

# Facility Automation Management Engineering (FAME) Systems

33 Hoffman Avenue, Lake Hiawatha, NJ 07034 – Tel. 973263-4843

Wednesday, 15 February 2006

## To Whom It May Concern:

The review that follows this introductory letter is a critical assessment of a copy of the paper, “When science is not enough — a risk/benefit profile of thiomersal-containing vaccines,” by C. John Clements and Peter B. McIntyre that was published in *Expert Opin. Drug. Saf.* (2006) 5(1):17-29; this copy was sent to me by the publisher as an email attachment on 18 January 2006.

In general, to clearly differentiate between my assessment comments and those of article, this reviewer’s remarks are written in a “News Gothic MT” font with the article’s statements indented and initially quoted in a “Times New Roman” font.

Quotations of or from other cited articles are generally in an “Arial” font except for quotations of or from US laws and statutes, which are in a “Lydian” font.

In general, except when quoting the article being reviewed and/or other sources and in footnotes, the *uppercase* identifiers “Thimerosal,” “Merthiolate,” and “Thiomersal” will be used interchangeably throughout this review, with preference being given to “Thimerosal” *because* these are/were trade names, even though the active mercury-containing ingredient in vaccines is, *in most cases*, the ethylmercurihydroxide that forms from the hydrolysis of Thimerosal, sodium ethylmercurithiosalicylate, in aqueous solutions.

When a text punctuation or word error is found that is considered significant, this reviewer has used a different font color for the correction and, when a word is changed, the word needing change is highlighted in a **red “Times New Roman”** font and the recommended change is presented in a **blue “News Gothic MT”** font.

Should any reader find any significant factual misrepresentations in this reviewer’s remarks, then this reviewer requests that you submit the factual error you have found along with the scientifically sound and appropriate documents that prove your point to this reviewer so that he can learn from you, incorporate that new knowledge into his understanding, and, where indicated, appropriately correct this document.

Respectfully,

A handwritten signature in black ink, appearing to read "Paul G. King". The signature is fluid and cursive, with the first name "Paul" being more prominent.

Paul G. King, PhD, MS, BA  
Founder, **F.A.M.E. Systems**

## Review of:

### **“When science is not enough — a risk/benefit profile of thiomersal-containing vaccine”**

#### **General Review Remarks**

First, this reviewer finds that a better title would have been:

“When the required scientific safety studies have not been conducted — a risk/benefit assessment for the use of thiomersal in vaccines.”

Second, as is often the case, the authors use the terms “ethyl mercury” and “methyl mercury” to refer to compounds that contain hydrolysable/metabolizable ethylmercuri- and methylmercuri- groups, which are ultimately metabolized into bio-accumulating “inorganic mercury” in the brain and other organs.

Based on the long-term, systemic effects of single bolus doses, this bio-accumulated “inorganic mercury,” having an estimated half-life of more than two decades, is the persistent toxin that accumulates in the human body.

That having been said, this reviewer will now assess each section of this article.

#### **The Review**

After the abstract, the authors begin by stating:

##### **“1. Introduction**

Since July 1999, the mercury-based vaccine preservative thiomersal (known as thimerosal in the US; for consistency, thiomersal is used throughout this article) has come under public and professional scrutiny because of an increasing awareness of its presence in childhood vaccines. Mercury has a reputation for causing diseases in man and animals, as well as damage to the environment.”

Contrary to the authors’ glib views, mercury, *in all forms (elemental, inorganic salts and organic and organometallic compounds)*, is generally recognized as the second most toxic element to mammals on the earth.

“However, this reputation of mercury as a toxic chemical rests predominantly on its effects as an element (e.g., mercury vapour from tooth fillings) and in its methylated form (e.g., in pesticides).”

Since Calomel (mercurous chloride; 86.96% mercury), a sparingly soluble form of mercury, was added to teething (soothing powders) legally sold in Australia from 1874 to 1959 and it has been unequivocally proven to cause a form of mercury poisoning that was labeled “Pink Disease” which maimed or killed thousands of Australian babies (as well as tens of thousands in the US and the UK) upon whom it was used, this reviewer is surprised that the authors, *both Australians*, would fail to note that an inorganic mercury compound, Calomel, knowingly added to baby teething powders, certainly adds to the “reputation of mercury as a toxic chemical.” [Note: Similar to Thimerosal, public pressure in the US led to the withdrawal of most of these Calomel-laced baby teething powders from the US market, starting in 1939, though poisoning cases continued to be found into the early-1950s until: **a**) the work of Warkany and others [r1-r3] proved the link between calomel and the form of mercury poisoning (intoxication) most commonly called “Pink Disease” or “Acrodynia,” and **b**) the governments finally banned their sale in the 1950s.]

However, bowing to the medical community’s position that the cause of “Pink Disease” was unknown and the pharmaceutical manufacturers’ unsubstantiated “its harmless” claims, Australia waited until there was unequivocal scientific “proof” that Calomel in teething powders caused “Pink Disease,” and the various states and territories, and *not* the federal

government, enacted the bans.

**Appendix A** contains one person's account of the lifelong effects of being mercury poisoned by Calomel.

As with each form of mercury poisoning, a "unique" symptom of Calomel-based mercury poisoning is the permanent damage to the teeth of those who were poisoned but survived the repeated application of these Calomel-laced powders.

"Concerns regarding the safety of thiomersal (containing the mercury compound ethyl mercury) were based on studies suggesting adverse effects in children from *in utero* exposure to methyl mercury at levels previously considered safe [1]. These concerns, however, cannot necessarily be extrapolated to ethyl mercury."

Factually, concerns about the toxicity of Thimerosal to humans have been raised since its introduction into US commerce in the 1930s (**see** the applicable references in the FDA petition and other relevant articles posted at <http://www.mercury-freedrugs.org/docs/>).

"This review first considers the data on mercury toxicity and the differences between ethyl and methyl mercury and then summarizes and reviews safety data on thiomersal in the vaccine context. Finally, a warning is sounded that the debate about the safety of the preservative could spill over into developing countries and result in its restriction or loss altogether from essential vaccines used there."

First, this reviewer finds that the authors only incompletely addressed the data on mercury toxicity.

Moreover, these authors fail to address:

- The similarities in the mercury poisoning outcomes observed in children,
- The knowing failure of the various governments, medical institutions, and pharmaceutical firms to conduct the appropriate scientifically sound acute, chronic and long-term toxicity studies required to prove the level of Thimerosal that is safe for all vaccines recipients, and
- The failure of these same entities to address the immune systems implications of the hypersensitivity (anaphylaxis) observed in a percentage of those administered Thimerosal-containing vaccines.

## **"2. Mercury toxicity**

### **2.1 History**

Elemental and methyl mercury have long been recognised as toxic. Clarkson [2] has fully described their toxicology. Women's makeup containing mercury that causes the lightening of the skin, reportedly caused the death of Queen Elizabeth I of England and still concerns health authorities [101]. Hat makers who used mercury in their trade were well known to frequently suffer impaired brain function – 'as mad as a hatter'."

This reviewer finds the authors' statements here problematic because mercury salts, and not elemental mercury, were the sources for the mercury poisoning cases cited here.

"More recently, catastrophic natural experiments when populations including pregnant mothers were inadvertently exposed to grain contaminated with methyl mercury insecticide have shown that damage to the CNS of the fetus occurs in large doses. Maternal methyl mercury exposure via the oral route in Iraq and Japan was documented to cause neurological abnormalities such as developmental delay in infants exposed *in utero* [3-6]."

This reviewer is dismayed to find that the authors failed to address the long, documented history of mercury poisoning by inorganic mercury compounds used as, or in, medicines.

Moreover, this reviewer is concerned because the authors failed to mention, much less address, the widespread, but unnecessary, mercury poisoning of infants by Calomel-laced “teething” or “soothing” powders, *represented as being safe (harmless) without any proof of safety*, from the 1800s until the 1950s in Australia, the United Kingdom and the United States.

The relative incidence (“1 in 500”) of this “Pink Disease” form of mercury poisoning (from Calomel in teething powders) and many of its symptoms have parallels to the “autism” form of mercury poisoning (from Thimerosal in topical drugs [finally “outlawed” but *not* recalled in the US in 1998] and injectable biological products [still being permitted without the required proof of safety in the US and elsewhere until today]), with an estimated US incidence of “1 in 250.”

Further, this reviewer notes that, in both instances, there has been a steadfast refusal of the medical community to accept the reality of mercury poisoning (intoxication) *until* decades after studies found unequivocal evidence of mercury intoxication in some of those children initially diagnosed with “Pink Disease” in the 1900s to the 1950s and, *to date*, in children diagnosed with “autism” from the mid-1900s to the mid-2000s.

Apparently, these authors have either:

- a. deliberately ignored the previous “Pink Disease” cases of the poisoning of babies by a mercury compound, Calomel, added to teething powders, and/or
- b. have apparently failed to properly investigate and understand the proven mercury poisoning of babies by Calomel (86.96% mercury by weight) added to teething powders (and other medicines) without proof of safety.

As was the case for “Pink Disease,” *where there was a latency period before the initial exposures began to have observable clinical symptoms, the incidence of mercury poisoning severe enough to be diagnosed as “Pink Disease” was estimated as “1 in 500,” and, for the same apparent levels of exposure, only a few had a significant severe reaction*, “autism” has a latency period, an estimated “1 in 250” children are diagnosed with DSM autism, and, *for the same levels of exposure*, the observed delayed outcomes range from no apparent adverse clinical effects to severe DSM autism. [**Note:** Since Calomel-laced teething powders were *not* universally used, this lower usage level may partially account for the lower incidence rate for the inorganic-mercury mercury poisoning labeled “Pink Disease (“1 in 500”) than for the organic-mercury mercury poisoning labeled DSM autism (“1 in 250”). However, unlike “Pink Disease,” *where the incidence rates were about the same for both sexes*, the incidence of DSM autism in boys is more than four times the incidence for girls – an apparent identifying characteristic for the form of mercury poisoning labeled/diagnosed as “autism.”]

“Guidelines created by various environmental agencies were designed to prevent such environmental disasters from happening due to methyl mercury, and to avoid subtle damage to the developing brain.”

