

Friday, 10 July 2009

To All:

The text following this page is a draft response to the FDA's: "**Thimerosal in Vaccines Questions and Answers**", last updated 1 July 2009, which was downloaded late on Tuesday, 7 July 2009 from:
<http://www.fda.gov/BiologicsBloodVaccines/Vaccines/QuestionsaboutVaccines/ucm070430.htm>

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This formal response, titled "**Draft Review of the FDA's: 'Thimerosal in Vaccines Questions and Answers'**," begins on the next page.

Introductory Remarks

First, to "*simplify*" this response, when portions of the article being reviewed are addressed in the review, the statements in this report will be quoted in a "Times New Roman" font.

Second, remarks by this reviewer, Paul G. King, PhD, are presented in indented text following the section of the article that is being reviewed.

In addition, this reviewer's remarks and suggested changes are in a dark blue "Georgia" font except, when he quotes: **a)** from or refers to any US or New Jersey statute or regulation, the text will be in a "Franklin Gothic Medium Cond" font or **b)** from other sources, the quotations will be in an "Arial Narrow" font.

When this reviewer quotes from statements made in the authors' article, this reviewer will use an italicized "Times New Roman" font; suggested corrections, if any, will be made in red.

Finally, should anyone find any significant factual error for which they have published substantiating documents, please submit that information to this reviewer so that he can improve his understanding of factual reality and revise his views and the final response.

Respectfully,

<ds>

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Draft Review of the FDA's: “Thimerosal in Vaccines Questions and Answers”

Introduction

The purpose of this review is to provide, where and as appropriate, an in-depth, fact-based, assessment of the FDA's statements presented in terms of the pertinent factual realities from the viewpoint of FDA's stated basis topic, “*Thimerosal in Vaccines*”. Thus, when the FDA's questions and answers veer from this reference frame, this reviewer has, in general, noted that either the question or the answer does not address the topic and proceeded to the next statement, question or answer, in the document.

However, this reviewer would be remiss if he did not point out that the original article is replete with the FDA's “interesting”, and carefully framed, questions as well as equally well-crafted answers that appear to be more Orwellian doublespeak¹ than honest discourse.

As disseminating false information to the public is illegal, this reviewer trusts that those in any government agency who receive a copy of this draft will independently: **a)** verify the accuracy of the statements made by the FDA or any other agency cited by the FDA and **b)** actively seek to correct any FDA statement that they confirm is inaccurate or false.

Finally, at times this document makes strong assertions. However, this reviewer has attempted to make objective assessments based on the facts, as he understands them.

¹ Doublespeak is “a deliberate, calculated misuse of language in which a statement is intended to do one or more of the following:

- mislead
- distort reality
- pretend to communicate
- make the bad seem good
- avoid, or shift, responsibility
- make the negative appear positive
- create a false view of factual reality
- limit, corrupt, and/or prevent thinking
- make the unpleasant seem attractive or tolerable, and
- create a disconnect between what is reality and what is being said, or not said”.

Thus, doublespeak can be viewed as a fusion of “doublethink” and “Newspeak”, constructs created by George Orwell in his book, **1984**. In Orwell's fictional world, using “doublethink”, the people could hold two opposing ideas in their minds at the same time without questioning the validity of either, and “Newspeak” was the official language used to express the ideas of doublethink. Thus, though Orwell never used the word “doublespeak” in **1984**, this reviewer will use the phrase “Orwellian doublespeak” to credit him for creating the etymological basis from which it was fashioned.

Table of Contents for the Review

The Review Headings	Page
1. The first important unasked question: “How does the vaccine maker prove its Thimerosal-preserved vaccines are safe?”	4
2. The second important unasked question: “Since: a. ‘Preservatives’ increase vaccine toxicity, b. Are <u>not</u> required in single-dose vaccines, and c. In 1986, 42 U.S.C. 300aa-27(a)(2) gave the U.S. FDA the statutory mandate to safen our vaccines, why hasn’t the FDA, charged with safening our vaccines: a. Complied with this mandate and b. i. Stopped licensing new vaccines that are <u>not</u> single-dose vaccines, and, <i>after giving sufficient notice to the vaccine makers</i> , ii. Revoked the existing licenses for all of the U.S. FDA-licensed multi-dose vaccines?”	11
3. The third important unasked question: “Why would the U.S. FDA, or any other governmental agency, knowingly allow Thimerosal, a highly toxic, bioaccumulation-mercury-based compound that is a known human teratogen, mutagen, carcinogen, and immune disruptor, to be added to any drug – much less to prophylactic vaccines given to our children or pregnant women?”	16
4. The fourth important unasked question: “Why, having been found, in 2003, by the U.S. Congress to be among the federal agencies that were ‘asleep at the switch’ concerning permitting any use of mercury in medicine, has the FDA <u>not</u> been: a) replaced by separate, focused, safety-only agencies for drugs, foods, nutritional supplements, medical devices, and clinical tests and b) charged with only protecting the health, financial and medical, of the American people?”	19
5. The fifth important unasked question: “Why is the FDA knowingly misrepresenting the mandate that Congress gave the FDA in ‘FDAMA 1997’?”	29
6. The sixth and seventh important unasked questions: “If the goal was set in 1999, as the FDA admits, why does any inactivated-influenza vaccine, which has to be reformulated and reapproved ‘every’ year, contain any level of Thimerosal whatsoever a decade later?” “Why has the FDA continued to license new suppliers of Thimerosal-preserved influenza vaccines after 1999, if the FDA’s goal were ‘eliminating thimerosal from vaccines’?”	34
7. The eighth important unasked question: “Why, by: a. Allowing deceptive terms, such as “preservative free” and “no preservative”, to be used on the label applied to the primary vaccine containers, and b. <u>Not</u> requiring all labeling, advertising, and each primary container of any Thimerosal-containing vaccine to prominently disclose the maximum mercury content of the vaccine dose or doses in that container (bottle, vial, syringe or other) is the FDA <i>knowingly</i> depriving each American of his or her constitutionally-guaranteed right to be able to give ‘informed consent’?”	41
8. The ninth important unasked question: “When it knows that, <u>unlike ingested</u> (eaten) mercury (where most [estimated as >75%] of the mercury in the foods we eat [e.g., fish] simply passes through the digestive system without being absorbed), injected mercury bypasses the digestive system’s mercury defenses and, when it is Thimerosal dissolved in a vaccine formulation, is readily transported throughout the body, then how can the FDA have so little real concern for <u>injected</u> mercury?”	43
9. The tenth important unasked question: “Why does the FDA expect anyone to believe the findings of any IOM committee named, “Immunization Safety Review Committee” reviewing the safety of Thimerosal in vaccines when they were hired and given their instructions by the CDC, the agency charged with promoting vaccines, given the “instructions” the committee received from the CDC directed it to make <u>no</u> recommendation that could threaten the status quo concerning the CDC’s vaccination programs?”	47
10. The eleventh important unasked question: “How can the FDA continue to tacitly and knowingly approve the injection of a Thimerosal-containing inactivated-influenza vaccine into pregnant women, when, since 1977, if <u>not</u> before, the FDA knew that, in retrospective studies, both topical Thimerosal and Thimerosal-preserved flu shots had been proven to be a human teratogen that caused serious birth defects in the offspring of women given a single flu shot (e.g., cleft palate, microcephaly, and pyloric stenosis) at hospital-adjusted rates up to 7 times the background rates for these birth defects?”	52

Table of Contents for the Review

[Continued]

The Review Headings [continued]	Page
<p>11. The twelfth and thirteenth important unasked question: “Why is the FDA failing to be truthful about the lack of proof of safety that the makers of preserved vaccines are required by law (21 CFR § 610.15(a)) to provide in their Biologic License Application (BLA)? “Why has the U.S. FDA <i>knowingly</i> continued to <i>illegally</i> license Thimerosal-preserved vaccines whose BLA did <u>not</u> contain proof of safety to the minimum standard (‘sufficiently nontoxic so that the amount present in the recommended dose of the product will not be toxic to the recipient, ...’) as required by law (21 CFR § 610.15(a))?”</p>	56
<p>12. The fourteenth important unasked question: “‘How can it be safe to give a Thimerosal-preserved flu shot to pregnant women when studies have shown that some of their unborn children, will, if they survive their initial <i>in utero</i> mercury poisoning, be born: a) prematurely, and b) with Thimerosal-induced birth defects?”</p>	59
<p>13. The fifteenth important unasked question: “Because the risk is related to, among other things, the dose and, <input type="checkbox"/> with: a. The CDC’s recommending that: i. Pregnant women get flu shots and ii. Currently, children from 6 months of age to 18 years of age get an annual flu inoculation, b. The CDC’s on-going refusal to even state a preference for the FDA-licensed “trace Thimerosal” vaccine and the “no Thimerosal” vaccines instead of the Thimerosal-preserved ones for pregnant women and children and c. The FDA’s on-going re-approval of the FDA-licensed Thimerosal-preserved vaccines without, at least, even adding an “indication” that states: “Not for Use in Pregnant Women and Children” or, at a minimum, “Not for Use in Pregnant Women”, the maximum mercury dose is increasing <input type="checkbox"/> so that a child born in 2003, a. Whose mother got a flu shot in pregnancy and b. Who received the current maximum number of injections of Thimerosal-preserved flu shots, may, <i>if nothing changes</i>, have received, by the age of 18, “twice” as much mercury from the flu shots alone as a child born in 1997, who gets <u>no</u> flu shots even though all of his early childhood vaccines were Thimerosal preserved, why is the FDA being knowingly deceptive here by focusing on the vaccines and <u>not</u> addressing the maximum dose issue at all?”</p>	63

The Review

1. The first important unasked question:

“How does the vaccine maker prove its Thimerosal-preserved vaccines are safe?”

“How does FDA evaluate vaccines to make sure they are safe?”

FDA's Center for Biologics Evaluation and Research is responsible for regulating vaccines in the U.S. Before new vaccines are licensed, they are tested *extensively* for safety in the laboratory, in animals, and in successive stages of human clinical trials called *phases*.”

When it comes to “**Thimerosal in Vaccines**”, the underlying subject of this question, all that this reviewer can accept from the preceding is:

- “FDA's Center for Biologics Evaluation and Research is responsible for regulating vaccines in the U.S.” and
- Before new vaccine formulations are licensed, the vaccines are required to be “tested for safety”.

Further, when the topic is “**Thimerosal in Vaccines**”, for Thimerosal-preserved vaccines, these pre-approval studies must include all of the applicable Thimerosal toxicity studies in which the applicable ~~no-observed-adverse-effect~~ levels (NOAELs) and the interspecies, intraspecies, and developmental scaling factors would be determined and the mechanisms of toxicity elucidated.

For Thimerosal-preserved vaccines, the preceding are required in order for the manufacturer/applicant to, as required by law (**21 CFR § 610.15(a)**), *unequivocally* establish the Thimerosal used as a preservative is “sufficiently nontoxic so that the amount present in the recommended dose of the product will not be toxic to the recipient”.

In addition, *for preserved vaccines*, the necessary toxicity and comparative toxicity studies for the preservative, the dose of preserved vaccine formulation, and the dose of formulation without the preservative would have to be conducted. Then, the NOAEL ^{maximum preservative level in vaccine formulation dose, human} would have to be determined for both sexes (male and female) in all age groups (i.e., all groups to which administration directly or indirectly is allowed) to meet this current good manufacturing practice (CGMP) requirement minimum of “sufficiently nontoxic ...” at the dose level, the CGMP requirement minimum under **21 CFR § 610.15(a)**. [Note: If the preservative, like, for example, Thimerosal, can form bioaccumulative metabolites (e.g., tissue-conserved mercury species in this instance) and other vaccines can be given concomitantly, then, the studies must evaluate the worst-case exposure from all pre-existing vaccines and the proposed new vaccine.]

To date, the FDA has produced no proof that the toxicity studies required to prove that each Thimerosal-preserved vaccine formulation met the legal safety requirement minimum that the “preservative used shall be sufficiently nontoxic so that the amount present in the recommended dose of the product will not be toxic to the recipient” (as required by **21 CFR § 610.15(a)** since at least 1973 [**38 FR** 32056, Nov. 20, 1973]):

- Were conducted by the manufacturer/applicant,
- Properly included in the manufacturer's/applicant's biologic license application (BLA),
- Fully available for inspection and review by the FDA (as required by **21 CFR § 601.2** since 1999 [**64 FR** 56450, Oct. 20, 1999])

The FDA has also failed to produce proof that the manufacture'/applicant' BLA met the preceding "preservative safety" requirement **before** the FDA licensed each Thimerosal-preserved vaccine formulation that it has approved since 1977 (as required by **21 CFR § 601.4** since 1977 [**42 FR** 4718, Jan. 25, 1977, as amended at **42 FR** 15676, Mar. 22, 1977; **42 FR** 19142, Apr. 12, 1977]).

Moreover, to date, neither the FDA nor the vaccine manufacturers have published the NOAEL levels for Thimerosal in each of their Thimerosal-preserved vaccine formulations to prove that "the recommended dose" of their vaccine "will not be toxic to the recipient".

In addition, under the same regulation, the safety studies for vaccine formulations containing bioaccumulative adjuvants, like the polymeric aluminohydroxy compounds typically used (where there is physical evidence of multi-year persistence of these polymeric adjuvants in the tissue near the injection site as well as established chronic activation of macrophagic layer of the immune system) should provide "satisfactory evidence that it" [the maximum level of adjuvant] "does not affect adversely the safety" [of the vaccine formulation] "...".

In other words, the firm applying for a vaccine license should determine the NOAEL_{adjuvant in the vaccine dose, human} and, in the case of multiple doses and multiple vaccines over an extended period, determine that the worst-case exposure added to all the other vaccines does not adversely affect the overall "vaccine safety" outcomes.

Sadly, few, if any, of the studies required seem have been done for either the bioaccumulative preservative Thimerosal or the bioaccumulative polymeric aluminohydroxy compounds used as systemic adjuvants. In fact, FDA CBER personnel have repeatedly testified that the manufacturers/applicants have neither conducted nor submitted (as required by **21 CFR 601.2(a)**) proof that they have conducted the scientifically sound and appropriate toxicity studies required to truly satisfy:

- a. The "preservative used shall be sufficiently nontoxic so that the amount present in the recommended dose of the product will not be toxic to the recipient" CGMP requirement minimum set forth in **21 CFR § 610.15(a)** for Thimerosal used as a vaccine preservative in a preserved vaccine formulation given to pregnant women and developing children, much less to all age groups approved to get the vaccine and/or
- b. The other "proof of safety" requirements set forth in **21 CFR 601.2(a)** for the maximum number of doses of all of the other licensed vaccines and the Thimerosal-preserved vaccines – required because all vaccines are known to interact with the immune system in a manner that each dose significantly alters each recipient's immune system in a manner that, at present, is difficult, if not impossible, to either predict or completely reverse.

Moreover, the FDA has neither provided nor referenced published studies that prove each FDA-licensed Thimerosal-preserved vaccine formulation licensed and approved for use contains an amount of Thimerosal "present in the recommended dose of" each Thimerosal-preserved vaccine that is below the amount that can be "toxic to the recipient" (**21 CFR § 610.15(a)**).

Furthermore:

- ❖ Under **21 CFR § 601.2(a)**, *since 1999*, "An application for a biologics license shall not be considered as filed until all pertinent information and data have been received by the Food and Drug Administration"; and
- ❖ Under **21 CFR § 601.4(a)**, "A biologics license shall be issued upon a determination by the Director, Center for Biologics Evaluation and Research or the Director, Center for Drug Evaluation

and Research that the establishment(s) and the product meet the applicable requirements established in this chapter”.

Thus, absent submitted proof of compliance with **21 CFR § 610.15(a)**, the preserved-vaccine’s manufacturer’s/applicant’s biologics license application (BLA) is incomplete and the FDA cannot legally license any preserved vaccine formulation. This is the case because, absent proof of compliance with 21 CFR 610.15, the named FDA directors cannot determine that “the product meet the applicable requirements established in this chapter” because **21 CFR § 610.15(a)** is one of the “applicable requirements established in this chapter” for Thimerosal-preserved vaccines.

Therefore, absent results from all of the applicable required toxicity tests (a set of NOEL values) that establish that a given Thimerosal-preserved vaccine formulation is “sufficiently nontoxic ...”, all that the FDA can *truthfully* say in regard to questions concerning “*Thimerosal in Vaccines*” is that said Thimerosal-preserved vaccine’s safety testing is incomplete – no matter what other *safety testing* has been conducted or how extensive that other “*safety testing*” may be.

Finally, since August of 2004, this reviewer has repeatedly formally and informally asked the FDA to provide the proof that the manufacturers of Thimerosal-preserved vaccines met the “sufficiently nontoxic ...” requirements set forth in **21 CFR § 610.15(a)** before the FDA licensed any Thimerosal-preserved vaccine formulation or drug product. As of 30 June 2009, the FDA has failed to provide or publish any such proof.

“When a new vaccine is first tested in humans, a sponsor (a vaccine manufacturer, academic investigator or other individual or organization) must first submit an Investigational New Drug Application to FDA. If data at any stage of clinical development raise significant concerns regarding the safety of the product, FDA may request additional information or may halt ongoing or planned studies.”

Given the weakness of the studies allowed by the FDA’s guidance for vaccine studies and the failure to require:

- a. The use of only a true placebo (i.e., sterile isotonic saline) in all safety studies;
- b. Comprehensive (full-pathology, effects, and gene expression) double-blind comparative safety evaluations in at least one vaccine-sensitive mammalian species (e.g., influenza vaccines in ferrets) over the animals’ normal lifespan;
- c. Comprehensive long-term double-blind adverse effects studies in human volunteers for at least 20 years with a post-approval commitment to track not less than 10 % of those in each recognized age group covered by the vaccine and matched (in distribution and age) by cohorts (of at least one-fourth the number in the vaccinated group for the first full year of post-approval use) who do not receive this vaccine; and
- d. True effectiveness studies where, *after determining that a group of volunteers post-vaccination “antibody titers” are at a level that provides disease protection*, this volunteer group is periodically exposed to the disease organism at the average interval between the historical peaks in the ebb and flow of the disease for an aggregate period of not less than 15 years (with at least 2 exposures prior to the granting of a license and the rest occurring after the vaccine has been licensed and approved),

this reviewer has little confidence in the manner in which vaccine safety studies are currently conducted.

“Phase 1 studies typically enroll less than 20 participants and are designed to look for very common adverse events.”

This reviewer notes that this “typical” plan is not appropriate for vaccines – especially, not for Thimerosal-preserved vaccines.

“Phase 2 studies may include up to several hundred individuals and are designed to look at the overall safety profile of the vaccine for local reactions such as redness and swelling at the injection site as well as general side effects that may occur with some vaccines such as fever. For *phase 3* studies, the sample size is often determined by the number required to establish efficacy of the new vaccine, which may be in the thousands or tens of thousands of subjects. *Phase 3* studies are usually of sufficient size to detect less common adverse events, such as those occurring at rates of 1 in 100 to 1 in 1000.

This reviewer notes that the FDA’s remarks here address, at best, tangential “*adverse events*” issues, but do not, in the context of “**Thimerosal in Vaccines**”, address the fundamental safety issues inherent in the use of Thimerosal as a preservative in a vaccine formulation (as required by **21 CFR § 601.15(a)**).

Further, without a fundamental determination that a single dose of a candidate Thimerosal-preserved vaccine “will not be toxic to the recipient”² using the applicable scientifically sound and appropriate pre-clinical toxicity testing during the “*Investigational New Drug Application*” phase of vaccine approval or prior phase of testing, how can the FDA, in good conscience, approve any subsequent clinical study (*Phase 1, Phase 2, or Phase 3*) in humans or approve post-approval study (*Phase 4*) until the manufacturer/sponsor/applicant has proven that said Thimerosal-preserved vaccine “will not be toxic to the recipient”?

“For vaccines given concomitantly with other vaccines under the routine immunization schedules, the safety of new vaccines typically is studied with concurrent administration of these other vaccines.”

To ensure that interactions are detected, the *Phase 3* studies should have a separate arm, at half the size of the vaccine only arm in which the persons to be inoculated have had all of the other currently recommended U.S.-licensed vaccines and half are also given all of the possible concomitantly administered vaccines. For preserved and adjuvated vaccines, to confirm vaccine safety, another arm, with one-third the number of U.S.-resident participants as in the main arm should, *in a random double-blind study*, be given an adjusted equivalent (in terms of “effectiveness”) vaccine formulation without the preservative or, if only an adjuvant is present, a the adjusted formulation without the adjuvant.

When both a preservative and an adjuvant are present, a third group with one-half the number as in the main study should be given an adjusted formulation without the preservative and the adjuvant. If the adjusted vaccine formulation without the preservative has a significant lower percentage of adverse events or less severe events than the formulation with the preservative, then the only formulation that may be licensed is the “no preservative” formulation.

If the adjusted vaccine formulation without the adjuvant has a significant lower percentage of adverse events or less severe events than the formulation with the adjuvant, then the only formulation that may be licensed is the “no adjuvant” formulation.

² Here, the term “recipient” means “any member of the most mercury-poisoning susceptible group of individuals for which an indication is being sought for a candidate vaccine.

If the adjusted formulation without both the preservative and the adjuvant has a significant lower percentage of adverse events or less severe events than the formulation with them, then only a “no preservative” and “no adjuvant” formulation may be licensed.

“In addition, FDA carefully reviews information on the manufacturing process of new vaccines, and testing is performed on individual lots for safety and potency. If product development is successful, the completion of all three phases of clinical development can be followed by submission of a Biologics License Application (BLA).”

Here, this reviewer generally agrees with the FDA, provided the submitted BLA contains, *at a minimum*, all of the required studies and reports that prove that the sponsor has met all of the applicable statutory and regulatory pre-licensing requirements for safety and effectiveness set forth for biological drug products, including, but not limited to, the applicable requirements set forth in **21 U.S.C. Chapter 9, 42 U.S.C., 21 CFR Parts 210 and 211, and 21 CFR Parts 600 through 680**, as well as made the appropriate commitments for *Phase 4*, post-marketing studies.

“Following FDA's review of a license application for a new indication” [and a determination by the FDA that the sponsor has met all of the applicable requirements for safety and effectiveness as set forth in **21 CFR § 601.4(a)**]“, the sponsor and FDA usually present their findings to an expert advisory committee in an open public meeting for comment and advice. The advisory committee provides advice to FDA on approval or disapproval. Vaccine approval also requires the provision of adequate information (labeling) to health care providers and the public on the vaccine's proper use, including its potential benefits and risks, and its indications and contraindications.”

Given the clear binding mandate set forth in **21 CFR § 601.4(a)** for safety and effectiveness and the limits on the use of administrative discretion that the 1988 U.S. Supreme Court decision ***Berkovitz v. USA*** (“Kevan Berkovitz, a Minor by his Parents and Natural Guardians Arthur Berkovitz, et ux., et al., Petitioners, v. *UNITED STATES*. Case No. 87-498. 108 S.Ct. 1954, 100 L.Ed.2d 531, 56 USL W 4549. (Cite as: **486 U.S. 531, 108 S.Ct. 1954**).”) established, the FDA cannot legally license a preserved vaccine **before** the manufacturer/sponsor/applicant has, *for example*, conducted and submitted all the required scientifically sound and appropriate toxicity studies required to prove that a Thimerosal-preserved vaccine meets the “sufficiently nontoxic ...” CGMP requirements set forth in **21 CFR § 610.15(a)** (in the formulation, for a single dose, in the most susceptible group of individuals for which a usage indication is being sought).

“The safety of new vaccines continues to be monitored following licensure in several ways. The Vaccine Adverse Event Reporting System, co-administered by FDA and CDC, is a national passive surveillance system for the collection of all reports of adverse events following vaccination.”

