control and Prevention. *Update: Multistate Outbreak of Mumps – United States, January 1 – May 2, 2006.* MMWR 2006;55(20): 559-63.

DATE[1]	TITLE
	unvaccinated workers born before 1957 who do not have evidence of mumps immunity."[27]
2006-10-27	"During January 1--October 7, 2006, a total of 45 states and the District of Columbia reported 5,783 confirmed or probable mumps cases to CDC. . . . In response to this nationwide mumps outbreak, ACIP recommendations for prevention and control of mumps were updated (4). Evidence of immunity through documentation of vaccination is now defined as 1 dose of live mumps vaccine for preschool-aged children and adults not at high risk for exposure and infection and 2 doses of live mumps vaccine for school-aged children (i.e., grades kindergarten--12) and adults at high risk for exposure and infection (i.e., health-care workers, international travelers, and students at post--high-school education institutions). Additional recommendations for outbreak control include administering a second dose of MMR for preschool children and adults not at high risk for exposure and infection if these persons are part of a group that is experiencing an outbreak (4). To ensure high levels of immunity, especially among groups at high risk for exposure and infection, every opportunity should be used to provide the first or second dose of MMR vaccine to those without adequate evidence of immunity (e.g., documentation of vaccination)."[28]
2008-03-14	"These updated recommendations remove ACIP's previous preference for administering combination MMRV vaccine over separate injections of equivalent component vaccines (i.e., measles, mumps, and rubella [MMR] vaccine and varicella vaccine). . . . In MMRV vaccine prelicensure studies, an increased rate of fever was observed 5--12 and 0--42 days after the first vaccine dose, compared with administration of MMR vaccine and varicella vaccine at the same visit (3,4). Because of the known association between fever and febrile seizures (5), CDC and Merck initiated postlicensure studies to better understand the risk for febrile seizures that might be associated with MMRV vaccination. . . . The preliminary results indicated a rate of febrile seizure of nine per 10,000 vaccinations among MMRV vaccine recipients compared with four per 10,000 vaccinations among MMR vaccine and varicella vaccine recipients (adjusted odds ratio = 2.3; 95% confidence interval [CI] = 1.6--3.2; $p<0.0001$). These results suggest that, in the 7--10 day postvaccination period, approximately one additional febrile seizure would occur among every 2,000 children vaccinated with MMRV vaccine, compared with children vaccinated with MMR vaccine and varicella vaccine administered at the same visit. Of the 166 children who experienced febrile seizures after vaccination and had hospitalization information available, 26 (16%) were hospitalized. No child who had a

[27] Centers for Disease Control and Prevention. *Notice to Readers: Updated Recommendations of the Advisory Committee on Immunization Practices (ACIP) for the Control and Elimination of Mumps.* MMWR 2006;55(22): 629-30.
[28] Centers for Disease Control and Prevention. *Brief Report: Update: Mumps Activity – United States, January 1-October 7, 2006.* MMWR 2006;55(42): 1152-153.

DATE[1]	TITLE
	febrile seizure died. . . . Given the availability of alternative options for vaccination against measles, mumps, rubella, and varicella and the limited supply of MMRV vaccine, ACIP voted to change the preference language for MMRV vaccine to read as follows: 'Combination MMRV vaccine is approved for use among healthy children aged 12 months--12 years. MMRV vaccine is indicated for simultaneous vaccination against measles, mumps, rubella, and varicella. ACIP does not express a preference for use of MMRV vaccine over separate injections of equivalent component vaccines (i.e., MMR vaccine and varicella vaccine).'"[29]
2008-10-10	"CDC, AAP, and HICPAC now recommend a 5-day period after onset of parotitis for 1) isolation of persons with mumps in either community or health-care settings and 2) use of standard precautions and droplet precautions. Postexposure recommendations remain unchanged. HCP with no evidence of mumps immunity who are exposed to patients with mumps should be excluded from duty from the 12th day after first exposure through the 26th day after last exposure."[30]
2009-11-20	"In August 2009, CDC was notified of the onset of an outbreak of mumps in a summer camp in Sullivan County, New York. The outbreak has spread and gradually increased in size and is now the largest U.S. mumps outbreak since 2006, when the United States experienced a resurgence of mumps with 6,584 reported cases (2)."[31]
2010-02-12	"State and local health departments, in collaboration with CDC, continue to investigate a mumps outbreak that began in New York in June 2009 (1). . . . The 1,521 outbreak-related mumps cases have been reported from several counties in New York and New Jersey; local transmission is continuing (Figure). . . . Although several factors play a role in mumps control in the United States (Box), maintenance of high 2-dose MMR vaccine coverage remains the most effective way to prevent and limit the size of mumps outbreaks."[32]
2010-05-07	"ACIP adopted new recommendations regarding use of MMRV vaccine for the first and second doses and identified a personal or family (i.e., sibling or parent) history of seizure as a precaution for use of MMRV vaccine. For the first dose of measles, mumps, rubella, and varicella vaccines at age 12–47 months, either MMR vaccine and varicella

[29] Centers for Disease Control and Prevention. *Update: Recommendations from the Advisory Committee on Immunization Practices (ACIP) Regarding Administration of Combination MMRV Vaccine.* MMWR 2008;57(10): 258-60

[30] Centers for Disease Control and Prevention. *Updated Recommendations for Isolation of Persons with Mumps.* MMWR 2008;57(40): 1103-05.

[31] Centers for Disease Control and Prevention. *Mumps Outbreak – New York, New Jersey, Quebec, 2009.* MMWR 2009;58(45): 1270-74.

[32] Centers for Disease Control and Prevention. *Update: Mumps Outbreak – New York and New Jersey, June 2009-January 2010.* MMWR 2010;59(5): 125-50.

DATE[1]	TITLE
	vaccine or MMRV vaccine may be used. Providers who are considering administering MMRV vaccine should discuss the benefits and risks of both vaccination options with the parents or caregivers. Unless the parent or caregiver expresses a preference for MMRV vaccine, CDC recommends that MMR vaccine and varicella vaccine should be administered for the first dose in this age group. For the second dose of measles, mumps, rubella, and varicella vaccines at any age (15 months–12 years) and for the first dose at age ≥48 months, use of MMRV vaccine generally is preferred over separate injections of its equivalent component vaccines (i.e., MMR vaccine and varicella vaccine)."[33]
2012-12-07	"On September 29, 2011, the California Department of Public Health (CDPH) confirmed by polymerase chain reaction (PCR) three cases of mumps among students recently evaluated at their university's student health services with symptoms suggestive of mumps. An investigation by CDPH, student health services, and the local health department identified 29 mumps cases. . . . This outbreak demonstrates the potential value of requiring MMR vaccination (including documentation of immunization or other evidence of immunity) before college enrollment, heightened clinical awareness, and timely reporting of suspected mumps patients to public health authorities. . . . CDC has evaluated use of a third dose of MMR vaccine for mumps outbreak control during two previous mumps outbreaks in which transmission was sustained, despite high 2-dose coverage (9,10). During both outbreaks, targeted vaccination was followed by a decrease in mumps incidence among the target group. Available data are insufficient to recommend for or against the use of a third dose of MMR vaccine for mumps outbreak control. Because control measures for mumps are limited, the ability to offer a third dose of MMR vaccine might be a tool that could be used in an attempt to limit the extent of mumps outbreaks, particularly in high-risk settings."[34]
2013-06-14	"At the October 24, 2012 meeting, ACIP adopted the following revisions, which are published here for the first time. These included: • For acceptable evidence of immunity, removing documentation of physician diagnosed disease as an acceptable criterion for evidence of immunity for measles and mumps, and including laboratory confirmation of disease as a criterion for acceptable evidence of immunity for measles, rubella, and mumps. . . . Data are insufficient to recommend for or against the use of a third dose of MMR

[33] Centers for Disease Control and Prevention. *Use of Combination Measles, Mumps, Rubella, and Varicella Vaccine – Recommendations of the Advisory Committee on Immunization Practices (ACIP).* MMWR 2010;59(RR-3): 1-12.
[34] Centers for Disease Control and Prevention. *Mumps Outbreak on a University Campus – California 2011.* MMWR 2012;61(48): 986-89.

DATE[1]	TITLE
	vaccine for mumps outbreak control. CDC has issued guidance for consideration for use of a third dose in specifically identified target populations along with criteria for public health departments to consider for decision making . . . . Persons who have written documentation of adequate vaccination for mumps at age ≥12 months, laboratory evidence of mumps immunity, laboratory confirmation of disease, or were born before 1957 have acceptable presumptive evidence of mumps immunity (Table 3)."[35]
2016-07-29	"On May 1, 2015, the Illinois Department of Public Health (IDPH) confirmed a mumps outbreak at the University of Illinois at Urbana-Champaign. IDPH and the Champaign-Urbana Public Health District (C-UPHD) conducted an investigation and identified 317 cases of mumps during April 2015–May 2016. . . . Because outbreaks occur despite high 2-dose coverage, a third dose has been provided as a control measure to targeted populations during previous outbreaks (4,5,7). . . . Currently there is no formal recommendation for a third dose of MMR vaccine during mumps outbreaks; the decision to implement this intervention needs to be carefully considered. In light of the recent increased incidence of mumps, CDC is gathering additional data to assess use of a third dose of vaccine to inform decision-making during outbreak responses and potential changes in the recommendations. Although evidence of its effectiveness is needed, a third dose of MMR vaccine may be considered as a control measure during mumps outbreaks occurring in settings in which persons are in close contact with one another, when transmission is sustained despite high 2-dose MMR coverage, and when traditional control measures fail to slow transmission. . . . Further evaluation is needed to determine if the reduction was a result of the recommendation for a third MMR dose."[36]
2017-04-14	"During July 2015–May 2016, a mumps outbreak occurred at the University of Iowa, which is located in Johnson County (1). A total of 301 cases of mumps were diagnosed among students."[37]
2017-12-01	"On February 8, 2017, a suspected case of mumps in a member of a fraternity or sorority at the University of Washington, Seattle campus (UW) was reported to Public Health—Seattle & King County (PHSKC). Additional confirmed and probable mumps cases were subsequently identified among UW students and staff members according to the

[35] Centers for Disease Control and Prevention. *Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, 2013: Summary Recommendations of the Advisory Committee on Immunization Practices (ACIP).* MMWR 2013;62(RR04): 1-34.
[36] Centers for Disease Control and Prevention. *Mumps Outbreak at a University and Recommendation for a Third Dose of Measles-Mumps-Rubella Vaccine – Illinois, 2015-2016.* MMWR 2016;65(29): 731-4.
[37] Centers for Disease Control and Prevention. *Complications of Mumps During a University Outbreak Among Students Who Had Received 2 Doses of Measles-Mumps-Rubella Vaccine – Iowa, July 2015 – May 2016.* MMWR 2017;66(14): 390-91.

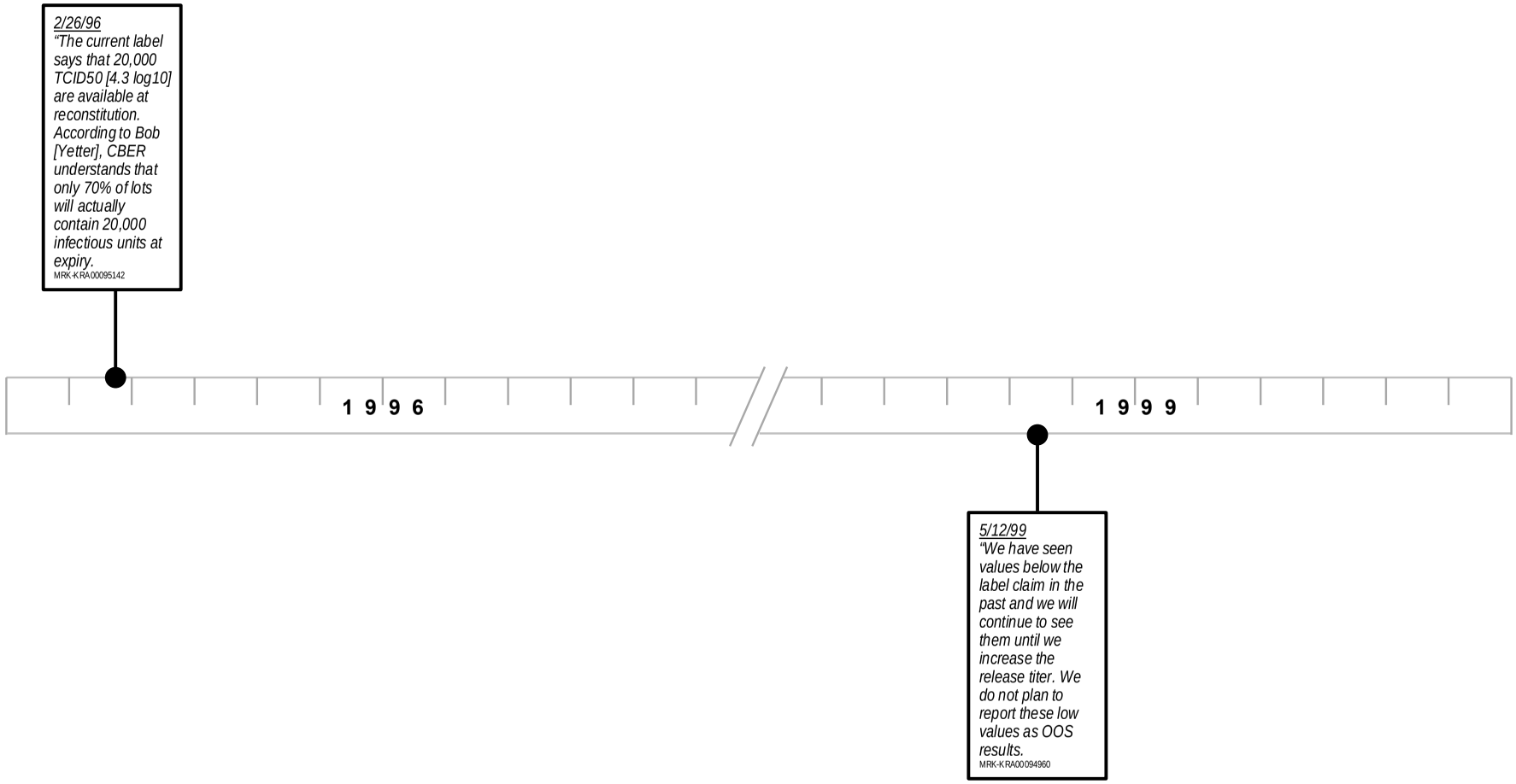
DATE[1]	TITLE
	national case definition. By July 19, 2017, a total of 42 (16 confirmed and 26 probable) mumps cases were reported among UW students and associated community members, with symptom onset February 6–June 4 (Figure)."[38]
2018-01-12	"A substantial increase in the number of mumps outbreaks and outbreak-associated cases has occurred in the United States since late 2015 (1,2). To address this public health problem, the Advisory Committee on Immunization Practices (ACIP) reviewed the available evidence and determined that a third dose of measles, mumps, rubella (MMR) vaccine is safe and effective at preventing mumps. During its October 2017 meeting, ACIP recommended a third dose of a mumps virus-containing vaccine for persons previously vaccinated with 2 doses who are identified by public health authorities as being part of a group or population at increased risk for acquiring mumps because of an outbreak. The purpose of the recommendation is to improve protection of persons in outbreak settings against mumps disease and mumps-related complications. This recommendation supplements the existing ACIP recommendations for mumps vaccination (3). . . . Recommendation Persons previously vaccinated with 2 doses of a mumps virus-containing vaccine who are identified by public health authorities as being part of a group or population at increased risk for acquiring mumps because of an outbreak should receive a third dose of a mumps virus-containing vaccine to improve protection against mumps disease and related complications."[39]

[38] Centers for Disease Control and Prevention. *Absence of Asymptomatic Mumps Virus Shedding Among Vaccinated College Students During a Mumps Outbreak – Washington, February – June 2017.* MMWR 2017;66(47): 1307-08.
[39] Centers for Disease Control and Prevention. *Recommendation of the Advisory Committee on Immunization Practices for Use of a Third Dose of Mumps Virus-Containing Vaccine in Persons at Increased Risk for Mumps During an Outbreak.* MMWR 2018;67(1): 33-8.