While this reviewer agrees that various environmental agencies created human mercury-consumption guidelines for organic mercurial compounds in fish, those guidelines rest on, among other things:

- an estimation of the levels of dietary mercury-exposure based on interview surveys for the studied groups who consume a mostly fish and/or marine mammal diet and
- an assumption that mercury-excretion levels in hair are universally correlated to the level of dietary mercury intake.

Recent reports by Gosselin *et al.* [r4] (which addresses the issue of the level of mercury from dietary exposure), Haley [r5] (which demonstrates that some individuals have impaired mercury excretion systems), and Camuel *et al.* [r6] (which shows there are population group variations in the correlation between mercury intake and the level of mercury in hair) have clearly proven that both of the preceding bases are *not* accurate.

“The human brain seems particularly vulnerable to methyl mercury during its developmental period due to the chemical’s highly and selective toxic effects on the CNS. The prenatal period is believed to be the most susceptible stage of the life cycle [7]. Mercury inhibits processes basic to brain development such as neuronal cell division and migration [8].”

Based on this reviewer’s understanding of the toxicity of mercury from studies in chicken eggs (Digmar *et al.* [r7]), during the developmental period, the toxic effects of alkyl mercury compounds, including Thimerosal, are systemic and not CNS selective.

At the cellular level, alkyl mercury compounds and their inorganic metabolism products seem to disrupt those biochemical processes that involve sulfur-containing proteins and/or are mediated by divalent cations (e.g., Ca, Mg, Cu, Zn) and, based on the abnormalities seen by Digmar *et al.* [r7] in the developing chicken embryos for Thimerosal at the 100 µg/egg (ca. 0.8 ppm – 1.1 ppm mercury [see: [http://www.sizes.com/food/chicken\\_eggs.htm](http://www.sizes.com/food/chicken_eggs.htm)]) level is a strong teratogen.

“From natural experiments, it has been possible to quantify to some extent the danger levels posed by methyl mercury. Organizations such as the World Health Organization (WHO), the US Environmental Protection Agency (EPA), the US Agency for toxic substances and Disease Registry (ATSDR), and the US FDA provide recommended limits on methyl mercury exposure in the diet [5,9-11]. Suggested safe levels range from 0.7 µg/kg body weight/week (EPA) to 3.3 µg/kg body weight/week (WHO). This variability results from the use of different primary data sources, differing intended applications for guidelines, and differing uncertainty factors or safety margins built into these recommendations. For example, the EPA dose takes into account the 95% confidence limit of the mean dose not associated with toxicity and adds a tenfold ‘safety factor’ that is intended to be protective of the developing fetus. Of note, the guidelines produced by these agencies were intended to indicate the starting points for the evaluation of mercury exposure, and not absolute levels above which toxicity occurs.”

While this reviewer does *not* disagree with the authors concerning the intent of the guidelines discussed, this reviewer notes that, in light of the findings by Gosselin *et al.* [r4], the current dietary guidelines for the ingestion of foods containing “methyl mercury” are probably 2 to 10 or more times higher than they should be.

Moreover, since about 80% of the mercury in fish is *not* adsorbed in the “normal” human gut, IF one were to attempt to project a tentative guideline for the ingestion of a non-tissue-bound organic mercury compound, THEN, an appropriate fish-derived science-based guideline might be from 0.02 µg down to 0.005 µg of mercury per kg of body mass per day, but certainly *not* the present EPA guideline of 0.1 µg per kg of body mass per day.

“It has been calculated that a typical infant exposure should not exceed 34 µg of total mercury (using EPA guidelines to determine recommended limits) or 159 µg (if WHO guidelines are used) [12,102]. Following a typical national immunisation schedule, during the first 14 weeks of life, an infant may receive three doses of diphtheria-tetanus-whole cell Pertussis (DTP) vaccine giving a maximum total dose of 75 µg of ethyl mercury. If hepatitis B vaccine (Hep B) is added to the immunisation schedule, the maximum exposure to ethyl mercury during the first 14 weeks of life is 112.5 µg and with Haemophilus influenzae type b (Hib) vaccine added, the total ethyl mercury dose reaches 187.5 µg.”

First, IF the adjusted EPA-based guidelines, *derived from the revised understanding of the most probable human exposure to ingested “methyl mercury”* [r4], were to be used, THEN, the corresponding daily infant exposure should *not* exceed 1.7 µg to 6.8 µg of total mercury.

Second, Thimerosal, having a formula weight of 404.8g per mole [r8], is “50%” (49.6%) by weight mercury (having an atomic weight of 200.6g per mole) and 56.7% by weight ethyl mercury (having a formula weight of 229.6g per mole); thus, Thimerosal is *not*, as the authors’ statements indicate, “50% ethyl mercury.”

Third, because the level of Thimerosal in a vaccine is permitted by most regulatory authorities to be up to 125% of the nominal level, the actual maximum total doses of “ethyl mercury” for the cited immunizations are about 106 µg, 159 µg, and 266 µg, respectively; and the corresponding maximum total doses of mercury are about 93 µg, 140 µg, and 232 µg, respectively.

Hopefully, the authors will, *after reviewing the referenced publications*, adjust their views concerning the maximum mercury dose and what an appropriate “reference” guideline should be for injected “ethyl mercury” – something that recent researchers have assiduously avoided doing.

Moreover, this reviewer finds the “comparative” mercury-dosing studies on baby monkeys by Burbacher *et al.* (the authors’ reference “[34]”) failed to use the same mode of administration for the methylmercurihydroxide (given orally) as the mode used for the Thimerosal (ethylmercurihydroxide) (given by injection), for reasons that seem to this scientist, *schooled in the design of comparative analytical studies of all kinds*, to have ignored the fundamental tox study design tenet that, *in a two-chemical, comparative, chemical-elimination (half-life) study*, the mode of administration for the tested methyl- and ethyl-substituted alkylmercury compounds being compared should be the same.

“In contrast, thiomersal is an organic mercurial compound whose mercury component is in the form of ethyl mercury. Although it has been used for > 60 years, knowledge of its toxicology was, until recently, mostly limited to topical application in very high doses.”

This reviewer finds that the authors’ statement here is, at best, misleading.

From the time in 1927, when Dr. Kharash filed the original patent (US patent 1,672,615 [1928]) for the alkyl mercuric sulfur compound (Thimerosal), the original studies failed to find that dilute solutions of Thimerosal (also commonly known as Merthiolate or, in the UK, Thiomerol) were bactericidal when injected intravenously (because that was what Dr. Kharash’s research was, *in a time before penicillin*, searching for).

Sometime in the period from 1929 to mid 1930, Eli Lilly contracted with a Dr. K. C. Smithburn, a well-respected physician, to conduct research on Lilly’s newly patented product on a local outbreak of “meningococcic meningitis” in the Indianapolis City Hospital.

Lilly assigned this human research project to Dr. Smithburn despite the fact that the doses that they planned to use on humans were, *in fact*, lethal to the animals used in Lilly’s animal toxicity studies.

After Smithburn’s study was completed, he reported to Eli Lilly that the Thimerosal treatment for “meningococcic meningitis” was *not* effective.

However, in 1931, in an effort to find a profitable role for Lilly’s newly patented drug, *which Smithburn had just demonstrated was not useful for treatment of a “bacterial” disease*, Jameson and Powell, scientists at Eli Lilly, authored an article, published in the American Journal of Hygiene [r9], in which they stated that Dr. Smithburn told them that he had injected Merthiolate (the brand name for Thimerosal) into 22 patients.



In their article, Jameson and Powell further stated, *without referencing any published study*, that Dr. Smithburn had told them that there appeared to be no positive affect with the use of intravenously Merthiolate.

Though the patients who were given intravenous Thimerosal doses by Dr. Smithburn all died, Jameson and Powell reported:

“Dr. Smithburn stated that in these cases ‘beneficial effect of the drug was not definitely proven. It did not however appear to have any deleterious action when used in rather large doses intravenously when all of the drug entered the vein.’”

Jamison and Powell used this alleged oral report from Dr. Smithburn to “conclude” that Thimerosal (Merthiolate), *though ineffective on bacterial meningitis*, had a low order of toxicity for man.

What Jameson and Powell omitted was that all of the patients, in fact, had meningitis, one third of the patients died within one day of receiving the first treatment with Thimerosal, none of those treated recovered, and, *by inference*, there were problems when the Thimerosal solution used was, by mistake or leakage, infused into patients’ muscle tissue.

Moreover, *in those who survived longer*, there was no way to tell whether the neurological or other damage observed was attributable to the toxicity of the Thimerosal or to the bacterial meningitis.

Obviously, Smithson’s study was fatally flawed and highly misleading.

Unfortunately, *for the generations that followed*, Jameson and Powell’s statements and conclusions were repeatedly cited by Eli Lilly, and subsequently by the pharmaceutical industry and Federal regulators, as evidence demonstrating that Merthiolate (Thimerosal [ethylmercurihydroxide]) had a low toxicity in humans when, in fact, Smithson *et al.* [r10] published no such finding of low toxicity in their report on the outbreak.

Dr. Kharash, the patent holder, filed a second patent (US patent 1,862,896 [1932]) in 1931.

In that patent, Dr. Kharash stated that in aqueous solution, Thimerosal breaks down into ethyl mercury hydroxide (ethylmercurihydroxide), which causes significant adverse reactions in humans.

Additionally, he noted that Thimerosal (Merthiolate), *which in an aqueous solution effectively kills bacteria*, rapidly loses its bactericidal potency when added to serum.

Contrary to Dr. Kharash’s reported patent findings, the Eli Lilly team of Marks, Jameson and Powell [r11] published an article in 1932 that reported:

“3. The tests indicate that merthiolate approaches the ideal germicide for skin disinfection because of the following properties demonstrated under conditions comparable to actual clinical use:

- a. High germicidal activity against surface skin organisms.
- b. High germicidal activity against deep skin organisms.
- c. Rapidity of skin disinfection.
- d. Maintenance of condition of antisepsis over a considerable period of time.
- e. Nonirritating to the most sensitive skin.
- f. Freedom from vapors irritating to the eyes of the operators and attendants.
- g. Promotion of the healing of abrasions by actively stimulating skin repair.”