Again, the FDA’s “*for the collection of all reports of adverse events following vaccination*” is, in fact, a misrepresentation of the facts. This is the case because there is: **a) no** reward for a healthcare provider’s reporting a problem or nominal reimbursement for the reporter’s time, **b) no** penalty for: **i)** failure to report an adverse event, **ii)** inaccurately reporting an adverse event, or **iii) not** reporting or misreporting the outcomes when a problem occurs – as the following narrative confirms. Moreover, when live-virus-vaccines are administered, the disease cases that do occur are not reported to the CDC and/or the FDA as a disease incident for whatever virus was the cause.

“As a spontaneous” [sic; voluntary] “reporting system, VAERS has several limitations including under-reporting, incompleteness of reports,” [misreporting, incomplete or nonexistent diagnostic work-up, lack of long-term post-event patient tracking,] “lack of consistent diagnostic criteria, and the inability in most cases to establish a cause and effect relationship. VAERS is useful, however,

for raising ‘red-flags’ and subsequently generating hypotheses that can be tested further in controlled clinical trials or epidemiological studies.”

However, this reviewer notes that no epidemiological study can establish the toxicity risk of any vaccine or vaccine component. Thus, *contrary to the FDA’s statements concerning vaccine safety and epidemiological studies*, epidemiological studies are incapable of establishing that a component of a vaccine is “sufficiently nontoxic ...” to the standards set forth in **21 CFR § 610.15(a) – only scientifically sound and appropriate toxicity studies can meet this CGMP requirement.**

“As part of a post-licensure commitment, FDA often asks the manufacturer to conduct additional clinical studies (sometimes called *phase 4* studies), to further evaluate safety, and to provide this information to FDA in a timely manner. In addition, controlled epidemiological studies may be conducted using pre-established large-linked databases, which have improved ability to evaluate whether rare adverse events are caused by vaccination.”

Factually, controlled epidemiological studies using pre-established large linked databases can only estimate the statistical probability that there may be a link between: **a)** some input (a vaccine [e.g., the MMR-V] or vaccine component [e.g., Thimerosal]) or the level of that input (e.g., total Thimerosal dose by 7 months of age or level of varicella virus administered [in Proquad vs. Varivax]) and **b)** the statistical risk, at some probability level, for a given outcome (e.g., the risk of brain damage, tics, or seizures). Therefore, for vaccines, this reviewer finds that long-term (≥ 10 years) clinical “*Phase 4*” studies should be routinely required by the Center for Biologics Evaluation and Research (CBER).

“One such system is the Vaccine Safety Datalink, administered by the CDC.”

Since:

- Access to the Vaccine Safety Datalink (VSD) system is actually controlled by the organizations, typically HMOs, that have gathered and maintain the data and not the CDC;
- Qualified independent researchers have had only limited access to portions of the VSD and, as of June 2009, no access to the post-2000 files;
- The CDC claims to have “lost” the original datasets used by Verstraeten et al. of the CDC in their epidemiological studies;
- There is clear and convincing evidence that CDC personnel actively participated in the distortion of the original findings by iterative manipulations that violated almost all of the basic precepts of epidemiology; and
- The CDC has tried, using unsupported statements, misleading claims and lies, to discredit the few studies that independent researchers have been able to conduct using a portion of the VSD data collections even though these independent studies used the same methodologies as the CDC has used and were subject to rigorous peer review by the journals in which they were published,

this reviewer finds that the FDA’s use of the VSD as its poster-child example of “*pre-established large-linked databases, which have improved ability to evaluate whether rare adverse events are caused by vaccination*” particularly revealing.

In the case of Thimerosal-preserved vaccines, in 2007, an NIEHS report dated August 24, 2006 and titled “**Thimerosal Exposures in Pediatric Vaccines: Feasibility of Studies Using the Vaccine Safety Datalink**” discredited all of the epidemiological studies and their underlying databases, upon which the 2004 Institute of Medicine committee on “vaccine safety” relied, including the CDC’s published VSD studies.

In addition, Julie Louise Gerberding, MD, MPH, then Director of the Centers for Disease Control and Prevention (CDC), testified before Congress in 2007 that the types of epidemiological studies that have been conducted were not appropriate to address the issue of cumulative injected Thimerosal exposure (as the level of mercury exposure in the first months of life) [the putative “causal” inputs] and the risk of mercury poisoning in susceptible individuals (the outcome) – an outcome that, as has been done since the 1940s, been covered by various medical labels (e.g., autism, autism spectrum disorders, and pervasive developmental disorders).

In spite of the published expert report and Gerberding’s testimony, apparently aimed at:

- Discrediting the independent studies published in peer-reviewed journals by that have clearly established a statistically significant link between Thimerosal exposure level and the risk of certain neurodevelopmental disorders (which are recognized symptoms of sub-acute mercury poisoning) and
- Further discouraging independent researchers from trying to access and use the accessible older portion of the VSD or further use the VAERS database,

the FDA continues to use and reference these invalidated studies to defend the FDA actions and decisions as if they established “no proof of harm” when, *at best*, all the published studies did, and are doing, is provide biased evidence of “a lack of evidence of harm” – not, what is required, proof of safety.

2. The second important unasked question:

“Since:

- a. ‘Preservatives’ increase vaccine toxicity,
- b. Are not required in single-dose vaccines, and
- c. In 1986, **42 U.S.C. 300aa-27(a)(2)** gave the U.S. FDA the statutory mandate to safen our vaccines,

why hasn’t the FDA, charged with safening our vaccines:

- a. Complied with this mandate and
- b.
 - i. Stopped licensing new vaccines that are not single-dose vaccines, and, *after giving sufficient notice to the vaccine makers,*
 - ii. Revoked the existing licenses for all of the U.S. FDA-licensed multi-dose vaccines?”

“What are preservatives and why are they added to vaccines?”

Preservatives are compounds that kill or prevent the growth of microorganisms, such as bacteria or fungi. They are used in vaccines to prevent bacterial or fungal growth in the event that the vaccine is accidentally contaminated, as might occur with repeated puncture of multi-dose vials. Vaccines, both in the United States and throughout other parts of the world, are commonly packaged in multi-dose vials.”

These statements are misleading because many countries in Western Europe only permit the use of single-dose vials. Moreover, *before 2000*, Thimerosal was found at preservative levels in some single-dose vials and syringes for Thimerosal-preserved biological drug products where the multi-dose-vial formulation was Thimerosal-preserved.

“In some cases, preservatives are added during manufacture to prevent microbial growth; with changes in manufacturing technology, however, the need to add preservatives during the manufacturing process has decreased markedly.”

Currently, except to reduce costs, in the USA, all vaccine formulations can be manufactured without any use of Thimerosal and packaged in pre-filled syringes with needles to minimize dispensing time costs. Moreover, since, based on the chronic adult rat study in Mason (1971), the putative NOAEL injected Thimerosal, fetus or developing child for an injected Thimerosal-containing vaccine formulation is $< 0.0086 \mu\text{g}$ of Thimerosal /kg/day, this precludes the injection of any Thimerosal-preserved vaccine (containing nominally about $100 \mu\text{g}$ of Thimerosal/mL in): **a)** directly into any child or **b)** indirectly, into the fetus by injecting pregnant women, unless, *for a nominal injection of $50 \mu\text{g}$ of Thimerosal*, the child or fetus weighs $> 50/0.0086 \text{ kg}$ or $> 5,814 \text{ kg}$ (12,818 pounds [> 6.4 tons])!

“Preservatives have been used in vaccines for over 70 years. The requirement for a preservative in multi-dose, multi-entry vials” [for some vaccine formulations] “was placed into the Code of Federal Regulations (21 CFR 610.15) in January 1968.”

Factually, **21 CFR § 610.15** was first published as a final regulation in **21 CFR § 610.15(a)** in the Federal Register in 1973 (*see 38 FR 32056*, Nov. 20, 1973).

However, there has never been a requirement that that preservative must be Thimerosal and several other compounds or mixtures of compounds have been and are being used as preservatives in the June 2009 list of FDA-licensed vaccines as the FDA’s “**Table 2**” in:

<http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/VaccineSafety/UCM096228>, that this reviewer has updated to include more example vaccines below:

“Table 2: Preservatives Used in U.S. Licensed Vaccines”

[augmented by this reviewer to reflect 2009 realities]

Preservative	Vaccine Examples (Tradename; Manufacturer)
Thimerosal	TT (one) Human Inactivated Influenza (several) Sanofi’s multi-dose Menomune “meningococcal” vaccine Sanofi’s inactivated “avian influenza” H5N1 vaccine JE-Vax “Japanese encephalitis vaccine” distributed by Sanofi.
Phenol	Typhoid Vi Polysaccharide (Typhim Vi; Sanofi Pasteur, SA) Pneumococcal Polysaccharide (Pneumovax 23; Merck & Co, Inc)
Benzethonium chloride (Phemerol)	Anthrax (Biothrax; Emergent BioDefense Operations Lansing Inc.)
2-phenoxyethanol	DTaP (Infanrix; GlaxoSmithKline Biologicals) DTaP (Daptacel; Sanofi Pasteur, Ltd) Hepatitis A/Hepatitis B (Twinrix; GlaxoSmithKline Biologicals) IPV (IPOL; Sanofi Pasteur, SA)

“There are exceptions to this requirement for preservative, primarily involving the live-attenuated viral vaccines.”

Actually, with respect to preservatives, **21 CFR § 610.15** states: “Products in multiple-dose containers shall contain a preservative, except that a preservative need not be added to Yellow Fever Vaccine; Poliovirus Vaccine Live Oral; viral vaccines labeled for use with the jet injector; dried vaccines when the accompanying diluent contains a preservative; or to an Allergenic Product in 50 percent or more volume in volume (v/v) glycerin”.

Yet, nowhere in the FDA’s “regulations” is there a requirement that the preservative must be a compound that is a known highly toxic bioaccumulative human teratogen, mutagen, carcinogen, and immune-system disruptor at injected levels below 1 ppm, like, for example, Thimerosal (sodium ethylmercurithiosalicylate), phenylmercuric acetate, phenylmercuric nitrate, or phenylmercuric borate.

In fact, given: **a)** common sense, **b)** the 1987 statutory mandate to safen vaccines in **42 U.S.C § 300aa-27**, and/or **c)** the current best practical technology for vaccine production, all FDA-licensed vaccines should be not only free of Thimerosal (also known as Merthiolate) as a preservative but also all vaccines should only be licensed in a single-dose preservative-free formulation. This is the case because, *for a given basis formulation*, the preserved vaccine formulation causes more adverse vaccine reactions than the corresponding preservative-free vaccine formulation because all of the compounds used as preservatives are toxic to human cells.

For Thimerosal (also known as Merthiolate), the findings from:

1. Nelson EA, Gottshall RY. Enhanced toxicity for mice of pertussis vaccines when preserved with Merthiolate. *Appl Microbiol.* 1967; **15**: 590-593, in which the “abstract” reported (with underlining added for emphasis)):

“Pertussis vaccines preserved with 0.01% Merthiolate are more toxic for mice than unpreserved vaccines prepared from the same parent concentrate and containing the same number of organisms. ... An increase in mortality was observed when Merthiolate was injected separately, before or after an unpreserved saline suspension of pertussis vaccine”;

2. Fagundes A, Mauro MCA, Perez M, Schubach A, Ferreira A, Silva JP, Schubach T, Marzochi KBF. Skin reactivity to thimerosal and phenol-preserved Montenegro antigen in **Brazil**. *Acta Tropica* 2007; **101**: 25–30, which found (with underlining added):

a. “Abstract

A randomized double-blind trial was performed to determine the frequency of positive reactions to the Montenegro antigen (leishmanin) preserved in thimerosal (Merthiolate™) 1:10,000 or phenol 0.4%. The respective products were tested separately in 400 young healthy individuals from a non-endemic area for *Leishmaniasis*. Each volunteer received one of the following reagents: merthiolated antigen, phenolated antigen, merthiolated saline, or phenolated saline. The frequency of positive responses to each reagent after the first application was as follows: 0% (phenolated saline), 9.2% (merthiolated saline), 34.6% (antigen in phenolated saline), and 41.1% (antigen in merthiolated saline). After 1 week, volunteers who had tested positive for merthiolated or phenolated antigen were retested with the respective preservative, while negatives were retested with the preservative they had not received during the first test. In all, 331 volunteers who received merthiolated saline during the study, of whom 41 (12.4%) tested positive. Meanwhile, 326 volunteers who received phenolated saline, 4 (1.2%) tested positive. Positive reactions in each group were similar in relation to gross appearance skin reactions. Considering the high frequency of hypersensitivity³ to thimerosal in the study population, it is recommended that this compound should be replaced as a preservative ...”,

b. “3. Results

... Frequency of positive responses to each reagent following the first application was: 0% (phenolated saline), 9.2% (merthiolated saline), 34.6% (antigen in phenolated saline), and 41.1% (antigen in merthiolated saline).⁴ Of the 87 volunteers who presented positive skin tests, 83 in were re-tested, which includes 41 positive to merthiolated antigen in group I, 33 positive to phenolated antigen in group II and 9 positive to merthiolated saline in group III. Of the 41 volunteers who were re-tested with merthiolated saline, 13 (31.7%) were positive. Of the 33 volunteers who were re-tested with phenolated saline, only 1 (3.0%) was positive. Of the 9 volunteers in group III who were retested with plain saline, none were found positive. Two hundred fifty seven of the 313 volunteers who did not react were re-tested; 125/257 received merthiolated saline where 14.4% of them tested positive. The remaining volunteers (132/257) received phenolated saline, only a minority (2.4%) tested positive ($\chi^2 = 11.80$, $p < 0.001$). All these negative volunteers received each reagent only once, to avoid double application of any product in the same volunteer. ... Adding the tests and retests, 331 volunteers received merthiolated saline during the study, of whom 41 (12.4%) were positive, while 326 volunteers received phenolated saline, of whom 4 (1.2%) were positive.⁵ The frequency of positive reactions to saline containing thimerosal among those who received it once was significantly less than among those who received

³ According to the www.wikipedia.org definition [emphasis added], “Hypersensitivity (also called hypersensitivity reaction) refers to undesirable (damaging, discomfort-producing and sometimes fatal) reactions produced by the normal immune system.”

⁴ Based on this data, the effect of the Thimerosal was “additive” indicating the lack of a synergistic effect.

⁵ These data indicate that Thimerosal in sterile saline at 0.01% produced roughly 10 times as many reactions as phenol in sterile saline at 0.4%; presuming the relative “reaction” effects for Thimerosal are approximately linear up to 0.5%, at the 0.4 % Thimerosal level, the intrinsic “Thimerosal” effect is roughly 400 greater than the intrinsic “phenol” effect.

it twice (14.4% versus 31.7%; $\chi^2 = 6.22$, $p < 0.05$, the same was true for phenolated saline (2.4% versus 3.0%, $\chi^2 = 4.98$ $p < 0.05$). ...”, and

c. “4. Discussion

... The development of hypersensitivity reactions is associated with different exposure routes to allergens and is regulated by different immune mechanisms. Although 86% of the volunteers used topical thimerosal, none reported signs or symptoms of current or past allergy to the product, even though 12.4% of them showed post-test delayed hypersensitivity, which was unfamiliar to them. The intradermal antigen inoculation route is associated with the development of delayed hypersensitivity, while the topical use of subcutaneous inoculations usually triggers reactions of the immediate type, which are more easily perceived by the patient. The high frequency of delayed hypersensitivity to thimerosal, the similarity between the reaction induced by this compound and that elicited by the MST, the association between receiving thimerosal and the higher frequency of side effects to thimerosal (Table 3) indicate that this compound should be replaced as the preservative ... The low sensitivity induced by phenolated saline in our study (1.2%) and the rare occurrence of side effects associated with this reagent suggest that it could be used to replace thimerosal ...”, and

- 3.** Byatt, Henderson A. Preoperative sterilization of the perineum: A comparison of six antiseptics. *J Clin Path*, 1973; **26**, 921-924, a study of antiseptics, including Thimerosal, which reported:

- a.** “SYNOPSIS Nine preparations of six antiseptic substances were applied to the perineum of pregnant women at term in order to assess their efficacy in sterilizing the skin. The efficacy, in descending order of effectiveness, after three minutes' exposure, was p-chlor-m-xylenol in alcohol (surgical Dettol); chlorhexidine gluconate in detergent (Hibiscrub), followed by the aqueous preparations p-chlor-m-xylenol (Dettol), chlorhexidine gluconate (Hibitane), cetrimide (Cetavlon), povidoneiodine (Disadine), benzalkonium chloride (Resiguard), and merthiolate. Surgical Dettol was the only alcohol-based preparation used”, and

b. “

No. of Patients	Antiseptic	Average Reduction in Bacterial Population (%)
1	Dettol (alcoholic)	100
6	Hibiscrub (concentrated)	98
6	Hibiscrub (diluted)	82
6	Dettol (aqueous)	77
6	Hibitane	68
6	Cetavlon	63
6	Disadine	60
6	Resiguard	54
6	Merthiolate	28
Total 54		
54	Water as control	24

Table II Reduction in bacterial population after
Application of antiseptic for three minutes”,

clearly indicate that Thimerosal at preservative (0.01%) levels significantly increases the toxicity of vaccines and the incidence of adverse reactions as well as, even at 10 times higher levels (0.1%) in aqueous solutions similar to those of vaccines, kill a significantly lower percentage of the mostly bacteria on human perineal skin within 3 minutes of application (28%) compared to the other antiseptics tested in the same manner ($\geq 54\%$) and is only marginally better than water in reducing the bacterial population on perineal skin (24%).

“The general need for preservatives in multi-dose vials has been underscored by cases in which multi-dose vials that did not contain preservatives become contaminated during use and caused fatal infections in vaccine recipients; cf. the Narrative Section on Thimerosal.”

While there may be a well-documented “*general need for preservatives in multi-dose vials*”, the problems with the use of Thimerosal at levels of up to 0.01% (100 ppm) as that preservative in a vaccine formulation have been well documented, including in:

1. Stetler HC, Garbe PL, Dwyer DM, et al. Outbreaks of group A streptococcal abscesses following diphtheria-tetanus toxoid-pertussis vaccination. ***Pediatrics*** 1985; **75**: 299-303;
2. Winship KA. Organic mercury compounds and their toxicity. ***Adverse Drug React Acute Poisoning Rev*** 1986; **5**: 141-180;
3. Cox NH, Forsyth A. Thiomersal allergy and vaccination reactions. ***Contact Dermatitis*** 1988; **18**: 229-233; and
4. Digar A, Sensharma GC, Samal SN. Lethality and teratogenicity of organic mercury (Thimerosal) on the chick embryo. ***J Anat Soc India*** 1987; **36**: 153-159

as well as in:

5. The 2004 incident in which “finished packaged” multi-dose vials of now Novartis’ Fluvirion were found to be contaminated with *Serratia marcescens* and the British regulators suspended then Chiron's manufacturing license to make Fluvirion over concerns about its manufacturing practices at the Liverpool plant (see: http://www.usatoday.com/money/.../2004-11-12-flu-cover_x.htm]), and
6. On 30 June 2006, the FDA issued Sanofi Pasteur, Inc a warning letter that included the following (with underlining added for emphasis):
“INVESTIGATION OF FAILURES

1. Eleven Fluzone® (preservative formula and no preservative formula) monovalent concentrate lots manufactured between February 2006 and April 2006 failed sterility.

There were significant deficiencies in the investigation of these sterility failures”

(<http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2006/ucm075964.htm>)

Based on the findings published in preceding peer-reviewed publications as well as the relatively recent (2004 and 2006) incidents where Thimerosal-preserved vaccine was found to be contaminated with reproducing bacteria either in the packaged undistributed containers (2004) or, worse, in the “monovalent concentrate lots”, it is clear that the FDA’s assertion that Thimerosal is an effective preservative even at Thimerosal levels that are *nominally* not less than 0.01% is, *at best*, problematic.

3. The third important unasked question:

“Why would the U.S. FDA, or any other governmental agency, knowingly allow Thimerosal, a highly toxic, bioaccumulation-mercury-based compound that is a known human teratogen, mutagen, carcinogen, and immune disruptor, to be added to any drug – much less to prophylactic vaccines given to our children?”

“What is thimerosal?”

Thimerosal is a preservative that has been used in some vaccines since the 1930's, when it was first introduced by Eli Lilly Company. It is 49.6% mercury by weight and is metabolized or degraded into ethylmercury and thiosalicylate.”

First, this reviewer can only agree that sodium ethylmercurithiosalicylate (having the common U.S. trade names of Merthiolate and Thimerosal and, in the U.K, Thiomersal) has been used in the manufacture of some serums and “*vaccines since the 1930s*”.

However, the FDA is *knowingly* and *apparently intentionally* mischaracterizing the nature of Thimerosal here because:

1. Factually, Thimerosal, the current U.S. trade name for “ethylmercury thiosalicylate, sodium salt” or “sodium ethylmercurithiosalicylate”, is one of the many ethylmercury (alkylmercury; organic mercury) compounds that are highly toxic.
2. In aqueous solutions containing sodium chloride, Thimerosal slowly degrades first into ethylmercury chloride, ethylmercury hydroxide, and sodium thiosalicylate.
3. In the presence of oxygen, the sodium thiosalicylate molecules oxidize the thio groups (R-SH) on two molecules into the corresponding disulfide (R-S-S-R), which drives the degradation process [Kharasch (1932)].
4. In a solution containing proteins with thio (“-SH”) groups, both Thimerosal and the initial ethylmercury degradation products are complexed by these proteins slowly rendering the added Thimerosal and its initial ethylmercury degradation compounds ineffective as even bacteriostatic agents [Kharasch (1935)].

“At concentrations found in vaccines, it meets the requirements for a preservative as set forth by the *United States Pharmacopeia*; that is, it kills the specified challenge organisms and is able to prevent the growth of the challenge fungi.”

Contrary to the FDA's statement here Thimerosal at 0.01% (1:10,000; 100 parts-per-million [ppm]) does not kill bacteria. Factually, Thimerosal at 0.01% only stops microbial growth (all that is required of a chemical used as a preservative of the type used in vaccines by the USP).

Further, as Morton, North and Engley reported in their 1948 paper (Morton HE Jr, North LL, and Engley FB, Jr. The bacteriostatic and bactericidal actions of some mercurial compounds on Hemolytic streptococci: In vivo and in vitro studies. *J. Am. Med. Assoc.* 1948; 136: 37–41) even at the 0.1% level (10 times higher than the preservative level) only the Thimerosal (Merthiolate) tincture (Thimerosal dissolved in alcohol) solutions killed the bacteria on or in human tissue – and these tinctures were not significantly more effective antiseptics than the corresponding alcohol solution.

Thus, Thimerosal, at preservative levels in the aqueous-based vaccine formulations is only bacteriostatic and, over time, as Morton et al. found in 1948, the solution slowly loses its ability to stop bacterial growth in the presence of proteins containing thio (-SH) groups.

Finally, as the sterility problems *previously* reported in the published literature as well as, in actual vaccine product that had not been distributed (Chiron now Novartis Vaccines and Diagnostics Ltd [2004]) or not even blended into the final trivalent dilute vaccine formulation for packaging (Sanofi Pasteur, Inc, 2006), Thimerosal at nominal levels of 100 ppm (0.01%) in inactivated-influenza vaccine is, at best, a marginal preservative.

“Prior to its introduction in the 1930's, data were available in several animal species and humans providing evidence for its safety and effectiveness as a preservative.”

Here, the FDA is either: **a)** sadly mistaken or, worse, **b)** knowingly misrepresenting the facts. All of the valid toxicity data in animals showed that Thimerosal was highly toxic.

Moreover, these “*humans*” had meningitis infections before the first penicillin antibiotics were available and died shortly after being given their first dose or, *in one case*, shortly after being given a second dose, of Thimerosal. Without any autopsies and tests looking for evidence of mercury toxicity in the tissues, the doctors conveniently attributed the deaths of these “*humans*” to the disease. They did this even though Eli Lilly studies of Thimerosal (Merthiolate) toxicity in animals showed significant toxicity and death at relatively dosing levels.

Finally, no “*effectiveness*” claims, antiseptic or otherwise, were reported in the experiments performed on these ailing humans, who were experimented on without obtaining the patients’ or their families’ consent.