Schedule 28

Potency Statement Timeline

Potency Statement Timeline



Appx1460

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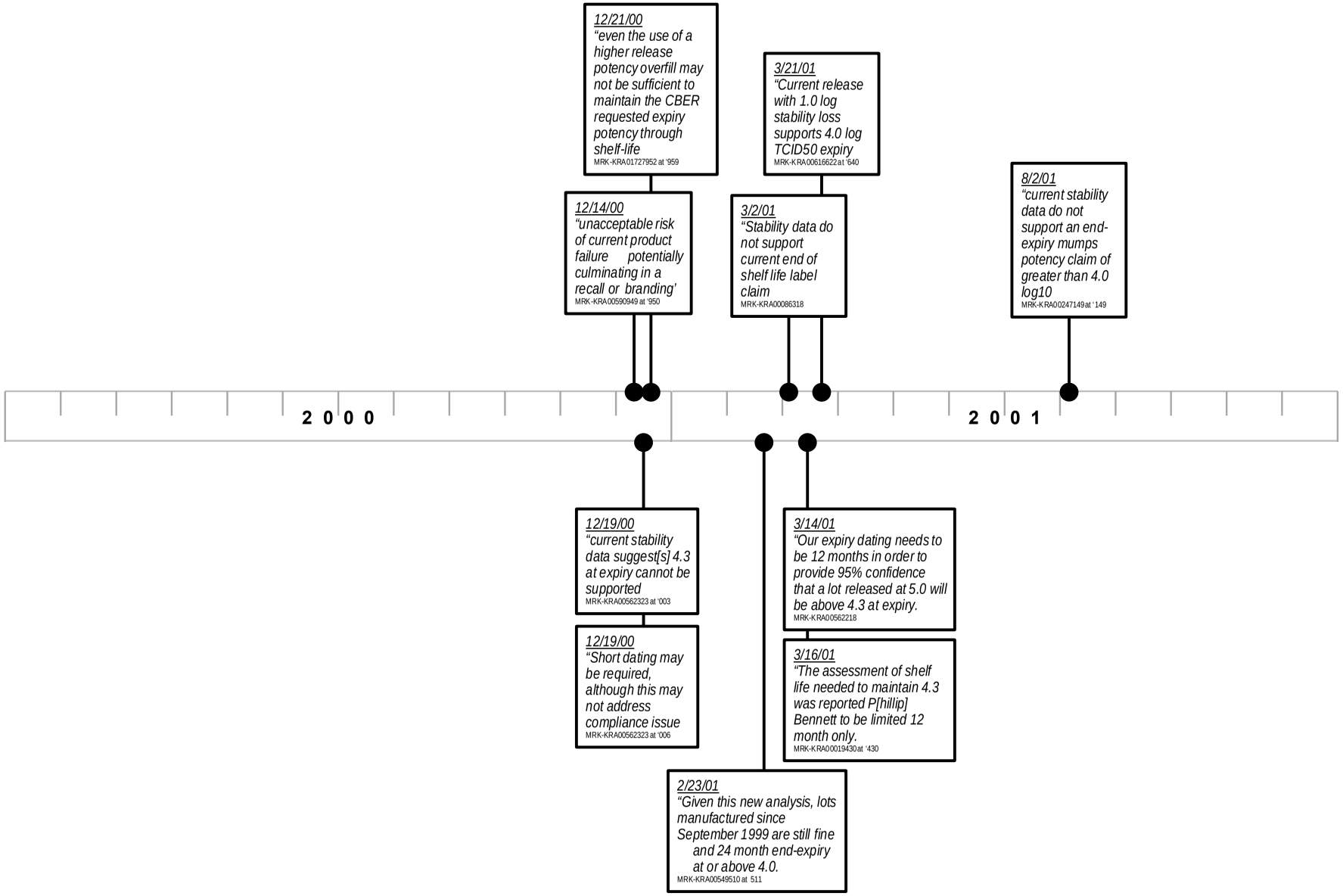
This is not intended to be an exhaustive timeline, nor a full description in detail.

Potency Statement Timeline



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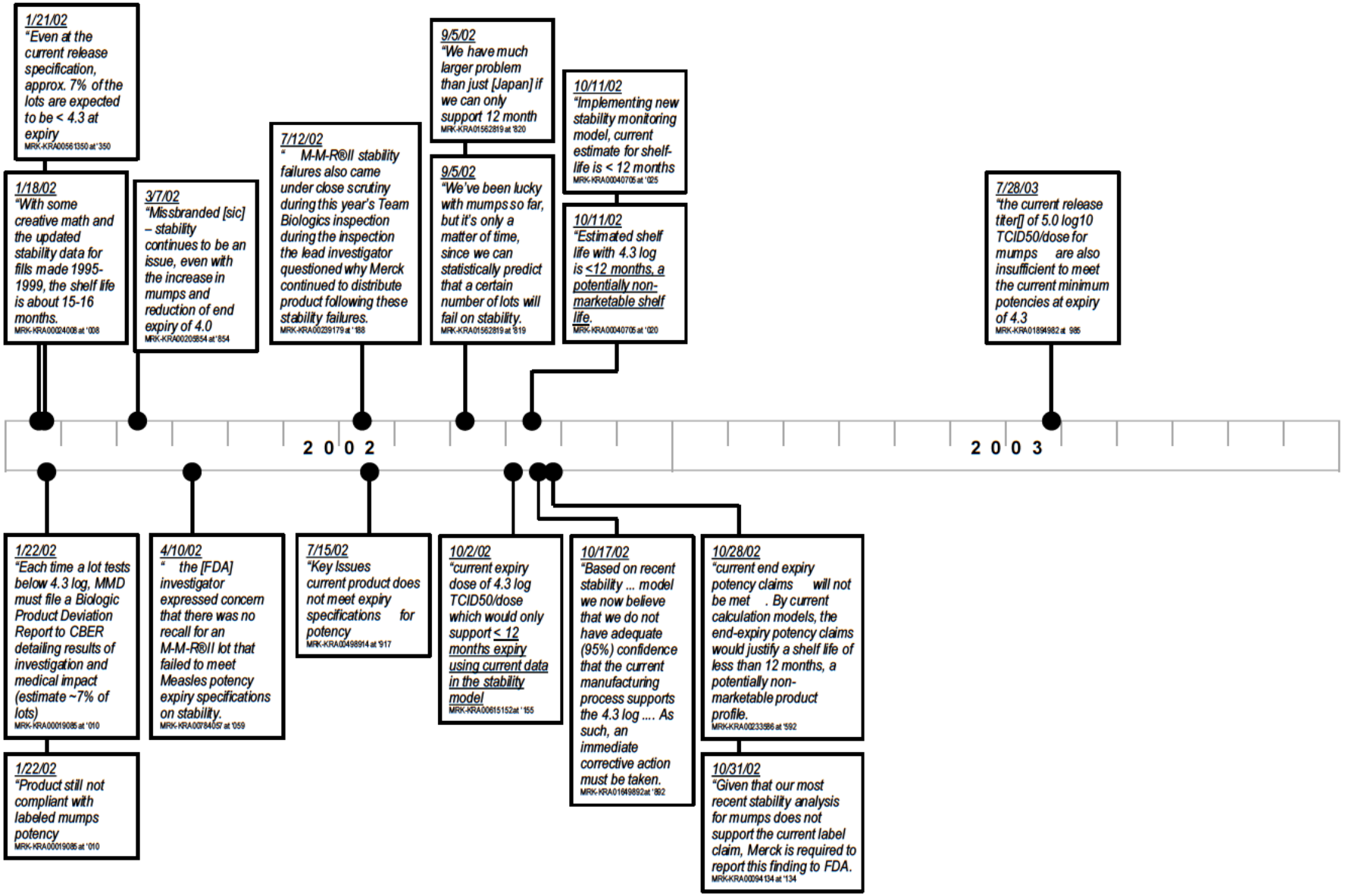
Potency Statement Timeline



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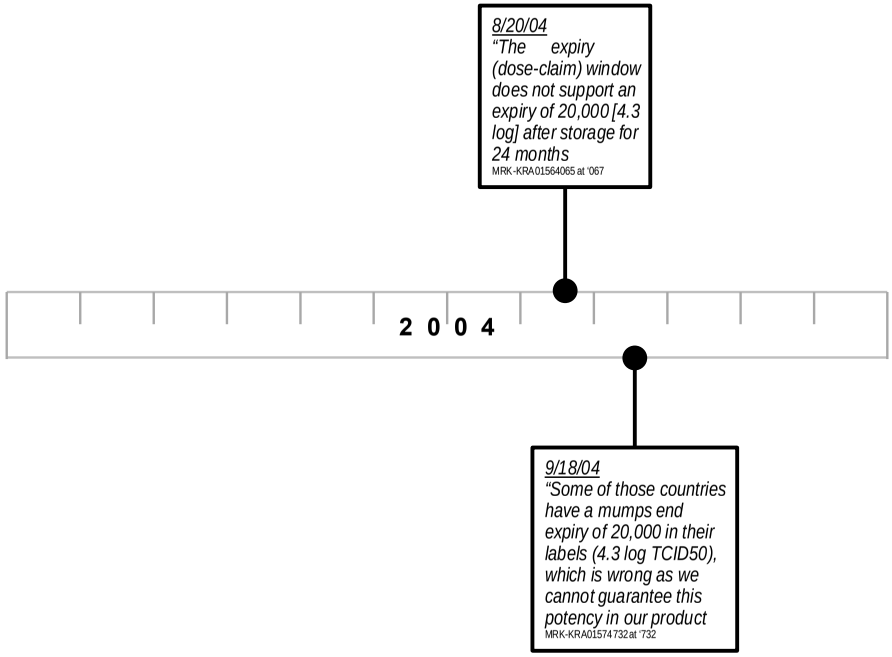
Potency Statement Timeline



Appx1463

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Schedule 29

Vaccine Courts

Program/Process/Law	Description[1, 2]
The National Vaccine Injury Compensation Program	The National Vaccine Injury Compensation Program ("Vaccine Program") was established on October 1, 1988 under the National Childhood Vaccine Injury Act as a no-fault system for resolving vaccine injury petitions. Under the Vaccine Program, petitions for monetary compensation may be brought by or on behalf of persons allegedly suffering injury or death as a result of the administration of certain compulsory childhood vaccines. Congress intended that the Vaccine Program provide individuals a swift, flexible, and less adversarial alternative to the often costly and lengthy civil arena of traditional tort litigation. All vaccine claims are managed and adjudicated by the congressionally created Office of Special Masters, which consists of eight special masters who are appointed to serve for four year terms. The Office of Special Masters is established within the U.S. Court of Federal Claims which appoints and removes the special masters and to which the special masters' decisions are appealed. Throughout the entire process, the special master makes every effort to balance Congress's vision of streamlined proceedings with parties' rights to a fair opportunity to present their cases. Any individual, of any age, who received a covered vaccine, and believes he or she was injured as a result, can file a petition. Parents, legal guardians, and legal representatives can file on behalf of children, disabled adults, and individuals who are deceased.
NVP Process	• An individual files a petition with the U.S. Court of Federal Claims. • The U.S. Department of Health and Human Services' medical staff reviews the petition, determines if it meets the medical criteria for compensation, and makes a preliminary recommendation.

[1] This is not intended to be exhaustive, nor a full description in detail.

[2] General Sources:

National Vaccine Injury Compensation Program, Pub. L. No. 99-660, 100 Stat. 3755 (1986) (codified as amended at 42 U.S.C. §§ 300aa-1 to -34).

https://www.hrsa.gov/vaccine-compensation/index.html.

Appendix B, Vaccine Rules of the United States Court of Federal Claims (available at https://www.uscfc.uscourts.gov/sites/default/files/170801VaccineRules.pdf).

https://www.uscfc.uscourts.gov/vaccine-programoffice-special-masters.

"What You Need to Know About the National Vaccine Injury Compensation Program (VICP)," Health Resources and Services Administration, September 2016 (available at https://www.hrsa.gov/sites/default/files/vaccinecompensation/resources/84521booklet.pdf).

https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/about/title-xxi-phs-vaccines-1517.pdf.

http://www.nvic.org/injury-compensation/origihanlaw.aspx.

Program/Process/Law	Description[1, 2]
	• The U.S. Department of Justice develops a report that includes the medical recommendation and legal analysis and submits it to the Court. • The report is presented to a court-appointed special master, who decides whether the petitioner should be compensated, often after holding a hearing in which both parties can present evidence. If compensation is awarded, the special master determines the amount and type of compensation.
Compensation	The Court orders the U.S. Department of Health and Human Services to award damages to compensate victims for their injuries. Even if the petition is dismissed, if certain requirements are met, the Court may order the Department to pay attorneys' fees and costs. Compensation awarded under the Vaccine Program for a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988 shall include the following:[3] (1) (A) Actual unreimbursable expenses incurred from the date of the judgment awarding such expenses and reasonable projected unreimbursable expenses which— (i) result from the vaccine-related injury for which the petitioner seeks compensation, (ii) have been or will be incurred by or on behalf of the person who suffered such injury, and (iii) (I) have been or will be for diagnosis and medical or other remedial care determined to be reasonably necessary, or (II) have been or will be for rehabilitation, developmental evaluation, special education, vocational training and placement, case management services, counseling, emotional or behavioral therapy, residential and custodial care and service expenses, special equipment, related travel expenses, and facilities determined to be reasonably necessary. (B) Subject to section 2116(a)(2) [42 USCS § 300aa-16(a)(2)], actual unreimbursable expenses incurred before the date of the judgment awarding such expenses which—

[3] 42 USCS § 300aa–15, Compensation.