In addition, their article closed with:

“We are indebted to Dr. G. H. A. Clowes, Director of Research, Eli Lilly and Company, for counsel and suggestions during the course of this study,”

which, *to this reviewer*, indicates that Lilly management “shaped” the research and findings to be more favorable than supported by Lilly’s knowledge of the properties of Thimerosal at the time. [Note: Although these remarkable claims helped Eli Lilly gain dominance in the market, *by encouraging consumers to switch their use from other safe and more effective products like iodine and*

*alcohol to Merthiolate*, to date, there has never been a mercury compound which actually promotes healing. In retrospect, this “Promotion of the healing of abrasions by actively stimulating skin repair” claim is the misrepresentation that Eli Lilly used to build itself into a major player in the pharmaceutical industry. Moreover, for many years, Thimerosal was Eli Lilly’s main cash cow, a cash cow that funded their ascent in the US pharmaceutical industry.]

In spite of the positive report by Lilly’s team, Dr. Kharash and Lilly filed yet another patent (US patent 2,012,820) in 1934, their third, that patented purported remedies for deficiencies in the stability of Thimerosal which, when Thimerosal solutions destabilized, lead to a loss of the ability to kill bacteria along with an increased tendency to produce undesirable side effects.

In sharp contrast to the preceding, in 1935 Salle and Lazarus [r12], *attempting to build on the comparative tissue/bacterial toxicity work of Dr. R. A. Lambert*, reported that dilute solutions of “Merthiolate” (Thimerosal) in embryonic chicken plasma were 35 to 44 times more toxic to embryonic chicken tissues than these solutions were to bacteria (“*E. Typhi*” and “*Staph. Aureus*”) indicating that, *in biological fluids*, Thimerosal is much more toxic to cellular tissues than it is to bacteria and that, *in biological tissues*, it does *not* support healing.

*Taken aback by these findings and accepting Lilly’s view about the efficacy of Merthiolate as a antibacterial agent*, Salle and Lazarus tried to rationalize their unexpected findings and closed by stating:

“Also chick rather than human plasma was used. Chick plasma may exert a bactericidal action on the organisms that may be wholly lacking, or almost so, in human plasma,”

which reminds this reviewer of the similar claim that Naproxen must be protective, which was used by Merck to rationalize the increased heart-attack rate in the Vioxx arm of a comparative outcomes study in humans.

With the ever-expanding use of Thimerosal came an ever-increasing number of peer-reviewed publications reporting on the adverse effects of Thimerosal in humans, animals, and tissue culture.

A search of the National Library of Medicines site (<http://www.ncbi.nlm.nih.gov/entrez>) using the search terms “Thimerosal” turned up over 1000 papers published since 1949, most of which addressed problems with, or issues associated with, the use of Thimerosal.

Furthermore, this reviewer suggests that the authors of this “expert opinion” article also carefully study the research reported in significant papers (with references to articles and communications starting from the mid-1930s) that

- Date from the 1940s to the present (**see** references in this reviewer’s other “Thimerosal (49.55% mercury) causes mercury poisoning”-series of articles published in the <http://www.mercury-freedrugs.org/docs/> webpage), and
- Have assessed of the toxicological properties of Thimerosal (also known as “Merthiolate” and “Thiomersal”); its hydrolysis product, ethylmercurihydroxide; and its end (in the human body) metabolite, “inorganic mercury” — at levels down to below 20 parts per billion in some cases.

“It is used as an antimicrobial agent in vaccines and other pharmaceutical products to prevent unwanted bacterial and fungal growth [13]. It is present in commonly used vaccines, such as DTP and tetanus toxoid, as well as certain formulations of diphtheria-tetanus-acellular Pertussis (DTaP), Hep B and Hib vaccines but not in live bacterial or viral vaccines.”



While the use of Thimerosal in vaccines is generally represented in most published papers to be as a preservative, Thimerosal “just happens” to be a strong vaccine “adjuvant” (a substance that enhances the immune response to an antigen) though this fact is, *for reasons that should be obvious, not* generally discussed in papers that, *like this article*, assess the risks associated with the use of Thimerosal.

Since Thimerosal in vaccines is, itself, known to cause anaphylactic shock and death in sensitized individuals, the reader can easily see why the authors would *not* wish to raise this obvious safety hazard to some of those injected with vaccines containing it.

“Vaccine preservatives, including thiomersal, have probably prevented illness and death in countless infants over the years by reducing the risk of contamination of opened multi-dose vials.

The use of thiomersal in vaccines has not been questioned until recently, presumably because its low dose and long use had not been associated with reported side effects.”

Since Thimerosal in vaccines has been repeatedly reported (**see** VAERS) to induce anaphylactic shock and death in those “sensitive” to Thimerosal, this reviewer finds either the authors do *not* consider Thimerosal-induced anaphylaxis and death as serious side effects, or they are guilty of “straining at the gnat and swallowing the camel” for failing to mention, *much less discuss*, these severe adverse side effects in this article.

“No studies have been carried out to measure possible adverse events due to the preservative, so it is not surprising that none have been reported.”

Contrary to the authors’ assertions, reports, *dating back to the 1930s*, from 1930s comparative studies in dogs (comparing biological formulations with Thimerosal at preservative levels to the same biological formulation without the Thimerosal) and similar 1960s studies in mice [r13], have clearly established that, based on repeated injection evaluations, a 100-ppm level of Thimerosal can cause severe adverse reactions, including anaphylactic shock and death, in sensitive individuals.

In addition, *until recently*, the US package inserts for all Thimerosal-preserved vaccines carried a specific warning about these severe side effects and a clear contraindication for administering these vaccines to individuals who were known to be sensitive to Thimerosal. [Note: For reasons that: **a)** have no scientific or medical validity and **b)** seem to be related to the public’s increased awareness of the dangers associated with the use of Thimerosal in vaccines, the FDA has permitted these “Thimerosal specific” warnings and contraindications (**see**, for example, the 2002 Package Insert for Fluzone®) that was replaced by general “if allergic to any component” warnings and contraindications (**see**, for example, the 2004-2005 and 2005-2006 Package Inserts for Fluzone®). Perhaps the authors’ failed to note these immediate severe and potentially fatal adverse reactions to injected Thimerosal-preserved vaccines for similar reasons.]

“None the less, it is argued, millions of doses of thiomersal-containing vaccines have been administered over the years, and if there had been consequential adverse events, it is reasonable to assume that they would have been noticed.”

This reviewer notes that the authors have again failed to address the anaphylactic shock and death which are “consequential adverse events” known to be linked to Thimerosal in vaccines as well as the immunostimulating adjuvant effect of Thimerosal that have been linked to **persistent** abnormal immunogenic and autoimmunogenic effects in humans over the years [r14-r22].

Based on the preceding references, it would seem that Thimerosal has, for some time, been recognized as harmful to the human immune system and a factor in the adverse autoimmune effects observed in some who have been mercury-poisoned by injected Thimerosal from vaccines and other Thimerosal-containing drugs and preparations.

“Opponents of the preservative use”(,) “use the same scenario to argue that none has been found because no-one has actually searched for more subtle, sequelae such as behavioral problems.”

This reviewer, one of the “opponents” of the use of any form of mercury in any drug formulation at any level *without* unequivocal proof of safety, finds the authors’ view to be flawed.

Since the 1930s, many medical researchers have repeatedly raised red flags about the toxicity and adverse effects of Thimerosal. [See “Appendix B” in [http://www.mercury-freedrugs.org/docs/051101\\_Thimerosal\(49\\_55\\_%20Hg\)CausesHgPoisoning\\_III\\_DrOrensteina.pdf](http://www.mercury-freedrugs.org/docs/051101_Thimerosal(49_55_%20Hg)CausesHgPoisoning_III_DrOrensteina.pdf).]

What opponents of the use of Thimerosal in vaccines and other drugs have lamented is that the drug companies, academic institutions, and the federal governmental agencies have apparently knowingly failed to conduct the appropriate scientifically sound acute, chronic and long-term toxicology studies to determine unequivocally what the safe level is for injected Thimerosal-containing formulations on fetuses, premies, full-term babies, toddlers, children, adolescents, young adults, and the elderly when these formulations are repeatedly injected into the most susceptible individuals (ones that have impaired mercury and heavy-metal detoxification systems) in each population segment.

“Soon after concerns were expressed in 1999 about thiomersal in vaccines, there arose anxiety that autism might be caused by the preservative. This concept was catalytic, bring together a number of disparate groups. First there were the parents of autistic children who, not unreasonably, were seeking an explanation for why their otherwise normal, healthy child should begin showing signs of autism in the second year of life. Second, medical epidemiologists were looking for a reason why the reported rates of autism were rising in many countries. Lastly, there were concerned parents who had read about the high doses of mercury in vaccines. They noted the apparently similarity between the symptoms of autism and symptoms of mercury poisoning [14]. These groups found what appeared to be an explanation — perhaps thiomersal in vaccines caused autism. In the eyes of the public, the onus of proof rapidly shifted to the medical world to show this was not the case. Also, the data were not there and the much-needed studies had not been done.”

Except to note that the start of the “recent” concerns about Thimerosal in vaccines can be traced back to the late 1960s (when the US FDA amended the regulations governing vaccines to require proof of safety to all for a preservative candidate before it could be used [21 CFR Section 610.15(a)]) and the early 1970s (when a US vaccine manufacturer found evidence of Thimerosal toxicity at the 1 ppm level and, shortly thereafter, abruptly exited the vaccines business), this reviewer agrees that the burden (the authors’ “onus”) of proof has been, and is, on the “medical world to show” that the level of Thimerosal in any injected, ingested or topical Thimerosal-containing drug is safe to be administered to those who may have “impaired” mercury detoxification systems.”

## **“2.2 Ethyl versus methyl mercury**

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Having differentiated between the clear danger posed to humans of elemental forms of mercury and high levels of methyl mercury, it is now important to show that methyl mercury and low-dose exposure to ethyl mercury (the form in thiomersal) pose very different levels of risk to humans. Even high doses of thiomersal applied to the skin are clearly high-risk. Clarkson describes the ‘three modern faces of mercury’. First, perceptions of risk from the exposure of billions of people to methyl mercury in fish. Second, exposure to mercury vapor from amalgam tooth fillings. And finally, ethyl mercury exposure from thiomersal [15].”