“Since then, thimerosal has a long record of safe and effective use preventing bacterial and fungal contamination of vaccines, with no ill effects established other than minor local reactions at the site of injection.”

Here the FDA is *knowingly* misrepresenting the facts (see: Geier DA, Sykes LK, Geier Mark R. A review of Thimerosal (Merthiolate) and its ethylmercury breakdown product – Specific historical considerations regarding safety and effectiveness. *Journal of Toxicology and Environmental Health, Part B* 2007, **10**: 575–596 – “**EARLY HISTORY OF THIMEROSAL**” pages 576 – 581).

“As a vaccine preservative, thimerosal is used in concentrations of 0.003% to 0.01%. A vaccine containing 0.01% thimerosal as a preservative contains 50 micrograms of thimerosal per 0.5 ml dose or approximately 25 micrograms of mercury per 0.5 mL dose. The use of mercury-containing preservatives in vaccines has declined markedly since 1999.”

The FDA is again *knowingly* misleading the reader. Factually, with the current CDC recommendations for annual inoculations for the inactivated-influenza vaccines for pregnant women and children 6 months to 18 years of age with no provision restricting the vaccines to those that are not Thimerosal-preserved, the maximum dose from the Thimerosal-preserved vaccines alone (425 – 450 µg of mercury {Hg}) will about double the fully vaccinated child’s total Thimerosal (mercury) dose over that from all of the Thimerosal-preserved vaccine doses that the CDC routinely recommended for children in 1999 (about 262.5 µg of Hg). In addition, if the child receives a multi-dose Menomune vaccine (25 µg of Hg), the 2 doses of the J-E Vax (35 – 70 µg of Hg), and, if allergic to the pertussis vaccine component, potentially 1 – 4 doses of the FDA-licensed Thimerosal-preserved DT vaccine (25 – 100 µg of Hg), the child’s maximum dose of Hg from Thimerosal could exceed 645 µg of Hg.

“FDA is continuing its efforts toward reducing or removing thimerosal from all existing vaccines.”

The FDA is again being misleading because it: **a)** has continued to license new Thimerosal-preserved vaccine formulations each year for the inactivated-human-influenza vaccines, including two new vaccine suppliers – one in 2005 and the other in 2007; **b)** has licensed a Thimerosal-preserved inactivated-“avian”-influenza vaccine for administration to adults; and **c)** will probably be licensing some Thimerosal-preserved inactivated “swine-flu” vaccines later this year.

In addition, the FDA apparently has not revoked the older licenses for the Thimerosal-preserved formulations of DTaP, Td, Hib, and Hep B.]

“Much progress has been made to date. FDA has been actively working with manufacturers, particularly those that manufacture childhood vaccines, to reach the goal of eliminating thimerosal from vaccines, and has been collaborating with other PHS agencies to further evaluate the potential health effects of thimerosal. In this regard, all vaccines routinely recommended for children 6 years of age or younger and marketed in the U.S. contain no thimerosal or only trace amounts (1 microgram or less mercury per dose), with the exception of inactivated influenza vaccine, which was first recommended by the Advisory Committee on Immunization Practices in ~~2004~~” [2002; Bridges CB, Fukuda K, Uyeki TM, Cox NJ, Singleton JA. Prevention and Control of Influenza Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2002 Apr 12; **51**(RR03): 1-31, with underlining added for emphasis, “The 2002 recommendations include five principal changes or updates, as follows: ..., influenza vaccination of healthy children aged 6–23 months is encouraged when feasible. ...”] “for routine use in” [pregnant women and] “children 6 to 23 months of age”, when feasible.”

Sadly, though this reviewer has repeatedly *formally* informed the Secretary of HHS and the FDA (in Citizen Petitions filed in 2004 (see FDA on-line docket: 2004P-0349/CP1) and in 2007 (FDA on-line docket: 2007P-0331/CP1) that the CDC’s recommendations to inoculate pregnant women and young children began in 2002, two years earlier than admitted here and that, as the information in **Birth Defects and Drugs In Pregnancy** (1977) confirms, informal recommendations that pregnant women receive flu shots have been being made since the late 1950s with an apparent uptake rate of about 3% then to an uptake rate of not less than 25% in the 2008 – 2009 flu season.

4. The fourth important unasked question:

“Why, having been found, in 2003, by the U.S. Congress to be among the federal agencies that were ‘asleep at the switch’ concerning permitting any use of mercury in medicine, has the FDA not been: **a)** replaced by separate focused safety-only agencies for drugs, foods, nutritional supplements, medical devices, and clinical tests and **b)** charged with only protecting the health, financial and medical, of the American people?”

“What has FDA done to address the issue of mercury containing preservatives in vaccines?”

Under the FDA Modernization Act (FDAMA) of 1997, FDA carried out a comprehensive review of the use of thimerosal in childhood vaccines. Conducted in 1999, this review found no evidence of harm from the use of thimerosal as a vaccine preservative, other than local hypersensitivity reactions.”

First, this FDA review was mandated by FDAMA.

Second, the FDA only reviewed the responses it received from those who chose to reply to the notices the FDA posted in the Federal Register, contacted some manufacturers, and reviewed its own files.

Third, not all firms responded to the FDA’s request for information on the products containing any form of added mercury.

Fourth, not all who responded provided complete information.

Fifth, the FDA did not confirm the validity and completeness of the responses it received or compel those whose answers it received were incomplete to provide the missing data much less check an appropriate sample of the firms who did not respond but were manufacturing products of the type that could contain some added mercury. The FDA even admitted that the agency knew that the list it published was incomplete. In the conclusions of a 1999 report titled “**Quantitative and Qualitative Analysis of Mercury Compounds in the List MERCURY COMPOUNDS IN DRUGS AND FOOD**”, the FDA stated:

“There may be some additional products in the marketplace that were not found in the sources that the agency reviewed.” [See Footnote 7 for the link to this report.]

Further, in 2005, this reviewer notified the FDA of an Over-The-Counter (O-T-C) antiseptic drug product called Butt Balm, advertised for diaper rash, that: **a)** was not on the FDA’s list but was being actively marketed and **b)** still listed Thimerosal as an active ingredient on its web site and in its labeling even though such O-T-C uses were proscribed by the FDA in 1998. [Note: The Product labeling subsequently changed but: **a)** there was no recall and **b)** as far as this reviewer could ascertain, The FDA made no assessment of how many more such products are still being marketed.]

In another instance, in 2005, a monoclonal antibody product appeared to contain Thimerosal at or below the lower end of the FDA’s implicit preservative range (nominally, 10 to 100 ppm Thimerosal) but neither the package insert nor the package labeling disclosed the presence of Thimerosal nor stated the maximum level in each dose of this twice-weekly-dosed drug product. [Note: This instance was also reported to FDA officials by this reviewer, but the FDA officials did not get back to this reviewer nor did the company revise its labeling later in 2005 or 2006 to disclose the presence, and/or level, of Thimerosal in that drug product. Moreover, to date, the FDA has not informed this reviewer that he was mistaken nor, *apparently*, has the 2002 Package Insert been updated.]

“As part of the FDAMA review, FDA evaluated the amount of mercury an infant might receive in the form of *ethyl*mercury from vaccines under the U.S. recommended childhood immunization schedule and compared these levels with existing guidelines for exposure to *methyl*mercury, as there are no existing guidelines for ethylmercury, the metabolite of thimerosal. At the time of this review in 1999, the maximum cumulative exposure to mercury from vaccines in the recommended childhood immunization schedule was within acceptable limits for the methylmercury exposure guidelines set by FDA, Agency for Toxic Substances and Disease Registry (ATSDR), and the World Health Organization (WHO). However, depending on the vaccine formulations used and the weight of the infant, some infants could have been exposed to cumulative levels of mercury during the first six months of life that exceeded EPA recommended guidelines for safe intake of methylmercury.”

Again, since there is at least one FDA-recognized peer-reviewed published chronic toxicity study in rats for injected Thimerosal (Mason M. *Clinical Toxicology*, 1971; 4(2): 185-204. Toxicology and Carcinogenesis of Various Chemicals Used in the Preparation of Vaccines {Mason 1971}), there has been no need for the evaluation of “comparative toxicities” since 1971. Thus, the FDA is *knowingly* misleading the reader and *intentionally not* disclosing the Mason (1971) chronic toxicity study for injected Thimerosal administered to adult rats of both sexes. This is the case even though the FDA recognizes, and has even cited, this article to this reviewer more than once – though it has not yet reported the correct average dose values though the study clearly stated: the dose levels for the twice-weekly-dosing plan used in the chronic toxicity arm of the study.

However, given the requirement minimum for preservative safety set forth in **21 CFR § 610.15(a)** (specifically, that the preservative “shall be sufficiently non-toxic so that the amount present in the recommended dose of the product will not be toxic to the recipient”), there is a clear need for the appropriate scientifically sound toxicity studies that:

- a. Establish the NOAEL(s) for injected Thimerosal in each vaccine formulation and
- b. Appropriately place the level of Thimerosal in said vaccine’s formulation appropriately below that NOAEL for Thimerosal-preserved vaccines that can be given to: **1)** pregnant women, **2)** developing children, **3)** adults and **4)** the elderly.

Given an estimated NOAEL_{injected Thimerosal, developing human} (based on Mason, 1971) of < 0.0086 µg of Thimerosal/kg of body weight/day with an imputed NOAEL_{injected mercury, developing human} of < 0.0042 µg of Hg/kg/day and a 3kg child, the safe dose from the standpoint of mercury, a known human bioaccumulative toxin, would be < 0.0126 µg of mercury. Thus, the maximum safe level of mercury injected in a 0.25-mL injection of a Thimerosal-containing vaccine would have to be less than (<) 4 times 0.0126 µg/mL or 0.05 µg Hg/mL and the upper limit on the safe level for Thimerosal would be < 0.1 µg/mL.

Therefore, the upper limit on Thimerosal in the formulation for a vaccine intended to be given to children weighing at least 3 kg should be < 0.1 µg Thimerosal/mL (< 0.1 ppm; < 0.0001 %).

Furthermore, provided there was a requirement that the fetus weigh at least 1 kg (only permitting pregnant women to be vaccinated in the later months of pregnancy), for a 0.5-mL dose of a vaccine that is allowed to be given to pregnant women, the limit on the level of Thimerosal in the vaccine would be on the order of < 0.0172 µg/mL (< 0.0172 ppm; < 0.00000172 %). This is the case because studies in rabbits and other animals have shown that most of the dose the mother receives is transferred to the fetus.

Based on these findings, Thimerosal cannot be used as a preservative in vaccines intended to be given to children and pregnant women.

This is the case because the lowest level of Thimerosal where the FDA has recognized Thimerosal as a preservative in a vaccine (the Mass Public Health's trade-nameless TD vaccine) is nominally 30 ppm (0.003%), a level > 300 times the < 0.1 ppm "safe" level for the example child and more than 1,500 times the "safe" level for the developing fetus when Thimerosal-preserved vaccines are administered to pregnant women.

Similarly, *for vaccines only given to adults who are not pregnant*, where the appropriate weight minimum for an adult might be 90 pounds (40.8 kg), not the FDA's "50 kg", and the appropriate NOAEL_{injected Thimerosal, adult humans} would be < 0.086 µg of Thimerosal/kg/day, the level of Thimerosal in a 0.5 mL dose of vaccine (the least dose given to adults) would have to be < 3.5 µg/0.5 mL or < 7 µg/mL (< 7 ppm; 0.0007%). Since the minimum nominal level of Thimerosal the FDA recognizes as a preservative is still 30 ppm (0.003%), the permitted level is still > 4 times the estimated NOAEL_{injected Thimerosal, adult humans} in this instance.

Thus, having this chronic toxicity data showing toxicity at low levels of chronic exposure in 1971 and appropriately computing the upper limit on the NOAEL_{injected Thimerosal, humans} in various groups of humans from that data, the FDA should have known that Thimerosal could not safely be used as a preservative in vaccines in 1971, if not before.

Moreover, as most toxicologists know, one cannot validly average bolus doses (in this case, a "bolus dose" can be considered to be a dose that exceeds the toxic threshold [taken as maximally being the lowest observed adverse effect level {LOAEL}] from Thimerosal-preserved vaccines given over some period of time).

Because the magnitude of the current Thimerosal bolus doses (nominally, "17.5", "25", "37" or "50" µg) that a child may receive from a single vaccine clearly exceed the imputed maximum toxic threshold (the LOAEL) of 0.0086 µg of Thimerosal/kg/day for children, a single dose of any Thimerosal-preserved vaccine should not be administered unless the child's weight were to exceed 2, 034 kg (> 4, 486 pounds) for even the "17.5 µg of Thimerosal" (lowest) bolus dose.

Because Thimerosal's maximum "toxic threshold" (LOAEL) for adults, *other than pregnant women*, is 0.086 µg of Thimerosal/kg/day and the Thimerosal bolus doses are nominally "37", "49 – 50" or "98" µg for these adults, for the lowest nominal bolus dose, "37" µg of Thimerosal, the adult need only weigh more than (>) 430 kg (> 949 pounds)!

Worse, all forms of mercury are bioaccumulative toxins!

Thus, if, *for example*, one takes the typical 187.5 µg dose of mercury given in the first "six" months of a child's life and presumes that the weight at each time point can be ignored (which, in the real world, it cannot), the "average daily dose" of 1.04 µg of mercury/day (or 2.08 µg of Thimerosal/day) exceeds the calculated (from a chronic toxicity study in rats using injected Thimerosal solutions {and not some other mercury compound or other mode of exposure}) toxic threshold, "LOAEL_{injected Thimerosal, developing child}" (0.0086 µg of Thimerosal/kg/day), unless, *on average*, the child weighs in excess of 242 kg (534 pounds {more than a quarter ton})!

Obviously, *based on the preceding realities*, no Thimerosal-preserved vaccine is "safe" to inject into pregnant women, developing children and/or, for that matter, adults.

Further, even Thimerosal-containing influenza vaccines that deliver about 2 µg of Thimerosal per dose are not safe for "developing children", who have a toxic threshold

(LOAEL) of 0.0086 µg Thimerosal/kg/day, unless they weigh more than 232.5 kg (512.7 pounds)!

For non-pregnant adults, where the toxic threshold is presumed to be 10 times higher (0.086 µg of Thimerosal/kg/day), a single 2-µg dose of Thimerosal is probably safe for adults weighing more than 23.3 kg (51.4 pounds). However, given:

- a. An estimated half-life of 18-20 years for mercury in the brain (Sugita M. The biological half-time of heavy metals. The existence of a third “slowest” component. *Int Arch Occup Environ Health* 1978; **41**(1): 25–40) and
- b. No proven upper limit on the maximum fraction of the Thimerosal dose’s mercury that is retained long-term in those with impaired mercury excretion,

it is clear to this reviewer that getting the annual “preservative free” inactivated-influenza-virus vaccine each year is, *given an adult’s existing accumulated mercury bioburden from the air, water, food, Thimerosal-containing vaccines and other drug products, and other sources, not “safe”, even if the adult has no mercury-amalgam dental filings.*

“As a precautionary measure, the Public Health Service (including FDA, National Institutes of Health [NIH], Centers for Disease Control and Prevention [CDC] and Health Resources and Services Administration [HRSA]) and the American Academy of Pediatrics issued a Joint Statement, urging vaccine manufacturers to reduce or eliminate thimerosal in vaccines as soon as possible. The U.S. Public Health Service agencies have collaborated with various investigators to initiate further studies to better understand any possible health effects from exposure to thimerosal in vaccines.”

These self-serving statements ignore the reality that the Secretary of HHS, the head of the “U.S. Public Health Service agencies”, has since January 1988, at the latest, *knowingly* failed to reduce the adverse reactions to vaccines whenever any of the Secretary’s subordinate agencies:

- a. Licensed a new vaccine that did not reduce the (overall) risks of adverse reactions or that increased the aggregate number of adverse vaccine reactions,
- b. Approved a preserved vaccine without pre-approval submitted scientifically sound and appropriate toxicological proof that that vaccine met the “sufficiently nontoxic ...” CGMP requirement *minimum* set forth for preservatives in **21 CFR § 610.15(a)**, or
- c. Recommended a new licensed vaccine for administration to any population segment

without ensuring that that the additional vaccine reduced the (overall) risks of adverse vaccine reactions as per **42 U.S.C. 300aa-27**, which states (with **bolding** added for emphasis⁶):

“**Sec. 300aa-27. Mandate for safer childhood vaccines**

(a) General rule

In the administration of this part and other pertinent laws under the jurisdiction of the Secretary, the Secretary shall -

⁶ The word “childhood” is not in bold because vaccines for adults have been included in the Secretary’s mandates under the National Vaccine Injury Compensation Program Act (NVICPA).]

- (1) **promote the development of childhood vaccines that result in fewer and less serious adverse reactions than those vaccines on the market on December 22, 1987, and promote the refinement of such vaccines, and**
- (2) **make or assure improvements in, and otherwise use the authorities of the Secretary with respect to, the licensing, manufacturing, processing, testing, labeling, warning, use instructions, distribution, storage, administration, field surveillance, adverse reaction reporting, and recall of reactogenic lots or batches, of vaccines, and research on vaccines, in order to reduce the risks of adverse reactions to vaccines.”**

“Available data has been reviewed in several public forums including the Workshop on Thimerosal, held in Bethesda in August 1999 and sponsored by the National Vaccine Advisory Committee, two meetings of the Advisory Committee on Immunization Practices of the CDC, held in October 1999 and June 2000, and by the Institute of Medicine's Immunization Safety Review Committee in July 2001 and February 2004.”

Here the FDA is knowingly misrepresenting the facts because at least two of these review meetings were not public forums but rather invitation only government-industry meetings held without public notice and closed to the press and the public.

Specifically, these unlawful meetings that the FDA is mischaracterizing are the “Workshop on Thimerosal” held in August 3-4, 1999 on the Bethesda campus of the National Institutes of health in the Lister-Hill Auditorium and the Simpsonwood conference held in June of 2000 at the United Methodist Church’s Simpsonwood Center in Georgia.

In both cases, the “Confidential” partial transcript of the first meeting and the “Confidential” report from the second meeting clearly established that the information discussed was to be withheld from the public and the press.

Further, since these “*two meetings*” were: **a)** closed to the public and the media, **b)** by invitation only, and **c)** included industry, World Health Organization, consultants, and FDA and CDC representatives who were clearly not members of the Advisory Committee on Immunization Practices (ACIP) of the CDC, these two meetings were *unlawfully* conducted meetings where, *in essence*, carefully screened government and industry representatives *illegally* met “in secret” to discuss: **a)** the toxicity of Thimerosal (in the first meeting), and **b)** the troubling outcomes found in the early epidemiological studies of the computerized data for US children in two California HMO groups, which showed statistically significant Thimerosal-dose-dependent neurodevelopmental toxicity (in the second meeting).

The findings, *in both cases*, were embargoed to collusively hide:

1. Damning information, or, *in the case of Thimerosal itself*, the glaring lack of the requisite toxicity studies (even though **21 CFR § 610.15(a)** had, *since 1973 at the latest*, mandated toxicity studies), and
2. Findings of harm as well as the significant risks of harm that was disclosed at both meetings

from the American people until:

- a.** The obvious lack of the mandated toxicity data for Thimerosal could be glossed over with appropriate propaganda and Orwellian newspeak;
- b.** The findings of statistically significant links between Thimerosal exposures and neurodevelopmental disorders in the initial epidemiological studies in the Vaccine Safety Datalink (VSD) database could be manipulated to make the statistically

significant linkages between Thimerosal dose and the most serious adverse outcomes “disappear”; and

- c. Other similarly flawed epidemiological studies could be initiated, conducted, and their similarly specious results published.

“Data reviewed did not demonstrate convincing evidence of toxicity from doses of thimerosal used in vaccines. In case reports of accidental high-dose exposures in humans to thimerosal or ethyl mercury”[,] “toxicity was demonstrated only at exposures that were 100 or 1000 times that found in vaccines.”

From the data presented at the August 1999 Lister-Hill meeting in the available portions of the transcript of that meeting and the “not unexpected” findings discussed at the 2000 Simpsonwood meeting, it is plain to this reviewer that the results reported presented convincing evidence of toxicity in humans from the doses of Thimerosal used as a preservative in vaccines, as some of the participants at both meetings were reported to have clearly stated during these meetings.

In addition, the literature available in 1999 and 2000 included studies clearly showing toxicity at levels of Thimerosal or ethylmercury compounds well below the 100-ppm (0.01%) nominal maximum level of Thimerosal in vaccines.

These studies included a closed system experiment using fertile chicken eggs and exposures to injected Thimerosal (injected into the yolk sack) at levels of about 1 ppm (Digar A, Sensharma GC, Samal SN. Lethality and teratogenicity of organic mercury (Thimerosal) on the chick embryo. **J Anat Soc India** 1987; **36**: 153-159). This egg study expanded the knowledge base regarding the marked toxicity of Thimerosal to the developing fetus when these researchers found:

“A single dose of 0.1 mg of Ethyl-mercury-thiosalicylate (Thimerosal) was injected into the yolk sac of chick embryos... Embryos were collected... It was found that 0.1 mg dose of Thimerosal was lethal in 46.46%. Gross malformations like syndactyly, thinning of the abdominal wall, visceroptosis and scanty feather, during Organogenesis as well as in the later period, have been noted in 36.03%... Significant change in the weight of embryo, crown-rump length, body and wing lengths were also observed... However, there was no gross reduction in the size of brain as compared to that of the control. The high incidence of lethality and malformations prove that organic mercury was transmitted from the yolk sac to the embryo. The deleterious effects of mercurials on cells and tissues seem to be due to action on a wide spectrum of enzymes by the organic mercury both on the surface and within the cell. The enzymes particularly involved are – Na – K activated ATPase and also sulfhydryl groups. Goldwater reported that mercury disrupts the normal function of mitochondria and lysosomes”.

“In its report of October 1, 2001, the IOM's Immunization Safety Review Committee concluded that the evidence is inadequate to either accept or reject a causal relationship between thimerosal exposure from childhood vaccines and the neurodevelopmental disorders of autism, attention deficit hyperactivity disorder (ADHD), and speech or language delay. At that time the committee's conclusion was based on the fact that there were no published epidemiological studies examining the potential association between thimerosal-containing vaccines and neurodevelopmental disorders. The Committee did conclude that the hypothesis that exposure to thimerosal-containing vaccines could be associated with neurodevelopmental disorders was biologically plausible. However, additional studies were needed to establish or reject a causal relationship. The Committee stated that the effort to remove thimerosal from vaccines was ‘a prudent measure in support of the public health goal to reduce mercury exposure of infants and children as much as possible’.”

If the IOM committee's true goal had been to review "Immunization Safety" as its title implies, then epidemiological studies are totally inappropriate because they cannot assess critical aspects of toxicity – fundamental aspects that must be assessed before one can determine "safety" to the required standard for a compound, like Thimerosal, that is being used as a preservative in vaccine formulations.

Obviously, the committee looked on the absence of epidemiological studies as fortunate "escape hatch", though which the committee could avoid having to assess the applicable toxicity studies, which had clearly demonstrated *in vivo* Thimerosal toxicity at levels at least 2 orders of magnitude below the levels of Thimerosal in most all Thimerosal-preserved vaccines.

"In 2004, the IOM's Immunization Safety Review Committee again examined the hypothesis that vaccines, specifically the MMR vaccines and thimerosal containing vaccines, are causally associated with autism. In this report, the committee incorporated new epidemiological evidence from the U.S., Denmark, Sweden, and the United Kingdom, and studies of biologic mechanisms related to vaccines and autism that had become available since its report in 2001."

Since:

- a. These studies were initiated by key CDC officials at the unlawful Simpsonwood conference who clearly wanted to cover up the damning findings reported at that illegal government/industry conference to "protect" the "immunization programs",
- b. These studies were overseen and/or underwritten by government officials in what, *at the time*, was the CDC's National Immunization Program, which was charged with promoting vaccination, and
- c. Reviews by qualified independent statisticians and epidemiologists of the published studies upon which the 2004 IOM report relied have established that each of these studies is fundamentally flawed and intentionally designed to exonerate and protect the existing vaccination programs that sanction the administration of mercury without informed consent,

this reviewer finds that the 2004 IOM committee's report lacks a scientifically sound foundation and that that report should be retracted and repudiated by the IOM before the few strands of credibility that the IOM has left with the public are irrevocably broken.