Program/Process/Law	Description[1, 2]
	(i) resulted from the vaccine-related injury for which the petitioner seeks compensation, (ii) were incurred by or on behalf of the person who suffered such injury, and (iii) were for diagnosis, medical or other remedial care, rehabilitation, developmental evaluation, special education, vocational training and placement, case management services, counseling, emotional or behavioral therapy, residential and custodial care and service expenses, special equipment, related travel expenses, and facilities determined to be reasonably necessary. (2) In the event of a vaccine-related death, an award of $250,000 for the estate of the deceased. (3) (A) In the case of any person who has sustained a vaccine-related injury after attaining the age of 18 and whose earning capacity is or has been impaired by reason of such person's vaccine-related injury for which compensation is to be awarded, compensation for actual and anticipated loss of earnings determined in accordance with generally recognized actuarial principles and projections. (B) In the case of any person who has sustained a vaccine-related injury before attaining the age of 18 and whose earning capacity is or has been impaired by reason of such person's vaccine-related injury for which compensation is to be awarded and whose vaccine-related injury is of sufficient severity to permit reasonable anticipation that such person is likely to suffer impaired earning capacity at age 18 and beyond, compensation after attaining the age of 18 for loss of earnings determined on the basis of the average gross weekly earnings of workers in the private, non-farm sector, less appropriate taxes and the average cost of a health insurance policy, as determined by the Secretary. (4) For actual and projected pain and suffering and emotional distress from the vaccine-related injury, an award not to exceed $250,000.
Punitive Damages[4]	Punitive damages are allowed under the Vaccine Program in cases in which the manufacturer engaged in—

[4] 42 USCS § 300aa–23, Trial.

Program/Process/Law	Description[1, 2]
	(A) fraud or intentional and wrongful withholding of information from the Secretary during any phase of a proceeding for approval of the vaccine under section 351 [42 USCS § 262], (B) intentional and wrongful withholding of information relating to the safety or efficacy of the vaccine after its approval, or (C) other criminal or illegal activity relating to the safety and effectiveness of vaccines, which activity related to the vaccine-related injury or death for which the civil action was brought.
Civil Court	A vaccine manufacturer may be subject to suit in civil court where the manufacturer engaged in fraud or misrepresentation relating to its vaccine. Under the Vaccine Program:[5] (1) **No vaccine manufacturer shall be liable in a civil action for damages** arising from a vaccine-related injury or death associated with the administration of a vaccine after the effective date of this part [effective Oct. 1, 1988] if the injury or death resulted from side effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings. (2) For purposes of paragraph (1), a vaccine shall be presumed to be accompanied by proper directions and warnings if the vaccine manufacturer shows that it complied in all material respects with all requirements under the Federal Food, Drug, and Cosmetic Act [21 USCS §§ 301 et seq.] and section 351 of the Public Health Service Act [42 USCS § 262] (including regulations issued under such provisions) applicable to the vaccine and related to vaccine-related injury or death for which the civil action was brought **unless the plaintiff shows**— (A) **that the manufacturer engaged in** the conduct set forth in subparagraph (A) or (B) of section 2123(d)(2) [42 USCS § 300aa-23(d)(2)(A) or (B)] [which includes "**fraud or intentional and wrongful withholding of information** from the Secretary during any phase of a proceeding for approval of the vaccine under section 351 [42 USCS § 262]," **or "intentional and wrongful withholding of information relating to the safety or efficacy of the vaccine after its approval**"], or (B) by clear and convincing evidence that the manufacturer failed to exercise due care notwithstanding its compliance

[5] 42 USCS § 300aa–22, Standards of Responsibility (emphasis added).

Program/Process/Law	Description[1, 2]
	with such Act and section (and regulations issued under such provisions).
Appeals	Finally, the special master's decision may be appealed and petitioners who reject the decision of the court (or withdraw their petitions within certain timelines) may file a claim in civil court against the vaccine company and/or the health care provider who administered the vaccine.[6]

[6] https://www.hrsa.gov/vaccine-compensation/index html.

Schedule 30

Chronology of Protocol 007

Chronology of Protocol 007

12/16/97
Merck: "in 1997, it was recognized that the minimum release potency specification ... 4.3 ... did not provide assurance that the labeled mumps potency was maintained through the end of shelf life in all lots released to the market." Merck made "a proposal for a clinical trial to investigate mumps immunogenicity at an end-expiry dose consistent with the EP mumps potency specification (3.7 log10 TCID50)."
MRK-KRA00000315 at '320

2/26/98
Merck: neutralization assay required because no "demonstrated correlation between the older assays and the ELISA-based assays
MRK-KRA00666494 at '558

3/25/98
GSK
[redacted]
'708

2/6/98
GSK
[redacted]
at '168

3/8/98
Merck's Margolskee: "We all agree that an MMR-II end expiry study is needed.
MRK-KRA00095320

9/17/98
Merck stated: "At this time, Merck Research Laboratories do not have any current and relevant data concerning the relationship between ELISA assay and virus neutralization capacity."
MRK-KRA00146417 at '429

9/8/98
CBER to Merck: Merck clinical study to have 5% equivalence margin; SCR lower limit > 90%; using wild-type antigens reflective of efficacy against disease; and "[S]eropositivity and seronegativity as indicators of protection require clinically valid justification."
MRK-KRA00001467 at '468-469

11/18/98
Merck: Regulatory Issues with CBER - "Neutralization assay necessary due to inability to re-establish clinical correlation; "interested in protection against wild-type, not vaccine strains; "possible to use alternate assay possible if correlation established; "Surrogate assay must be highly specific (100%) for WT neutralizing response; "CBER considers WT neutralizing antibody assay to be 'gold standard'
MRK-KRA01731773 at '778-779

2/26/99
Initiation date of Protocol 007
MRK-KRA0001270

2/5/99
Merck in Serial 027: Ongoing studies include evaluation of assay specificity. One year persistence objective added.
MRK-KRA01646761 at '760 '787

9/1/99
Merck: "CBER requires that SCR reflect protective efficacy
MRK-KRA00198876 at '878

8/16/99
Merck: 2 assays confirmed: "seroprotection rates against wild type virus isolates are not ~95%, per CBER's expectations.
MRK-KRA00015686

9/16/99
Merck: "A requirement was set forth by CBER to use a functional neutralization assay due to: 1- The efficacy statement in M-M-R®II label are based on old, limited data and an assay that is no longer used by Merck 2- Lack of data that correlates currently used ELISA assays and efficacy for M-M-R®II 3- Emergence of out breaks in highly vaccinated populations.
MRK-KRA00020425

10/26/99
(MMRV) CBER to Merck: False positive and false negative results are frequently observed when using mumps ELISA assays; "it is essential ELISA ... be validated against ... neutralization assay." Required ELISA cut-off to be justified.
MRK-KRA00761482 at '83

1998

1999

12/16/97
Merck: at 12/16/97 meeting, CBER requested clinical trial protocol to support expiry claim for mumps.
MRK-KRA00756256

2/26/98
Merck: If claimed potency is lower than available data, then "must provide clinical data
MRK-KRA00666494 at '525

3/6/98
Merck's Chirgwin: "trial is necessary for regulatory purposes have only limited clinical data at [4.3] and no data at all with the trivalent below 4.1. [T]herefore clinical data at the expiry is required.
MRK-KRA00095320

3/8/98
CBER to GSK:
[redacted]
R-IND-0000221 at
'222

5/8/98
CBER to Merck re IND 7068: "demonstrate a direct correlation of ELISA seroconversion data and GMT with presence of protective levels of neutralizing antibody"
MRK-KRA0146375 at '376

6/23/98
Merck: data limited to 4.1 - 4.3; no data below 4.1 log; MRL will demonstrate at 3.7 log. No correlation between the older neutralization assays and ELISA, thus CBER requested neutralization assay. Assumed SCR for neutralizing assay would be 96%, "which is the rate in the package circular."
MRK-KRA00137711 at '719-720 '723

10/2/98
Merck stated: "CBER has repeatedly requested 'clinically valid justification' for serologic criteria.
MRK-KRA00086290 at '290

12/10/98
Merck: "Merck has undertaken a clinical study to evaluate the immunogenicity of mumps at a targeted expiry titer of 3.7 log10 TCID50/dose.
MRK-KRA00756233 at '235

2/22/99
Merck: CBER does not use IgG to enhance sensitivity and feels not necessary. CBER encouraged Merck to correlate PRN and ELISA assay. If it can correlate, Merck can use ELISA for future clinical trials.
MRK-KRA0062710

3/7/99
Merck: ELISA antibody may not be a good measure of protection.
MRK-KRA00577001 at '032.

8/30/99
Merck: PRN results - JL SCR = ~90%, and LO1 SCR = ~70-80%; If CBER raises 96% SCR in the label as an issue and Merck defends unsuccessfully, "one option may be to propose range of observed SCRs in the label.
MRK-KRA00273309

9/14/99
Merck: approved "Mumps Plaque Reduction Neutralization Assay (the "1999 PRN) SOP No. 874.3422 Rev00.
MRK-KRA00002202

9/27/99
Merck: "PRN performance 70-75% Neut. WT; "PRN no correlation with ELISA; "Label change UNDERSIREABLE at the present time delay label change; "Have time to develop a more sensitive functional Neut. assay
MRK-KRA00020420

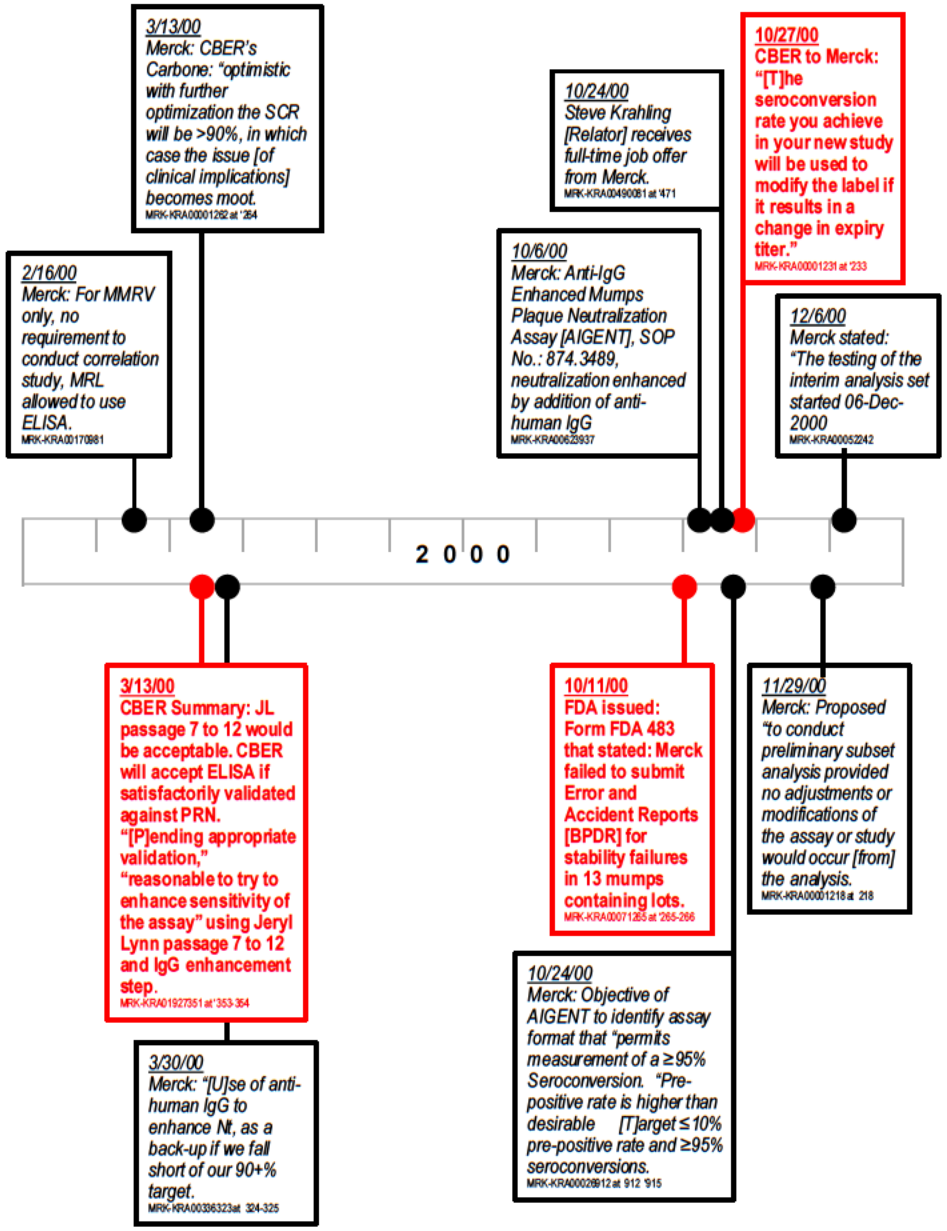
12/30/99
Merck: PRN designed as "correlate of protection from disease." "[W]e propose to use Jeryl Lynn™ as the target strain."
MRK-KRA00001470 at '631
MRK-KRA01620035 at '050

Appx1471

KEY: **Formal Merck to CBER**; *Merck internal*; **Formal CBER to Merck/GSK**; **Formal GSK to CBER**; *GSK internal*; **Relator statement**

This is not intended to be an exhaustive timeline, nor a full description in detail.