This reviewer finds that the authors' failure to define what constitutes "high levels of methyl mercury" and "low-dose exposure to ethyl mercury" anywhere in this publication is a major deficiency.

Based on their remarks about consumers' becoming sick from eating fish contaminated with "methyl mercury" in fish and the FDA's setting of a 1-ppm concern level for "methyl mercury" in fish, there seems to be a disconnect between what has been proven to be safe and the authors' rhetoric.

Obviously, though the authors seem *not* consider 1 ppm to be a high level for "methyl mercury" in food, the US health authorities and the public do.

Further, though toxicity has been proven in tissue and developing nerve studies for mercury in the form of ethylmercurihydroxide from Thimerosal and "inorganic mercury" from levels below 0.02-ppm, how is it that the authors' can present 100-ppm levels of Thimerosal (which represent the author's "ethyl mercury") as "low-dose exposure to ethyl mercury," *without any independent experimental toxicological of proof of safety at this level in the appropriate "susceptible" surrogate mammalian species.*

Finally, *notwithstanding the authors' view of Clarkson's views and Clarkson's views*, historically, the faces of mercury poisoning include the deliberately forgotten and knowingly concealed face of the medical mercury poisoning of hundreds of thousands of children by "inorganic mercury," principally Calomel, widely used, *without proof of safety*, in drug products given to babies and children, *mainly teething powders and worming preparations*, in the English-speaking world from the 1800s to the mid 1900s.

Calomel, 86.96% mercury by weight, is mercurous chloride ( $\text{Hg}_2\text{Cl}_2$ ).

The Calomel (or "inorganic mercury") face of medical mercury poisoning overlaps the much more insidiously toxic face, the Thimerosal (or "organic mercury") face of mercury poisoning that appeared in the 1930s and continues to exist today.

Since widespread use of Calomel-laced drug formulations persisted into the mid-20<sup>th</sup> century, it is one of the faces of "modern faces of mercury" poisoning even though the medical communities and governments have, for the most part, attempted to bury this face and the thousands of survivors (**see Appendix A**) who were once diagnosed with "Pink Disease," a disease that was "officially" buried in 1966 about 5 years after the sale of Calomel in drug products was outlawed in most of the English-speaking world.

The Thimerosal (or "organic mercury") face of medical mercury poisoning encompasses the addition of organic mercury compounds, mainly Thimerosal (and, to a lesser extent, phenyl mercuric salts [acetate and nitrate]) to vaccines and other drug formulations also without any direct scientifically sound toxicological proof (not speculation or inferential assessment [epidemiological study]) of safety — as statutorily required for all US drugs by Title 21 of the United States Code (21 U.S.C.) Section 351(a)(2)(B) since 1938 and explicitly required for preservatives in vaccines by FDA regulation since 1968 (21 CFR Sec. 610.15(a)).

Thus, the true primary faces of modern mercury poisoning are environmental in nature and should properly be labeled:

- ❖ The ingested-food mercury-poisoning face, where the major human source is the "methyl mercury" found principally in fish, dolphins and whales.
- ❖ The dental mercury-poisoning face, where the mercury emissions from mercury amalgams used in dentistry without proof of safety are a major source of the mercury.

❖ The two medical faces of mercury poisoning:

- The inorganic mercury-poisoning face, where inorganic mercury compounds, principally Calomel, were widely used in English-speaking countries in teething (soothing) powders, worming medicines and some other medicines, and
- The organic mercury-poisoning face, where organic mercury compounds, principally Thimerosal (also commonly known as Merthiolate and Thiomersal), were used in medical preparations, including vaccines, sera, infusion solutions, eye and ear drops, antiseptics, and spermaticides.

“For elemental mercury and methyl mercury, the evidence is unequivocal. People who eat fish with high mercury content become sick. Although rare outbreaks of methyl mercury poisoning have occurred, human exposure is almost entirely from fish and other seafood. Inorganic mercury occurring naturally or from pollution can be converted to methyl mercury by micro-organisms and accumulated up the food chain [5]. Ingested methyl mercury is almost is almost totally absorbed and readily crosses the placenta and blood-brain barrier. Pregnant women who consume fish may expose their fetus to methyl mercury, possibly resulting in a range of abnormalities [1,16-24].”

This reviewer finds that the authors’ statements here acknowledge the “dental face” of mercury poisoning and briefly address the “food face” of mercury poisoning.

However, the authors again overlook the medical use of Calomel and other inorganic mercurials that make up the inorganic aspect of the “medical face” of mercury poisoning.

“The initial assumption was that because the ethyl and methyl mercury are chemically similar, they must have the same toxicological effects. So that the question that needed answering was: ‘Does ethyl mercury behave the same way as elemental and methyl mercury, does it accumulate and does it cause the same or similar effects?’”

While this reviewer finds the authors’ approach to the issue of “does Thimerosal cause mercury poisoning?” is one often employed by apologists for the use of Thimerosal in medicine, this reviewer must note that the questions asked ignore the body of human case data that shows that vaccine-level doses of “ethyl mercury” apparently produce symptoms in some individuals that appear to be the same as those for mercury poisoning and, *in many instances*, the same as some of the symptoms reported for subjects diagnosed with “Pink Disease” — a disease that has been proven to be a form of mercury poisoning.

In addition, the authors seem to ignore the human case data showing that children with diagnosed DSM autism who are found by chelation challenge to be mercury and/or heavy metal poisoned often gradually lose their DSM autism diagnosis after repeated heavy-metal-chelation treatment cycles, even though such cases are well documented in many instances.

“The question is crucial — if the answer is ‘yes’, then there can be no argument, vaccines should not contain ethyl mercury. But the question could not be answered because toxicity data from low-dose human exposure to ethyl mercury were not available in 1999.”

First, as far as this reviewer can tell, the authors’ previous question is actually three (3) questions:

- “Does ethyl mercury behave the same way as elemental and methyl mercury?”
- Does “ethyl mercury” “accumulate”?
- Does “ethyl mercury” “cause the same or similar effects” as “methyl mercury”?

and not one question.

As far as this reviewer can tell, one important question is,

“Does repeatedly injecting 0.25-mL to 0.7-mL aliquots of *nominally* 61-ppm-ethylmercurihydroxide-containing drug formulations into pregnant women, newborns, babies, toddlers, and others produce mercury-poisoning symptoms that are the same as, or similar to, the mercury-poisoning symptoms for the better-studied “methyl mercury” compounds of which the authors’ speak?

However, in the US, another crucial question is,

“Have appropriate, scientifically sound toxicology studies proven that 100-ppm Thimerosal is safe, as it is required by law (21 CFR Sec. 610.15(a)) to be, for use as a preservative in a vaccine formulation?”

As far as this reviewer has been able to ascertain, the answer to the second question this reviewer has posed is “No”!

Moreover, until the answer to this crucial question is an unequivocal “Yes,” all Thimerosal-Preserved vaccines manufactured for introduction into commerce in the US and its commonwealths and territories are adulterated — making their sale illegal and their manufacturers and the key responsible manufacturing officials subject to the penalties prescribed by statute, the US Food, Drug, and Cosmetic Act.

However, both have been and are currently being protected by the US FDA’s steadfast refusal to prosecute either group for their knowing violation of the applicable US drug law.

“But they were assumed to be similar to that from low-dose exposure to other organic mercurial compounds such as methyl mercury [25]. There had been little concern about ethyl mercury in the past, and as a result, specific studies in animals were limited and no studies at all were available in humans comparing ethyl and methyl mercury adverse reactions. The only available human data described hypersensitivity reactions following topical application of thiomersal-containing antimicrobial solutions and eye drops in doses vastly in excess of doses in vaccines [26-29].”

While this reviewer has no problems with the authors’ first two statements here, this reviewer finds the authors’ third statement is problematic because the authors’ reference “[28]” seems to address “hypersensitivity” associated with the injection of Thimerosal-preserved drugs and not topical applications. {“[28] Matheson DS, Clarkson TW, Gelfand EW: Mercury toxicity (acrodynia) induced by long-term injection of gamma globulin. J. Pediatr. (1980) 97:153-155.”}

Moreover, since the documented “hypersensitivity” reactions to injected preservative-level solutions of Thimerosal include anaphylaxis and death, it should be obvious that, as such, Thimerosal does *not* meet the safety expectations of 21 CFR Sec. 610.15(a) which, in part, states:

“...Any 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, ...”

“Thiomersal is 49.6% mercury by weight and metabolized to ethyl mercury and thiosaliclylate [13,15].”

Factually, notwithstanding the authors’ references, dissolving Thimerosal in an aqueous vaccine environment leads to the rapid *hydrolysis* of the Thimerosal into ethylmercurihydroxide (EMH) and sodium thiosaliclylate and, thus, Thimerosal is *not* “metabolized to ethyl mercury and thiosaliclylate.”

Moreover, on standing in solutions containing oxygen, the thiosaliclylate oxidatively converts to the corresponding disulfide ensuring the complete hydrolysis of the Thimerosal.

Based on the preceding information, EMH is the mercury-containing species present in vaccine formulations containing added Thimerosal.

“The metabolic pathway of ethyl mercury is different from that of methyl mercury in that it is actively excreted into the gut.”

The authors’ statement is an incomplete generalization of the facts.

Factually, the metabolic excretion pathway for *injected* ethylmercurihydroxide, mainly excreted in the feces, is apparently different than the excretion pathway for *ingested* “methyl mercury” which is mainly excreted through the kidneys.

However, since, as far as this reviewer has been able to ascertain, there are no mercury transport, excretion and accumulation studies comparing the *injection* of a 100-ppm ethylmercurihydroxide solution to the *injection* of a corresponding methylmercurihydroxide solution.

For whatever reasons, even the most recent comparative research studies by Burbacher *et al.* (the authors’ reference “[34]”) using baby monkeys illogically chose to compare *ingested* methylmercurihydroxide solution dosing in one arm of their study to *injected* Thimerosal (ethylmercurihydroxide) in the other mercury challenge arms — leading this reviewer to conclude that the choice of differing modes of administration may have contributed to:

- a. the observed differences in the transport, excretion and accumulation data, and
- b. misleading the casual reader into accepting the proposition that the metabolism of these two mercury compounds was different in several aspects when *some* of the differences may be attributable to the differences in the mode of administration—*intramuscular injection* for the Thimerosal treatments versus *oral dosing* for the methylmercurihydroxide treatments.