"The committee concluded that this body of evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism, and that hypotheses generated to date concerning a biological mechanism for such causality are theoretical only."

Because this IOM committee refused to consider and/or inappropriately rejected the available human toxicity evidence and independent epidemiological studies in favor of the uninformative CDC-lead and/or CDC-funded epidemiological studies that cannot assess vaccine safety and had other fundamental flaws (as a report by the NIEHS dated August 24, 2006 and titled: "Thimerosal Exposures in Pediatric Vaccines: Feasibility of Studies Using the Vaccine Safety Datalink" reported and as Julie Louise Gerberding, MD, MPH, then Director of the Centers for Disease Control and Prevention (CDC), subsequently confirmed to Congress in 2007 [in a document titled, "DEPARTMENT OF HEALTH AND HUMAN SERVICES CENTERS FOR DISEASE CONTROL AND PREVENTION REPORT TO CONGRESS ON VACCINE SAFETY DATALINK House Appropriations Committee"]), this reviewer finds that all that should be rejected is this 2004 IOM committee's report.

“Further, the committee stated that the benefits of vaccination are proven and the hypothesis of susceptible populations is presently speculative, and that widespread rejection of vaccines would lead to increases in incidences of serious infectious diseases like measles, whooping cough and Hib bacterial meningitis.”

While this reviewer agrees that these positions were adopted by the 2004 IOM committee’s report, this reviewer notes that **none** of this IOM committee’s stated concerns have:

- ❑ Anything to do with vaccine safety as well as
- ❑ Little to do with the reality of susceptible population segments that has clearly been demonstrated by:
 - a. Population-wide exposures of fetuses, and developing children to Thimerosal-preserved vaccines, *without all of the requisite proofs of safety*, at levels well above the toxic threshold (LOAEL_{injected Thimerosal}) for such exposures and
 - b. The resultant observed variable risk of sub-acute mercury poisoning’s established harmful effects on the brains and other organs (e.g., the gastrointestinal, cardiovascular, and endocrine systems) of those receiving “identical doses” of these vaccines at a given time point as well as
 - c. The 3- to 5- fold greater incidence of these effects in male children than in female children of the same age.

“FDA is continuing its efforts toward reducing or removing thimerosal from all existing vaccines. Much progress has been made to date. FDA has been actively working with manufacturers, particularly those that manufacture childhood vaccines, to reach the goal of eliminating thimerosal from vaccines, and has been collaborating with other PHS agencies to further evaluate the potential health effects of thimerosal. Since 2001, all vaccines recommended for children 6 years of age and younger have contained either no thimerosal or only trace amounts, with the exception of inactivated influenza vaccines, which are marketed in both the preservative-free and thimerosal-preservative-containing formulations. Thimerosal-preservative free influenza vaccine licensed for use in children six to 59 months of age is available in limited supply. Nevertheless, FDA is in discussions with manufacturers of influenza vaccine regarding their capacity to increase the supply of vaccine without thimerosal as a preservative. Additionally, new pediatric vaccines that have received licensure do not contain thimerosal.”

What the FDA fails to disclose here is that, *with*:

- a. *The addition of the CDC’s recommendations, starting in early 2002, to give the inactivated-influenza vaccine to” i) pregnant women and ii) young children, where feasible and*
- b. *The CDC’s 2008-2009 updated recommendation for annual inactivated flu shots for children up to 18 years of age,*

the total lifetime dose of Thimerosal that a child born in 2002, and after, MAY receive by the age of 18 (presuming full compliance and the administration of only Thimerosal-preserved flu shots) from the flu shot alone (nominally 475 µg of mercury) is about double the total dose that a child would receive by age 18 under the CDC’s late-1990s recommended vaccination program (about 265 µg of mercury)!

So much for reducing the maximum mercury exposure that a child may receive!

Of course, you can:

- ❑ Get your child a safer “preservative free” inactivated-influenza shot, for which there are only 2 FDA-licensed inactivated-influenza vaccine suppliers approved for administration to children under 18 (Novartis and Sanofi, which do each produce a less risky inactivated flu shot):
 - a. A “reduced-Thimerosal” flu shot if your child is 4 or older and Novartis starts shipping that formulation to the USA again (for the past 5 flu seasons, it has either not been available or only a few doses have been distributed), or
 - b. A “no Thimerosal” Sanofi Fluzone shot if you can find a dose; or
- ❑ Get your 2-year or older child the live-virus influenza vaccine FluMist produced by MedImmune and risk your child’s:
 - a. Getting a severe or lethal case of influenza from it or
 - b. Spreading influenza to yourself or others, or
 - c. Being “case 0” for a nationwide or worldwide flu pandemic should one of the FluMist’s vaccines’ live viruses mutate into a pandemic highly virulent strain.

Further, currently, the population of children that the CDC recommends get an annual inoculation for influenza is clearly expanding faster than the supply of no-Thimerosal inactivated-influenza vaccine doses. For example, the number of children in the recommended population has expanded from about 8 million with the CDC’s 2002 recommendation to vaccinate children 6 months of age to 23 months of age with a flu vaccine, to more than 72 million since the CDC revised its annual influenza inoculation recommendation to cover all children up to age 18. Moreover, the only current supplier of a no-Thimerosal inactivated human influenza vaccine that the FDA has approved for administration to children, Sanofi Pasteur, Inc. has stated (in a written communication in 2009) that:

- a. The supply for the 2008-2009 flu season of its no-Thimerosal Fluzone influenza vaccine was about 14 million doses for people of all ages, where the general guidelines covered all children 6 months to 5 years of age, some to age 9 and “at risk” groups to 18 or about 27 million children (or doses for less than {LT} 52% of the covered children because this vaccine is also approved for adults),
- b. It may be able to distribute “up to 30 million” doses of its no-Thimerosal Fluzone influenza vaccine for the upcoming 2009-2010 human flu season for about 75 million children 6 months to 18 years of age, the CDC’s newest guideline, (or projected doses for LT 40% of the covered children because this vaccine is also approved for adults), and
- c. It may be able to distribute “up to 50 million” doses for the 2010-2011 human flu season for about 78 million children (or projected doses for LT 64 % of the covered children because this vaccine is also approved for adults).

Moreover, this reviewer notes that the FDA’s statement: “*new pediatric vaccines that have received licensure do not contain thimerosal*” is intentionally misleading. It conceals the reality that the supply of said no-Thimerosal inactivated human influenza vaccine doses is insufficient.

In spite of the known cumulative risk to sub-acute mercury poisoning in susceptible individuals, the FDA has also continued to license Thimerosal-preserved vaccines for adults.

In spite of no population-wide evidence of effectiveness in preventing influenza infection in those over 50 years of age, the CDC continues to recommend that older Americans get an annual flu shot. Since most doses continue to be Thimerosal-preserved doses because the FDA has continued to license: **a)** the existing Thimerosal-preserved inactivated-influenza vaccines and **b)** additional manufacturers to distribute Thimerosal-preserved vaccines, older adults continue to be exposed to unnecessary risk for sub-acute mercury poisoning from the cumulative effect of doses of ineffective Thimerosal-preserved inactivated-influenza vaccines.

5. The fifth important unasked question:

“Why is the FDA knowingly misrepresenting the mandate that Congress gave the FDA in ‘FDAMA 1997’?”⁷

“Why did FDA wait until mandated by Congress under FDAMA 1997 to examine the use of preservatives containing mercury?”

Several factors led to examination of mercury-containing preservatives in childhood vaccines. Over the past decade there has been increased attention focused on the health effects of human exposure to mercury, particularly methyl mercury. In 1994, the EPA revised its Reference Dose (RfD) for methylmercury exposure, lowering its guideline for safe exposure from 0.3 to 0.1 microgram per kilogram body weight per day. Prospective studies (in the Seychelles, Faroe Islands and others) of the effects of low dose exposure to methylmercury in the diet were published, and some of these studies raised concern that neurodevelopmental outcomes in children may be subtly affected when their mothers were exposed to methylmercury from dietary sources at levels that were previously thought to be safe. Also in the 1990's, the CDC's Advisory Committee on Immunization Practices (ACIP) and other recommending bodies added new vaccines (e.g., hepatitis B, Hib), some of which contained thimerosal as a preservative, to the routine childhood immunization schedule. Additionally, beginning in 1996, the replacement of whole cell DTP-Hib combination vaccines with separately administered DTaP and Hib vaccines increased the amount of thimerosal that some infants might have received (depending on vaccine formulation(s) received). In light of efforts by various federal agencies to decrease human exposure to mercury from various sources, and the potential increase in infant exposure to thimerosal from vaccines, FDA undertook review of this issue.”

This reviewer finds the FDA's statements here to be an attempt to rewrite reality by omitting unfavorable realities from its abridged version of history. Most tellingly, these omissions include the FDA's 1980 review of the use of Thimerosal in antiseptics at nominal levels of 0.1

⁷ Under section 413(a) of the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Pub. L. 105-115), entitled ‘Food and Drug Administration Study of Mercury Compounds in Drugs and Food,’ the Food and Drug Administration (FDA) is required to: (1) Compile a list of drugs and foods that contain intentionally introduced mercury compounds, and (2) provide a quantitative and qualitative analysis of the mercury compounds in this list. Thus, the statute did not differentiate between mercury as an active or an inactive ingredient nor did it limit the mandate to vaccines or, for that matter, drugs – since the mandate included foods. Furthermore, there was no mandate to “*examine the use of preservatives containing mercury*” – Congress only mandated compilation of a list and either the qualitative or the quantitative amount of mercury in each drug or food. Finally, the FDA failed to fully comply with this Congressional mandate and admitted that the list they did provide to Congress was incomplete and inaccurate. This was the case because essentially all the FDA did was ask the drug makers to provide the information FDAMA 1997 was requesting because, as the FDA had admitted, it had no list. Apparently, the FDA did not even verify it had received a response from every registered drug maker because, in 2005, this reviewer found and reported one illegal O-T-C drug product, whose manufacturer had been making this diaper-rash treatment product, which contained about 0.1% Thimerosal for decades, but had obviously failed to respond to the FDA's request. See: <http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAAct/SignificantAmendmentsToTheFDCAAct/FDAMA/ucm100219.htm>

% (a level only 10-fold higher than the nominal maximum level in Thimerosal-preserved vaccines {0.01%}).

This review found that topical application of even small amounts of Thimerosal-containing antiseptics to superficial cuts and abrasions was more toxic to the human cells than it was to the bacteria, fungi and molds in these wounds. In addition, this review clearly established that Thimerosal is not even an effective microbial growth inhibitor.

Based on these findings of a lack of safety and lack of effectiveness, this review panel recommended banning Thimerosal from the list of allowed ingredients in O-T-C antiseptics and O-T-C vaginal spermicidal preparations. However, the FDA did not act on the 1982 report (formalizing and publishing the 1980 review's findings) until 1998 – 16 years after the report.

Moreover, it overlooked the reality that, since a 0.1% solution of Thimerosal formulated in an aqueous carrier without alcohol is not even bacteriostatic, much less bactericidal, when applied topically, a 0.01% level of Thimerosal in an essentially aqueous vaccine formulation containing proteins is a less-than-effective preservative, just as the results reported by Morton, North and Engley in their 1948 paper indicate.

“Thus, while enactment of FDAMA 1997 provided an official mechanism for review of this issue, the use of thimerosal as a preservative in vaccines had already begun to be considered by FDA.”

Factually, for drugs, “*FDAMA 1997*” only mandated compilation of a list of all mercury compounds and their level in all drugs. Thus, “*FDAMA 1997*” did not provide the FDA Thimerosal in vaccines as a preservative. Moreover, the FDA’s “*the use of thimerosal as a preservative in vaccines had already begun to be considered by FDA*” is simply self-serving empty rhetoric on the part of the FDA. Factually, the 2003 Congressional report titled, “Mercury in Medicine – Taking Unnecessary Risks” (May 2003, Subcommittee on Human Rights & Wellness of the Government Reform Committee, US House of Representatives (Chairman Dan Burton – following a 3 year congressional investigation), “Mercury in Medicine – Taking Unnecessary Risks” pgs 1-80) presents a much clear picture of the FDA’s performance when it states (with **bolding** added for emphasis):

“II. FINDINGS AND RECOMMENDATIONS

A. Findings

Through this investigation of pediatric vaccine safety, the following findings are made:

1. **Mercury is hazardous to humans. Its use in medicinal products is undesirable, unnecessary and should be minimized or eliminated entirely.**
2. For decades, ethylmercury was used extensively in medical products ranging from vaccines to topical ointments as preservative and an anti-bacteriological agent.
3. **Manufacturers of vaccines and thimerosal**, (an ethylmercury compound used in vaccines), have **never conducted adequate testing on the safety of thimerosal. The FDA has never required manufacturers to conduct adequate safety testing on thimerosal** and ethylmercury compounds.
4. **Studies and papers documenting the hyperallergenicity and toxicity of Thimerosal (ethylmercury) have existed for decades...**
- ...
8. **The FDA acted too slowly to remove ethylmercury from over-the-counter products like topical ointments and skin creams.** Although an advisory committee determined that

ethylmercury was unsafe in these products in 1980, a rule requiring its removal was not finalized until 1998.

9. **The FDA and the CDC failed in their duty to be vigilant as new vaccines containing thimerosal were approved and added to the immunization schedule.** When the Hepatitis B and Haemophilus Influenzae Type b vaccines were added to the recommended schedule of childhood immunizations, the cumulative amount of ethylmercury to which children were exposed nearly tripled.
10. **The amount of ethylmercury to which children were exposed through vaccines prior to the 1999 announcement exceeded two safety thresholds established by the Federal government for a closely related substance - methylmercury.** While the Federal Government has established no safety threshold for ethylmercury, experts agree that the methylmercury guidelines are a good substitute. Federal health officials have conceded that the amount of thimerosal in vaccines exceeded the EPA threshold of 0.1 micrograms per kilogram of bodyweight. In fact, the amount of mercury in one dose of DTaP or Hepatitis B vaccines (25 micrograms each) exceeded this threshold many times over. Federal health officials have not conceded that this amount of thimerosal in vaccines exceeded the FDA's more relaxed threshold of 0.4 micrograms per kilogram of body weight. In most cases, however, it clearly did.
11. **The actions taken by the HHS to remove thimerosal from vaccines in 1999 were not sufficiently aggressive...**
12. **The CDC's failure to state a preference for thimerosal-free vaccines in 2000 and again in 2001 was an abdication of their responsibility.** As a result, many children received vaccines containing thimerosal when thimerosal-free alternatives were available...
...
14. **The CDC in general and the National Immunization Program in particular are conflicted in their duties to monitor the safety of vaccines,** while also charged with the responsibility of purchasing vaccines for resale as well as promoting increased immunization rates. ...
...
17. **To date, studies conducted or funded by the CDC that purportedly dispute any correlation between autism and vaccine injury have been of poor design, under-powered, and fatally flawed.** The CDC's rush to support and promote such research is reflective of a philosophical conflict in looking fairly at emerging theories and clinical data related to adverse reactions from vaccinations...

The Food and Drug Administration's (FDA) mission is to 'promote and protect the public health by helping safe and effective products reach the market in a timely way, and monitoring products for continued safety after they are in use.' However, the FDA uses a subjective barometer in determining when a product that has known risks can remain on the market. According to the agency, 'at the heart of all FDA's product evaluation decisions is a judgment about whether a new product's benefits to users will outweigh its risks. No regulated product is totally risk-free, so these judgments are important. FDA will allow a product to present more of risk when its potential benefit is great—especially for products used to treat serious, life-threatening conditions.' **This argument—that known risks of infectious diseases outweigh a potential risk of neurological damage from exposure to thimerosal in vaccines—is one that has continuously been presented to the Committee by government officials. FDA officials have stressed that any possible risk from thimerosal was theoretical: that no proof of harm existed. However, the Committee, upon a thorough review of the scientific**

literature and internal documents from government and industry, did find evidence that thimerosal did pose a risk...

...

Thimerosal used as a preservative in vaccines is likely related to the autism epidemic. This epidemic in all probability may have been prevented or curtailed had the FDA not been asleep at the switch regarding the lack of safety data regarding injected thimerosal and the sharp rise of infant exposure to this known neurotoxin. Our public health agencies' failure to act is indicative of institutional malfeasance for self-protection and misplaced protectionism of the pharmaceutical industry".

"During the past ten years, FDA has provided informal and formal advice to manufacturers recommending that new vaccines under development be formulated without thimerosal as a preservative."

Since, the FDA has:

- a. Ignored the statutory mandates for safer vaccines set forth in **42 U.S.C. § 300aa-27**,
- b. Persisted in *unnecessarily* licensing additional Thimerosal-preserved vaccine formulations including a Thimerosal-preserved inactivated "avian influenza" vaccine even though the clinical trials were apparently conducted using a "no preservative" formulation, and
- c. Continued to *illegally* license (by ignoring the FDA-binding law set forth in **21 CFR § 601.4(a)** that requires all of the applicable safety requirements to be met before the FDA can license these vaccines) Thimerosal-preserved vaccines for which the manufacturers/sponsors have not conducted all of the applicable required scientifically sound toxicity studies to meet the CGMP requirement minimums that the preserved vaccine formulation be proven to be "sufficiently nontoxic ..." (see **21 CFR § 610.15(a)**) and submitted proof of compliance and safety (as required in **21 CFR § 601.2(a)**),

it seems that the FDA has colluded, and is colluding, with the vaccine makers to ignore the applicable laws rather than, as claimed here, providing "*informal and formal advice to manufacturers recommending that new vaccines under development be formulated without thimerosal as a preservative*".

"FDA had previously reviewed thimerosal use in biological products, including vaccines, in 1976. This review evaluated exposure to thimerosal from biological products using the 1974 American Academy of Pediatrics 'Red Book' immunization schedule and concluded that, with the exception of long term immune globulin replacement therapy, 'no dangerous quantity of mercury is likely to be received from biologic products in a lifetime.' Of note, immune globulin products licensed in the U.S. no longer use thimerosal as a preservative."

As the subsequent FDA reviews of Thimerosal have done, it is obvious that the less-than-comprehensive literature review conducted by the FDA in 1976 apparently missed the hundreds of prior articles that found evidence of toxicity at Thimerosal levels 100 times or more lower than the nominal maximum Thimerosal levels in Thimerosal-preserved vaccines.

While the currently supplied immune globulin drug products may currently not use Thimerosal as a preservative, this reviewer finds no proof that the FDA has: **a)** revoked all of the existing FDA-licenses for Thimerosal-preserved immune globulin drug products; **b)** proscribed the inclusion of Thimerosal or any other mercury-based compound in any manufacturing process for immune globulin products so that these products contain no added mercury compound at any level; and **c)** required the manufacturer of any immune globulin product, other biological product or other drug product to disclose the names and levels of any mercury compounds present in any still-approved drug formulation down to the nanograms-per-dose level in parts per million (micrograms per gram [or mL] of the drug product).

6. The sixth and seventh important unasked question:

“If the goal was set in 1999, as the FDA admits, why does any inactivated-influenza vaccine,⁸ which has to be reformulated and reapproved ‘every’ year, contain any level of Thimerosal whatsoever a decade later?”

“Why has the FDA continued to license new suppliers of Thimerosal-preserved influenza vaccines after 1999, if the FDA’s goal were ‘*eliminating thimerosal from vaccines*’?”

“What progress has been made towards the goal of eliminating thimerosal from vaccines?”

Great progress has been made in removing thimerosal from vaccines. Manufacturers have been able to accomplish this goal through changing their manufacturing processes, including a switch from multi-dose vials, which generally require a preservative, to single-dose vials or syringes. Since 2001, all vaccines manufactured for the U.S. market and routinely recommended for children ≤ 6 years of age have contained no thimerosal or only trace amounts (≤ 1 microgram of mercury per dose remaining from the manufacturing process), with the exception of inactivated influenza vaccine. In addition, all of the routinely recommended vaccines that had been previously manufactured with thimerosal as a preservative (some formulations of DTaP, Haemophilus influenzae b conjugate (Hib), and hepatitis B vaccines) had reached the end of their shelf life by January 2003.”

This reviewer finds the FDA’s claim of “(g)reat progress” to be a smoke screen hiding the reality that the maximum childhood exposure to Thimerosal from before birth to “adulthood” is now about double the maximum childhood exposure to Thimerosal under the CDC recommended vaccination protocols for the late 1990s and 2000.

Moreover, contrary to the FDA’s assertion, this reviewer finds that some distributed lots of the Thimerosal-preserved formulations for some of the FDA’s list of vaccines did not expire (“reach the end of their shelf life”) until some point in 2005 and, *worse*, Thimerosal-preserved lots of FDA-licensed vaccine formulations that are not being distributed in the USA in 2009 are still being distributed in many other nations around the world.

“In the past, prior to the initiative to reduce or eliminate thimerosal from childhood vaccines, the maximum cumulative exposure to mercury via routine childhood vaccinations during the first six months of life was 187.5 micrograms. With the introduction of thimerosal-preserved-free formulations of DTaP, hepatitis B, and Hib, the maximum cumulative exposure from these vaccines decreased to less than three micrograms of mercury in the first 6 months of life. With the addition of influenza vaccine to the recommended vaccines, an infant could receive a thimerosal-containing influenza vaccine at 6 and 7 months of age. This would result in a maximum exposure of 28 micrograms via routine childhood vaccinations.”

Since, without the requisite proofs of safety and with proof of significant risks for teratogenic effects (serious birth defects) in their offspring, *as this reviewer has reported*, pregnant women are allowed to be administered a Thimerosal-preserved inactivated-influenza vaccine

⁸ This reviewer notes that the FDA has repeatedly used the phrase “*inactivated influenza vaccines*”, indicated that the vaccines are inactivated, rather than “*inactivated-influenza vaccines*”, which correctly indicates that the influenza is inactivated. Perhaps this is a “Freudian” slip, a subconscious compulsion to admit that the current inactivated-influenza vaccines are “inactive” when it comes to preventing those given such from subsequently contracting influenza.

shot during their pregnancy, the maximum exposure level up to the time the child is seven months of age is nominally 53 micrograms (53 µg) of mercury (though, worst case, it can exceed 65 µg) or 106 µg of Thimerosal (worst case, >130 µg of Thimerosal).

“This level is well below the EPA calculated exposure guideline for methylmercury of 65 micrograms for a child in the 5th percentile body weight during the first 6 months of life.”

Crudely, the FDA’s “calculation” duplicitously attempts to equate the adverse effect from, for example, a child’s taking an “aspirin” dose about every other day between the ages of 2 months and 7 months of age (or about 53 “aspirin” doses in all), when taking more than 0.5 “aspirin” doses in a “day” causes toxic effects, to a child’s taking 1 “aspirin” dose on the days they are 2 months and 4 months of age, 26 “aspirin” doses on the day they are 6-months old and 25 “aspirin” doses on the day they are 7-months old (53 “aspirin” doses in all).

Obviously, whenever the dose of medicine at any time point exceeds the toxic threshold, *as it does in the easily understood “aspirin” example*, it is wrong to calculate the average dose (about 0.5 “aspirin” a day) in such cases!