Chronology of Protocol 007



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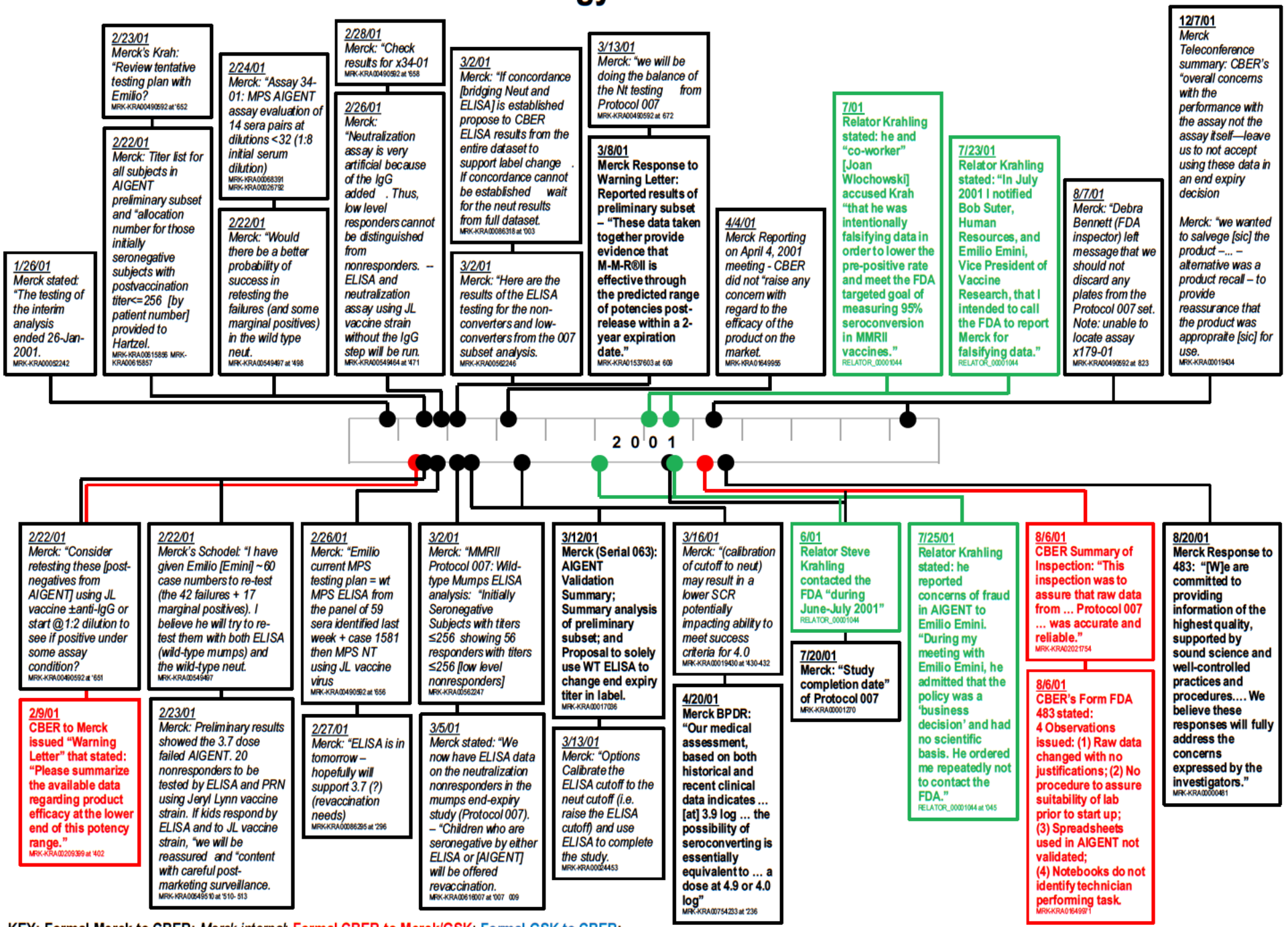
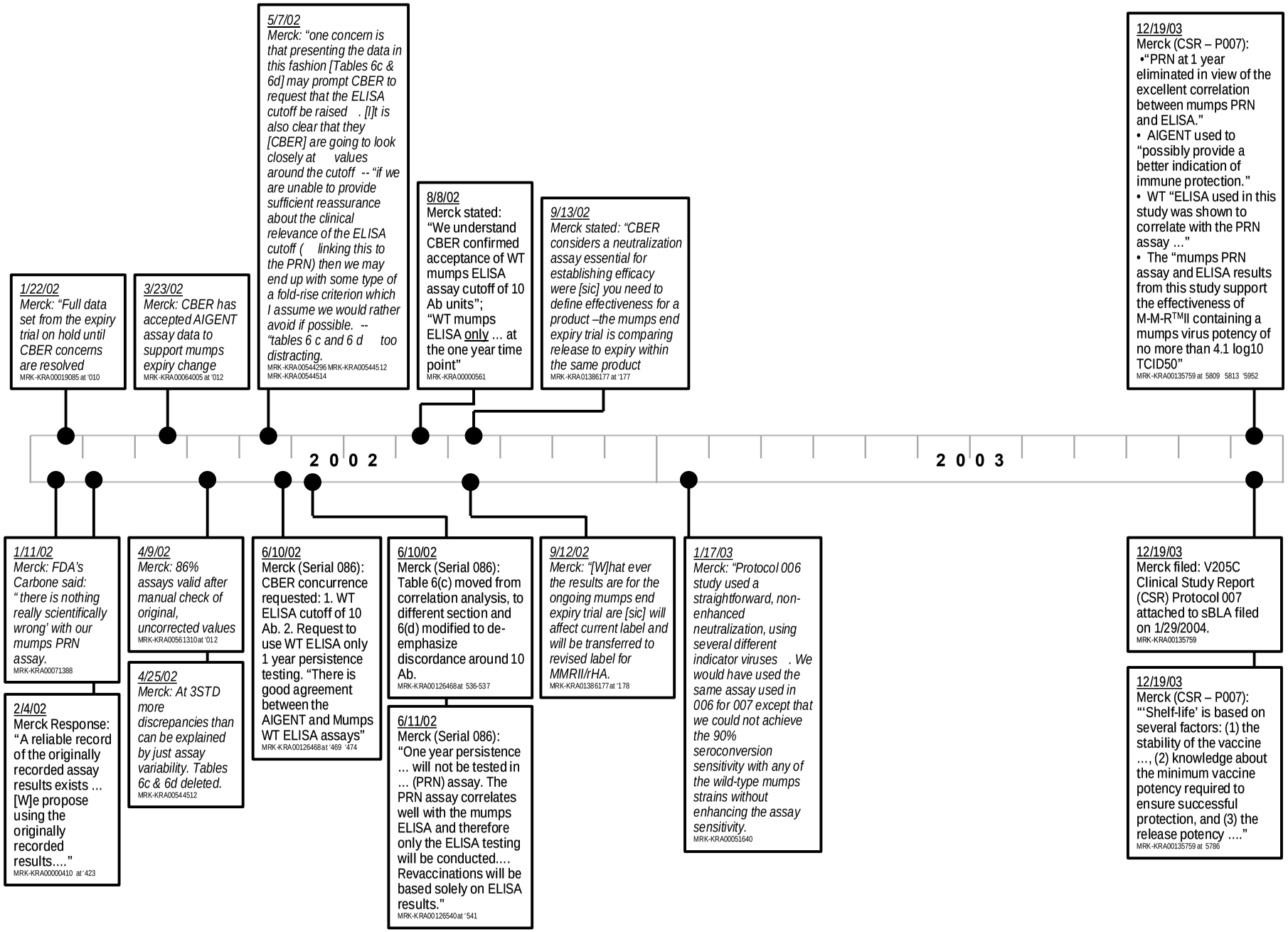
Chronology of Protocol 007



Appx1473

KEY: Formal Merck to CBER; *Merck internal*; Formal CBER to Merck/GSK; Formal GSK to CBER; *GSK internal*; Relator statement

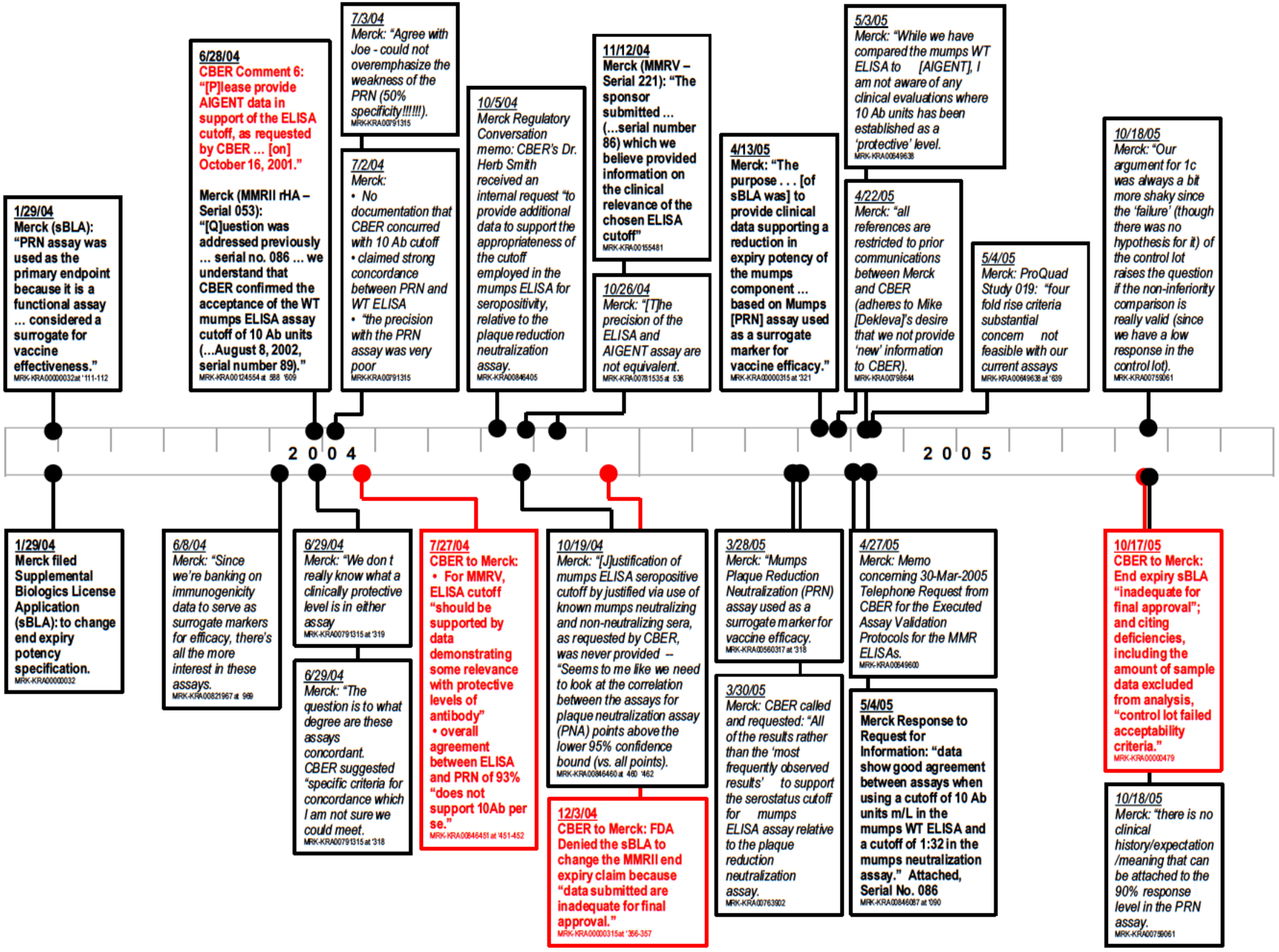
Chronology of Protocol 007



Appx1474

KEY: Formal Merck to CBER; *Merck internal*; Formal CBER to Merck/GSK; Formal GSK to CBER; *GSK internal*; Relator statement

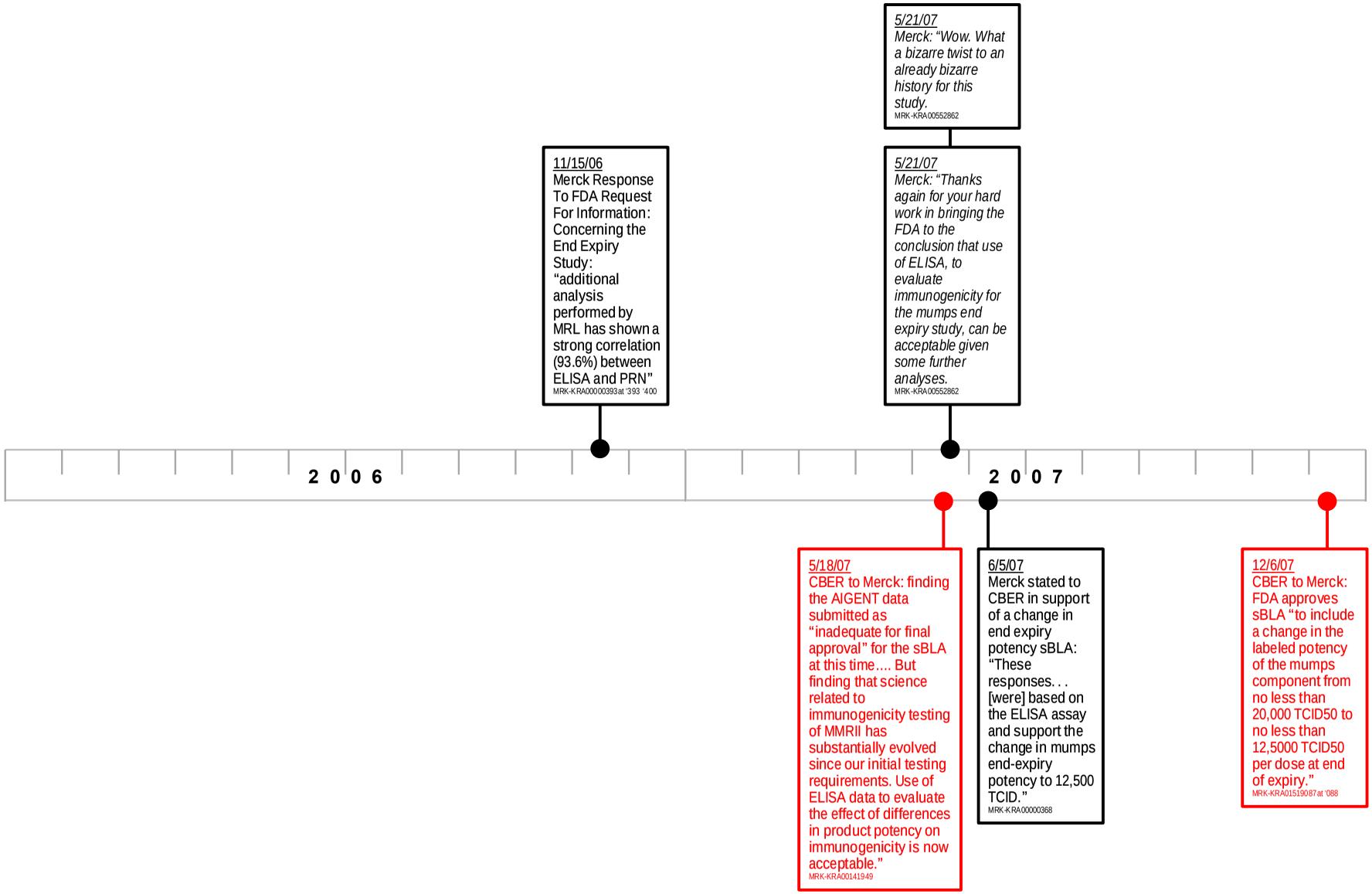
Chronology of Protocol 007



Appx1475

KEY: Formal Merck to CBER; *Merck internal*; Formal CBER to Merck/GSK; Formal GSK to CBER; *GSK internal*; Relator statement

Chronology of Protocol 007



Appx1476

KEY: Formal Merck to CBER; *Merck internal*; Formal CBER to Merck/GSK; Formal GSK to CBER; *GSK internal*; Relator statement

Schedule 31

Legislative History of the
National Childhood Vaccine Injury Compensation Act

In 1986, Congress enacted the National Childhood Vaccine Injury Compensation Act (the "NCVIA"). The NCVIA consists of two parts: (1) the National Vaccine Program ("NVP"), which is concerned with improving vaccines, monitoring and tracking adverse reactions to vaccines, and supporting efforts by the Department of Health and Human Services to improve immunization programs; and (2) the National Childhood Vaccine Injury Compensation Program ("NCVIP"), which establishes a "no-fault" compensation program designed to efficiently and expediently compensate vaccine-injured children and their families.

Program	Description[1, 2]
National Vaccine Program	The NCVIA requires the Secretary to establish in the Department of Health and Human Services a NVP to achieve optimal prevention of human infectious diseases through immunization and to achieve optimal prevention against adverse reactions to vaccines. The NVP shall be administered by a Director selected by the Secretary. The Director of the NVP has several responsibilities, including:[3] (1) Vaccine research. The Director of the NVP shall coordinate and provide direction for research carried out in or through the National Institutes of Health, the Centers for Disease Control and Prevention, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development on means to induce human immunity against naturally occurring infectious diseases and to prevent adverse reactions to vaccines. (2) Vaccine development. The Director of the NVP shall coordinate and provide direction for activities carried out in or through the National Institutes of Health, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development to develop the techniques needed to produce safe and effective vaccines. (3) Safety and efficacy testing of vaccines. Clinical trials to establish safety and efficacy are required for all vaccines. Difficulty in organizing clinical trials and their cost may deter the development of important vaccines. The NVP will assure that clinical testing of vaccines proceeds efficiently, so that the basic

[1] This is not intended to be exhaustive, nor a full description in detail.