“Ethyl mercury has been reported to cause neuro- and nephrotoxicity in accidental poisoning episodes at doses 2 – 6 times the lethal dose in rats (LD<sub>50</sub> 60 mg/kg), — much higher than those used in vaccines [30,31]. However, the precise dose-response relationship of thiomersal toxicity remains uncertain.”

This reviewer notes that the authors cited but failed to discuss the important work of D. G. Fagan, J. S. Pritchard, Thomas W. Clarkson and M. R. Greenwood, “Organ mercury levels in infants with omphaloceles treated with organic mercurial antiseptic,” ***Archives of Disease in Childhood*** (1977) **52**:962-964 (authors’ reference “[27]”), in which ten of thirteen infants so treated died after Thimerosal exposures at levels significantly lower than the LD<sub>50</sub> for rats.

These researchers reported, in a study funded by the National Institute of Environmental Health Sciences, that, between 1969 and 1975, they found 13 cases of exomphalos treated by Thimerosal in their hospital.

Though unknown amounts of a 0.1% (0.1mg/mL) Thimerosal solution (merthiolate tincture) were repeatedly applied to the umbilical area of these infants, their work indicates that the average level of Thimerosal (in the deceased infants where fresh post-mortem samples were available for analysis) was less than 12 mg/kg (12 ppm) with the least level being about 5 mg/kg (5 ppm).

In the one infant case with reported liver, kidney, brain and blood levels for unpreserved samples, those levels, in ppm, were: 15.5, 2.36, 0.650 (0.460 – 1.14), and 1.340, respectively.



Since the infants were newborns and the treatments were believed to be safe, no assessments of neurological dysfunction were conducted.

Contrary to this article's authors' statements, the Canadian researchers stated:

"Though thiomersal is an ethyl mercury compound, it has similar toxicological properties to methyl mercury (Friberg and Vostal, 1972) and the long-term neurological sequelae produced by the ingestion of either methyl or ethyl mercury-based fungicides are indistinguishable (Kantarjian, 1961; Damluji, 1962; Bakir *et al.*, 1973; Rustam and Hamdi, 1974). The clinical notes of the 6 cases studied, showed that 3 had developed vomiting, acidosis, or convulsions, but none of these findings alone is specific or indeed unusual in neonates." [Note: The references cited are: "Bakir, F., Damluji, S. F., Amin-Zaki, L., Murradha, M., Khaladi, A., Alrawi, N.Y., Tikriti, S., Dhahir, H. I., Clarkson, T.W., Smith, J.C., and Doherty, R.A. (1973). Methyl mercury poisoning in Iraq. An inter-university report. *Science* **181**, 230–241." "Damluji, S. (1962). Mercurial poisoning with fungicide Granosan M. *Journal of the Faculty of Medicine (Baghdad)*, **4**, 83–103." "Friberg, J and Vostal, L (1972). (Editors.) *Mercury in the Environment—A Toxicological and Epidemiological Appraisal*, CRC Press, Cleveland." "Kantarjian, A. D. (1961). A syndrome clinically resembling amyotrophic lateral sclerosis following chronic mercurialism. *Neurology*, **11**, 639–644." "Rustam, H. and Hamdi, T. (1974). Methyl mercury poisoning in Iraq. A neurological study. *Brain*, **97**, 499–510."]

A follow up in one of the three identified infants, a 10-year-old male, who survived this treatment, included the statement (with **bolding** added for emphasis):

"We are unable to comment on his intellectual development, though the school reports **he is restless, easily distracted and not interested in schoolwork.**"

These researchers concluded:

"Although thiomersal is an ethyl mercury compound, it has similar toxicological properties to methyl mercury and the long-term neurological sequelae produced by the ingestion of either methyl or ethyl mercury-based fungicides are indistinguishable."

These researchers also noted the scientific community seemed to have forgotten:

- a. "Mercury and mercury-containing compounds are highly toxic,"
- b. "Alkyl mercury compounds (e.g., methyl mercury and ethyl mercury [the initial mercury-containing metabolite from Thimerosal]) penetrate intact membranes," and
- c. Even in 1977, "Equally effective and far less toxic broad-spectrum antifungal and antibacterial antiseptics" were available.

"Studies by Magos were undertaken on rats and mice that had been exposed to high levels of mercury — much higher than exposure to thiomersal in human vaccines [25,32]. In these comparisons, brain levels of total mercury in the laboratory animals were lower than for methyl mercury, and kidney levels of inorganic mercury that had split off from ethyl mercury were higher. Extrapolating directly from experiments in rats to humans must be done with caution as the toxicological profile of humans may be different, and when these studies were published, there was no yard stick to facilitate this comparison."

This reviewer agrees with the much of what the authors state here concerning the comparative studies by Magos because both the methyl and the ethyl mercury compounds used the same mode of dosing (oral) so that the differences seen are not biased by a study that doses one orally and injects the other, like the more recent studies by Burbacher *et al.* did.

However, because the mercury compounds used were methylmercurichloride and ethylmercurichloride and *not* methylmercurihydroxide and ethylmercurihydroxide, the general applicability of the findings to Thimerosal may be limited to the general finding that ethylmercurichloride is more rapidly converted into "inorganic mercury" than the methylmercurichloride.

“However, since 1999, enough evidence has accumulated to indicate the metabolic/toxicological profiles of the two compounds are actually different in crucial respects.”

Based on Magos’ findings, this reviewer not only agrees that “the metabolic/toxicological profiles of the two compounds are actually different” but also that they may differ significantly in aspects that are crucial to understanding the long-term neurotoxicity of injected Thimerosal in humans, which, based on animal studies, seems to be associated with the “inorganic mercury” trapped in the brain and other tissues.

However, the authors have presented no study that addressed the effect of Thimerosal (ethylmercurihydroxide) or a similar compound, ethylmercurichloride, on reproduction. Factually, rodent studies have been reported that clearly show significant adverse reproductive effects when ethylmercurichloride was tested at levels below the LD<sub>50</sub>.

In 1971, G. A. Goncharuk [r28] published a paper in Russia titled, “Eksperimental’ noe issledovanie vliyaniya pestitsidov gruppy rtut’ organicheskikh soedinenii na generativnyuyu funktsiyu i potomstvo” [in translation: “Experimental investigation of the effect of organomercury pesticides on generative functions and on progeny”] where the Granosan, a commercial ethylmercurichloride (EMC) (*in vivo*, EMC hydrolyzes to ethylmercurihydroxide) and various other mercury preparations were studied to assess their reproductive effects.

In studies where female rats were repeatedly (every other day for 1.5 months) perorally dosed with EMC solutions at 1/20<sup>th</sup> the LD<sub>50</sub> and then mated at about 1 month after dosing started.

The EMC-dosed females had more trouble conceiving (4 – 5 matings required vs. 1 – 2 matings for control females) and produced smaller litters of pups than the control females.

Moreover, the offspring of the EMC-treated females had “impaired viability” (25–30 % died during their first month of life while only 11% of the offspring of the untreated control mothers.

Further, though the birth weights in the EMC arm were slightly higher than the controls, the progeny from the EMC arm of the study lagged in growth, especially in the first two months after birth, had delayed skeletal ossification, and, at birth and one week, had detectable mercury levels in their stomach and intestines, but was absent after weaning.

However, no changes in the activity of the SH groups in proteins of the blood and internal organs was detected.

The EMC arm’s first-generation progeny had diminished fertility (only 1.3 litters of pups vs. 4.8 litters for the controls in the first year of life); the second-generation progeny in the EMC arm of the study also had low viability and lagged in maturation like the first-generation progeny, in line with later chick embryo teratogenicity seen by Digmar *et al.* [r7].

Finally, the second-generation females also had reduced fertility (0.6 litters vs. 2.3 litters for the controls).

Based on these EMC fertility and progeny studies, it is clear that the effects of poisoning by EMC adversely impact not only the first generation but also the second-generation progeny in the areas of growth and reproduction.

While these results cannot be directly extrapolated to humans, the effects observed seem similar to those observed in humans mercury-poisoned by Calomel.

In children diagnosed with “Pink Disease,” some females have reported difficulty in conceiving and, in the males, sterility was often observed (**see Appendix A**).

Based on the preceding findings, it is even more imperative that the appropriate reproductive toxicity and mutagenicity studies be conducted for Thimerosal as a part of the required safety studies under 21 CFR Sec. 610.15(a).

### “2.3 Laboratory measurements and animal studies

A number of factors make laboratory estimation of ethyl mercury difficult. First, laboratory measurements of mercury tend to overestimate ethyl mercury. Mercury in human blood can come from two main sources: diet and vaccines. Laboratory tests do not generally distinguish between methyl, ethyl and inorganic mercury, but measure ‘total mercury’. If an individual is exposed to dietary methyl mercury, most (> 90%) of the total measured will be from methyl mercury. So the total mercury measured will reflect quite accurately the methyl mercury level. But if an individual is exposed to ethyl mercury from vaccines, its conversion to inorganic mercury is quite rapid and only ~ 75% of the total mercury will be accounted for by ethyl mercury [15]. Thus, testing for total mercury will over estimate the level of ethyl mercury in the blood.”

While the authors’ points are valid, there are analytical tests that can differentiate and assess the differing forms of mercury present in the human body.

However, this reviewer notes that, before Thimerosal was introduced in the 1930s, most of the clinical mercury poisoning cases diagnosed in infants and young children were from teething children treated with Calomel-laced teething powders (“inorganic mercury” poisoning) and not from the ingestion of fish (“methyl mercury” poisoning)

Moreover, though commonly labeled “Pink Disease” by the medical community at the time, it is clear that these “Pink Disease” cases were severe mercury poisoning by Calomel, an inorganic mercury compound.

Further, though the treatments stopped, the damage caused by this inorganic-mercury poisoning persisted for decades (see **Appendix A** for one affected person’s account), indicating that, for the “1 in 500” who were clinically mercury poisoned by Calomel and survived, some of the “inorganic mercury” that poisoned them seems to have been retained for decades and/or the damage caused was “permanent.”