Yet, in spite of the reality that even a 1 µg dose of Thimerosal (0.5 µg of Hg) dose exceeds the EPA RfD of 0.1 µg/kg/day unless the child weighs 5 kg (11 pounds) and the 25 µg and 26 µg doses exceed the EPA’s RfD unless the child weighs more than 125 kg (276 pounds) and 130 kg (287 pounds), respectively, the FDA *knowingly* makes this totally misleading calculation, ignoring the reality that each dose probably exceeded the toxic threshold for Thimerosal exposure at even the lowest dose given. [Note: Using the more appropriate LOAEL ^{injected Thimerosal, developing child,} of 0.0086 µg of Thimerosal/kg/day estimated from the 1971 Mason chronic toxicity study that injected adult rats twice weekly with Thimerosal doses in the 0.03 µg Thimerosal/kg/day, the LOAEL level, to 1.0 µg Thimerosal/kg range and found an adverse effect at the lowest dose, averaging is inappropriate unless the dose of Thimerosal is, *based on the ratio of the administered dose to the average dose that Mason (1971) used*, no more than 3.5 times the toxic threshold for the daily dose:

- Thus, using this 3.5 multiplier, for children, the total dose of Thimerosal on any given day should be less than 0.03 µg/kg and, for adults, less than 0.3 µg/kg. Obviously, when: **a)** many toxicity and autopsy studies have established that Thimerosal and other and inorganic mercury compounds are bioaccumulative toxins and **b)** the doses injected on a given day are bolus doses that are tens to thousands of times higher than the estimated upper limit on the NOAEL ^{injected Thimerosal, developing human} of < 0.0086 µg of Thimerosal/ kg/day (derived from Mason, 1971, where, in a chronic feeding study using rats, where the twice-weekly doses were only 3.5 times the average dose so that the computation of an average exposure level is appropriate), it is *obviously wrong* to average an infant’s total exposure to Thimerosal over any time period.
- Moreover, unlike the Mason’s study using adult rats, it is also inappropriate to simply average the exposures over time because, unlike the adult, the child is developing.
- Further, the adverse impact of any Thimerosal exposure depends not only on the specific exposure (exposure amount divided by the developing child’s body mass at the time of exposure) but also the developing child’s susceptibility to being mercury poisoned at each individual exposure time point.
- In addition, the calculation also depends upon the developing child’s exposures to other sources of mercury.

- At a minimum, because the initial bolus-dose exposure (to nominally 50 µg of Thimerosal) may occur *in utero*, where the developing child can weigh less than a kg and the brain is not only rapidly growing but also accounts for half or more of the body's mass, the specific exposure must be appropriately weighted.
- Furthermore, absent proof that 90+ % of each dose clears the body (not just the blood) before the next dose is administered in the closest dosing interval, the exposure level for those children who belong to the population of “poor mercury excretors” should be estimated by adding the amount from the previous dose or doses and the average background exposure {typically estimated as an average daily intake retention level of mercury from other sources that may cumulatively equal or exceed the total dose from the vaccines (for example, some data indicates that the total mercury burden in the nursing child's first year of life is roughly “twice” the post natal vaccine burden in nursing children)} to the current dose and then dividing that total dose by the child's weight at that time point.])

Based on the preceding realities, it is clear that the FDA is *knowingly* attempting to mislead the public here.

“Currently, all hepatitis vaccines manufactured for the U.S. market contain either no thimerosal or only trace amounts. Also, DT, Td, and Tetanus Toxoid vaccines are now available in formulations that contain no thimerosal or only trace amounts (see Table 3).”

First this reviewer notes that the “Table 3” to which the FDA refers to here, *though incomplete and flawed in some instances*, contains numerous FDA-approved vaccines that: **a)** the FDA has failed to mention and **b)** are still Thimerosal preserved, including: Sanofi Pasteur, Ltd's trade-nameless TD vaccine; Sanofi Pasteur, Inc's trade-nameless TT vaccine, Sanofi Pasteur, Inc's trade-nameless, inactivated "avian" (H5N1) influenza vaccine; Research Foundation for Microbial Diseases of Osaka University's JE-VAX Japanese Encephalitis vaccine, Sanofi Pasteur, Inc's Menomune A, C, AC and A/C/Y/W-135 multidose meningococcal vaccine.

Thus, except for instances where there is:

- a.** No FDA-licensed “no Thimerosal” vaccine for two of these (i.e., Sanofi Pasteur, Inc's trade-nameless TT vaccine and Sanofi Pasteur, Inc's trade-nameless, inactivated "avian" {H5N1} influenza vaccine, currently only approved for adults) or

- b.** No licensed vaccine for children for another of these (i.e., Research Foundation for Microbial Diseases of Osaka University's JE-VAX Japanese Encephalitis vaccine),

this reviewer does not understand why the FDA licenses for these Thimerosal-preserved vaccines along with those for the Thimerosal-preserved inactivated-influenza vaccines have not been revoked by the Secretary of HHS under the explicit authorities granted to the Secretary in **42 U.S.C. § 300aa-27**.

Thus, the dose of Thimerosal in any vaccine should be less than (<) 0.086 µg) because:

- a.** Neither the vaccine manufacturers nor the FDA – the licensor of vaccines – nor the CDC – the recommender of vaccines – nor any other recognized governmental body have established a scientifically sound value for the dose of injected Thimerosal in any vaccine that has no toxic effect to meet the legally binding CGMP requirement that each dose of vaccine be “sufficiently nontoxic ...” (see 21 CFR § 610.15(a));

- b. For injected pediatric vaccines and injected vaccines allowed to be administered to pregnant women, this reviewer's estimated no-effect level ($< 0.0086 \mu\text{g}$ of Thimerosal/kg/day $\{< 0.0042 \mu\text{g}$ of Hg/kg/day $\}$ is the only estimate appropriately derived from a chronic toxicity study in which Thimerosal was injected into adult rats (which are known to be much more resistant to mercury poisoning than humans, much less children developing *in utero* and in childhood); and
- c. The FDA's "trace" nomenclature permits the level of mercury to be up to $1 \mu\text{g}$ of mercury/dose ($2 \mu\text{g}$ of Thimerosal), or, for the typical 0.5-mL dose, $4 \mu\text{g}$ of Thimerosal/mL (4 ppm), "trace" amounts **may** exceed the estimated NOAEL for injected Thimerosal unless the Thimerosal dose, in μg , is less than 0.0086 times the child's weight in kg (e.g., if the child weighs 10 kg [22 pounds]).

Based on the FDA's June 2009 "Table 3" that shows some level for "Thimerosal in Vaccines" (<http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/VaccineSafety/UCM096228>, **Table 3**), this reviewer notes that the lowest reported Thimerosal dose (for Sanofi Pasteur, Inc's DTaP vaccine, Tripedia®, is $\leq 0.6 \mu\text{g}$ of Thimerosal/ 0.5 mL dose) would be below this reviewer's estimated "no effect" level (NOAEL) only for "children" who weigh at least 70 kg (154 pounds).

Conversely, for human children typically weighing $2\text{-}4 \text{ kg}$ at birth, the maximum "safe" dose of Thimerosal would appear to be in the range of $< 0.017 \mu\text{g}$ – $< 0.034 \mu\text{g}$ of Thimerosal (< 0.0086 – $< 0.017 \mu\text{g}$ of Hg). Thus, for young children the maximum "safe" level of Thimerosal, for 0.5-mL doses, appears to be $< 0.034 \mu\text{g/mL}$ $\{< 0.034 \text{ ppm Thimerosal}\}$.

Based on Tripedia, which has a Thimerosal level of not more than $1.2 \mu\text{g/mL}$, the truly safe Thimerosal levels for Thimerosal in vaccine formulations for children are apparently below the lowest residual levels obtainable in vaccine formulations. **Given this reality alone, the FDA should immediately ban the use of Thimerosal in the manufacture of vaccines and other drug products administered to pregnant women and children.**

In addition, *for developed adults*, where the appropriate NOAEL is $< 0.086 \mu\text{g}$ of Thimerosal/kg/day, the use of Thimerosal as a preservative should be banned and the maximum trace level restricted to not more than (\leq) $4 \mu\text{g}$ of Thimerosal/mL (4 ppm) for the influenza vaccines to provide a safety level for the cumulative effect of both double dosing a month apart initially and the currently recommended annual dosing, provided: **a)** the dose is restricted to $\leq 0.5 \text{ mL}$ and **b)** these vaccines cannot be administered to pregnant women.

"Furthermore, all new vaccines licensed since 1999 are free of thimerosal as a preservative."

Since:

- a. Two Thimerosal-preserved human influenza vaccines are "relicensed licensed" because their viral composition changes each year or two (Fluzone and Fluvirin),
- b. Two additional Thimerosal-preserved human influenza vaccines have been licensed since 1999 (FluLaval {licensed and relicensed since 2006} and Afluria {licensed and relicensed since 2007}), and
- c. A new Thimerosal-preserved inactivated "avian" influenza vaccine, sponsored by Sanofi Pasteur, Inc was licensed in 2007, the FDA is apparently knowingly and intentionally lying here!

"Inactivated influenza vaccine was added to the routinely recommended vaccines for children 6 to 23 months of age in 2004."

The FDA is again being duplicitous because, **starting in 2002**, the CDC has issued written recommendations recommending that not only children but also pregnant women be given the influenza vaccine annually (Bridges CB, Fukuda K, Uyeki TM, Cox NJ, Singleton JA. Prevention and Control of Influenza Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2002 Apr 12; **51**(RR03): 1-31), “where feasible”.

Additionally, The FDA’s “... *recommended vaccines for children 6 to 23 months of age* ...” is, at best misleading. While the 2002 CDC-published recommendation was for children 6 to 23 months of age, the CDC continually widened its recommendation:

- a. First to 23 months with 2 shots the first year, then to 35 months with 2 shots the first year,
- b. Then to 59 months with 2 doses the first year (because the FDA approved a live-virus vaccine for children at least 5 years of age),
- c. Then to 59 to 107 months with 2 doses the first year, and
- d. Finally, to the present CDC recommendation is 6 months to 18 years of age (essentially to 215+ months of age).

Moreover, the FDA has intentionally failed to address the CDC’s off-label recommendation that pregnant women get an annual flu shot.

Ignoring:

- a. The proven increased risk of serious birth defects to their offspring (Heinonen et al. in **Birth Defects and Drugs in Pregnancy** [1977]),
- b. The fact that all influenza vaccines were, and they still are, “Pregnancy Category C”⁹ drugs though, given the findings of teratogenicity by Heinonen et al., as published

⁹ The United States FDA has the following definitions for the pregnancy categories with added emphases:

U.S. FDA Drug Labeling [21 CFR § 201.57(c)(9)(i)(A) Teratogenic effects and ...(A)(1) –(A)(5)]	
...(A)(1) Pregnancy Category A	If adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of a risk in later trimesters), the labeling must state: “ Pregnancy Category A. Studies in pregnant women have not shown that (name of drug) increases the risk of fetal abnormalities if administered during the first (second, third, or all) trimester(s) of pregnancy. If this drug is used during pregnancy, the possibility of fetal harm appears remote. Because studies cannot rule out the possibility of harm, however, (name of drug) should be used during pregnancy only if clearly needed. ” The labeling must also contain a description of the human studies. If animal reproduction studies are also available and they fail to demonstrate a risk to the fetus, the labeling must also state: “ Reproduction studies have been performed in (kinds of animal(s)) at doses up to (x) times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to (name of drug). ” The labeling must also contain a description of available data on the effect of the drug on the later growth, development, and functional maturation of the child.
...(A)(2) Pregnancy Category B	If animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women, the labeling must state: “ Pregnancy Category B. Reproduction studies have been performed in (kind(s) of animal(s)) at doses up to (x) times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to (name of drug) . There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. ” If animal reproduction studies have shown an adverse effect (other than decrease in fertility), but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus during the first trimester of pregnancy (and there is no evidence of a risk in later trimesters), the labeling must state: “ Pregnancy Category B. Reproduction studies in (kind(s) of animal(s)) have shown (describe findings) at (x) times the human dose. Studies in pregnant women, however, have not shown that (name of drug) increases the risk of abnormalities when administered during the first (second, third, or all) trimester(s) of pregnancy. Despite the animal findings, it would appear that the possibility of fetal harm is remote, if the drug is used during pregnancy. Nevertheless, because the studies in humans cannot rule out the possibility of harm, (name of drug) should be used during pregnancy only if clearly needed. ” The labeling must also contain a description of the human studies and a description of available data on the effect of the drug on the later growth, development, and functional maturation of the child.
...(A)(3) Pregnancy Category C	If animal reproduction studies have shown an adverse effect on the fetus, if there are no adequate and well-controlled studies in humans, and if the benefits from the use of the drug in pregnant women may be acceptable despite its potential risks, the labeling must state: “ Pregnancy Category C. (Name of drug) has been shown to be teratogenic (or to have an embryocidal effect or other adverse effect) in (name(s) of species) when given in doses (x) times the human dose. There are no adequate and well-controlled studies in pregnant women. (Name of drug) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. ” The labeling must contain a description of the animal studies. If there are no animal reproduction studies and no adequate and well-controlled studies in humans, the labeling must state: “ Pregnancy Category C. Animal reproduction studies have not been conducted with (name of drug) . It is also not known whether (name of drug) can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. (Name of drug) should be given to a pregnant woman only if clearly needed. ” The labeling must contain a description of any available data on the effect of the drug on the later growth, development, and functional maturation of the child. [Pregnancy Categories “D” and “X” are on the bottom of the next page]

in **Birth Defects and Drugs in Pregnancy** (1977), the FDA should have reclassified Thimerosal-preserved influenza vaccines as “Pregnancy Category D” drugs but, as the FDA continually appears to be, the agency was apparently ignoring the risks whenever they are vaccine-related.

- c. The mandates set forth in **42 U.S.C. 300aa-27**,
- d. The reality that making a recommendation for use in pregnant women was a knowing promotion of an off-label use, and
- e. The manufacturers’ failure to conduct toxicity studies that provided the requisite proofs of safety,

the CDC, through its ACIP, began recommending that pregnant women get a dose of influenza if they were going to be in their second or third trimesters of pregnancy during the “flu” season in April 2002 (Bridges CB, et al. Prevention and Control of Influenza Recommendations of the Advisory Committee on Immunization Practices (ACIP). **MMWR** 2002 Apr 12; **51**(RR03): 1-31), even though the CDC knew that almost all doses that would be available for the 2002 – 2003 flu season were Thimerosal-preserved inactivated-influenza vaccine doses.

Worse, to increase the risk of birth defects in some offspring (since the supply of “preservative free” vaccines was increasing), in 2004 the CDC removed the restriction on the time during pregnancy that a pregnant woman could get a “flu” shot (**MMWR** 2004 May 28; **53**(RR06):1-40):

“Vaccination with inactivated influenza vaccine is recommended for the following persons who are at increased risk for complications from influenza: ...

- women who will be pregnant during the influenza season...”

“FDA has approved thimerosal–preservative free formulations (containing either no or only trace amounts of thimerosal) for the inactivated influenza vaccines manufactured by Sanofi Pasteur and Chiron. These influenza vaccines continue to be marketed in both the preservative free and thimerosal-preservative containing formulations. In addition, in August 2005, FDA licensed GlaxoSmithKline's inactivated influenza vaccine, which contains 1.25 micrograms mercury per dose. Of the three licensed inactivated influenza vaccines, Sanofi Pasteur's Fluzone is the only one approved for use in children down to 6 months of age. Chiron's Fluvirin is approved for individuals 4 years of age and older, and GSK's Fluarix is approved for individuals 18 years of age and older.”

Apparently, the FDA has trouble keeping up with the list of inactivated-influenza vaccines that are currently licensed – from nominally five suppliers and, in 2009, “Chiron” is now “Novartis Vaccines and Diagnostics Ltd”.

...(A)(4) Pregnancy Category D	If there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks (for example, if the drug is needed in a life-threatening situation or serious disease for which safer drugs cannot be used or are ineffective), the labeling must state: “ Pregnancy Category D. See ‘Warnings and Precautions’ section. ” Under the “Warnings and Precautions” section, the labeling must state: “(Name of drug) can cause fetal harm when administered to a pregnant woman. (Describe the human data and any pertinent animal data.) If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.”
...(A)(1) Pregnancy Category X	If studies in animals or humans have demonstrated fetal abnormalities or if there is positive evidence of fetal risk based on adverse reaction reports from investigational or marketing experience, or both, and the risk of the use of the drug in a pregnant woman clearly outweighs any possible benefit (for example, safer drugs or other forms of therapy are available), the labeling must state: “ Pregnancy Category X. See ‘Contraindications’ section. ” Under “Contraindications,” the labeling must state: “(Name of drug) may (can) cause fetal harm when administered to a pregnant woman. (Describe the human data and any pertinent animal data.) (Name of drug) is contraindicated in women who are or may become pregnant. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.”

In addition to Sanofi Pasteur, “CSL Limited” (Afluria) has been approved for both its “*preservative free*” (actually, “no Thimerosal) and its “Thimerosal-preserved” formulations; and ID Biomedical Corporation of Quebec (FluLaval), a subsidiary of GSK has been approved for its “Thimerosal preserved” formulation.

Finally, while the initial approval for GSK’s Fluarix for adults had a nominal Thimerosal level of 1.25 µg/0.5-mL dose, in 2006, GSK reformulated it to contain nominally < 1 µg/0.5-mL dose.

“The live attenuated influenza vaccine (FluMist, manufactured by MedImmune), which contains no thimerosal, is approved for individuals 5 to 49 years of age.”

Apparently, the FDA again has trouble accurately reporting the facts or wishes to hide the fact that it knowingly increased the risk of adverse effects when it widened the age range for FluMist to 2 – 49 years from the original 5 – 49 years.

Specifically, although the initial approval for MedImmune’s FluMist was for those 5 to 49 years of age, in 2007, the FDA approved the widening of the range to 2 to 49 years of age even though the adverse respiratory reactions in children less than 5 years of age occurred more frequently.

Thus, the FDA’s decision was, and is, at odds with the statutory mandate for the Secretary of HHS to whom the FDA supposedly answers “safely vaccines” by reducing adverse reactions (**42 U.S.C. § 300aa-27(a)**).

“For the 2005-2006 season, Sanofi Pasteur was able to manufacture up to 8 million doses of thimerosal-preserved free influenza vaccine. Based on an estimated annual birth cohort in the United States of 4 million, there are 6 million infants and children between the ages of 6 and 23 months, most of whom would need two doses each. Thus, the amount of thimerosal-preserved-free vaccine that is available based on current manufacturing capacity is well below the number of doses needed to fully vaccinate this age group.”

Here, the FDA is again bending reality because: **a)** the number of doses distributed was closer to 6 million because the CDC has continually refused to state a preference for the “*thimerosal-preserved free influenza vaccine*” and **b)** the usage of the doses was not restricted to children “*between the ages of 6 and months*”.

“FDA is in discussions with manufacturers of influenza vaccine regarding their capacity to further increase the supply of preservative-free formulations.”

Again, this reviewer finds the FDA’s statement here is, at best, misleading

Troublingly, there has been no change in the CDC’s and the FDA’s posture toward: **a)**, *on the part of the FDA*, complying with the applicable laws and statutes that mandate “proof of safety” to the standard “sufficiently nontoxic ...” set forth in **21 CFR § 610.15(a)** by the manufacturers of preserved drug products, and licensing by the FDA only after the manufacturer of preserved drug products has met and submitted proof that its preserved products have met the aforesaid safety standard, and **b)**, *on the part of both agencies*, complying with all the vaccine safety mandates set forth in **42 U.S.C. § 300aa-27** that, among other issues, addresses the licensing and the administration of vaccines.

7. The eighth important unasked question:

“Why, by:

- a. Allowing deceptive terms, such as ‘preservative free’ and ‘no preservative’, to be used on the label applied to the primary vaccine containers, and
- b. Not requiring all labeling, advertising, and each primary container of any Thimerosal-containing vaccine to prominently disclose the maximum mercury content of the vaccine dose or doses in that container (bottle, vial, syringe or other)

is the FDA *knowingly* depriving each American of his constitutionally-guaranteed right to be able to give ‘informed consent’?”

“Why are some vaccines noted to be ‘thimerosal-free’ while some are ‘thimerosal-reduced’? What is the difference between ‘thimerosal-free’ and ‘preservative-free’?”

Thimerosal may be added at the end of the manufacturing process to act as a preservative to prevent bacterial or fungal growth in the event that the vaccine is accidentally contaminated, as might occur with repeated puncture of multi-dose vials. When thimerosal is used as preservative in vaccines, it is present in concentrations up to 0.01% (50 micrograms thimerosal per 0.5 mL dose or 25 micrograms mercury per 0.5 mL dose). In some cases, thimerosal is used during the manufacturing process and is present in small amounts in the final vaccine (1 micrograms mercury or less per dose).

The term "preservative-free" indicates that no preservative (thimerosal or otherwise) is used in the vaccine; however, traces used during the manufacturing process may be present in the final formulation. For example, some vaccines may be preservative-free but may contain traces of thimerosal (1 micrograms mercury or less per dose); in such settings, this information is noted in the package insert. Similarly, the term "thimerosal-reduced" usually indicates that thimerosal is not added as a vaccine preservative, but trace amounts (1 micrograms mercury per dose or less) may remain from use in the manufacturing process. Such trace amounts are not felt to be clinically significant, nor would they result in exposure exceeding any federal guideline for mercury exposure. Vaccines may be termed "thimerosal-free" if no thimerosal can be measured; i.e., thimerosal content is below the limit of detection.”

First, this reviewer notes that the FDA did not address the “no Thimerosal” formulations, which apparently address those formulations in which “no Thimerosal” is used in the manufacturing process for the product or the components used to make the product.

Second, this reviewer notes that, absent a defined FDA-accepted methodology that has a “*limit of detection*” for Thimerosal, not Thimerosal and Thimerosal’s ethylmercury solvolysis products or mercury, which is below 0.1 ppm Thimerosal, the terms “thimerosal-free” and “thimerosal-reduced” imply that Thimerosal was used in, at some stage, in the manufacture of the vaccine formulation.

Third, because the term “preservative” strictly applies to the usage of a compound and, in the FDA’s current view, usage at a level sufficient to conform to the USP’s current expectations for “Preservative Effectiveness”, no chemical compound “is” a preservative.

Therefore, the FDA’s first statement:

“The term ‘preservative-free’ indicates that no preservative (thimerosal or otherwise) is used in the vaccine”,

is inaccurate and should be revised to read:

“The term ‘preservative-free’ indicates that no ~~preservative~~ compound (Thimerosal or otherwise) is ~~used~~” added to “the vaccine” or present in the distributed vaccine as a ‘preservative’”.

Finally, given:

- a.** This reviewer’s understanding of the properties of Thimerosal in vaccine formulations and the published 2004 failure of the contents of some released vials of some lots of released Thimerosal-preserved inactivated-influenza vaccine doses to prevent the growth of the *Serratia marcescens* bacteria with which some vials of some lots had been somehow contaminated during the manufacturing process (http://www.usatoday.com/money/.../2004-11-12-flu-cover_x.htm) – as well as published “preservative” failures in which some partially used vials were found to be contaminated with viable pathogenic bacteria, including *Streptococcus Aureus*, when evaluated, and
- b.** The USP’s legally binding post-release requirement that the “preservative” system be effective, whenever post-release samples are tested under the current applicable USP evaluation conditions for “Preservative Effectiveness” until after the expiration date for the lot of vaccine released by the manufacturer,

this reviewer asks that the FDA publish proof that, at expiration, each Thimerosal-preserved vaccine formulation still meets the USP’s definition for an effective microbial preservative.

8. The ninth important unasked question:

“When it knows that, unlike ingested (eaten) mercury (where most [estimated as >75%] of the mercury in the foods we eat [e.g., fish] simply passes through the digestive system without being absorbed), injected mercury bypasses the digestive system’s mercury defenses and, when it is Thimerosal dissolved in a vaccine formulation, is readily transported throughout the body, how can the FDA have so little real concern for injected mercury?”

“Why is exposure to mercury a concern?”

Mercury is an element that is dispersed widely around the earth. Most of the mercury in the water, soil, plants and animals is found as inorganic mercury salts.”

This reviewer notes that the FDA *misleadingly* fails to disclose: **a)** mercury, in all of its forms, is recognized as the most toxic of all of the non-radioactive elements on the earth, **b)** mercury compounds are recognized as being 10 to 100 times more toxic than the corresponding lead compounds, **c)** mercury is also found in the air, and **d)** mercury compounds, like Thimerosal and other forms of mercury, that are used in medicine are *totally avoidable exposure sources unlike* the mercury in air, water, soil, plants and animals.