[2] General Sources:
H.R.5546 – 99th Congress (1985-1986) (available at https://www.congress.gov/bill/99th-congress/house-bill/5546).
https://www.cdc.gov/vaccinesafety/ensuringsafety/history/index html.
House Report No. 99-908, 1986 WL 31971, National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-1 to 300aa-34.
http://www.nvic.org/injury-compensation/origihanlaw.aspx.
Health Resources & Services Administration National Vaccine Injury Compensation Program Fact Sheet (available at https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/faq/vicp-fact-sheet.pdf).
Guidance for Industry, FDA Review of Vaccine Labeling Requirements for Warnings, Use Instructions, and Precautionary Information, FDA, September 2004 (available at https://permanent.access.gpo.gov/LPS112955/ucm092196.pdf).

[3] 42 USCS § 300aa–2, Program Responsibilities.

Program	Description[1, 2]
	public health goals of immunization programs can be met. The Director of the NVP shall coordinate and provide direction for safety and efficacy testing of vaccines carried out in or through the National Institutes of Health, the Centers for Disease Control and Prevention, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development. Under Section 314 of the NCVIA, FDA was required to review warnings, use instructions and precautionary information that states: "Not later than 1 year after the effective date of this title and after consultation with the Advisory Commission on Childhood Vaccines established under section 2119 of the Public Health Service Act [42 USCS § 300aa-19] and with other appropriate entities, the Secretary of Health and Human Services shall review the warnings, use instructions, and precautionary information presently issued by manufacturers of vaccines set forth in the Vaccine Injury Table set out in section 2114 of the Public Health Service Act [42 USCS § 300aa-14] and shall by rule determine whether such warnings, instructions, and information adequately warn health care providers of the nature and extent of dangers posed by such vaccines. If the Secretary determines that any such warning, instruction, or information is inadequate for such purpose in any respect, the Secretary shall at the same time require the manufacturers to revise and reissue such warning, instruction, or information as expeditiously as practical, but not later than 18 months after the effective date of this title."[4] "If FDA determined that any such warnings, use instructions or precautionary information were inadequate, then manufacturers were required to revise and reissue such warnings, use instructions or precautionary information as expeditiously as practical."[5] "On June 13, 1988, the Secretary delegated authority to implement section 314 of the NCVIA to the Assistant Secretary of Health (ASH). On September 16, 1988, the ASH delegated authority to implement section 314 of the NCVIA to the Commissioner of the Food and Drugs. On April 1, 1993, FDA delegated to the Center of Biologics Evaluation and Research Authority to implement Section 314 of the NCVIA."[6] (4) Licensing of vaccine manufacturers and vaccines. The Food and Drug Administration licenses vaccine manufacturers and vaccines. The NVP will, by coordinating these licensure activities with other Federal agencies that are

[4] Note to 42 U.S.C. § 300aa–1.
[5] Guidance for Industry, FDA Review of Vaccine Labeling Requirements for Warnings, Use Instructions, and Precautionary Information, FDA, September 2004, available at (https://www fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/UCM092196.pdf).
[6] *Id.*

Program	Description[1, 2]
	engaged in research, development, and clinical testing, seek to make the licensure program responsive to the public health priorities of immunization. The NVP will assist the Food and Drug Administration to assign resources to vaccine licensure activities, so that these activities may best contribute to rapid licensure of important vaccines. The Director of the NVP shall coordinate and provide direction for the allocation of resources in the implementation of the licensing program. (5) Production and procurement of vaccines. The Director of the NVP shall ensure that the governmental and non-governmental production and procurement of safe and effective vaccines by the Public Health Service, the Department of Defense, and the Agency for International Development meet the needs of the United States population and fulfill commitments of the United States to prevent human infectious diseases in other countries. (6) Distribution and use of vaccines. The Director of the NVP shall coordinate and provide direction to the Centers for Disease Control and Prevention and assistance to States, localities, and health practitioners in the distribution and use of vaccines, including efforts to encourage public acceptance of immunizations and to make health practitioners and the public aware of potential adverse reactions and contraindications to vaccines. (7) Evaluating the need for and the effectiveness and adverse effects of vaccines and immunization activities. The Director of the NVP shall coordinate and provide direction to the National Institutes of Health, the Centers for Disease Control and Prevention, the Office of Biologics Research and Review of the Food and Drug Administration, the National Center for Health Statistics, the National Center for Health Services Research and Health Care Technology Assessment, and the Centers for Medicare & Medicaid Services in monitoring the need for and the effectiveness and adverse effects of vaccines and immunization activities. (8) Coordinating governmental and non-governmental activities. The NVP would constitute the central focus in the Federal government for gathering and analyzing information about non-government vaccine and immunization activities. Because [] the success of immunization efforts, including vaccine research and development, is dependent on close collaboration and cooperation between government, industry, universities, and others, the NVP will encourage the investment of non-government resources in a manner that they will complement government activities. The Director of the NVP shall provide for the exchange of information between Federal agencies involved in the implementation of the Program and non-governmental entities engaged in the development and production of vaccines and in vaccine research and encourage the investment of non-governmental resources complementary to the governmental activities under the Program.

Program	Description[1, 2]
	(9) Funding of Federal agencies. The Director of the NVP shall make available to Federal agencies involved in the implementation of the plan issued under the NCVIA funds appropriated to supplement the funds otherwise available to such agencies for activities under the plan.
National Childhood Vaccine Injury Compensation Program[7]	Created under the NCVIA, the National Vaccine Injury Compensation Program ("NVICP") is a no-fault alternative to the traditional legal system for resolving vaccine injury petitions. It was created after lawsuits against vaccine companies and health care providers threatened to cause vaccine shortages and reduce U.S. vaccination rates. Any individual, of any age, who received a covered vaccine and believes he or she was injured as a result, can file a petition. Parents, legal guardians and legal representatives can file on behalf of children, disabled adults, and individuals who are deceased. The NVICP is administered through the Department of Health and Human Services. The Department of Justice represents HHS in Court. The U.S. Court of Federal Claims makes the final decision regarding whether a petitioner should be compensated. The NVICP compensates those injured by vaccines on a "no fault" basis. The United States Court of Federal Claims and the United States Court of Federal Claims special masters shall have jurisdiction over proceedings to determine if a petitioner is entitled to compensation under the NVICP and the amount of such compensation.
Liability under the NCVIA[8]	(b) Liability. The first stage of such a civil action shall be held to determine if a vaccine manufacturer is liable under section 2122 [42 USCS § 300aa-22]. (c) General damages. The second stage of such a civil action shall be held to determine the amount of damages (other than punitive damages) a vaccine manufacturer found to be liable under section 2122 [42 USCS § 300aa-22] shall be required to pay. (d) Punitive damages. (1) If sought by the plaintiff, the third stage of such an action shall be held to determine the amount of punitive damages a vaccine manufacturer found to be liable under section 2122 [42 USCS § 300aa-22] shall be required to pay. (2) If in such an action the manufacturer shows that it complied, in all material respects, with all requirements under the Federal Food, Drug, and Cosmetic Act and this chapter applicable to the vaccine and related to the vaccine injury or death with respect to which the action was

[7] *See* Schedule 29 Vaccine Courts for more details.
[8] *Id.*; 42 USCS § 300aa–23, Trial.

Program	Description[1, 2]
	brought, the manufacturer shall not be held liable for punitive damages unless the manufacturer engaged in— (A) fraud or intentional and wrongful withholding of information from the Secretary during any phase of a proceeding for approval of the vaccine under section 351 [42 USCS § 262], (B) intentional and wrongful withholding of information relating to the safety or efficacy of the vaccine after its approval, or (C) other criminal or illegal activity relating to the safety and effectiveness of vaccines, which activity related to the vaccine-related injury or death for which the civil action was brought.

10/25/2019
Declaration of G. Reilly
EXHIBIT 4

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

UNITED STATES OF AMERICA, ex rel., STEPHEN A. KRAHLING and JOAN A. WLOCHOWSKI, Plaintiff, v. MERCK & CO., INC., Defendant.	Civil Action No. 10-4374 (CDJ) Volume I of II 9:20 a.m. - 7:28 p.m.
IN RE: MERCK MUMPS VACCINE ANTITRUST LITIGATION THIS DOCUMENT RELATES TO: ALL ACTIONS	Master File No. 12-03555 (CDJ)

- - -

Friday, September 28, 2018

- - -

Videotaped deposition of DAVID KESSLER, M.D., taken at the offices of VENABLE LLP, 600 Massachusetts Avenue, N.W., Washington, D.C., beginning at 9:20 a.m., before Nancy J. Martin, a Registered Merit Reporter, Certified Shorthand Reporter.

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I N D E X

EXHIBITS
(CONTINUED)

NUMBER	DESCRIPTION	MARKED
Exhibit 20	Letter dated December 16, 1998, MRK-KRA01629294 - -1629307, 30 pages	178
Exhibit 21	E-mail dated May 12, 1999, MRK-KRA00094960, 1 page	182
Exhibit 22	E-mail dated October 25, 2000, MRK-KRA00784029 - -784046, 22 pages	188
Exhibit 23	Measles, Mumps, and Rubella Virus Vaccine Live Statistical Analysis of Potency on Stability, STN 101069, October 24, 2000, MRK-KRA01899087 - -1899253, 168 pages	191
Exhibit 24	Warning Letter dated February 9, 2001, MRK-KRA00209399 - -209403, 6 pages	197
Exhibit 25	Letter dated March 8, 2001, MRK-KRA01537603 - 1537611, 10 pages	201
Exhibit 26	Memorandum dated April 8, 2001, MRK-KRA01649955 - -1649956, 2 pages	212
Exhibit 27	Biological Product Deviation, Report Form, MRK-KRA00754239 - -754244, 6 pages	217
Exhibit 28	Biological Product Deviation, Report Form, MRK-KRA00754233 - -754238, 6 pages	219

EXHIBITS
(CONTINUED)

NUMBER	DESCRIPTION	MARKED
Exhibit 29	Team Biologics Inspection, May 20, 2002, MRK-KRA-00783949 - -783977, 30 pages	225

WASHINGTON, D.C., SEPTEMBER 28, 2018, Friday, 9:20 A.M.

THE VIDEOGRAPHER: Good morning. We're going on the record at 9:20 a m. on September 28, 2018. Please note that the microphones are sensitive and may pick up whispering, private conversations, and cellular interference. Please turn off all cell phones or place them away from the microphones as they can interfere with the deposition audio. Audio and video recording will continue to take place unless all parties agree to go off the record.

This is Media Unit 1 of the video recorded deposition of David Kessler taken by counsel for defendant in the matter of United States of America, et al., vs. Merck & Co., Inc. filed in the United States District Court for the Eastern District of Pennsylvania, Civil Action 10-CV-4374 (CDJ).

This deposition is being held at Venable, located at 600 Massachusetts Avenue, Northwest, Washington, D.C. My name is Gene Aranov from the firm Veritext Legal Solutions, and I'm the videographer. The court reporter is Nancy Martin from the firm Veritext Legal Solutions. I'm not authorized to administer an oath. I'm not related to any party in this action, nor am I financially interested in the

outcome.

Counsel and all present in the room and everyone attending remotely will now state their appearances and affiliations for the record. If there are any objections to proceeding, please state them at the time of your appearance, beginning with the noticing attorney.

MS. HARDWAY: Kathleen Hardway from Venable for Merck.

MR. MANCANO: Jamar Mancano from Venable for Merck.

MR. SANGIAMO: Dino Sangiamo from Venable for Merck.

MS. ROBERTS: Michaela Roberts from Venable for Merck.

MS. DYKSTRA: Lisa Dykstra, Morgan Lewis, for Merck.

MS. LERNER: Kellie Lerner, Robins Kaplan for private plaintiffs.

MR. SCHNELL: Gordon Schnell, Constantine Cannon for relators.

MS. WYSOCKI: Sarah Wysocki, Keller Grover for relators.

MS. SCANLAN: Kathleen Scanlan, Keller Grover, for relators.

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MR. HOWARD: Tim Howard, in-house counsel for Merck.

DAVID KESSLER,
having been first duly sworn/affirmed,
was examined and testified as follows:

EXAMINATION

BY MS. HARDWAY:

Q. Good morning, Dr. Kessler.

A. Good morning.

Q. We met right before the deposition. My name is Kathleen Hardway, and I represent Merck in these matters.

Could you please state your name and address for the record.

A. David Kessler, 2715 Steiner Street, San Francisco, California, 94123.

Q. You've been deposed several times, Dr. Kessler; is that right?

A. Yes.

Q. And you understand in the deposition you're to testify fully and accurately as if you're at trial?

A. Correct.

Q. And that you're to make audible responses?

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A. I will try.

Q. And you understand that the court reporter is trying to take down everything that both of us say. So I will give you the respect of trying to let you finish your answer before I start asking my question. I'd ask for you to let me finish my question before you begin your answer. Is that fair?

A. Good idea.

Q. You know you can take a break at any time. I would just ask that, if you need a break, that you would wait until providing an answer to a question before asking for a break.

A. Of course.

Q. Is there any reason today that you cannot give complete and accurate testimony?

A. No.

Q. What is your understanding of the claims in this case?

A. They're set out in my report in certain paragraphs. Specifically, I believe there's actions under the False Claims Act. I believe there's antitrust actions. There are a number of matters, but I can refer you to -- specifically, I laid that out in Paragraph 10 and 11 of my report more specifically.

MS. HARDWAY: We're going to go ahead and mark your report and the appendices as Exhibit 1.

(Deposition Exhibit 1 was marked for identification.)

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BY MS. HARDWAY:

Q. Now, you're looking at -- excuse me -- a version of your report that you brought with you. We marked it 1 in this binder here, as Exhibit 1. Do you recognize this as your report?

A. I don't have it in front of me, but I will take your representation that it has every page.

Q. It does.

A. Then I'll take your representation, and I'll work from this copy unless you have a specific request that's different.

My microphone just fell apart.

Q. Now, about five minutes before the deposition started I was handed an errata to your report, which is nearly four full pages long with a three-page attachment; is that correct?

A. It's an errata plus a supplemental reliance, supplemental list of materials.

Q. Did you prepare this errata?

A. It was prepared at my request by counsel and under my direction.

Q. When did you direct it to be prepared?

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A. The last couple of days.

Q. When, specifically, did you ask it to be prepared?

A. I don't remember specifically. As I was pulling articles and looking at things, I asked counsel to, on citations, if anyone noticed any changes from the actual Bates numbers, whether there's any mistakes, that they keep that, and I've asked that to be kept for the last several months.

If anyone noted, as they helped me put together books, et cetera -- oh, actually, over probably a period of more than a year, anything that changes.

Q. So you asked counsel to keep a record of any errors or changes that had been made over the course of the last year?

A. No. I asked -- the report's obviously signed somewhere, what, March, I believe. But as I -- I asked counsel to print out also some documents, and then they see certain things, and if they see any errors in Bates numbers, to keep it -- keep a record of that. I did some, and then those were put together the last couple of days.