Finally, in areas where fish and other seafood were the mainstays of the people’s diet and teething powders and/or Thimerosal-containing drugs were *not* used, neither “autism” nor “Pink Disease” seems to have occurred.

“Second, studies in Rochester, NY [33], suggest that the half-life of ethyl mercury is only 6 days (95% CI: 3 – 10 days) compared with 40 – 50 days for methyl mercury. It is actively excreted in the gut, not accumulated in the body. It rapidly converts to inorganic mercury that is less toxic to the brain than ethyl or methyl mercury.”

Though this reviewer does *not* dispute the comparative *initial* half-life data for ingestion of the methyl and ethyl mercury compounds studied, this reviewer finds no evidence that unequivocally establishes that the toxicity of these alkyl organic mercury compounds is significantly more than the toxicity of the “inorganic mercury” trapped in the brain.

Moreover, since the “inorganic mercury” formed in the brain has an estimated two-plus-decades-long half-life, the cumulative long-term toxicity of the “inorganic mercury” trapped to the brain easily exceeds the short-term toxicity of these alkyl mercury compounds.

Finally, this reviewer questions the usefulness of the *initial* half-life data for highly toxic organic mercury compounds (like ethylmercurihydroxide and methylmercurihydroxide) that are partially metabolized into other highly toxic mercury (“inorganic mercury”) species that bio-accumulate in the body.

“Thus, it is highly likely that all or virtually all the ethyl mercury is already lost from the body by the time the next vaccine dose is given. The peak levels will be determined by the amount of ethyl mercury administered – a function of which of the combination of vaccines is administered.”

Given:

- The established reality that some individuals have an “impaired” ability to excrete heavy metals that they absorb, ingest, or with which they are injected,
- Prior or concomitant administration of certain drugs, *including some antibiotics*, impairs the human body’s ability to excrete mercury, and
- Diet and illness can adversely affect mercury excretion,

this reviewer finds the authors’ statements to be both simplistic and misleading.

Since, during the peak dosing period in the US for Thimerosal-preserved vaccines administered to young children in vaccines (1987 – 2000), the percentage of those dosed who are subsequently developed the form of mercury poisoning that is labeled DSM autism is, based on the most rigorous data (from California’s diagnosed/confirmed/included database), only about 0.4 percent of the children vaccinated (1 in 250) and, based on the “informal survey” data from the Amish community and the “case” data from a Chicago pediatric practice that does *not* favor vaccination of young children, DSM autism is *not* found when children are *not* vaccinated (and, in the Chicago practice, the documented, confirmed level of asthma is more than an order of magnitude lower), this reviewer notes that these small half-life studies did *not* address the long-term mercury-poisoning of a *susceptible* population.

“Having demonstrated the actual (as opposed to modeled) values, the subsequent question is what proportion (if any) of blood mercury crosses the blood-brain barrier, what brain levels of ethyl mercury are attained, and whether the level is damaging in any way. A study from the Rochester group indicated that administration of thiomersal-containing vaccines did not seem to raise blood levels of mercury in human infants above safe limits which are well below those potentially associated with toxicity, even in the fetus [33]. This study, however, was not able to measure how much ethyl mercury crossed the blood-brain barrier, a virtual impossibility in human trials of infants, nor whether any neurological damage had occurred as a result of immunization. A step closer to the human situation was taken by a study sponsored by the National Institutes of Health in 2004 when blood level measurements in monkeys confirmed a much shorter half-life of ethyl mercury as compared to methyl mercury, as well as confirming the actual blood and brain levels of mercury after injection of vaccines containing thiomersal [34].”

In general, with the caveats stated previously, this reviewer accepts the authors’ views here.

## “2.4 Laboratory studies of thiomersal

Three studies on the pharmacokinetics of mercury after administration of vaccines were identified; two in humans and one in monkeys.

### 2.4.1 Human studies

Pichichero *et al* [33] studied 40 full-term infants aged  $\leq 6$  months who were given vaccines that contained thiomersal” ( “DTaP, Hep B vaccine, and in some children, Hib vaccine). Twenty-one control infants received thiomersal-free vaccines. Samples were obtained of blood, urine, and stools 3 – 28 days after vaccination. Concentrations of mercury were low in urine after vaccination, but were high in stools of the thiomersal-exposed infants. Blood-sampling did not, however, take place until at least 5 days in most of the thiomersal-exposed infants. Estimated half-life of ethyl mercury was 7 days (95% CI: 4 – 10 days). The authors concluded that administration of vaccines containing thiomersal did not seem to raise blood concentrations of mercury above safe values in infants. Ethyl mercury appeared to be eliminated from blood rapidly via the stools after parenteral administration of thiomersal in vaccines. Based mainly on the already published results of Stajich [35] (see below), they also concluded that thiomersal in routine vaccines poses extremely little risk to full-term infants, but thiomersal-containing vaccines should not be administered at birth to very low birth weight premature infants (who were not included in their study). Both Pichichero and

Stajich assume that the lower body mass of the low birth weight/premature infant would increase proportionately thiomersal concentrations.

A study of human infants was undertaken by Stajich [35]. Total mercury levels were measured before and after the administration of hepatitis B vaccine to 15 preterm and 5 term infants. Comparison of the pre- and postvaccination mercury levels showed a significant increase in both preterm and term infants after vaccination. Additionally, postvaccination mercury levels were measured. They showed that preterm infants had > 10-fold higher mean mercury levels at the baseline reading compared to term infants, although this difference was not statistically significant. Preterm infants may not be able to metabolize mercury as well because of immature livers that are not able to synthesise the metal-binding protein metallothionein [36]. After vaccination, they had five times higher mercury levels compared to term infants (this was statistically significant). There is clearly an incomplete understanding of the metabolism of mercury in general and ethyl mercury, particularly around the time of birth.”

Again, this reviewer generally accepts and agrees with the authors’ understanding of the studies reviewed here.

However, this reviewer notes that these studies shed little, if any, light on the long-term toxicity of Thimerosal, ethylmercurihydroxide, or “inorganic mercury” from the metabolism of ethylmercurihydroxide.

#### “2.4.2 Simian studies

Studies of human infants measuring brain levels of mercury or ethyl mercury after administration are impossible. Instead, attempts have been made to use simian models. The appropriateness of simian models is assumed, but not proven. Burbacher [34] and his team measured the systemic and brain distribution of total and inorganic mercury in infant monkeys following thiomersal exposure and compared them with infant monkeys exposed to methyl mercury.”

This reviewer again notes that Burbacher *et al.* inexplicably choose to compare *injected* Thimerosal to *ingested* methylmercurihydroxide.

“The initial and terminal half-life of mercury in blood following thiomersal exposure was much shorter (2.1 and 8.6 days) than the elimination half-life of mercury following methyl mercury exposure (21.5 days). Brain concentrations of total mercury were significantly lower by ~ 3-fold for the thiomersal infants when compared to the methyl mercury infants, while the average brain to blood concentration ratio was slightly higher for the thiomersal-exposed infants ( $3.5 \pm 1.0$  versus  $2.5 \pm 0.6$ ). A higher percentage of the total mercury in the brain was in the form of inorganic mercury for the thiomersal-exposed infants (34% versus 7%). The authors concluded that methyl mercury was not a suitable reference for risk assessment from exposure to thiomersal-derived mercury. In addition, it appears that blood levels are not necessarily good markers for brain levels of mercury. The study also suggests that inorganic mercury may accumulate in the brain, although the levels noted in the study were very modest (~ 16 ng/ml;” [sic; should be ‘/gram’]“.”

Except for the authors’ last statement, this reviewer finds that the authors’ review fairly reports the findings from their study and their significance.

Though the half-life of “inorganic mercury” could *not* be accurately computed because the data acquired were variable and, in the methylmercurihydroxide arm of the study, incomplete, the brain half-life values reported in the literature from longer-term animal studies are in the 20 – 30 year range for this “inorganic mercury.”

Together, these findings (and case data from chelation detox studies on:



- a. children diagnosed with mercury and heavy metal poisoning and
- b. adults diagnosed with an impaired mercury-excretion metabolism)

indicate that, on the human-life-expectancy timescale, “inorganic mercury” accumulates in the human brain and other organs.

Since, in 2001, Leong *et al.* [r23] reported significant “inorganic mercury” toxicity in growing neurons, *at effective concentrations below 0.2 ng/mL (< 0.2ppb)*, the “~ 16 ng/g” (~ 16 ppb) values reported by Burbacher are anything but “very modest.”

“It has not been possible within the scope of this review to discuss the toxicology of mercury very fully. For more detail, readers are referred to Clarkson and Magos who have probably contributed most of our understanding of this subject [2,32,37-39]. Between them in the 1970s and 1980s, they laid the fundamentals of mercury toxicology. Their latest publications are mostly reviews but the paper reviewed above by Burbacher [34] was also co-authored by Clarkson. Magos’ recent publication in the field [39] describes the decomposition rate of organo-mercurial compounds. Because metabolic rates (e.g., basal metabolism, daily loss of mercury in per cent of body burden) in different weight are related to the fractional power of body weight, mercury clears from the infant body faster than from the adult body.”

Based on this reviewer’s research into mercury, the origins of the study of the toxicity and toxicology of Thimerosal date back to the 1930s when the compound was introduced into medicines and would suggest that the readers and the authors study the seminal articles by Morton and Engley [r24-27].

In addition, these statements do *not* address the reality that those who are clinically mercury poisoned by injected Thimerosal-preserved vaccines have, *based on the research and case studies into the levels of mercury in the hair and fingernail clippings of those having diseases thought by this reviewer and other researchers to have any form of mercury as a causative factor (e.g., autism) or a major contributive factor (e.g., Alzheimer’s),* a much less efficient (impaired) mercury-excretion metabolism than the majority of the public.

Furthermore, this reviewer finds it problematic that authors neglected to discuss the experimental work of Hornig *et al.* [r27], where, *using mice*, not only was Hornig able to induce symptoms similar to human autism in mice but also, *because the susceptibility induced was mouse-strain dependent*, able to add credence to a genetic predisposition component to the development of autism following vaccine exposure.