“Mercury accumulates in the aquatic food chain, primarily in the form of the methylmercury, an organomercurial. Methylmercury is more easily absorbed and is less readily eliminated from the body than inorganic mercury. Exposure to one chemical with mercury, i.e., methylmercury, has been shown to pose a variety of health risks to humans.”

The FDA’s statements here misrepresent reality. Actually:

- Mercury accumulates in the aquatic food chain, primarily in the form of methylmercury compounds, which are organomercurials (organic mercury compounds).
- The common, environmentally generated, methylmercury compounds, are mainly produced today by the methylation of the naturally occurring inorganic mercury species, and
- These methylmercury compounds are more readily absorbed and less readily eliminated from the human body than inorganic mercury compounds.
- Exposure to organomercury compounds, mostly short-chain alkylmercury compounds (like methylmercury hydroxide and chloride and dimethylmercury), and aryl mercury compounds (like phenylmercury acetate, nitrate, and borate) have been shown to pose a variety of health risks to humans at mercury tissue levels below 1 ppm.
- Furthermore, Thimerosal, sodium ethylmercury thiosalicylate, is: **a)** highly toxic and **b)** a recognized teratogen, mutagen, carcinogen, and immune-system disruptor, which unlike methylmercury chloride or methylmercury hydroxide, has significant auto-immunogenic properties, as well as a reproductive toxin at nominal Thimerosal levels below 1 ppm (0.0001%; 1 part in 1,000,000).
- In early studies of organomercurials by Morton, North and Engley reported in their 1948 paper (Morton HE Jr, North LL, and Engley FB, Jr. The bacteriostatic and bactericidal actions of some mercurial compounds on Hemolytic streptococci: In vivo and in vitro studies. *J. Am. Med. Assoc.* 1948; 136: 37–41) that of the many mercury compounds they evaluated, Thimerosal (Merthiolate) was the second most toxic.

“Extremely high levels, such as that observed in poisoning episodes in Japan and Iraq has caused neurological damage and death. The fetus is considered more sensitive to health effects of methylmercury than adults. In recent years[,] some studies have found adverse health effects of methylmercury at levels previously thought to be safe. Other studies, however, have shown conflicting results.”

Here, the FDA appears to be intentionally and *knowingly* misrepresenting factual reality. Based on knowledgeable reviewer’s understanding of reality the following text accurately portrays the current realities:

“Factually, confirmed cases of systemic mercury poisoning, neurological damage and death from food consumption have been observed in instances of: **a)** direct human exposures to a variety of methyl- and ethyl- mercury compounds from seeds coated with a variety of methylmercury and ethylmercury fungicides that periodically occurred in poisoning episodes in Iraq, Russia, Egypt and elsewhere when it was legal to use these alkylmercury compounds as agricultural fungicides, and **b)** indirect exposures such as eating animals contaminated at low ppm levels from being fed mercury-compound-treated seed such as occurred in the USA or from eating fish contaminated with ppm-levels of methylmercury compounds, such as those which occurred in Japan, where the authorities initially labeled the problem “strange disease”.

In addition, deaths from the topical use of Merthiolate (as a 0.1% solution Thimerosal in alcohol) on babies in a hospital setting have been reported (e.g., Fagan DG, Pritchard JS, Clarkson TW. Organ mercury levels in infants with omphaloceles treated with organic mercurial antiseptic. *Arch Dis Child*. 1977; **52**: 962-964).

Based on the available published toxicological literature, it is clear that, though, in humans and other mammals, as a group, the fetuses are most sensitive, the developing children are more sensitive and adults are the less sensitive to mercury poisoning from exposures to alkylmercury compounds, there is a wide range in the sensitivity of individuals within any group to exposures at sub-acute mercury intoxication levels.

In addition, limited studies in animals have established a 2- to 5- fold lower threshold for the onset of mercury poisoning symptoms in males compared to females, which even extends to the lethal single-dose level.

As the scientific study of the toxicity of alkylmercury compounds has progressed, the level of exposure associated with toxic effects has declined to the point that, in 2009, persistent harmful effects in developing primates and children are being observed from doses of organic mercury compounds below 10 µg of Hg/kg.”

For those wishing to read more concerning Thimerosal and these toxicity issues, this reviewer recommends:

- “A review of Thimerosal (Merthiolate) and its ethylmercury breakdown product: Specific historical considerations regarding safety and effectiveness” published in 2007 by Geier DA et al. (*Journal of Toxicology and Environmental Health, Part B* 2007; **10**: 575–596) for the period from the 1920s through 2006 and
- The recent published toxicological literature for the period from 2007 onwards.”

“It is important to note that the preservative thimerosal contains ethylmercury, a related though distinct chemical from methylmercury. Moreover, recent studies in animal models exposed to thimerosal containing vaccines or oral methylmercury suggest that methylmercury may not be a suitable reference to assess the risk from exposure to thimerosal (Burbacher et al, 2005).”

First, this reviewer agrees with the FDA that, as with all alkyl mercury compounds, substituting a methyl group with an ethyl group produces a “distinct chemical”.

However, with respect to Burbacher (2005), since:

- a. The methyl mercury compound used (methylmercury hydroxide) was not the methylmercury analog of Thimerosal (i.e., sodium ethylmercury thiosalicylate) and
- b. The modes of exposure differed (the methylmercury compound was force fed to the monkeys in the “methylmercury” test group of monkeys, while the “ethylmercury” test group of monkeys were injected with Thimerosal-containing vaccines),

the differences in:

1. The mode of delivery (force fed versus injected) and
2. The alkylmercury compound’s type (a neutral hydroxide in the “methylmercury” case and a thiosalicylate salt in the “ethylmercury” case)

preclude any unbiased assessment of whether or not a given “methylmercury” analog is a suitable “model compound” for the testing of the toxicity of some ethylmercury compound.

Had the researchers, using a similar experimental design:

- a. Injected sodium methylmercury thiosalicylate into a “methylmercury” test group of three times as many developing monkeys,
- b. Injected sodium ethylmercury thiosalicylate into the “ethylmercury” test group of the same number of monkeys,
- c. Injected methylmercury hydroxide into a similar third group and
- d. Injected sterile saline into a similar “placebo control” group, **e**) reared them on the same mercury-level-controlled rat chow,
- f. Carefully performed similar assessments for a significant portion of the monkey’s life span (e.g., for 3 years) instead of a few months and
- e. Found significant differences between the half-lives for the various mercury species in group “a” as compared to group “b” but similar mercury-type half-lives in groups “a” and “c”,

then some *unbiased* valid assessment of the suitability of the use of methylmercury hydroxide as a surrogate for Thimerosal could have been found.

However, *for whatever reasons*, the researchers in Burbacher et al. (2005) confounded the experiments by using different modes of exposure (force feeding and injection) and compounds that had significant structural (–hydroxide and –thiosalicylate sodium) and type differences (simple alcohol and the sodium salt of a weak acid).]

“In addition, data from studies in human infants that were given routine immunizations with thimerosal-containing vaccines showed that mercury levels in blood and urine were uniformly below safety guidelines for methyl mercury and that unlike methylmercury excretory profiles, infants excreted significant amounts of mercury in stool after thimerosal (ethylmercury) exposure, thus removing mercury from their bodies (Pichichero ME, et al, 2002).”

Here, again, as the researchers, for whatever reasons, did, the FDA misrepresents the findings of the experiment.

First, having essentially claimed that “methylmercury” compounds probably cannot be used as models for Thimerosal based on the work of Burbacher et al. (2005), the FDA now is essentially claiming that it is valid to use a “methylmercury” estimated guideline for the “safe” level for “methylmercury” in infant blood and urine (the FDA’s “*mercury levels in blood and urine were uniformly below safety guidelines for methyl mercury*”).

Moreover, since the Pichichero (2002) failed to:

- a.** Use Thimerosal that contained an identifiable mercury isotopic pattern different from the naturally occurring one and
- b.** Do a mass balance study on any infant that showed that 99+% of the mercury dosed was recovered in the feces, urine, hair, and fingernails, the principal sources for excretion and
- c.** Collect and test all of the stools for each child so that the cumulative percentage of “mercury” recovered in the stool could be estimated, the FDA’s claim that “*infants excreted significant amounts of mercury in stool after thimerosal (ethylmercury) exposure, thus removing mercury from their bodies*” is a clever distortion.

This is the case because, *absent the experiments outlined by this reviewer*, all that this Pichichero (2002) study found was that the infants excreted some mercury in their feces, which obviously removed some mercury from their bodies. However, since:

- a.** This study did no mass balance assessments that established a significant percentage of the mercury injected (e.g., > 50%) was recovered in the feces and the values determined were “level” values (e.g., ng of mercury per gram of feces tested),
- b.** The experimental details reported neither the total weight of the fecal samples nor the steps taken to render the total feces homogeneous with respect to mercury, and
- c.** These researchers reported no cumulative “amount values” (i.e., µg of mercury) derived by multiplying the “level” values by the grams of feces,

it is neither scientifically sound nor scientifically appropriate to state, as has been done here, that the “*infants excreted significant amounts of mercury in stool after thimerosal (ethylmercury) exposure, thus removing mercury from their bodies*”.

9. The tenth important unasked question:

“Why does the FDA expect anyone to believe the findings of any IOM committee named, ‘Immunization Safety Review Committee’ reviewing the safety of Thimerosal in vaccines when they were hired and given their instructions by the CDC, the agency charged with promoting vaccines, given the ‘instructions’ the committee received from the CDC directed it to make no recommendation that could threaten the status quo concerning the CDC’s vaccination programs?”

“I understand that the Institute of Medicine (IOM) has reviewed the issue of thimerosal in vaccines. What were the IOM’s findings?”

In its report of October 1, 2001, the IOM’s Immunization Safety Review Committee concluded that the evidence is inadequate to either accept or reject a causal relationship between thimerosal exposure from childhood vaccines and the neurodevelopmental disorders of autism, attention deficit hyperactivity disorder (ADHD), and speech or language delay. At that time[,] the committee’s conclusion was based on the fact that there were no published epidemiological studies examining the potential association between thimerosal containing vaccines and neurodevelopmental disorders. The Committee did conclude that the hypothesis that exposure to thimerosal-containing vaccines could be associated with neurodevelopmental disorders was biologically plausible. However, additional studies were needed to establish or reject a causal relationship.”

This reviewer hopes everyone finds it very odd that the IOM “Immunization Safety Review Committee” titularly, charged with reviewing immunization safety, would have restricted its review to links between a causeless “psychiatric” disorder characterized by fuzzy symptoms and: **a)** the MMR vaccine and **b)** vaccines containing Thimerosal as a preservative.

Moreover, the review that this IOM committee conducted was anything but comprehensive. There were, and are, numerous key pre-2000 peer-reviewed publications in which ethylmercury compounds were studied, including several instance of mass poisonings from the consumption of grain treated with ethylmercury-based fungicides, which clearly showed evidence of the neurotoxicity of low-level dietary exposures in developing children to ethylmercury compounds (which are clearly structurally related to Thimerosal, ethylmercury thiosalicylate, sodium salt), which this IOM committee apparently failed to review. [**Note:** Based on the list of references, the committee’s review included only one of the papers {Jalili & Abbasi, 1961} that addressed sub-acute ethylmercury-compound exposure in developing children.]

In contrast, though by no means complete, the published peer-reviewed historical review paper, “A review of Thimerosal (Merthiolate) and its ethylmercury breakdown product: Specific historical considerations regarding safety and effectiveness” published in 2007 by Geier DA et al. (***Journal of Toxicology and Environmental Health, Part B* 2007; 10: 575–596**) reported (pages 584-586):

“ E THYLMERCURY POISONING IN HUMANS

Spanning the 1950s and 1960s, a series of population outbreaks of ethylmercury poisonings occurred in Iraq, following ingestion of Granosan M, an antifungal that was used to prevent plant root disease in grain products. Beginning in 1955, the Iraqi Ministry of Agriculture supplied farmers with seeds dusted with the fungicide. Farmers had been given frequent warnings against using the treated seed for food, and as a result, most of them were aware of the highly lethal effect of eating dusted seed. Out of ignorance or neglect, however, some unfortunate farmers and their families consumed the seed and became the victims of mercury poisoning. Consequently, these

farmers developed a number of serious mercury-related conditions (Jalili & Abbasi, 1961; Al-Kassab & Saigh, 1962; Dahhan & Orfaly, 1962; Damlugi, 1962). Specifically, it was reported:

"Poisoning by a fungicide used for seed-borne diseases of cereals, ethyl mercury p-toluene sulfonamide (Granoson M, Dupont) is described. It affected a large number of farmers and their families who used the dressed seed in the preparation of home-made bread. Many systems were involved, including the kidneys, the gastrointestinal tract, the skin, the heart, and the muscles, but involvement of the nervous system was the most constant with disturbance of speech, cerebellar ataxia, and spasticity. Mental abnormalities were occasionally observed ... In 1956 many cases of mercury poisoning were observed in the North of Iraq, and more than 100 cases were admitted to Mosul Hospital with 14 deaths. In 1960, many farmers from the central part of Iraq were affected and 221 patients were admitted to one hospital in Baghdad. Other patients went to other hospitals. (Jalili & Abbasi, 1961, p. 303)"

Later, a significant series of patients in Russia was observed to suffer from serious toxic outcomes following ingestion of ethylmercury and occupational exposure to ethylmercury (Shustov & Syganova, 1970; Nizov & Shestakov, 1971). Early signs of exposure included general weakness, pains, tachycardia, and headache. Thereafter, it was observed that appetite decreased until, at last, food was refused; there was also nausea, liquid stool, disordered sleep, decreased memory, and pain in the extremities. Most of the patients recovered, but death was observed following exposure in some of the patients. Such case studies clearly demonstrate the severe toxicity of this compound to humans and document its effect on multiple systems of the human body due to acute exposure.

Not only acute exposure, however, but also low-dose exposure has produced significant impairment in human beings, a fact documented by Mukhtarova (1977). Mukhtarova (1977) examined the late after-effects upon the nervous system following chronic low-dose exposure to ethylmercury. The researcher reported:

A total of 25 persons exposed to multiple effects of low ethyl-mercuric-chloride concentrations were subjected to a clinical examination in dynamics 1 ½ and 3 years after exposure to the compound. In investigations clinicophysiological (EEG, Asschner-Dagnini reflexes, etc) and biochemical (catecholamines, sugar, mercury, DDT, DDE in the urine, etc) methods were employed. The pathology of the nervous system presented certain peculiarities by comparison with early period. In evidence were changes in the simpatico-adrenal system function, vascular lesions of the brain after the type of transient derangements of the cerebral circulation in the vertebro-basilar basin and angiospasm, diffuse changes in the nervous system with predominant involvement of the hypothalamic cerebral structures and in some cases psychiatric disturbances were on record. (p. 4–7)

Over time, further incidents of mercury poisonings by ethylmercury compounds continued to offer substantial evidence and disclose a pattern of extreme toxicity produced by ethylmercury in humans. For example, Cinca et al. (1980) reported on accidental ethylmercury poisoning with nervous system, skeletal muscle, and myocardium injury and stated, 'Four case reports are presented of patients who ate the meat of a hog inadvertently fed seed treated with fungicides containing ethyl mercury chloride. The clinical, electrophysiological, and toxicological, and in two of the patients the pathological data, showed that this organic mercury compound has a very high toxicity not only for the brain, but also for the spinal motor neurons, peripheral nerves, skeletal muscles, and myocardium' (p. 143).

As another example, Zhang (1984) evaluated clinical symptoms observed in patients with ethylmercury chloride poisoning and reported, 'Forty-one patients in the Peoples Republic of China were poisoned by ethyl mercury chloride, caused by the ingestion of rice that had been treated with the chemical. A dose-response relationship was found. Five months after the onset of the intoxication, the patients were still in poor condition' (p. 251).

Derban (1974) even reported on clinical symptoms observed in children following ethylmercury poisoning of 144 people in a rural Ghana village, 'Four children developed disturbance of speech which led to stammering and scanning. Mental abnormality was observed in one boy who showed occasional outburst of anger unrelated to circumstances. A girl developed encephalitis and became completely paralyzed in both upper and lower limbs, with incontinence of urine and feces and complete loss of speech' (p. 50).

Paramount in the historical scientific record of exposures to ethylmercury compounds are the first reports of human fetal poisonings. Bakulina (1968) described in a study on a human fetal poisoning:

Granoson (ethylmercury chloride) is capable of passing through the placental barrier and penetrating into the fetus, causing in the organs of the latter grave pathological changes. The permeability of the placental barrier for organic mercury compounds finds its confirmation in the presence of mercury in the placenta and organs of the fetus ... Breast feeding was found to be conducive to accumulation of mercury in the organism of newborns, since the mothers' milk, as a rule, disclosed the presence of this element. A very important point was that fetal intoxication was possible for as long as 3–4 years after the mother poisoned. (p. 63)

By the early 1970s, researchers developed an overall clinical picture of ethylmercury poisoning in fetuses following large-scale ethylmercury poisoning episodes (Mal'tsev, 1972; Ramanauskayte & Baublis 1973). Ramanauskayte and Baublis (1973) stated that, after exposure to ethylmercury-treated seeds:

Intrauterine poisoning in infants was observed(.) ... (C)hildren on the whole are more susceptible to mercury than adults(.) ... Serious functional disorders of the central nervous system, hydrocephalus, cerebral paralysis, and spasms were observed in infants. Toxic encephalomyeloradiculoneuritis with prevalence of the syndromes of lesions of the cerebral cortex, brain stem, cerebellum, myelitis, peripheral neurites, lesions of the motor centers, of the pyramidal tracts, and encephalitis with irregular alphas rhythm were observed ... Epilepsy lasting up to 2 years was observed in 10% of all cases. Prevalence of vegetoneurotic syndromes, tachycardia, bradycardia, arrhythmia, acrocyanosis, liability of the arterial pressure, and reduction of the blood cholinesterase activity were found in older children with chronic poisoning. The lesions of the liver, kidney, heart and gastrointestinal tract were much less pronounced than those of the central nervous system. Sodium thiosulfate, glutamic acid, vitamin B and C complexes, glucose, and diuresis are essential for detoxification. (Ramanauskayte & Baublis, 1973, p. 56–60)

Confirming the tremendous danger of ethylmercury compounds to children, Mal'tsev (1972) reported that in cases of children poisoned with ethylmercury, the onset of symptoms usually occurred many weeks following exposure. The first symptoms of ethylmercury poisoning in children included asthenia, fatigability, and loss of appetite, followed by nausea, vomiting, liquid feces, abdominal pains, and elevated temperature. Subsequently, the neurological syndrome developed and consisted of symptoms such as ataxia, dysarthria, psychomotor disturbances, and sleep disturbances.

The researcher reported that damage to the nervous system may be irreversible even following low-dose exposure. Mal'tsev (1972) also commented that, upon autopsy of children who died of ethylmercury exposure, degenerative, inflammatory, and necrotic alterations were seen, as well as hemorrhages in the central nervous system, kidney, liver, heart, and intestines. Mal'tsev (1972) also reported that ethylmercury appeared to be the most dangerous to the embryos during the third and four months of pregnancy”.

In addition, the FDA's: *“At that time the committee's conclusion was based on the fact that there were no published epidemiological studies examining the potential association between thimerosal containing vaccines and neurodevelopmental disorders”* is a clear example of Orwellian “new speak” and pseudo-scientific “mumbo jumbo”.

Factually, the human-exposure safety limits for a chemical compound that is injected into humans can only be determined by the appropriate scientifically sound toxicological assessments.

Epidemiology cannot determine the safety of vaccinating humans with Thimerosal-preserved vaccines or Thimerosal-containing vaccines because:

- **At best**, honest epidemiology can only estimate the probability that some potential causal factor (e.g., injecting Thimerosal-preserved vaccines into pregnant women and developing children without first obtaining the legally mandated proofs of safety, minimally to the CGMP standard of “sufficiently nontoxic ...” as set forth in **21 CFR § 610.15(a)**) is linked to the risk of some subsequent outcome (e.g., sub-acute mercury poisoning manifesting as neurological damage that is “diagnosed” as “autism” and other “neurodevelopmental disorders”).
- **At worst**, through the use inappropriate study designs, misclassification of information, inappropriate data culling criteria, problematic data sets, and inappropriate outcome-directed iterative assessment, epidemiology can be used to hide the evidence of possible causal linkages, as the NIEHS report, “REPORT OF THE EXPERT PANEL TO THE NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, Thimerosal Exposure in Pediatric Vaccines: Feasibility of Studies Using the Vaccine Safety Datalink, August 24, 2006”, established.

Though only a journeyman statistician at best, even this reviewer remembers the classic tobacco-industry-funded epidemiological study that showed that the rate of increase in cases

of lung cancer was linked to the increase in sales of refrigerators and, therefore, refrigerators (and not cigarettes and other tobacco products) were the “cause” of lung cancer.

“The Committee believed that the effort to remove thimerosal from vaccines was ‘a prudent measure in support of the public health goal to reduce mercury exposure of infants and children as much as possible.’ Furthermore, in this regard, the Committee urged that ‘full consideration be given to removing thimerosal from any biological product to which infants, children, and pregnant women are exposed.’”

Here, this reviewer finds it odd that this IOM committee failed to note that this lack of evidence for Thimerosal-preserved vaccines had been caused by: **a)** the vaccine makers’ *knowing* and *intentional* failure to conduct the appropriate scientifically sound toxicity studies on the vaccine formulation and Thimerosal that are required by law to prove the Thimerosal used as a preservative used was “sufficiently nontoxic ...” (**21 CFR § 610.15(a)**) and/or publish the results of said toxicity studies and **b)** the FDA’s failure to enforce compliance by denying the licensing of any new Thimerosal-preserved vaccine formulation whose BLA did not contain proof of compliance with **21 CFR § 610.15(a)** as required by **21 CFR § 601.4** before licensing that formulation or, for existing licensed Thimerosal-preserved vaccines, suspending said licenses under the authorities granted to the Secretary of HHS to safe vaccines (**42 U.S.C § 300aa-27**).

In addition, given the availability of the Mason (1971) chronic toxicity study using adult rats and injected Thimerosal solutions and finding clear evidence of an adverse dose-level-dependent effect at all dosing levels (“broncopneumonia”), this IOM committee should have, *at a minimum*, found that Thimerosal was too toxic to be used as a preservative in vaccines given to pregnant women and developing children!

Finally, this reviewer simply notes that, *like the many previous “urgings”*, this one fell upon ears that did not want to hear much less truly heed them.]

“In 2004, the IOM’s Immunization Safety Review Committee again examined the hypothesis that vaccines, specifically the MMR vaccines and thimerosal containing vaccines, are causally associated with autism. In this report, the committee incorporated new epidemiological evidence from the U.S., Denmark, Sweden, and the United Kingdom, and studies of biologic mechanisms related to vaccines and autism that had become available since its report in 2001.”

First, since access to the raw data sets used in these studies has been denied to qualified independent reviewers (for example, in the U.S. study [Verstraeten et al. 2003], the CDC has claimed to have “lost” the datasets in order to preclude any review) and the published studies contain many obvious violations of the fundamental precepts of the study of the statistics of large populations of living entities, including epidemiological studies, this reviewer must again:

- Relegate the studies to the dustbin reserved for studies whose soundness cannot be *independently* verified and whose findings *cannot* be independently confirmed, and
- Reject any use of the studies as the basis for any decision concerning the evidence of a linkage, or lack thereof, between “autism” and either the MMR vaccines or the dose-related Thimerosal risk from vaccinating young children with Thimerosal-preserved vaccines.

In addition, this reviewer must again ask why any “immunization safety committee” would attempt to use epidemiological studies that cannot prove “safety” as the basis for its decisions on “safety”?

“The committee concluded that this body of evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism, and that hypotheses generated to date concerning a biological mechanism for such causality are theoretical only. Further, the committee stated that the benefits of vaccination are proven and the hypothesis of susceptible populations is presently speculative, and that widespread rejection of vaccines would lead to increases in incidences of serious infectious diseases like measles, whooping cough and Hib bacterial meningitis.”