Q. But the record was being kept longer than just during the last couple of days; is that right?

A. If anyone noted any citation changes -- the vast majority of these my guess is 98 percent would be considered citation. Just proofreading kind of things.

Q. But there are other substantive changes to your report; correct?

A. There are several substantive changes, probably two, to my recollection.

Q. Which two to your recollection?

A. So there is -- I'd have to go through this. There's the swap-out, to use a -- just a colloquial term. I asked Dr. Stark over the last several days. My understanding is Dr. Shenerman is ill and can't testify, and for that and other reasons I asked Dr. Stark to do the calculation that Dr. Shenerman had done, and I attached that.

As you see, there's an E-mail to me, and I asked Dr. Stark to do that, and that's my handwriting is Attachment 1. So that swaps out calculation of Stark for Shenerman, and I believe I deleted -- I noted one error. I can find it here. I can do it now or at the break. One error where I deleted a certain paragraph.

MS. HARDWAY: Okay. We're going to go ahead and mark this, the errata as Exhibit 2.

(Deposition Exhibit 2 was marked for identification.)

BY MS. HARDWAY:

Q. And Exhibit 2 is the errata that we've been discussing; right, Dr. Kessler?

A. Right. And a supplement to materials considered.

Q. The error that you were just describing, would that be errors in Paragraphs 366 and 434 on Page 2?

A. I believe so. By memory I can double-check. I can pull those. I believe those are the paragraphs by memory. I'd be happy to get it in front of me.

Q. And could you explain to me why Paragraph 366 is in error.

A. Well, it's not entirely in error. I think that it's primarily -- it was a question of my reading of the four-fold rise, and I didn't think it was quite right in one part of this as it was phrased, and certain parts of the paragraph are correct, but I didn't like the way it was phrased.

Q. Explain to me specifically why you didn't like the way it was phrased.

A. So it says, "In my opinion Merck's Proquad label is misleading because it admitted that the WT

ELISA used in the --

REPORTER MARTIN: Can you slow down just a little, please "Admitted that the" --

THE WITNESS: "...admitted that the WT ELISA used in the clinical studies to support the licensure of Proquad did not include the --

REPORTER MARTIN: Slow down, please.

"...did not" support the...

THE WITNESS: "It did not include the four-fold rise criteria reported to be correlated with protection against mumps infection. Furthermore, the label omitted that the WT ELISA assay with a 10 AB cutoff did not have a connection to whether a subject was protected from disease. Moreover, the label is misleading because it did not state that the seroconversion rates measured in the clinical studies to support the Proquad were not measured using the four-fold rise criteria used in previous clinical studies."

That's the part that's inartful because this four-fold rise is used several times -- several different ways when you deal with seroconversion, and I thought this was ambiguous and it was better to be struck. I'm happy to go into how four-fold rise is used, but it's used both diagnostically in terms of

mumps diagnosis in clinical studies, and it's also used as an immunological surrogate. So for that ambiguity, I decided it was better to strike it.

BY MS. HARDWAY:

Q. And then Paragraph 434.

A. I think that just should be the corresponding conclusions, if my memory serves me right, but let me look.

(The witness reviewed the document.)

THE WITNESS: It should be the corresponding paragraph to that. Hold on a second.

(The witness further reviewed the document.)

THE WITNESS: I have to check. It's just that that exact, same -- those sentences that relate -- it's a way to those. So it's the sentences that I just told you about that I meant to strike. It's the reference to the four-fold. So the conclusions just bring down -- tries to summarize the opinions at the end, and the conclusions at the end that relate to four-fold is what I meant to strike.

BY MS. HARDWAY:

Q. Okay. You also struck Paragraphs 259.6 to 259.11.

A. Yeah, that should be Shenerman if I'm correct. Let's just go do it. If I got my numbers

right -- yeah. 259.6 to 259.11 is the striking of Shenerman and the replacement of Shenerman with, in essence, the E-mail on the second page of the E-mail of Dr. Stark's calculation.

Q. The supplement materials considered, which is pages -- it starts on Page 3 and continues onto Page 4.

A. Yes, ma'am.

Q. Were these materials that you requested?

A. No. These may be -- well, these are materials that I probably -- let me just take a look. So I'm sure there's articles on here. I may have downloaded articles from PubMed. I've been looking at -- these are articles that I may have found off the database of provided documents. These may be documents that I requested. So they're a compilation.

Q. When is the earliest time that you either obtained one of these documents or articles yourself or that you requested them from counsel?

A. I don't recall. A number of these were supplemental to or added to the database, either an FOI subsequent to the report, and I don't remember exactly when I looked at them, but they weren't available. Some of these were not available, such as the FDA FOI request that -- and some of these I just

saw on the database myself and searched.

Q. Why is it that you were performing additional searches on PubMed for certain articles?

A. Well, because as you know, Counsel, science continues -- things continue to be published, and things continue to be published throughout, even after the report. So it's an effort to be thorough.

Q. Well, the first article was published in 2016 by Gumer, et al?

A. Yes.

Q. So that was published before you drafted your report.

A. I didn't see it. I did a search. I was very interested in the computational genetics that go into the mumps vaccine. And this is a paper on certain epitopes, and I continued to study in that area. I didn't see it until after -- I didn't do the search until after my report was done. So I saw it after.

Q. The Latner article, the next one, do you have a date or a period in which it was published?

A. Yeah. So the Latner was published. As you know, the Latner was CDC. I can give that you if you just wait for just a second, Counselor.

Actually, I have a printout of Latner, as well as Gumer, but you asked me for Latner. So I can

tell you that Latner was published in clinical and vaccine immunology. That's where it was published.

Q. What year?

A. 2014. And I believe Latner should be on my material. There may be some duplication, but Latner, I thought, was in my original reliance list. It may be duplicated here. I thought Latner was on my original reliance list. They were searching Gumer articles, just also to be clear, that were published that are on my reliance list. So this just may be a duplication because what I did was I gave my stack of articles to counsel and said, "Just make sure these are on the reliance list."

So that may be a duplication is my guess.

Q. But the Nalen article, that was published in 1998; correct?

A. Yes. And, again, these represent here, but they should be cross-checked against my original reliance list. These are things that I've printed out.

Q. The Stohaniv article at the bottom of Page 3, what year was that published in? In what periodical was that published?

A. So let me see. I may have to check on that. I may have it here.

(The witness reviewed the document.)

THE WITNESS: I'd have to check on-line, Counselor. I just don't have that in my hand.

BY MS. HARDWAY:

Q. Page 4, the Usonis article, when was that published and in what periodical?

A. Yeah. So there's several Usonis articles. These are on the GSK vaccine on PEDIARIX, and I think they also may be originally on my original reliance list. I can get it for you if you'd like. We can double-check this.

Q. Let me ask you this, Dr. Kessler --

A. I think -- hold on one second. Let me just answer your question if I may. I think this is a duplicate. I'm pretty sure Usonis is on the original reliance list. Yeah. So there's several -- so the one Usonis is -- the one that I've just referred to is 1999. That is on my reliance list.

Q. The first one?

A. The reactor *geneceity article is on my reliance list. And I'd have to check the dates on the others.

Q. Which materials on Pages 3 and 4 were sent to you by counsel not at your request?

A. Certainly the expert reports were sent to me

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by counsel. I'd have to go back and check and go through and look and see which of the MRKs. I can go through individually. I'd have to look at it and see which ones I found on the database and which I may have asked counsel to send me.

And it is also possible there's a third category, I apologize, just to finish the question. I have a problem printing off from the database at times. So there are a number of times where I ask counsel -- or I gave them a Bates number and I was able to look at something on-line and --

Q. Hang on a second, Doc.

A. Did I do it again?

(Pause in proceedings to adjust microphone.)

THE WITNESS: There are a number of times where I've asked counsel to print a document for me or send me a PDF or something like that.

MS. SCANLAN: And if I just caution the witness, there is a stipulation in place that protects against the disclosure of communications between counsel and the witness, and just to remind the witness not to disclose communications in the context of answering the questions.

THE WITNESS: You're citing the federal rule to me. Thank you very much, Counsel.

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BY MS. HARDWAY:

Q. Did you read all the expert reports on Page 4?

A. No. I mean I think it's fair to say I probably -- it depends on your definition of the word "read." I didn't read them from the beginning to end. That would be impossible. But I am sure that I have searched them as a collection for certain terms over time.

Q. Is it fair to say, Dr. Kessler, that you've had the materials on Pages 3 and 4 prior to this week?

A. That wouldn't be a complete -- that would not be completely accurate.

Q. Which materials did you get prior to this week, Dr. Kessler?

A. I can't -- I'd have to go through individually, and I'm not sure I would recall exactly the time frame. The answer is I don't know the answer to that exact question.

Q. But certainly some of the materials on Pages 3 and 4 you got prior to this week. Is that fair?

A. Well, the FOI documents were produced subsequent to the report, and they were on the database and I looked at them prior to this week, yes.

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Q. And any other ones that -- any other materials that you can recall looking at -- without going back to the materials themselves, any other materials that you can recall looking at prior to this week?

A. Sure. I certainly recall reading Gumer and reading Latner, and furthermore, I remember -- and certainly the expert reports that cite me, Norman Baylor, Bruce Burlington, a number of these. Leanne Arvin. A number of these other reports. I have Patriarca I read before this week.

Q. Turning to the Attachment 1.

A. Yes.

Q. When were you advised that Dr. Shenerman was no longer going to be an expert in this case?

A. I don't remember exactly.

Q. Was it prior to this week?

A. I believe so. I believe that was correct.

Q. What was your request to Dr. Stark?

A. My request to Dr. Stark was that he take his regression analysis and -- with his calculation -- I'd like to look at it if we want to talk about it in detail. But that the rate of loss that he calculated from his slope and that he could kindly calculate the variance, the total variance, then drew the square

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root -- calculate the total variance correctly and come up with the minimum release per their equation in the table that is referenced in the E-mail. So I asked him to do the calculation, as I would normally do of any statistician.

Q. When did you make that request to him?

A. Several days ago.

Q. Prior to this week?

A. No.

Q. How did you make that request of him?

A. Through counsel.

Q. You did not E-mail him?

A. I did not. I asked counsel to contact him. I did not E-mail him. As you can see, he E-mailed me.

MS. HARDWAY: I'm just going to state an objection for the record. We were handed this errata sheet five minutes before the deposition started. It contains a significant number of changes, including substantive changes to Dr. Kessler's report, as well as a significant number of additional materials reviewed.

We had an agreed-upon 10 hours for Dr. Kessler's deposition, but I'm going to reserve the right to ask for more time based on this errata and these additional materials reviewed.

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MS. SCANLAN: You've now spent 20 minutes going through the errata that he gave. He described that 90 percent of the changes in here are typographical changes for citation errors. There were two substantive changes to which you have already addressed, and the supplemental materials, he's already described what the context was that he used. Many of them are already on his reliance list. They're already duplications.

MS. HARDWAY: Well, we have no way of knowing what's on his reliance list, and I'm not going to waste anymore time on this. I'm just stating my objection for the record and reserving the right to seek more time.

MS. SCANLAN: I would appreciate you giving me the time to put my response on the record before you interrupt me in response, please.

We've already gone through these in the course of the day. Your objection is understood. You have asked in various other depositions whether our experts have reviewed the report of your experts, and he has simply provided you the list showing which ones he actually reviewed.

MS. HARDWAY: It's a lot more than just expert reports.

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Q. Dr. Kessler, what was the general assignment that was given to you by relator's counsel in terms of what opinions they wanted you to offer?

A. So I think the specific questions that I grew to understand that the matter involved are laid out in the report beginning on Page 6, I believe. But that's certainly not what -- counsel didn't phrase it that way, but as I sat and did my report, those were the questions in my head.

Q. How did you go about preparing your report?

A. Reading a lot of materials.

Q. Did your assignment change at all over time in terms of what opinions you were asked to offer?

A. No, I was not -- I think, simply put, I mean the assignment -- there was no restrictions on the assignment. Obviously I'm the -- you know, I deal with the interface between the regulatory and the scientific aspects of the matter at hand in these cases, but it really had to do with Merck's conduct with regard to issues of potency and efficacy surrounding the MMR II Proquad, et al., applications.

Q. How much time did you spend preparing your report in this case?

A. The report itself?

Q. Yes.

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A. Hundreds.

Q. Hundreds of hours?

A. Yeah.

Q. More than 500?

A. No.

Q. More than 100?

A. I can -- I mean I billed -- I kept track of about -- I don't know. Does anyone have an invoice? My guess is about 225 hours. There may be hours beyond that that I didn't -- that I spent that I didn't bill, where I was reading things.

Q. Are those hours that you haven't billed yet and you intend to bill?

A. No, I'm talking about -- you asked -- your question was about in preparation of the report.

Q. Okay. So about 225 hours in preparation of the report. Are you confident in that estimate?

A. You can look at an invoice. Happy to do that at a break. I know it's 225 or 250. Something of that magnitude.

Q. If you could look at an invoice during the break, I would appreciate that and we can --

A. I didn't want to interrupt.

Q. -- and we can get that number on the record.

A. I don't have it. I'm sure you're entitled to

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it. So I'm happy to have counsel give it to you. If not -- if they don't have it at the break -- I don't have it with me today, but if counsel has it, I'm happy to have them share it with you.

Q. In addition to the time spent preparing your report, are there other hours that you've billed on this matter?

A. No.

Q. So just the 225 hours?

A. 225 to 250. Whatever the invoice says.

Q. Okay. Did anyone help you, assist you in reviewing documents for your report?

A. No.

Q. Did anyone assist you in writing your report?

A. Other than in the traditional way that counsel helps as far as typing, et cetera.

Q. So only typing?

A. Yeah. No. This report is my report. It's only me. I tend to dictate or direct how things -- you know, "Please type these lines," et cetera. So I direct all that.

Q. Did anyone help you form your opinions in this case?

A. Absolutely not.

Q. Are you affiliated with any consulting firm?

A. "Consulting firm." That's an interesting question. I don't -- affiliated. So I'm on the board of several organizations. I'm a senior advisor. None of those are consulting firms.

Q. Okay. Do you anticipate doing any additional work before trial?

A. There's always preparation for trial. There's always new information that occurs. I will do as counsel requests.

Q. Do you have any specific intention, as we sit here today, to do any additional work in this case?

A. Yes.

Q. What is that?

THE WITNESS: Could you make sure that any principals that you want in this matter are on the phone for both sides, please.

MS. SCANLAN: I can represent my firm.

THE WITNESS: I just want to make sure that all principals are here. I want this to be on the record. I just want to make sure that people have had -- that any principals in this matter for any parties hear this.

So I have done some work. I'm sure we'll talk about it. But in preparation of this work -- and counsel -- just for the record, counsel does not know

I'm going to say this. I've not spoken to anyone about this.

I have done certain work in this matter that's led me, as obviously it's in the report and subsequently. I have a document that's in front of me that I have worked on that's called "Release Lots" filed after March 28, 1998 through -- actually, this goes complete through 2007.