Using an injection scheme developmentally and weight-proportionally mimicking the 2001 US immunization schedule for Thimerosal-containing vaccines with both Thimerosal-only solutions and Thimerosal-Preserved vaccine arms but without the other vaccines, these researchers found effects (in behavior and, *after sacrifice*, brain structure for one of the strains (SJL/J) that they studied) that seem to parallel the effects found in autism.

These researchers concluded:

“The pattern of behavioral and neuropathologic findings described here in SJL mice suggests a strain-dependent, ethylmercury-based disruption of normal programs of neural development and synaptogenesis. These findings implicate genetic influences and maturational factors as critical determinants of postnatal thimerosal-related sequelae and highlight the importance of interactions of gene, environment, and timing in the pathogenesis of neurodevelopmental disorders.”

Hopefully, the reader will carefully study these findings and realize that they should have been reviewed by the authors in this section (as a “**2.4.3 ‘Mus musculus’ studies**” subsection) because they provide significant support for a genetic predisposition component to the observed form of mercury poisoning diagnosed as autism and support the reality that injecting ethylmercurihydroxide into babies can cause significant damage to



the developing CNS and other systems in susceptible individuals.

Factually, the current toxicology data clearly supports the reality that repeatedly injecting young children with 100-ppm Thimerosal (49.55% mercury by weight) in drugs formulations causes some of these children to exhibit a form of mercury poisoning that, based on the neurological symptoms exhibited, is diagnosed as DSM autism (**see Appendix B** for another's views on the issue of Thimerosal in vaccines).

However, rather than conducting the appropriate safety studies, the Establishment has continued to stonewall and to assert that, *contrary to sound toxicological science*, epidemiological studies are “safety” studies.

With the preceding in mind, let us examine the epidemiological studies offered by the authors as indirect measures of the risks associated with Thimerosal-preserved vaccines.

## “2.5 Epidemiological

The published literature prior to 1999 consists primarily of studies on the toxicology of methyl mercury and the clinical syndromes associated with the topical application of medicinal compounds containing thiomersal. From 1999, there was a predictable increase in studies examining the neurodevelopmental effects of thiomersal. There were 105 published papers containing the words ‘thiomersal’ or ‘thimerosal’ in their title identified using PubMed with publication dates after 1999. Of these, 31 papers were concerned with the chemical nature of thiomersal or its metabolism or were announcements by official organisations such as national paediatric associations, 9 were extensive reviews and most of the remaining 65 were less extensive comments on various aspects of thiomersal. Only 12 publications were identified as containing new data or new ways of analysing existing data. Six concluded there was no convincing evidence that early exposure to thiomersal had any deleterious effects on neurological or psychological abnormalities, (Table 1). In dramatic contrast, one pair of authors (Geier and Geier) has published six papers claiming a relationship between the preservative and neurological or psychological abnormalities, and generating a flurry of high-powered criticism of their methodology in their wake. Because there are so few original papers and because the debate hinges on them, they are each reviewed in depth

**Table 1. Primary epidemiological data sources and the possible link between receipt of vaccines containing thiomersal and the onset of neurodevelopmental conditions.**

Author	Type of Study	Link with neurodevelopmental conditions	Possible but unproven association
Andrews [40]]	Retrospective cohort	None proved	Tics
Heron [41]	Prospective cohort	None proved	None
Haviid [42]	Retrospective cohort	None proved	None
Madsen [43]	Retrospective cohort	None proved	None
Verstraeten [44]	Retrospective cohort	Inconclusive: None proved	Tics, attention deficit disorder, speech and language disorders
Stehr-Green [45]	Ecological	None proved	None
Geier [46-51]	Retrospective cohort and ecological	Links claimed in all six papers	Various associations claimed

and have been summarised in Table 1.”

In general, this reviewer has no problem with the authors' introductory remarks until the authors begin to speak of the “conclusions” of the 12 studies they discuss in “depth.”

This reviewer finds that epidemiological studies, as with all statistical human-population studies, can only be used to measure the probability of a cause-and-effect link at some confidence level and uncertainty.

In addition, general human-population studies often miss causal relationships when, as *seems to be the case for DSM autism*, the portion of the population susceptible to the “disease” is low (less than 0.5 % for autism in the US to less than 0.09 % for autism in Denmark and Sweden; in the UK, the autism estimate is less than 0.2%).

Finally, though the authors state: “Because there are so few original papers and because the debate hinges on them, they are each reviewed in depth,” this reviewer finds the authors: **a)** only reviewed six of the twelve in any depth and **b)**, contrary to their statement, simply lumped the other six into a single “review.”

With the preceding factors in mind, let us now examine the authors’ findings and views on the studies they claim to have “reviewed in depth.”

#### **“2.5.1 Andrews *et al*, United Kingdom**

In a retrospective cohort study, Andrews *et al.* [40] examined data on 109,863 children born from 1988 to 1997 and registered in general practices in the UK, contributing to a research database. The outcomes investigated were general developmental disorders, language or speech delay, tics, attention deficit disorder (ADD), autism, unspecified developmental delays, behaviour problems, encopresis and enuresis. There was some evidence of a higher risk with increasing dose for only one outcome, tics. There were statistically significant negative associations for the other outcomes of general developmental disorders, unspecified developmental delay and ADD. For the other disorders, there was no statistically significant evidence of an association. The authors concluded that, with the possible exception of tics, there was no evidence that thiomersal exposure via DPT/DT vaccines caused neurodevelopmental disorders.”

Where does this reviewer begin to address the problems with this epidemiological study?

First, the conflicts of interest of the authors as well as the US CDC’s direct involvement (through the Robert Chen) in funding and crafting this study, and GlaxoSmithKline’s Thomas Verstraeten in providing input into this study and reviewing the study’s definition and interpreting the results are *not* disclosed (**see** the FOIA-discovered emails in the Adobe Acrobat file “.../Miller-CDC&GSK\_EmailDocumentsRe\_Andrews\_et.al.pdf”).

Second, in an obvious (to this reviewer anyway) attempt to minimize the magnitude of the statistical effects found, the researchers reported the results as “HR per dose” instead of simply calculating and reporting the overall “HR” as they should have.

Using this “per dose” approach minimizes and, effectively, hides the real risks.

In addition, *similar to some of the manipulations of the data by Verstraeten et al. in the US study*, exclusion criteria were manipulated to further reduce the cause by, among other exclusions, eliminating those who had a higher exposure from other Thimerosal-preserved vaccines.

Further, *as admitted in a FOIA-discovered email from Verstraeten (GSK) to Chen (CDC)*, the General Practice Research Database (GPRD) data for the “comparison group” are suspect or, as Verstraeten put it in an email:

“I am not sure if the GPRD is that reliable that you can be sure that low exposure is really low exposure and not underascertainment in the in the database.”

or, in layman’s terms, the “low exposure” data may simply be failures of the immunization data to have been entered into the database.

Given these flaws, it should be obvious that the conclusions reached are biased and *not* supported by sound science.

Finally, these authors mischaracterized that studies findings as “no evidence that thiomersal exposure via DPT/DT vaccines caused neurodevelopmental disorders” when the study actually concluded that, except for tics, there was no statistically significant “HR per dose” effects (and *not* “no statistically significant ‘HR’ effects”) for the diagnostic codes evaluated in this population and that the significant “HR per dose” effect for tics could have been the result of other-factor confounding. [Note: Another oddity in these data was that about 89% of the autism cases included were males (an 8:1 ratio) when the generally accepted male:female ratio for DSM autism in the US is 4:1.]

Overall, this study seems to be fundamentally flawed and the reader should, therefore, disregard its findings.

#### “2.5.2 Heron *et al.*, United Kingdom

This population-based cohort study [41] was derived from a longitudinal study on childhood health and development. The study had been monitoring > 14,000 children who were from the geographical area of Avon, UK and were born in 1991 – 1992. Associations were examined between exposure to mercury and outcomes measured in the study of impaired childhood cognitive development and early motor skills. The age at which doses of thiomersal-containing vaccines were administered was recorded, and measures of childhood cognitive and behavioural development covering the period from 6 to 91 months of age. For many of the outcomes examined, the unadjusted results suggested a beneficial effect of thiomersal exposure. For example, exposure at 3 months was inversely associated with hyperactivity at 47 months; motor development at 6 months and at 30 months; difficulties with sounds at 81 months; and speech therapy, special needs at 91 months. Only one result of the 69 criteria tested was found to be in the direction hypothesized. They concluded they could find no evidence that early exposure to thiomersal had any deleterious effect on neurological or psychological outcome.”

Without access to the original data, this reviewer first notes that the choices of the cutoff percentages in the adverse outcomes set were subjectively selected.

Second, the conflicts of Heron *et al.*, if any, and their collaboration with the US CDC, if any, are *neither* addressed *nor* disclosed.

Third, the names of the “variety of medical research charities and commercial companies,” who provided financial support, were *not* disclosed.

In addition, there is no evidence that the “completed” questionnaires were validated for accuracy, or that the children with “incomplete” questionnaires had the same distribution and severity of adverse effects as those with completed questionnaires.

Further, the small number of the cases in any actual evaluation (< 9,000) precludes any statistically valid general population inferences or conclusions in which one can have a high degree of confidence ( $p < 0.001$ ) for most of the factors studied.

Finally, the scientific justification for the numerous confounders used was *not* presented and, like the studies of Andrews *et al.* and Verstraeten *et al.*, gives the impression that these were prejudicially selected to reduce the size of the effects seen.

In this study, the “researchers” apparently got carried away with the manipulation of the data to the point that they may have “accidentally” excluded all the cases with a significant adverse outcome, which, *given the small initial size (12,956) and the fact that the putative confounders were used to eliminate 24% (leaving 9882) to 52 % (leaving 6170) of the 12,956 cases*, is highly probable since, based on Andrews *et al.*, the percentage of those apparently significantly adversely affected by something is on the order of < 1 % of the population treated with the DTP/DT vaccines.

Though, *in most cases*, the results reported for the residual data *nonsensically* found that

Thimerosal was “protective,” in the “**CONCLUSION**” section of the cited paper, these epidemiologists actually stated:

“We could find no convincing evidence that early exposure to thimerosal had any deleterious effect on neurologic or psychological outcome when given according to an accelerated schedule.”  
which is slightly different than the authors’ reported, “They concluded they could find no evidence that early exposure to thiomersal had any deleterious effect on neurological or psychological outcome.”