Factually, all of the assertions reported here are simply examples of the clever use of Orwellian “new speak” to obscure the truth cover it with misdirective statements that changed the focus:

- ❑ **From:** the obviously unproven vaccine safety, which the IOM committee was supposed to establish but: **a)** had not established and **b)**, based on the toxicity data, could not establish for Thimerosal in vaccines (or, for that matter, for the MMR vaccine)
- ❑ **To:** **a)** the “*benefits of vaccination*”, **b)** a proven generality, “*susceptible populations*”, cast as an “*hypothesis*” that, contrary to the committee’s view, was well-established, and **c)** a vacuous, fabricated, vague, fear-based warning, “*widespread rejection of vaccines would lead to increases in incidences of serious infectious diseases like measles, whooping cough and Hib bacterial meningitis*” that were, and are, clearly outside of the scope of what this IOM committee was supposed, based on its title, “Immunization Safety Review Committee”, to be reviewing – namely, “immunization safety”.

10. The eleventh important unasked question:

“How can the FDA continue to tacitly and knowingly approve the injection of a Thimerosal-containing inactivated-influenza vaccine into pregnant women, when, since 1977, if not before, the FDA knew that, in retrospective studies, both topical Thimerosal and Thimerosal-preserved flu shots had been proven to be a human teratogen that caused serious birth defects in the offspring of women given a single flu shot (e.g., cleft palate, microcephaly, and pyloric stenosis) at hospital-adjusted rates up to 7 times the background rates for these birth defects?”

“The IOM urged that ‘full consideration be given to removing thimerosal from any biological product to which infants, children, and pregnant women are exposed’ (IOM 2001). Routine administration of influenza vaccine is recommended in pregnant women, yet currently available U.S. licensed influenza vaccines contain thimerosal. Why are pregnant women receiving influenza vaccine containing thimerosal?”

This issue was reviewed by the CDC's Advisory Committee on Immunization Practices (ACIP) in 1999 and again in 2001. At that time, the ACIP recommended no changes in the influenza vaccination guidelines, including those for children and pregnant women. The ACIP stated that ‘because pregnant women are at increased risk for influenza complications and because a substantial safety margin has been incorporated into health guidance values for organic mercury exposure, the benefit of influenza vaccine outweighs the potential risks for thimerosal’.”

Here, this reviewer is taken aback. Again rather than citing the scientific studies that prove the safety of Thimerosal-preserved influenza vaccines, the FDA is simply paraphrasing a portion of an unreferenced self-serving statement that the ACIP, a pro-immunization advisory committee to the pro-vaccination-without-regard-to-its-cost-effectiveness CDC, purportedly made: *“because pregnant women are at increased risk for influenza complications and because a substantial safety margin has been incorporated into health guidance values for organic mercury exposure, the benefit of influenza vaccine outweighs the potential risks for thimerosal”*.

Based on the only published U.S.-wide population study of the effectiveness of influenza vaccination in preventing influenza (Geier DA, King PG, Geier MR. Influenza Vaccine: Review of effectiveness of the U.S. immunization program, and policy considerations. **J. Am Phys Surg** 2006 Fall; **11**(3): 69-74), the influenza vaccination program is, *for a number of reasons*¹⁰, not effective in reducing: **a)** the number of influenza cases, **b)** influenza-related hospitalizations or **c)** influenza-related (mostly pneumonia) deaths that occur each year during the U.S. “flu” season.

Since the influenza vaccines are not effective in preventing disease, the only proven direct benefits of influenza vaccines are the benefits to: **a)** the revenues of the vaccines’ manufacturers who make the vaccines, **b)** the increased income from more well-baby visits to those who provide such, and **c)**, through the \$ 0.75 federal tax on each dose, the federal government.

¹⁰ The reasons for ineffectiveness include, but are not limited to, **a)** “strain mismatch” between the actual circulating strains and the strains for which the vaccines may provide some protection, **b)** the presence of many other strains of influenza virus in the population, and **c)** the lack of effectiveness of the vaccine dose in providing protection from even the vaccine strains of influenza (typically, “efficacy” values as low as “65”% are allowed).

Further, since inoculation with Thimerosal-preserved vaccines has known adverse risks that include anaphylactic shock, Guillian-Barré syndrome, and death, it is clear that the FDA's "*potential risks*" for those inoculated with Thimerosal-preserved influenza vaccines are real.

Finally, among its findings, a collaborative study (Heinonen OP, Slone D, Shapiro S. **Birth Defects and Drugs in Pregnancy**. Littleton, Massachusetts: Publishing Sciences Group, Inc., 1977) reported:

"Between 1958 and 1965, under the auspices of the National Institute of Neurological and Communicative Disorders and Stroke, a prospective study of over 50,000 pregnancies was undertaken with the main objective of determining whether there are factors during pregnancy or delivery that are related to the risk of cerebral palsy or other neurological outcomes. This study ultimately became known as the Collaborative Perinatal Project. Among many items of data obtained, drug use was recorded during pregnancy, and birth defects identified in the children were recorded subsequently. With the growing realization that drugs are sometimes teratogenic, it became mandatory to evaluate the data from the perspective... The purpose of this book is to present data on drugs used by 50,282 gravidæ in relation to birth defects identified in children.' The conclusion of these researchers with regard to Thimerosal, '(t)he measure of association presented is a standardized relative risk (SRR) with its 95% confidence limits. The SRR is the ratio of the observed number to the expected number of malformed children. Since the SRR takes into account potential confounding variables, it represents the best estimate of the relationship between a drug and a malformation...' Finally, thiomersal...was associated with malformations overall and with uniform malformations".

Specifically, the study found that Thimerosal exposure during the first 4 months of pregnancy was associated with a statistically significant increased risk (SRR = 2.69) for birth defects.

Furthermore, in "**Birth Defects and Drugs in Pregnancy**", Heinonen et al. also reported evidence of serious birth defects in children born to mothers who had had an influenza shot:

- In **Appendix 4, "Drug Exposure During the First Four Lunar Months of Pregnancy in Relation to Specific Malformation Entities"**, on page 474, the book reports, for "Influenza Virus Vaccine", which was at that time only Thimerosal preserved, a "Hospital Standardized Relative Risk" for 650 "Mother-Child Pairs Exposed" of 7.1 for "Cleft Palate Only".
- In addition, in **Appendix 5, "Drug Exposure Anytime During Pregnancy in Relation to Specific Malformation Entities"**, the book reports, on page 488, a "Hospital Standardized Relative Risk" based on 2,283 "Mother—Child Pairs Exposed" of 2.6 for "Microcephaly" and 2.0 for "Pyloric stenosis".

Thus, the findings actually reported in the appendices of the 1977 book, "**Birth Defects and Drugs in Pregnancy**", clearly show a significant increased risk for birth defects in a cohort of children whose mothers were given a single dose of a Thimerosal-preserved flu vaccine during pregnancy.

Given the obvious increased risk for serious birth defects in the offspring of pregnant women who : **a)** had a recorded topical Thimerosal exposure or **b)** were given a single 50-µg dose of Thimerosal in a Thimerosal-preserved "flu" shot, either:

1. The reviews conducted by the CDC's Advisory Committee on Immunization Practices (ACIP) "*in 1999 and again in 2001*" were incredibly slipshod or
2. The ACIP and the CDC should have known since 1977 and did know before these reviews were conducted that giving a Thimerosal-preserved "flu" shot to a pregnant women risked the health of her unborn child and, *at a minimum*, significantly increased the risk that their offspring would be born with a serious birth defect.

Finally, to protect their interests, it appears that both the CDC and the FDA have been *knowingly* lying to the American public from some time in 1977, if not before, until the present (June 2009).

“Furthermore, in its most recent recommendation regarding prevention and control of influenza the ACIP stated ‘The risks for severe illness from influenza infection are elevated among both young children and pregnant women, and both groups benefit from vaccination by preventing illness and death from influenza. In contrast, no scientifically conclusive evidence exists of harm from exposure to thimerosal preservative-containing vaccine, whereas evidence is accumulating of lack of any harm resulting from exposure to such vaccines. Therefore, the benefits of influenza vaccination outweigh the theoretical risk, if any, for thimerosal exposure through vaccination’ (MMWR 54 [RR08]: 1-40, 2005). Nonetheless, FDA is in discussions with manufacturers of influenza vaccine encouraging them to further increase the supply of preservative-free formulations.”

Here, this reviewer finds that the FDA is simply reporting additional instances in which the ACIP and the CDC are *knowingly* lying to the American public about the harm that injecting pregnant women with a Thimerosal-preserved “flu” shot can cause – harm that has been known for more than 30 years – understanding that continually repeating a lie is one of the more effective tactics for intentionally misleading the public.

Moreover, there is no proof that any manufacturer of a Thimerosal-preserved vaccine has proven that its preserved vaccine formulation is safe to standard “sufficiently nontoxic ...”, the CGMP minimum required by law, by establishing the applicable scientifically sound toxicologically valid “no effect” levels for their Thimerosal-preserved vaccine formulations (e.g., **a**) the fetus (NOAEL indirectly administered Thimerosal-preserved influenza vaccine, fetus), **b**) the developing child (NOAEL injected Thimerosal-preserved influenza vaccine, developing child), **c**) the adult (NOAEL_injected Thimerosal-preserved influenza vaccine, adult), and **d**) the elderly (NOAEL injected Thimerosal-preserved influenza vaccine, adult over 60).

Thus, Sanofi Aventis (Fluzone) and Novartis (Fluvirin) would need to have established all four (4) NOAEL values because their Thimerosal-preserved vaccines are approved for pregnant women, children, adults and the elderly. Since the corresponding vaccines from the other makers of FDA-licensed Thimerosal-preserved inactivated-influenza vaccines are not approved for administration to developing children, they would only need to establish the three (3) applicable NOAEL values.

To the extent that:

1. The manufacturers have *knowingly* failed to comply with the “sufficiently nontoxic ...” law,
2. The FDA has *knowingly* failed to:
 - a. Enforce that law and
 - b. Comply with 21 CFR § 601.4(a) by refusing to license preserved vaccines that have not been proven “sufficiently nontoxic ...”, and
3. The FDA has, *contrary to its claims*, continued to license new Thimerosal-preserved vaccine formulations since 1999,

it is apparent to this reviewer that the Secretary of HHS, the FDA, the CDC, and the manufacturers are acting in concert to not only blatantly violate drug law but also to continue the manufacture and use of Thimerosal-preserved and Thimerosal-containing vaccines as they see fit – a with no genuine regard for:

- ❑ The health of the public,
- ❑ The harm that the Thimerosal-preserved vaccines,
- ❑ The harm that the other Thimerosal-containing vaccines have caused, are causing and will continue to cause to the offspring of pregnant women, young children and susceptible older children and adults, who are inoculated with them, until their use is prohibited or
- ❑ The wasted dollars spent in a national influenza vaccination program that cannot be cost effective because all of the current influenza vaccines:
 - Are not truly effective in preventing those who are vaccinated from getting influenza,
 - Cause serious harm to some who are vaccinated, and
 - In the case of the live-virus vaccines, actually infect not only those who are inoculated with them with three strains of live influenza viruses but also can infect others who have contact with them for up to 21 days after they are inoculated with these live viruses.

Moreover, since the number of children in the recommended population has expanded from about 8 million with the CDC's 2002 recommendation for children 6 months of age to 23 months of age to more than 72 million and the only current supplier of a no-Thimerosal inactivated human influenza vaccine that is approved for children, Sanofi Pasteur, Inc. has announced:

- a. The supply for the 2008-2009 flu season of its no-Thimerosal Fluzone influenza vaccine was about 14 million doses for people of all ages, where the general guidelines covered all children 6 months to 5 years of age, some to age 9 and “at risk” groups to 18 or about 27 million children (or doses for less than {LT} 52% of the covered children because this vaccine is also approved for adults),
- b. A projected “about 30 million” doses for the up-coming 2009-2010 human flu season for about 75 million children 6 months to 18 years of age, the CDC's newest guideline, (or projected doses for LT 40% of the covered children because this vaccine is also approved for adults), and
- c. A projected “about 50 million” doses for the 2010-2011 human flu season for about 78 million children (or projected doses for LT 64 % of the covered children because this vaccine is also approved for adults,

it is evident that the supply of “no Thimerosal” inactivated-influenza for children (and pregnant women) is not truly increasing relative to the indicated population in the short run and, *given the reality that Sanofi has, to date, shipped less than 90% of its projected doses and other adults are increasingly demanding a “no Thimerosal” shot*, the actual availability of this vaccine, *in terms doses available per child*, may actually continue to decrease from last year's less-than-50% level to certainly the less-than-40% level for this year's human flu season. Certainly, if, *contrary to the available evidence*, the FDA is “talking the talk” as it claims, the vaccine makers are apparently not listening.]

11. The twelfth and thirteenth important unasked question:

“Why is the FDA failing to be truthful about the lack of proof of safety that the makers of preserved vaccines are required by law (**21 CFR § 610.15(a)**) to provide in their Biologic License Application (BLA)?”

“Why has the U.S. FDA *knowingly* continued to *illegally* license Thimerosal-preserved vaccines whose BLA did not contain proof of safety to the minimum standard (‘sufficiently nontoxic so that the amount present in the recommended dose of the product will not be toxic to the recipient, ...’) as required by law (**21 CFR § 610.15(a)**)?”

“Is it safe for children to receive an influenza vaccine that contains thimerosal?”

Yes. There is no convincing evidence of harm caused by the small doses of thimerosal preservative in influenza vaccines, except for minor effects like swelling and redness at the injection site.”

First, the FDA’s unqualified “Yes” is an obvious lie because vaccination for influenza is clearly contraindicated for certain groups of children (see: the “Contraindications” and the “Warnings and Precautions” sections in the package inserts for the FDA-licensed influenza vaccines).

In addition, the legal expectation (**21 CFR § 610.15**) is for proof of safety – not the FDA’s all-too-clever, “*no convincing evidence of harm*”.

Moreover, the FDA is knowingly mischaracterizing the Thimerosal exposures as “small doses” when, relative to the toxic threshold for injected Thimerosal (LOAEL_{injected Thimerosal}) based on chronic toxicity studies in adult rats (0.0086 µg/kg/day), the current maximum single dose of Thimerosal for the vaccines in the CDC’s national vaccination program for the U.S. is, for the developing child/fetus, weighing under 5 kg, one- to six- thousand times the toxic threshold.

Further, even for adults weighing 100 kg, the single dose can exceed the toxic threshold by more than a factor of 5.

Thus, for the fetus and the developing children weighing 5kg or less, single 50-µg doses of Thimerosal are “huge doses”, not “*small doses*”, for this group. To be “*small doses*” for young children, the doses would have to be below the toxic threshold or, for a 5-kg child, < 0.043 µg of Thimerosal. Similarly, for “50-kg adults”, “*small doses*” of Thimerosal would be ones that were < 4.3 µg.

Second, a 0.5-mL dose of a Thimerosal-preserved influenza vaccine nominally delivers 50 µg of Thimerosal, a dose at least an order of magnitude larger than the dose that, *in 1971*, in an internal memo, Eli Lilly researchers reported was toxic.

Since, based on the FDA-recognized Mason (1971) study of chronic toxicity in rats using injected Thimerosal, after appropriately correcting the observed LOAEL_{injected Thimerosal}, adult rat of “8.6 µg/kg/day” for:

- a. The *recognized minimum* inter-species factor of 10 for rats compared to humans,
- b. The *recognized minimum* 10-fold factor needed to correct for human population diversity, and
- c. The *accepted* (by researchers, the EPA and the FDA) factor of 10 to account for the established higher susceptibility to mercury in the developing child,

and converting that LOAEL into an NOAEL, the resultant NOAEL_{injected Thimerosal, developing child} is: < 0.0086 µg Thimerosal/kg/day.

For adult humans, the similarly derived value for adults, NOAEL_{injected Thimerosal, human adult} is: < 0.086 µg Thimerosal/kg/day.

Given the preceding realities, even a 0.25-mL dose of a Thimerosal-preserved influenza vaccine (nominally 100 µg Thimerosal/mL) injects the child with 25 µg of Thimerosal – a dose that exceeds the NOAEL_{injected Thimerosal, developing child} of < 0.0086 µg Thimerosal/ kg/day on the day of injection unless the developing child were to weigh more than 2,907 kg (6,409 pounds [3.2 tons])!

Finally, the FDA’s claim of “*no convincing evidence of harm*” statement is a blatant misrepresentation of the reality that, for a Thimerosal-preserved influenza inoculation, besides death, the listed possible inoculation-related adverse reactions include: (See manufacturers’ “Package Inserts”; since this example is derived from Fluzone and FluLaval inserts, there is some overlap between the categories in some cases)

- **Blood and Lymphatic System Disorders:** Thrombocytopenia, lymphadenopathy
- **Immune System Disorders/Allergic Reactions:** Anaphylaxis, other allergic/hypersensitivity reactions (including urticaria, angioedema), allergic edema of the face, allergic edema of the mouth, allergic edema of the throat, hives, allergic asthma
- **Eye Disorders:** Conjunctivitis, eye pain, photophobia.
- **Gastrointestinal Disorders:** Dysphagia, vomiting.
- **Infections and Infestations:** Pharyngitis, rhinitis, laryngitis, cellulitis.
- **Musculoskeletal and Connective Tissue Disorders:** Muscle weakness, back pain, arthritis.
- **Nervous System Disorders:** Guillain-Barré syndrome (GBS), convulsions, myelitis (including encephalomyelitis and transverse myelitis), facial palsy (Bell’s palsy), optic neuritis/neuropathy, brachial neuritis, syncope (fainting) shortly after vaccination), dizziness, paresthesia, partial facial paralysis, and brachial plexus neuropathy, hypoesthesia, hypokinesia, tremor, somnolence, convulsions/seizures, facial or cranial nerve paralysis, limb paralysis.
- **Psychiatric Disorders:** Insomnia.
- **Respiratory, Thoracic and Mediastinal Disorders:** Dyspnea (difficulty in breathing), pharyngitis (sore throat), rhinitis, bronchospasm, throat tightness
- **Skin and Subcutaneous Tissue Disorders:** Stevens-Johnson syndrome, urticaria, localized or generalized rash, pruritus (intense itchiness), periorbital edema, sweating
- **Vascular Disorders:** Vasculitis (microscopic polyangitis), vasodilation/flushing, pallor
- **General Disorders and Administration Site Conditions:** Fever, pain, pruritis (intense itchiness), asthenia/fatigue, pain in extremities, chest pain, injection site inflammation, rigors, influenza-like symptoms, abnormal gait, injection site bruising, injection site sterile abscess

- some of which are known to be either associated with Thimerosal exposure or exacerbated by Thimerosal in the vaccine dose administered.

Recent research suggests that healthy children under the age of 2 are more likely than older children and as likely as people over the age of 65 to be hospitalized with flu complications. Therefore, vaccination with thimerosal-preservative containing influenza vaccine and thimerosal-reduced influenza vaccine is encouraged when feasible in children, including those that are 6-23 months of age.

Since several small-scale studies, meta reviews studies by Dr. Thomas Jefferson, and the only long-term retrospective U.S. study have found the influenza vaccines are not effective in preventing those inoculated, including “*healthy children under the age of 2*” and “*people over the age of 65*” from contracting the influenza virus, *which is the supposed reason we should prophylactically vaccinate against any “contagious” disease*, this reviewer again finds the FDA’s statements here to be simply Orwellian newspeak.

Since the retrospective large-population studies show that the vaccines do not reduce the risk that those vaccinated will contract some strain of influenza, the FDA apparently feels compelled to draw the readers’ attention away from this reality and focus it on hospitalizations and flu complications.

Finally, the language the FDA uses in their second statement, “*Therefore, vaccination with thimerosal-preservative containing influenza vaccine and thimerosal-reduced influenza vaccine is encouraged when feasible in children, including those that are 6-23 months of age*”, clearly reflects the realities in 2002, when the CDC’s recommendations were to vaccinate children 6 to 23 months of age, “*when feasible*”, with the then-FDA-licensed Thimerosal-containing inactivated-influenza vaccines and not realities in 2009, where the CDC’s recommendations are to vaccinate all children 6 months to 18 years of age with one or, for the first time, regardless of the child’s age, two doses of influenza vaccine, and the FDA-licensed influenza vaccines approved for children include “Thimerosal-preserved”, “reduced-Thimerosal”, and “no-Thimerosal” inactivated flu vaccines as well as a “no Thimerosal” live-virus vaccine.

12. The fourteenth important unasked question:

“How can it be safe to give a Thimerosal-preserved flu shot to pregnant women when studies have shown that some of their unborn children, will, if they survive their initial *in utero* mercury poisoning, be born: **a)** prematurely, and **b)** with Thimerosal-induced birth defects?”

“Is it safe for pregnant women to receive an influenza vaccine that contains thimerosal?”

Yes.”

The FDA’s answer of “Yes” is, *as this reviewer has previously shown, knowingly false.*

“A study of influenza vaccination examining over 2,000 pregnant women demonstrated no adverse fetal effects associated with influenza vaccine.”

First, the FDA fails to cite the study. Second, an in depth review of the birth outcomes data from a national multi-center study charting delivery outcomes in the late 1950s and early 1960s for those children whose mothers were exposed to a variety of drugs during pregnancy, the researchers found and reported statistically significant relative risks for serious birth defects in the offspring of those mothers who were exposed to Thimerosal topically or administered a Thimerosal-preserved flu shot. Thus, a single dose of a Thimerosal-preserved flu shot during pregnancy has been shown to increase the risk of serious birth defects in the delivered child. Are not these facts evidence of “*adverse fetal effects from a single Thimerosal-preserved flu shot given during pregnancy?*” These studies were published in a book titled, “**Birth Defects and Drugs in Pregnancy**”. Finally, in that book (Heinonen OP, Slone D, Shapiro S. **Birth Defects and Drugs in Pregnancy**. Littleton, Massachusetts: Publishing Sciences Group, Inc., 1977), the researchers reported (with underlining added for emphasis):

““Between 1958 and 1965, under the auspices of the National Institute of Neurological and Communicative Disorders and Stroke, a prospective study of over 50,000 pregnancies was undertaken with the main objective of determining whether there are factors during pregnancy or delivery that are related to the risk of cerebral palsy or other neurological outcomes. This study ultimately became known as the Collaborative Perinatal Project. Among many items of data obtained, drug use was recorded during pregnancy, and birth defects identified in the children were recorded subsequently. With the growing realization that drugs are sometimes teratogenic, it became mandatory to evaluate the data from the perspective ... The purpose of this book is to present data on drugs used by 50,282 gravae in relation to birth defects identified in children.’ The conclusion of these researchers with regard to Thimerosal, ‘(t)he measure of association presented is a standardized relative risk (SRR) with its 95% confidence limits. The SRR is the ratio of the observed number to the expected number of malformed children. Since the SRR takes into account potential confounding variables, it represents the best estimate of the relationship between a drug and a malformation...’ Finally, thiomersal...was associated with malformations overall and with uniform malformations.”

Specifically, the study found that topical Thimerosal exposure during the first 4 months of pregnancy was associated with a statistically significant increased risk (SRR = 2.69) for birth defects. In addition, in an appendix, the study reported an adjusted 7.1-fold increased relative risk for cleft palate, a serious birth defect, in the children of mothers who received a Thimerosal-preserved flu shot during the first four lunar months of pregnancy. Finally, in a second appendix, the study reported adjusted relative risks of 2.0 or greater for micro-

cephaly and pyloric stenosis, two other serious birth defects, in children born to mothers who were given a Thimerosal-preserved “flu” shot.

Given the obvious increased risk for serious birth defects from:

- a. Topical Thimerosal exposure or
- b. A single 50-µg dose of Thimerosal in a Thimerosal-preserved “flu” shot,

either:

1. The FDA has failed to review the applicable scientific data or
2. The CDC and the FDA should have known since 1977 and/or did know that giving a Thimerosal-preserved “flu” shot to a pregnant women risked the health of her unborn child and, at a minimum, significantly increased the risk that their offspring would be born with a serious birth defect.