This is of great -- this is an important public health concern. This is by lot, in essence, the subpotency of some 60 million doses of MMR II that have been released either below 4.3 or 4.1.

I think public health -- I think there's public health significance to this data. I need -- I'm happy to talk to both sides in this matter, but my plan is to seek -- in the next 10 days to seek out private counsel to represent me. The complexity of that is that there needs -- I understand this is material subject to a protective order.

My current thinking is to move the Court -- and it has to be done in a thoughtful way. I don't know what a reasonable period of time is, 45 days, 60 days -- to move the Court to make sure that certainly at least the secretary of health and human services have this information, and maybe broader. I have to

think through that. I don't want to do anything without permission of both sides.

But this matter is, at this point, enough of a public concern -- and also for the Court -- and that's why I want to do this on the record. I think the fact that there are some 60 million doses that have been released that have been subpotent that still have implications for immunity in young adults who get exposed to this disease.

It is of such import that that needs to be thoughtfully done. I don't profess, sitting here, how to do this, and again, I seek counsel from both sides. I want to do it completely subject to the protective orders, to follow the rules to the T, but my intention is to petition the Court, as I sit here, so that this information is appropriately -- people are appropriately informed of this.

BY MS. HARDWAY:

Q. Dr. Kessler, that the 60 million doses you're referring to, are those listed on this spreadsheet that you've prepared?

A. Yes. I'd be happy to go through the spreadsheet with you --

(Telephonic interruption.)

MS. HARDWAY: Did someone just join us?

MR. MACORETTA: Yeah, hi. John Macoretta from Spector Roseman & Kodroff, just joining.

BY MS. HARDWAY:

Q. You brought copies of the spreadsheet?

A. I did. I brought one for -- yes. I'd be happy to share that at this point.

MS. LERNER: And this is Kelley Lerner for the plaintiffs. This is something that's been previewed with us. He's raising the prospect of bringing a separate matter retained by separate counsel. So I just don't want to undermine what we're doing today in these cases by belabored discussion of what that might look like. He says he wants it to be thoughtful, and we need to be thoughtful but don't want to take from the record of today's proceedings to discuss what Dr. Kessler may be doing separately in his own capacity represented by other counsel. So I just want to put that on the record.

THE WITNESS: And just, Counsel, I mean it perhaps -- I mean my request is that both of you -- both sides confer. I am -- I will also put on the record for Mr. Howard, you know, I got a phone call back a number of years ago from Ken Frazier saying if I ever -- it was a very nice phone call I think when he assumed the CEO-ship. I don't remember the call

exactly, but if there were issues ever involving Merck that I thought were important, that I should feel free to call him.

I understand this is a matter of litigation. I didn't pick up the phone and do that, but I certainly do think this rises to that level and am prepared to do that. But I'm willing to do this thoughtfully, but I am not willing to just to sit silent. And, again, I don't want to distract from today. I think this document is relevant to today's inquiry because it supports what's in the record. The number may be a little different than the 12 million in the report. This comes out to 60 million, but this is of such import that I think everyone will understand the matter.

But you asked me whether I intend to do other work. So the answer to your question is a belated yes.

MS. HARDWAY: Let's go ahead and mark this as Exhibit 3.

You know, obviously this is something we were not aware of. It's significant both in its substance and in what Dr. Kessler is saying he intends to do with it. Whether we ask him about it today or not -- and he also just said it's relevant to his opinions in

this case -- it's certainly not something that -- because of that, it's something that I'm going to want to ask him about today, but again, because this is significant both in terms of the substance and what he's saying he's going to do with it, I'm going to go on the record for a second time and say we're going to need more time with him.

THE WITNESS: I'm just going to respond. If that's the case, why don't you decide -- if you want more time, then let's adjourn, and you can pick up when you're ready because my time is very limited. So if you're going to reserve other time, that's fine. Make your decision. You get 7 hours under the federal rule. I'm respectful of the two sides agreeing to 10. I'm prepared to stay here throughout the night.

But if you're not ready to take this deposition -- this is just -- this just is part of my -- this is just supplement. Just so there shouldn't be any mistake, this just supports the opinions in my report.

If you are gaming for more time, if you don't think 10 hours is enough time, then please adjourn, go talk to the Court, get that solved and call me back when you are ready to depose me. I just don't have endless time. I just want to represent to you,

Counsel, I'm prepared to stay here throughout the night. I think that 10 hours gets to be excessive, but I'm prepared to stay here.

But if that's not enough for you, Counselor, then let's adjourn right now, and we'll pick up when you're ready.

BY MS. HARDWAY:

Q. We're going to continue with the deposition today and tomorrow, if necessary, to complete the 10 hours. In terms of additional time that we're going to be seeking, we'll seek it when -- at the appropriate time and get however much time we're going to get, and we'll be together again at some point in the future.

A. I just want the record to show it's my understanding, just so we're on the same wavelength, is because I have meetings tomorrow, you know, I am prepared to sit here as late as you want to complete your 10 hours. I just want to make sure because I requested from counsel everyone is aware that there should be enough court reporters and videographers to last as long as you would like, but I'm prepared to do this because I would like to be at those medical meetings tomorrow in this town.

If I can't because the 10 hours is not yet

completed, I will stay here, but I'm going as long as humanly possible if you want 10 hours. So just make sure there's court reporters and videographers and enough coffee for everybody.

MS. HARDWAY: And respectfully, Dr. Kessler, because of the time limit that I have, at least at this sitting, I would ask for you to refrain from some of these longer answers and speeches because we're going to be here -- we're going to ask for even more time if your answers are not specific to the questions, and I would ask that you refrain from giving speeches and instructions because that's just really taking up unnecessary time.

MS. SCANLAN: Objection. You asked him a question about what he intended to do separate from here before trial, and he gave his answer. You have to allow him to give his answer to the fullest extent possible.

MS. HARDWAY: He just gave a speech about adjourning and about how long we're going to go today. So I'm, again, not going to waste time with that.

Have you had a chance to mark that exhibit yet?

(Deposition Exhibit 3 was marked for identification.)

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BY MS. HARDWAY:
Q. Is this the only copy you brought, Dr. Kessler?
A. No. There should be one other that -- there's one other copy.
MS. LERNER: On the record, I just want to confirm that you are not retreating on what was memorialized in correspondence, I believe -- I don't have it in front of me, but between John Macoretta and Lisa Dykstra that this deposition would go on until Dr. Kessler said he could no longer go on for 10 hours or until Dr. Kessler says, "I can't go on." I don't think he got an answer to his question.
MS. HARDWAY: Yeah, that's fine.
MS. LERNER: Okay. Great.
BY MS. HARDWAY:
Q. Towards the end of your report, Dr. Kessler, there's an issue timeline. It's Appendix D?
A. Yes. Can we just roll it out, please.
MS. HARDWAY: I'm going to mark this separately as Exhibit 4.
(Deposition Exhibit 4 was marked for identification.)
BY MS. HARDWAY:
Q. Did you personally prepare these materials?

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A. I'm graphically challenged. So the answer is no. As you can see, I am not capable of doing these. These were done under my direction, but as the -- as like some of the schedules, these were done subject to my direction and review.
Q. Do you plan on using this timeline or any of your other schedules as exhibits or demonstratives at trial?
A. It's not my choice, Your Honor -- Your Honor, sorry. Counselor. It depends on what counsel decides to do. The purpose of these are to objectively just make it easier, as we're talking today, to be able to have facts in front of us. I think the matter is of -- again, of such importance that I think as complete a record. But as you know, counsel gets to ask the questions and decides what demonstratives. I don't.
MS. HARDWAY: Appendix C of your report is a list of materials provided. I'm going to mark this separately as Exhibit 5.
(Deposition Exhibit 5 marked for identification.)
BY MS. HARDWAY:
Q. Did you review each of the documents in this list?

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A. Define the word "review." There's some -- probably tens of millions of pages. I have all of this material on hard drives. I've searched these hard drives, but I have not -- I make no representation that I have read every single page. It would be beyond human possibility to do that, but I wanted, again, to make sure that these materials were searchable for me and that I was able to consider this.
Q. So when you say, "database," what is it that you're referring to?
A. Well, some of these documents are, as you know, produced by you. They go into a database that I can sit in front of a screen, and more specifically, I have a hard drive, and I have these documents in OCR format, and they are searchable.
Q. What percentage of these documents would you say that you've reviewed?
A. I wouldn't want to -- I couldn't give you an estimate. I can tell you that 100 percent gets searched but that I don't -- certainly there's -- I think there's -- I have the record. I think there's 37 gigabytes. You can translate to how many pages that is.
Q. With that appendix, as well as the

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materials -- or the errata and additional list of materials provided that you gave us today, would that be everything that you've reviewed in this matter?
A. So the intent -- yes. With the caveat that I always -- there's always a chance that I was on-line looking at things on PubMed or on the FDA website, or even on the database that I may have seen that I can't -- you know, when you get back certain searches and you're scrolling through things, but I think that that reflects the four corners of what I consider sort of a reliance list or a considered list.
Q. There are a list of depositions in Appendix C. Did you review all those depositions?
A. So, again, some of them I read. All of them I searched. And, again, I tend to put these things -- either search them through a hard drive, through a root directory or sometimes a combined binder, as it's called in Adobe.
Q. Are there specific documents that you requested from counsel?
A. Oh, sure. I mean many of these are large documents, and so there are many documents that I requested from counsel.
Q. Are there any specific categories of documents that you requested from counsel that you can

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recall?
A. Oh, sure. I mean the regulatory files. The BLAs, et cetera. Oh, FDA correspondence, FDA internal documents. I asked for all those documents. I asked for all the depositions. I asked for all the -- I asked for all those documents.
Q. Any other documents or categories of documents that you recall requesting?
A. Oh, I mean on certain subject areas there certainly were substantive areas within this that are in my report that I may have asked for. So there are numerous documents that I requested.
Q. Anything that you reviewed or relied on, prior to forming your opinions in this case, that is not listed either in Appendix C or in Exhibit 2?
A. I tried to be comprehensive. Not that I can recall.
Q. When were you first contacted about this litigation?
A. May, 2015.
Q. Who contacted you?
A. Kathleen Scanlan.
Q. Did you begin working on the case in May of 2015?
A. I don't want to waste your time, counselor,

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to ask you what you mean by working on the case. I took that as a -- from the first phone call, that that was a -- privilege would attach, and I didn't agree. You know, certainly -- so that's when -- I guess "working on," but it depends how you define "working on."
Q. Let me ask you this: When did you agree to be an expert witness in this case on behalf of relators and plaintiffs?
A. So I mean I guess the answer to that question is the day -- again, you asked when did I agree? Sometime between -- I mean I'm not sure I can point to a specific time. I considered the matter. I considered myself bound by privilege from that beginning in May 2015. I may not have considered -- I may not have, in my own head, considered to be an expert witness in this matter until I signed my report.
Q. So you had not agreed to be an expert for relators and plaintiffs until you signed your report in 2018?
A. I certainly didn't bind myself to certain opinions until I signed my report.
Q. That wasn't my question. My question was when did you agree to be an expert witness and provide

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expert opinions on behalf of relators and plaintiffs?
A. When I had my -- well, again, maybe it's semantics. I'm not sure I can answer that question exactly. I mean my sense was when I signed my report, then I had my opinions formed, and then I was, in essence, committing to testify, as I understand the process. But I considered myself bound from the first time we talked, but certainly from the first time I talked, I didn't have any opinions. I didn't know whether I would testify or what I would testify about or whether I was willing to testify. So I didn't know that from the first call.
Q. So when did you know that you'd be willing to testify and provide opinions in this case?
A. Well, when I signed my report.
Q. So up to that point in 2018, you did not know whether you were going to be providing opinions or testifying in this case?
A. You never -- until I am sure of what my opinions are, until I finish the process, I'm not sure of anything, ma'am.
Q. Did you -- when did you agree to be -- let me ask you this: When did you start drafting your report?
A. I don't know exactly. My guess is somewhere

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less than a year before I signed it. Probably the actual draft date.
Q. Was it your intent -- so that would have been in 2017 that you began drafting your report?
A. That would be accurate.
Q. And in the first half of 2017?
A. Probably more toward latter part of 2017, but I don't have it exactly.
Q. When you began drafting your report in 2017, was it your intention to provide opinions in this case, expert opinions?
A. Again, I think I've answered your question, Counselor.
Q. I don't think you have, Dr. Kessler. I'm asking you when -- this is now the third time, I think, that I've asked this question.
A. Third time I've answered it, Counselor.
Q. I disagree.
What I'm asking you, Dr. Kessler, is when you started drafting your report in 2017, was it your intention to offer expert opinions in this case?
MS. SCANLAN: Objection. Asked and answered.
THE WITNESS: My intention to offer expert opinions was on the date -- that was when I had a formal intention to do that, when I signed my report,

as I stated.
BY MS. HARDWAY:
Q. Have you ever worked with relator's counsel before?
A. I'd have to go back and think about that. I don't recall whether there were any whistle blower -- whether there were any whistle blower matters that I've testified in to -- as an expert that -- I mean, for example -- I just want to be careful. I've testified in Philadelphia and in California on a certain matter, and I know they were tangential whistle blowers, but I don't believe I was involved in those relator cases, but they were relator cases that were attached to those. So I'd have to do the homework to make sure I'm exact -- answering your question exactly.
Q. And I'm not limiting to whistle blower cases. I'm just asking whether you've worked with relator's counsel on any case before?
A. I'd have to go back and check.
Q. And same question for private plaintiff's counsel. Have you ever worked with private plaintiff's counsel before?
A. Define "private plaintiff counsel," if you'd be so kind.

Q. Some of the lawyers sitting in this room or people from their firm.
A. Oh, I'm sorry. Have I worked with these folks before, these specific lawyers before?
Q. Yes, or their firm.
A. Their firm. I don't recall. I've not worked with Keller Grover before. I have -- I may have been involved in a matter -- certainly I was involved in tobacco with Robins Kaplan going back decades, and there may have been other matters with Robins Kaplan.
MS. LERNER: And to the extent that those matters are sealed and are not public, I would just caution Dr. Kessler not to divulge anything that may not be public.
BY MS. HARDWAY:
Q. Prior to the phone call that you got in 2015 from Ms. Scanlan, did you have any knowledge of the claims that were being brought in this case?
A. No.
Q. Do you have a financial stake in the outcome of this litigation?
A. No, nothing whatsoever.
Q. Did you interview or speak with anyone other than relator's counsel before preparing your opinions in this case?

A. I speak to a lot of people.
Q. Did you speak to anybody, other than relator's or private plaintiff's counsel, about your opinions in this case prior to forming those opinions?
A. About my opinions, no.
Q. Do you know Dr. Norman Baylor?
A. I know of him from reading his report and from reading documents and E-mails that are -- that were produced in this matter. I don't believe -- I don't remember meeting Dr. Baylor, but I think he probably goes back when he joined the agency, from his CV. I think I looked that up. I don't recall.
Q. He was at CBER during the relevant time period; right?
A. I'm talking about whether -- you're asking me whether I met with him, whether I knew him. So my relevant time frame to that question was when I was there. So the question is was he there when I was there, to answer your question, but I don't recall meeting him.
Q. So since you don't recall meeting him, you don't have a personal opinion about Dr. Baylor?
A. I have a professional opinion about Dr. Baylor.
Q. What is your professional opinion?