Thus, to protect their interests, it appears that the CDC and the FDA have been *knowingly*¹¹ lying to the American public from some time in 1977, if not before, until the present (June 2009).

“Case reports and limited studies indicate that pregnancy can increase the risk for serious medical complications of influenza. One study found that out of every 10,000 women in their third trimester of pregnancy during an average flu season, 25 will be hospitalized for flu related complications.”

First, this reviewer must again note that the proceeding statements have nothing to do per se with “*Thimerosal in Vaccines*”, the supposed topic of this set of “*Questions and Answers*”, or with the answer to the question asked here, “*Is it safe for pregnant women to receive an influenza vaccine that contains [T]himerosal?*”

Moreover, this reviewer is again taken aback.

Based on the only published U.S.-wide population study of the effectiveness of influenza vaccination in preventing influenza (Geier DA, King PG, Geier MR. Influenza Vaccine: Review of effectiveness of the U.S. immunization program, and policy considerations. *J Am Phys Surg* 2006 Fall; **11**(3): 69-74), the influenza vaccination program is, *for a number of reasons*, not effective in reducing the number of influenza cases, influenza-related hospitalizations and influenza-related (mostly pneumonia) deaths that occur each year during the U.S. “flu” season. From this study and another peer-reviewed study (Jefferson T. Influenza vaccination: Policy versus evidence. *BMJ* (British *Medical Journal*) 2006 October 28; **333**: 912-915), it is clear that the benefits of influenza vaccination for “*pregnant women*” are THEORETICAL. Further, since vaccination is not known to be effective in preventing any vaccinated person from contracting influenza, the FDA’s statements are, at best, off-the-topic, Orwellian newspeak, fear mongering intended to mislead and confuse the public.

What does the risk of complications from a disease have to do with the “safety” of administering the Thimerosal-preserved influenza vaccine to a pregnant woman and her unborn child or children? Little or nothing when the legal requirement is that a preserved vaccine must be proven to be “sufficiently nontoxic so that the amount present in the recommended dose of the product will not be toxic to the recipient, ...” (**21 CFR § 610.15(a)**), a requirement that “Thimerosal

¹¹ **21 U.S.C. § 321(bb)**: “(bb) The term ‘knowingly’ or ‘knew’ means that a person, with respect to information -
(1) has actual knowledge of the information, or
(2) acts in deliberate ignorance or reckless disregard of the truth or falsity of the information”.

preserved” influenza vaccines administered to pregnant women have not been proven to meet!

Further, even if the findings of this unidentified study were valid, what percentage of the 25 women in 10,000 who are “*hospitalized for flu related complications*” had an influenza infection? If that percentage is similar to the percentage of those who die from flu-related disease (during the “flu” season, any case of pneumonia is typically counted as a flu-related medical complication) that percentage may easily be in the 2 to 8 percent range.

Why is it that pneumonia deaths during the flu season are counted as “flu-related deaths” without any definitive proof, in most cases, that the person who died actually had a serious influenza infection and not a “cold” virus or some other virus? Apparently, these flu-season pneumonia deaths are counted as “*flu-related*” deaths to inflate the body count so that this inflated body count can be used to frighten the public into being vaccinated!

Of those who have “*flu related complications*”, what is the risk for a “*serious medical complications of influenza*”? Is it 1 in 1,000 or 1 in 1,000,000? This reviewer cannot answer because the government health agencies have failed to report accurate risk data for “*serious medical complications of influenza*” based on data that only includes “healthy” individuals with a proven case of influenza and no other underlying serious or chronic illnesses or habits (like smoking, heavy drinking and drug addiction or abuse).

Finally, this reviewer again asks what does any of the preceding have to do per se with the “proof of safety” required under **21 CFR § 610.15(a)** before one can legally market Thimerosal-preserved influenza vaccines for use in pregnant women? Nothing!

“Additionally, influenza-associated excess deaths among pregnant women have been documented during influenza pandemics.”

This reviewer is bemused by this statement because it reminds him of the Vietnam-era, where the only “body counts” were those reported by a military desperate to conceal its failure to beat the enemy. Similarly, this reviewer must discount this “*excess deaths*” claim because those who reported this are part of the same group of “public health” officials who count all pneumonia deaths during a “flu season” as “flu-related deaths” and use an adjustable mathematical model to derive their specious claim that “36,000 die from influenza-related disease annually” Finally, this reviewer notices that the wording is not “excess influenza deaths ...” but rather the Orwellian “*influenza-associated excess deaths ...*”.

“Because pregnant women are at increased risk for influenza-related complications and because a substantial safety margin has been incorporated into the health guidance values for organic mercury exposure, the benefits of thimerosal-reduced influenza vaccine or thimerosal-preserved influenza vaccine outweighs the theoretical risk, if any, of thimerosal.”

Since the influenza vaccines are not generally effective in preventing the disease in those who are vaccinated, there does not seem to be any real benefit of these vaccines to the person vaccinated but the risks for a serious adverse reaction are real and the cumulative risk for sub-acute mercury poisoning and all of the harm such mercury poisoning is known to cause is all too real.

Further, inoculation with Thimerosal-preserved vaccines has known adverse risks that include: **a)**, *for the mother*, anaphylactic shock, Guillian-Barré syndrome, and death, and **b)**, *for the unborn child*, death, premature birth, low birth weight, serious birth defects (cleft palate, microcephaly [the condition of having a small head or having reduced space for the

brain in the skull, often associated with diminished mental abilities], and pyloric stenosis [abnormal constriction of the pyloric sphincter that controls the emptying of the stomach]), and post-natal developmental disorders.

Thus, it is clear that the risks from being inoculated with a Thimerosal-preserved influenza vaccine are all too real and, contrary to the FDA position, the benefits to the individual vaccinated are only theoretical. Yet again, the federal health agencies, including the FDA, fail to even disclose what these risks are to the American public, choosing to deny that there are serious risks from being inoculated with a Thimerosal-preserved influenza vaccine or, for that matter, any influenza vaccine – much less reveal the probable rates for serious adverse outcomes like, for example, Gillian Barré syndrome.

13. The fifteenth important unasked question:

“Because the risk is related to, among other things, the dose and,

□ with:

- a. The CDC’s recommending that:
 - i. Pregnant women get flu shots and
 - ii. Currently, children from 6 months of age to 18 years of age get an annual flu inoculation,
- b. The CDC’s on-going refusal to even state a preference for the FDA-licensed “trace Thimerosal vaccine and the “no Thimerosal” vaccines instead of the Thimerosal-preserved ones for pregnant women and children, and
- c. The FDA’s on-going re-approval of the FDA-licensed Thimerosal-preserved vaccines without, at least, even adding an “indication” that states: “Not for Use in Pregnant Women and Children” or, at a minimum, “Not for Use in Pregnant Women”,

the maximum mercury dose is increasing

□ so that a child born in 2003,

- a. Whose mother got a flu shot in pregnancy and
- b. Who have received the current maximum number of injections of Thimerosal-preserved flu shots,

may, *if nothing changes*, have received, by the age of 18, “twice” as much mercury from the flu shots alone as a child born in 1997, who gets no flu shots even though all of his early childhood vaccines were Thimerosal preserved,

why is the FDA being knowingly deceptive here by focusing on the vaccines and not addressing the maximum dose issue at all?

“You have said that thimerosal is no longer used as a preservative in vaccines routinely recommended for children 6 years or less of age, with the exception of influenza vaccine. What is being done about the thimerosal content of other vaccines and other biological products given to infants, children, and pregnant women?”

Since the FDA is responsible for all drugs and the FDA’s question extended beyond vaccines to “*other biological products*”, the question that this reviewer wants answered and the public should want answered is:

“What is being done to ban the use of Thimerosal and other mercury compounds in all the drugs, including vaccines and other biological drug products, given to pregnant women, infants, children, and other adults?”

Why was this question not asked? Perhaps, as with vaccines, a general shell game exists where the overall reduction in worst-case mercury exposures from vaccines, *if any*, are being “carefully” balanced by: **a)** increasing the worst-case cumulative mercury exposure to mercury compounds in other drugs, *which, in some cases, are apparently not even being disclosed in the drug products’ package inserts and/or labeling* or **b)** increasing the cumulative worst-case exposures to mercury and other “bioaccumulative” harmful components, like polymeric-aluminum-based adjuvants in a manner that maintains a slow

growth in the number of American of all ages who have one or more the now “epidemic” chronic diseases that, in the 1940s, 1950s and 1960s, were either unknown or rare.

Certainly, in the case of Thimerosal-preserved vaccines, this shell game is obvious. While the manufacturers have reduced and removed Thimerosal from some types of vaccines (e.g., DTaP, DT, Td, Hib, and Hep B), the FDA’s actions in conjunction with those taken by the CDC have actually increased the availability of Thimerosal-preserved influenza vaccine doses for influenza. “Coincidentally”, *as the supply of these other types of Thimerosal-preserved vaccines was waning*, in April 2002, the CDC (Bridges CB et al. Prevention and Control of Influenza Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2002 Apr 12; **51**(RR03): 1-31) began recommending giving influenza vaccines to: **a)** women who will be in their second and third trimesters in the “flu season” and **b)** children 6 months to 23 months of age in the “flu season”.

Moreover, the CDC refused, *and has continued to refuse*, to even state a preference for the then Aventis Pasteur (now Sanofi Pasteur) “preservative-free” Fluzone influenza vaccine (first approved in September 2002). The CDC made the recommendation to vaccinate pregnant women and young children in 2002, even though the CDC knew that the required multiple-generation reproductive toxicity, fetal toxicity, carcinogenicity, mutagenicity and teratogenicity studies for the available Thimerosal-preserved formulation approved for administration to children in this age group had not been conducted and that, *for pregnant women*, all the then-approved influenza vaccines were, like so many others, Pregnancy Category C drugs – drugs whose reproductive and fetal safety in humans were not proven. Moreover, the CDC made these recommendations even though it knew flu shots are not effective in preventing young children from contracting influenza.

Moreover, the underlying “reason” for the CDC’s 2002 recommendation for pregnant women appears to be the desire to, at least, “replace” the loss in Thimerosal exposure in pregnant women to conceal the reality that injecting pregnant women with Thimerosal-preserved RhoGAM sub-acutely mercury poisons the fetus to varying degrees. This is the reality because, *prior to 2002*, about half of the 10% to 15% of pregnant women in America whose Rh blood type is Rh negative were given at least one dose of Thimerosal-preserved RhoGAM at about 28 weeks into their pregnancy as well as at birth, with a few getting additional doses. However, on April 16, 2001, Ortho Clinical Diagnostics, the last supplier of a Thimerosal-preserved Rho(D), was approved by FDA to produce RhoGAM without Thimerosal. As a part of the approval process Ortho Clinical Diagnostics had committed to only shipping the Thimerosal-free RhoGAM into the US market. However, Ortho did not agree to voluntarily recall all the unexpired doses of Thimerosal-preserved RhoGAM (www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/BloodSafety/ucm095529.htm). Thus, in early 2002, the supply of in-date Thimerosal-preserved RhoGAM was declining.

In contrast, the Thimerosal exposure in pregnant women eligible for a “flu shot” during the flu season in 2002 and who, *if they were inoculated*, would receive a Thimerosal-preserved “flu shot” was, *given “market realities”*, more than sufficient to offset the decline in the percentage of Rh-negative mothers who received Thimerosal-preserved RhoGAM shots.

Moreover, *as vaccine uptake increased*, it was clear to the healthcare establishment that, even with some pregnant women receiving “reduced-Thimerosal” or “no-Thimerosal” flu shots, the annual number of pregnant women being injected with a Thimerosal-preserved flu shot would certainly surpass the annual number of Rh-negative women who had received Thimerosal-preserved RhoGAM during their pregnancy when the annual percentage of

pregnant women getting a flu shot exceeded 10 %¹², provided the healthcare establishment could stop the states from passing laws mandating that pregnant women can only be given a “reduced Thimerosal or “no Thimerosal” flu shot.

So now, the reader should understand why: **a)** the CDC has refused to state a preference for a flu shot with no Thimerosal and **b)** the healthcare establishment has consistently fought to stop states from enacting laws to ban pregnant women and young children from getting a Thimerosal-preserved flu shot.

Moreover, as the “supply” of the other types of Thimerosal-preserved vaccines that it recommends for children has declined, the CDC “coincidentally”: **a)** removed the restriction on administration to only women who will be in their 2nd and 3rd trimesters of pregnancy, **b)** introduced the “need” for 2 doses of vaccine the first time the child is vaccinated, and **c)** widened the age range to first “6 months to 35 months”, then “6 months to 59 months”, then to 6 months to 59 – 107 months, and finally to “six months to 18 years” in 2008.

Collectively, the CDC’s actions have, in spite of a “increasing” supply of influenza vaccine doses that contain no Thimerosal (the current “no Thimerosal” inactivated-influenza Fluzone formulation and the current “no Thimerosal” live-influenza FluMist [which is not recommended by the CDC for administration to pregnant women]), **increased the worst-case mercury exposure** provided by flu shots for those who FULLY comply only because of the CDC’s recommendations **from “o” in 2001 to:**

- a.** 50 – 62.5 µg by 23 months of age in 2002;
- b.** 62.5 – 75 µg by 23 months of age in 2003;
- c.** 87.5 – 100 µg by 35 months of age in 2004 and 2005;
- d.** 137.5 – 150 µg by 59 months of age in 2006;
- e.** 237.5 – 250 µg by 9 of age in 2007; and
- f.** 462.5 – 500 µg by 18 years of age in 2008 and beyond.

Thus, rather than decreasing childhood exposure to mercury in medicine, the actions of the FDA and the CDC, which both report to the Secretary of Health and Human Services, have actually increased the **maximum** childhood mercury exposure and, *for the pregnant woman*, has unnecessarily: **a)** increased the mercury exposure of the mother and her unborn child, and **b)** significantly increased the risk of harm from the Thimerosal-related mercury exposure to the unborn child (or children) whom she is carrying.

“FDA is continuing its efforts to reduce the exposure of infants, children, and pregnant women to mercury from vaccines.”

If: licensing and approving two new Thimerosal-preserved inactivated-influenza vaccine sources that can be given to pregnant women, apparently without their manufacturer’s proving they are “sufficiently nontoxic ...” is an example of the FDA’s “efforts”,

Then this reviewer must again note that, *besides being prohibited actions on the FDA’s part under 21 CFR s 601.4(a)*, these “efforts” do not reduce the exposure of pregnant women to mercury from vaccines because they add more doses of Thimerosal-preserved vaccine to the supply.

Moreover, given the 1999 commitment to remove Thimerosal (mercury) from vaccines as soon as possible (Center for Disease Control and Prevention. Thimerosal in vaccines: A joint

¹² According to the CDC, the current uptake for influenza shots in pregnant women is about 25% and increasing.

statement of the American Academy of Pediatrics and the Public Health Service. *MMWR* 1999 July 9; **48**(26): 563-565), the FDA's "efforts to reduce" should be efforts to ban the use of Thimerosal in the manufacture of vaccines and all other drugs.

"FDA is in discussions with manufacturers of influenza vaccine regarding their capacity to further increase the supply of preservative-free formulations. Of note, all hepatitis B vaccines for the U.S., including for adults, are now available only as thimerosal-free or thimerosal-reduced containing formulations."

Since the 1999 commitment established by the manufacturers and the DHHS and its subordinate agencies (including the FDA) was to remove Thimerosal from the manufacturing process for all vaccines, why is the FDA "in discussions with manufacturers of influenza vaccine regarding their capacity to further increase the supply of preservative-free formulations" instead of discussions as to when those who make "Thimerosal-preserved" formulations or "Thimerosal-preserved" and "reduced-Thimerosal (*preservative free*)" formulations will have converted their facilities to only make "no Thimerosal" formulations? Perhaps, the answer is:

"The FDA appears willing to permit the sub-acute mercury poisoning of children to continue (via the mercury doses they receive from their Thimerosal-containing vaccines)".

Why is the FDA not suspending the licenses of all Thimerosal-preserved influenza vaccine formulations until their manufacturers can prove that these are "sufficiently nontoxic ..." as required by a law with which the vaccine manufacturers have admitted to *knowing* non-compliance? Perhaps because the discussions between the FDA and the vaccine manufacturers are actually about how best to maintain the shell game and continue to mislead the American public.

Given the CDC's general recommendation to administer flu shots to pregnant women each year, why has the FDA not banned the use of all flu shot formulations in pregnant women until their manufacturers can conduct the appropriate scientifically sound toxicity testing, find that there is no reproductive or fetal risk of harm, and certify that their influenza vaccine formulations present no reproductive or fetal risk? Apparently, because maintaining the status quo for mercury poisoning, profit making, and law breaking is more important to the FDA than protecting the physical and mental health of unborn children.

"Tetanus and Diphtheria toxoids (Td) which is indicated for children 7 years of age or older and adults, is now also available in thimerosal-free formulations."

Having: **a)** searched the FDA website (<http://www.fda.gov>) using the FDA's search box and the sequential search terms, "tetanus"; "diphtheria" within the "tetanus" set; and "thimerosal-free" within the "tetanus diphtheria" subset and **b)** found no supporting documentation for the availability of a Thimerosal-free Td vaccine as of 25 June 2009, this reviewer must conclude that either the FDA is mistaken or that, somehow, *though such supporting documentation is supposed to be posted on the FDA web site*, this information has been inadvertently misplaced.

Therefore, this reviewer respectfully requests the FDA to either: **a)** provide proof that said Thimerosal-free Td vaccine is both licensed and was currently available for sale in the U.S.A. on or shortly before June 10, 2009, the "last updated" date on the web page this reviewer copied and is currently reviewing or **b)** publish a notice of correction with, and delete this

statement from, every published FDA document in which some unsubstantiated version of it appears.

“In addition, all vaccines licensed since 1999 with the exception of inactivated influenza vaccine have not contained thimerosal as a preservative.”

First, this reviewer notes that the FDA’s statement here confirms that its previous statement, “Furthermore, all new vaccines licensed since 1999 are free of thimerosal as a preservative”, is false.

Second, to be accurate the FDA’s statement should be corrected to read:

“... with the exception of inactivated-influenza vaccines”, because:

- a. The FDA has licensed more than one inactivated-influenza vaccine;
- b. The “influenza” in the vaccines is “inactivated” but, *hopefully*, the vaccines are not inactivated as the FDA’s wording implies;
- c. The FDA:
 - i. Has approved two (2) additional suppliers of a “Thimerosal-preserved” inactivated-influenza vaccines since 1999 (ID Biomedical Corporation of Quebec’s FluLaval [2005] and CSL Limited’s Afluria [2007]) apparently without manufacturer-supplied proof of their safety to the CGMP standard minimum, “sufficiently nontoxic ...” set forth in **21 CFR § 610.15(a)**, and
 - ii. Annually “relicenses” a new “Thimerosal-preserved” inactivated-influenza vaccine formulation, again apparently without manufacturer-supplied proof of their safety to the CGMP standard minimum, “sufficiently nontoxic ...” set forth in **21 CFR § 610.15(a)**, from two other suppliers whose “Thimerosal-preserved” flu-shot formulations were apparently first licensed in 1999 (Sanofi’s Fluzone) or before 1999 (Novartis’ Fluvirin); and
- d. In 2007, the FDA licensed Sanofi’s nameless, “Thimerosal-preserved” inactivated-avian-H5N1 vaccine even though:
 - i. Most all of the clinical trials were conducted using a “preservative-free” formulation,
 - ii. The mercury-dose approved (about 49 µg) for each inoculation is almost twice the dose from the other “Thimerosal-preserved” inactivated-influenza vaccines (about 25 µg), and
 - iii. The license was apparently granted without manufacturer-supplied proof of their safety to the CGMP standard minimum, “sufficiently nontoxic ...” set forth in **21 CFR s 610.15(a)**.

Thus, the FDA is apparently admitting that, in spite of being put on notice since 2004 of its need to: **a)** enforce the safety laws with which vaccine makers are required to comply as well as **b)** comply with the laws governing the FDA’s own conduct, today’s FDA is doing neither.

Moreover, this reviewer notes that the FDA’s statement here is an admission that neither removing Thimerosal from vaccines nor reducing the level of Thimerosal in vaccines is apparently at the top of the FDA’s vaccine priorities because there are now two approved “no Thimerosal” inactivated-influenza vaccine formulations. If two vaccine firms can make a “no Thimerosal” inactivated-influenza vaccine, then there is obviously no compelling capability-

related need to continue licensing the “Thimerosal-preserved” formulations of either these two (2) firms or the other firms who make “Thimerosal preserved” influenza vaccines.

Thus, *given the preceding realities*, at present, the *only* inactivated-influenza vaccines or other vaccines that the FDA should be licensing are “no Thimerosal” vaccines for pregnant women and children under 45 kg (99.2 pounds) in weight and, possibly, “reduced-Thimerosal” vaccine formulations for children over 45 kg in weight and adults if the FDA were truly interested in reducing the public’s exposure to mercury in vaccines.

“Also, all immune globulin preparations including hepatitis B immune globulin, and Rho(D) immune globulin preparations are manufactured without thimerosal.”

To the extent that the FDA’s carefully worded statement actually means that none of these are also manufactured with Thimerosal or any other mercury-containing compound, this reviewer applauds both the FDA and the manufacturers of immune globulin preparations for the removal of Thimerosal from these drug products.

However, this reviewer understands that the makers of any immune globulin preparation distributed in the U.S. had a much greater incentive to remove mercury from their products – they are not shielded from litigation by the National Vaccine Injury Compensation Program (**42 U.S.C. §§ 300aa-10 through -34**) [NVICP].

Should the Secretary and the FDA continue to act in a manner that does not continually safen and/or ensure the safety of vaccines to all applicable standards, then, *at a minimum*, the American public should rise up en masse and demand that **42 U.S.C. §§ 300aa-10 through -34** be repealed.

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Related Information

- [Thimerosal in Vaccines](#) [Link to the “Table 3” mentioned in this Q&A narrative]
- [Vaccine Safety](#)

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REVIEWER'S CONCLUDING REMARKS

Hopefully, the Secretary of Health and Human Services and the relevant agencies that report to the Secretary, including, but not limited to, the FDA, CDC, NIH and the Public Health Service will provide this reviewer, the readers of this review and the American public, with scientifically sound and factual studies that address the toxicity and risk issues as well as the court case citations that establish that the CDC, FDA and/or the vaccine manufacturers are not bound by the U.S. policies, laws and statutes governing vaccines, in specific, and drugs, in general.

Absent a satisfactory response that addresses all of the salient points raised in this review with proof and not, as the original mostly document does, unsupported rhetoric, this reviewer must recommend that CoMeD take appropriate action, under the applicable provisions of the applicable codified statutes and current regulations issued to comply with the “Data Quality Act” as enacted by Congress in the FY 2001 Consolidated Appropriations Act (Public Law 106-554) at section 515 (with underlining added for emphasis):

“Sec. 515. (a) In General. – The Director of the Office of Management and Budget shall, by not later than September 30, 2001, and with public and Federal agency involvement, issue guidelines under sections 3504(d)(1) and 3516 of title 44, United States Code, that provide policy and procedural guidance to Federal agencies for ensuring and maximizing the quality, objectivity, utility, and integrity of information (including statistical information) disseminated by Federal agencies in fulfillment of the purposes and provisions of chapter 35 of title 44, United States Code, commonly referred to as the Paperwork Reduction Act.

(b) Content of Guidelines. – The guidelines under subsection (a) shall –

(1) apply to the sharing by Federal agencies of, and access to, information disseminated by Federal agencies; and

(2) require that each Federal agency to which the guidelines apply –

(A) issue guidelines ensuring and maximizing the quality, objectivity, utility, and integrity of information (including statistical information) disseminated by the agency, by not later than 1 year after the date of issuance of the guidelines under subsection (a);

(B) establish administrative mechanisms allowing affected persons to seek and obtain correction of information maintained and disseminated by the agency that does not comply with the guidelines issued under subsection (a); and

(C) report periodically to the Director –

(i) the number and nature of complaints received by the agency regarding the accuracy of information disseminated by the agency; and

(ii) how such complaints were handled by the agency”.