A. So my professional opinion, based on what I've read, is that there were certain -- again, maybe "professional opinion" is too strong a term. There's some E-mails that strike me as -- what's the right word -- as concerning. There's one in particular that strikes me as concerning. Let's say it that way.
Q. What E-mail is that?
A. Well, there's an E-mail, and I think it's an E-mail -- it's a Merck E-mail. It's actually cited in my report, where he says -- actually, let me get it so I can be exact, please. I'm just looking at my report, and I'm just going to search so I can quote it exactly.
So there's an E-mail -- it's in Paragraph 251.7 of my report. I guess it's Keith Sherwin at Merck to himself. So this is a Merck document, to be fair. This is not Dr. Baylor writing it, but it's Dr. Baylor -- it's referenced to Dr. Baylor. And so, again, I can't represent these facts are correct. Others would have to determine that.
But he says from his perspective, and in there -- I assume that goes to the prior sentence of Norman Baylor. By having this filing plan submitted with risk assessment -- this is Merck's filing plan --

this allows CBER to just come back and say that they would concur with the plan and allows them to be silent on the label noncompliance issue. That strikes me as concerning.

Q. Why does that strike you as concerning?

A. Well, if anyone wants to be -- if an FDA official at the time is talking about being silent on noncompliance with the statute, I think that's concerning. Now, again, I'd want to be very careful that -- and make no aspersions, but you're asking me questions about why that's concerning. Again, this is not Dr. Baylor saying this. This is Merck saying this and representing. But if one is talking about being silent about noncompliance with the Act, that's not the way I would consider an FDA official to act.

Then he goes -- "Norm Baylor, somewhat nervous. We will need to do some negotiation internally." That actually is -- can someone pull the actual document for me because there's a typo in that. If you look at that underlying document in my report, I know I made a typo in there. If you'd pull the underlying document. He's saying, yes, check with compliance. He's somewhat nervous about that, but I would not expect Merck to say -- of an FDA official to say that we can be silent on an issue of -- on a

noncompliance issue.

Merck gets us this, and that allows us to be noncompliant. So that, obviously, just needs to be looked at, but that would be concerning.

Q. Anything else regarding your professional opinion about Dr. Baylor other than this particular E-mail that you just referred us to?

A. That's the one that strikes me for the moment. I mean there were other E-mails that I've looked at, and I'm sure other things may jog my memory. Let me just make sure because there is an error in my transcription of that.

It says, "and be somewhat nervous and will need to do some negotiation internally." So why is he -- he's nervous, and he's going to need to negotiate about a Merck issue internally, and he's going to be silent on noncompliance. Again, this needs to be explored.

Q. Do you know Peter Patriarca?

A. Not personally, I don't believe. I may have met him.

Q. Do you have a professional opinion about Dr. Patriarca?

A. I have no opinion.

Q. Do you know Bruce Burlington?

A. I do.

Q. Do you have a professional opinion about Bruce Burlington?

A. I appointed Bruce, I believe, to several positions. I hold Bruce in -- not that we agree necessarily on matters, but I certainly hold Bruce in high personal regard.

Q. Do you know Kathy Carbone, Dr. Kathy Carbone?

A. I don't know if I've ever met her. I don't -- sitting here, I can't tell you one way or the other.

Q. You'll agree that Dr. Carbone is in regular contact with Merck on issues related to its stability testing of MMR; correct?

A. For a certain period of time. I believe she left the agency at a certain point in time.

Q. And you agree that she evaluated data for both MMR II and Proquad; right?

A. In certain regards. She was, in essence, the medical review officer, yes.

Q. And you'd agree that she's an expert on both mumps and the mumps vaccine?

MS. SCANLAN: Objection.

THE WITNESS: Yeah. I think as any physician -- again, I have nothing -- no challenge to

Dr. Carbone's knowledge, but no physician is going to be expert on all matters, on all molecular biology matters, on all compliance matters. There's certainly things that I would take significant issue with her in her E-mails but -- as I read them.

But, again, I don't have the ability to talk to her. So I don't know what she knows or knows about the issues that I would want to raise with her about what she's written.

BY MS. HARDWAY:

Q. Dr. Kessler, my question was whether you'd agree that she's an expert on both mumps and the mumps vaccine.

MS. SCANLAN: Objection. Asked and answered.

THE WITNESS: I understand that's your question.

BY MS. HARDWAY:

Q. And what is your answer to that question?

A. Exactly as I said. I'd be happy to repeat it. I think she's expert on certain aspects of the mumps vaccine. I don't think she -- from what I can tell, I don't think she's expert on all aspects of the mumps vaccine.

Q. Do you have an opinion about Dr. Carbone or her work at CBER?

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MS. SCANLAN: Objection. Compound.
BY MS. HARDWAY:
Q. Do you have a professional opinion about Dr. Carbone?
A. I'm thinking, Counselor. You asked your question. I'm thinking.
Q. I was restating it so as not to make it compound, Doctor.
A. Thank you. I'm happy to talk to you about Dr. Carbone's opinions. I don't have a general -- I don't have a general overview opinion that I think would be fair of her in general. I think I'd be happy to talk to you about specific statements that she made and whether I think those are right. Were they on target, whether they're wrong. But I think we'd have to discuss individual statements to be fair.
Q. Do you know Steve -- Dr. Steve Rubin?
A. I don't believe -- I know of him, certainly.
Q. And Dr. Rubin evaluated Merck data for both MMR and Proquad; correct?
A. Sure.
Q. Would you agree that he's an expert on mumps and the mumps vaccine?
MS. SCANLAN: Objection.
THE WITNESS: He's certainly expert on

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certain aspects of the mumps vaccine. He has national reputation on certain aspects of the mumps vaccine, yes.
BY MS. HARDWAY:
Q. Do you have a professional opinion about Dr. Rubin?
A. Again, I have certain -- in this matter? Are you asking me specifically about in this matter?
Q. I'm just asking if you have a professional opinion about Dr. Rubin.
A. Yeah. Again, there are certain things that I find striking in the database that concern Dr. Rubin, but I don't think it goes to his -- I don't form a professional opinion about it. But there are certain things that are striking in this matter that concern Dr. Rubin.
Q. What things are striking that concern Dr. Rubin?
A. So there's a -- this is an E-mail that's August -- dated August 24, 2011 from Dr. Rubin to David Krah, and they're talking -- I mean these are two scientists talking to each other, and in the CBER tradition they're being colleagues. I respect that, but Rubin is a scientist, he's not -- I mean he's talking as a scientist to a scientist, and I respect

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this.
And when he's talking about looking at the effectiveness of the vaccine induced immune response, again, the vaccine strain. And he's saying this would not be an acceptable practice to David Krah for measuring vaccine immunogenicity as a surrogate for efficacy in a clinical trial. Given that we are not interested in the protection against vaccine virus exposure -- of course they're talking about they're interested in vaccine, again, exposure against circulating virus, the reality of today. Instead a wild type will have to be used.
Many years ago Merck argued for use of a -- it says, "Many years ago Merck argued for use of a low passage version of JL," Jeryl Lynn, "in such an assay, and we accepted (not my decision. I would not have been in favor of stacking the deck)."
So, you know, this whole matter, I mean certainly the whole agent test, the whole wild-type ELISA deals with a significant part of this matter in assessing whether in fact Merck studies were done under a low passage strain. And the JL135 -- again, it's a Passage 7 or something like that strain, and that all these tests -- some of these tests, not all of these tests, there were other earlier, preliminary

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tests done against other strains, he's saying, that doesn't have anything -- that's not the way you test effectiveness. Merck argued to use this -- a low passage strain. I would not have done that. That doesn't measure effectiveness. The agency approved that.
So I guess my question to Dr. Rubin -- and I understand he's the scientist -- if you didn't think this was appropriate that this agent test or these -- the JL 135 were not a measure of wild type, which they are not -- right? I think we can agree on that, because they have low passage -- why did you allow that? He says, "Well, it wasn't my decision." The question is whose decision was it.
So my sense is he's in the role of scientist letting other people make decisions on the regulatory, certainly, in this matter. He's signing off on other things. I think people are representing that he made certain approval decisions. But he's clearly saying it makes sense you would never use a low passage strain in your serological tests if you wanted to test effectiveness. So what's going on here at CBER and with Merck? I don't know. Others can figure that out.
Q. Anything else that's striking that concerns

Dr. Rubin?
A. Again, he's basically saying there are decisions being made that I would not have approved. So, again, that just opens questions to me.
Q. And you're referring to that one E-mail?
A. His E-mail to David Krah, yes. And that's not fair. I have looked at a lot of other E-mails of him with David Krah and back and forth where they're talking scientist to scientist. They're talking as colleagues, not as regulator to regulator.
Q. Are those E-mails that you have issues with, Dr. Kessler?
A. It's a longer discussion.
Q. Well, let me withdraw that question.
Are there any other E-mails specifically that you can think of, as you sit here today, that concern you that were authored by Dr. Rubin?
A. Concern, maybe not. I mean there is a -- I think when you look at the totality of the E-mails when I went back and I tried to search for the correspondence, you can see them in both the data you produced and the documents you produced and in the FDA FOI documents.
I think -- again, this is one of the issues with CBER and the long-standing issues with CBER.

CBER was set up at the National Institute of Health campus. It was the biologics center, and there were scientists who had their own laboratories who became national experts, world class experts in their respective fields, and they may be narrow fields, but they were world class. And CBER had a tradition of allowing them to be involved in the regulatory decision.
That model came under significant criticism over the last two decades because they were acting as scientist to scientist, and if you and I are acting as colleagues, then what role do I have as a regulator. So you see this familiarity or this sort of symbiotic relationship, which is appropriate scientist to scientist and is good and may have a role for the FDA because you want the FDA to have the knowledge and the science. So you want their scientists.
But there's a blurring with CBER between regulator and colleague with the regulated industry, and I think that's -- again, one can have different opinions on whether that's a good thing or not a good thing. And, again, that's part of a longer discussion, but you see that relationship between Dr. Steve Rubin and David Krah.
Q. Both Drs. Carbone and Rubin have published

extensively on mumps and the mumps vaccine; correct?
A. I've seen articles -- I've certainly seen Dr. Rubin has published extensively. Dr. Carbone's name has been on a number of those articles.
MS. HARDWAY: I'm going to show you what we're going to mark as the next exhibit.
(Deposition Exhibit 6 was marked for identification.)
MS. SCANLAN: Kathleen, we've been going for an hour and 15. So at some point if you want to plan a break.
MS. HARDWAY: All right. Just a couple more questions.
MS. SCANLAN: Sure.
BY MS. HARDWAY:
Q. Exhibit 6, Dr. Kessler, is a collection of at least some of the peer-reviewed articles and textbook chapters authored by Drs. Rubin and Carbone. Do you see that, the index at the front there?
A. Yes, I do.
Q. And these are peer-reviewed publications; correct?
A. Probably Plotkin's vaccines. Certainly the books are not peer reviewed, but some -- I assume the majority of these are peer reviewed. We can go

through them, but some are clearly not.
Q. Do you recall seeing at least some of these publications prior to forming your opinions in this case?
A. Yes, ma'am.
Q. Do you know Dr. Suresh Rastogi?
A. I don't believe I know Dr. Rastogi. I don't believe I know Dr. Rastogi.
Q. He's a biostatistician at CBER?
A. Again, I don't recall.
Q. Do you have a professional opinion about Dr. Rastogi?
A. I do not.
MS. HARDWAY: All right. We'll go ahead and take a break.
THE VIDEOGRAPHER: We're going off the record. This is the end of Media Unit No. 1. The time is 10:40 a m.
(A recess was taken from 10:40 a m. to 11:00 a m.)
THE VIDEOGRAPHER: We're back on the record. This is the beginning of Media Unit No. 2. The time is 11:00 a m.
BY MS. HARDWAY:
Q. Dr. Kessler, earlier we were talking about

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Dr. Bruce Burlington, and I'm not sure if I asked you this question. Do you have a professional opinion about Dr. Burlington?

A. I think you asked me that question, and I think I said Bruce and I may agree and disagree on certain issues, but I appointed Bruce. I think my answer was I hold him in the highest personal regard. I think it's probably fair to say I hold him -- in general, I respect Bruce certainly in a professional capacity, not that -- that doesn't mean we would agree on all issues, et cetera.

Q. Are you being compensated for your work in this case?

A. I am.

Q. Are you being reimbursed for expenses related to preparing for and attending this deposition?

A. Yes.

Q. What did you do to prepare for your deposition today?

A. Just read a lot of materials.

Q. Just read a lot of materials?

A. Read a lot of materials.

Q. About how many hours did you spend reading materials to prepare for your deposition?

A. I don't know exactly. I don't have that in

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my head.

Q. Is it more than 50 hours?

A. Potentially.

Q. More than 100 hours?

A. It's possible. I don't know the answer to that question.

Q. Is it more than 200 hours?

A. Probably not, but again, I don't know the answer to that question.

Q. Did you meet with counsel to prepare for your deposition?

A. I did.

Q. About how many hours did you meet with counsel to prepare for your deposition?

A. I don't know exactly. I came yesterday. I insisted on watching TV most of the time. So I don't know whether you'd consider that meeting or not meeting. I don't know exactly. But, again, we've had -- again, we've had conversations since my report was signed.

Q. About how many hours have you spent having conversations with counsel after your report was signed prior to today?

A. Oh, probably -- I don't know exactly. Probably several dozen is my guess, but I don't know.

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Q. Several dozen hours?

A. I'm sure.

Q. Which attorneys have you spoken with since your report was signed?

MS. SCANLAN: Objection. Vague and ambiguous.

THE WITNESS: Which attorneys? I think the three attorneys -- four attorneys sitting here today I've had conversations with.

BY MS. HARDWAY:

Q. Who did you meet with yesterday?

A. So yesterday, Sarah and Kate. Again, came, tried to get my attention, pretty much unsuccessfully.

Q. Have you agreed to testify at trial in these matters?

A. I think the answer to that -- no one has asked me that question specifically, but my sense is the answer to that is generally yes. You going to trial?

MS. HARDWAY: I'm going to mark the next exhibit, which is your CV.

(Deposition Exhibit 7 was marked for identification.)

MS. HARDWAY: Exhibit 7.

Q. Is your CV accurate and up to date?

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A. My CV is never accurate or up to date. There's always errors or dates that are wrong, and it's always a little behind. And I'm sure this is behind. At a certain point I just stopped putting things on my CV.

Q. When did you stop putting things on your CV?

A. Whenever I did this -- I don't know what version this is, but there's a certain number of pages, and you just sort of stop. So I'm not -- it's generally accurate. I'm being a little flip. I apologize, Counsel. I'm just saying there may be dates that are not exactly correct here, things that maybe -- to the present that are a little old. No. This looks pretty -- this looks pretty right, but there may be other things that are not on here.

Q. Does this include all of your relevant experience?

A. No. I mean I've had experience in these matters for some 40 years. So is everything listed, no.

Q. Does it include all of your education?

A. Yes. Formal education, yes.

Q. Does it include all of your specialties?

A. I think so. Well, include specialties, I don't know what that means by that question.