Overall, the obvious flaws in this study have completely undermined the usefulness and validity of this study’s findings.

#### “2.5.3 Hviid *et al.*, Denmark

This study [42] examined a population-based cohort study of all children born in Denmark from 1990 until 1996 (n = 467,450). In Denmark, childhood vaccines with and without thiomersal were in use and both vaccination status from the national register and autism diagnosis (which is determined at a central health clinic) were available for the whole cohort. During 2,986,654 person-years, 440 children were identified as cases of autism and 787 with other autistic-spectrum disorders. The risk of autism and other autistic spectrum disorders did not differ significantly between children vaccinated with thiomersal-containing vaccine and children vaccinated with thiomersal-free vaccine. The paper concluded that the results did not support a causal relationship between childhood vaccination with thiomersal-containing vaccines and the development of autistic-spectrum disorders.”

Deferring to the comprehensive rebuttal to the work of Hviid *et al.* by Safe Minds, this reviewer recommends that reader consult their paper, “**Analysis of the Danish Autism Registry Data Base in Response to the Hviid *et al* Paper on Thimerosal in JAMA (October, 2003)**” ([http://www.safeminds.org/research/docs/Hviid\\_et\\_alJAMA-SafeMindsAnalysis.pdf](http://www.safeminds.org/research/docs/Hviid_et_alJAMA-SafeMindsAnalysis.pdf)) – a copy of which is posted in **Appendix C**.

Safe Minds’ key problems with the Hviid *et al.* paper are:

- ❖ A large percentage of diagnosed autism cases are lost from the Danish registry each year.
- ❖ The vast majority of those lost cases would represent older children in the 2000 registry.
- ❖ Since the relative risk of the Hviid study is based on finding fewer older thimerosal-exposed children than younger unexposed children, the validity of their conclusion exonerating thimerosal in autism is questionable.
- ❖ More likely, the finding is a result of missing records rather than true lower incidence rates among the exposed group.
- ❖ In Safe Minds’ view, the incidence among the Thimerosal-free group is about 1 in 1,500, *which is much lower than the US and UK rates*, while the incidence of autism in the thimerosal group is about 1 in 500, similar to US and UK rates, — 3 times higher than the Thimerosal-free group.
- ❖ The Denmark registry has a number of inconsistencies and has experienced large recordskeeping-practice changes during the study period, making trend analysis difficult.
- ❖ Interpretation of the data in the manner the Hviid *et al.* used is subject to biases that may be hard to detect.
- ❖ Analysis of this data set should have been conducted by independent researchers.

Based on the validity of the Safe Minds’ rebuttal, it should be obvious to the reader, *as it was to this reviewer*, that the findings by Hviid *et al.* are *not* scientifically sound.

**“2.5.4 Madsen et al., Denmark**

Another Danish study [43] using a cross-sectional analytical design, examined longitudinal data from the Danish Psychiatric Central Research Register which recorded all psychiatric admissions since 1971, and all out-patient contacts in psychiatric departments in Denmark since 1995. The records identified all children between 2 and 10 years of age who were diagnosed with autism during the period from 1971 – 2000. A total of 956 children had been diagnosed with autism during that period. There was no trend towards an increase in the incidence of autism during that period when thiomersal was used in Denmark, up until 1990. From 1991 until 2000 the incidence increased and continued to rise after the removal of thiomersal from vaccines, including increases in children born after the discontinuation of thiomersal. This study showed that the discontinuation of thiomersal-containing vaccines in Denmark in 1992 was actually followed by an increase in the incidence of autism. The authors concluded that their data did not support a correlation between thiomersal-containing vaccines and the incidence of autism.”

In addition to the fundamental reality that the true case incidence of autism actually remained about the same over the period of time studied (**see** the FOIA-discovered emails in the Adobe Acrobat file .../Madsen\_FOIA\_EmailDocument.pdf) and concealment of the CDC's participation in this paper, the study contained numerous flaws.

Rather than recount them personally, this reviewer has again included a copy of the detailed and highly cogent review of Madsen et al. by Blaxhill of SafeMinds.org (**see**: <http://www.safeminds.org/research/docs/Blaxill-DenmarkAutismThimerosalPediatrics.pdf>) in **Appendix D**.

Based on the numerous significant flaws documented by Blaxill, the reader should reject the authors' statements concerning Madsen et al. because, *if nothing else*, they are based on a scientifically unsound epidemiological study.

**“2.5.5 Verstraeten et al., US**

This study was conducted under the auspices of the Vaccine Safety Datalink (VSD) system established by the Centers for Disease Control (and Prevention), Atlanta, to assess a wide range of adverse events from vaccines using records derived from participating managed care organisations, in this case from the VSD of the US [44]. These large linked data sets enable a wide range of outcomes and exposure levels to be examined. The screening analysis found weal (relative risk < 2), but statistically significant associations between exposure to thiomersal-containing vaccines before the age of 6 months and tic disorders, ADD and speech and language disorders. This screening analysis did not find an association with other neurological and renal disorders. To examine with more rigor the specific hypothesis emerging from the screening analysis that tic disorders, ADD and speech and language disorders are associated with thiomersal exposure before 6 months of age, a more detailed study was undertaken at one site. This study did not confirm the tentative association suggested by the screening analysis suggesting that it may have been due to bias. Taken together, the results of the two studies were inconclusive as to the effect of thiomersal on neurological outcomes.”

This reviewer must reject the authors remarks here because they are based on the published Verstraeten paper which, *based on the FOIA-accessed records obtained by Safe Minds and others*, constitute reporting based on knowing, less-than-ethical, multiple iterations of the study by Verstraeten, and his fellow epidemiologists.

These manipulations of the data and the evaluation criteria were obviously directed toward reducing the relative risk ratios to below 2 for the critical outcomes, autism and ADD.

One clear view of problems with the Verstraeten et al. paper can be found at:

[http://www.safeminds.org/research/library/VSD\\_SafeMinds\\_critique.pdf](http://www.safeminds.org/research/library/VSD_SafeMinds_critique.pdf).

Because this critical assessment is 46 pages long, this reviewer has *not* included a copy of it as an appendix to the review of this paper.

In its “**SUMMARY**,” Safe Minds reported:

- ❖ “The CDC’s approach to analysis of the VSD database demonstrates a pervasive pattern of bias and conscious manipulation of samples, statistics and findings to produce a negative finding regarding the dangers of thimerosal exposure to children”
- ❖ “Despite significant problems with study design and data quality and contrary to public statements by the CDC, the VSD analyses of autism, NDDs and speech delay provide support for a causal relationship between thimerosal exposure and childhood developmental disorders”
- ❖ “Comparisons at a population level across HMOs suggest that compliance with the recommended vaccine schedule of thimerosal exposure was associated with high rates of neurological disorders and developmental delay.”
- ❖ Fully vaccination-schedule-compliant ‘populations reported to HMOs’ had ‘disease frequencies exceeding 5% of the birth populations. Extrapolating these rates to a national level suggests that the population harmed by thimerosal exposure may number in the millions.’”

This reviewer strongly recommends that the reader and the authors study this Safe Minds’ report.

In addition to this report, which starts with the “Generation 1 (2/29/00)” findings, based on FOIA-discovered emails, the actual study of the VSD for the effects of Thimerosal in vaccines started in 1999.

The “Generation Zero” relative-risk ratios, *generated before any apparent conscious manipulative attempts to reduce the relative ratios found*, have also been reported by the “Safe

Condition (Diagnostic Code) • Inoculation time point	Generation 0 1999 analyses (relative risk)	Generation 1 2/29/00 report (relative risk)	Percentage Reduction
<b>Autism (399.0)</b>			
• 1 month	7.62/11.35	1.58	79–86
• 3 month	2.00/2.19	2.48	19–12
<b>Attention deficit disorder (314.0)</b>			
• 1 month	3.76/3.96	2.14	43–46
• 3 month	2.88/2.84	2.45	15–14
<b>Developmental speech delay (315.39)</b>			
• 1 month	2.32	0.80	66
• 3 month	0.99	1.30	(31)
<b>Sleep disorders (307.4)</b>			
• 1 month	4.98/4.64	1.74	65–62
• 3 month	2.75/2.74	n.a.	n.a.
<b>Low &amp; high exposure levels</b>			
• 1 month	0 to > 25 mcg	0 to > 12.5 mcg	
• 3 month	0 to ≥ 75 mcg	<37.6 to >62.5 mcg	

Minds” group.

The actual Verstraeten summary statistics can be found at:

<http://www.safeminds.org/research/library/SummaryStatisticsThimerosalStudy-CDC.pdf>



<http://www.safeminds.org/research/library/SummaryStatisticsThimerosalStudy-CDC2.pdf>.

Safe Minds compared the “Generation Zero” findings to the “Generation One” ones, and tabulated their review findings as shown on the previous page:

Based on this reviewer’s study of the FOIA-recovered 1999 data and the Safe Minds’ findings, this reviewer must reject the findings published by Verstraeten *et al.* as well as the authors’ review remarks.

In addition, this reviewer notes that the CDC now claims to have “lost” all the VSD datasets generated by the “Verstraeten” group, precluding an independent review thereof.

#### **“2.5.6 Stehr-Green *et al.* multi-country comparison**

This study [45] was an ecological study which compared the prevalence/incidence of autism in California, Sweden and Denmark from the mid-1980s to the late-1990s coinciding with the periods of differing average exposures in the three countries. Graphs compared population-based data from the US (national immunisation coverage surveys and counts of children diagnosed with autism-like disorders seeking special education services in California); Sweden (national in-patient data on autism cases, national vaccine coverage levels, and information on use of all vaccines and vaccine-specific amounts of thiomersal); and Denmark (national registry of in-patient/out-patient – diagnosed autism cases, national vaccination coverage levels, and information on use of all vaccines and vaccine-specific amounts of thiomersal). In all three countries, the incidence and prevalence of autism-like disorders began to rise in the 1985 – 1989 period, and the rate of increase accelerated in the early 1990s. However, in contrast to the situation in the US, where the average thiomersal dose from vaccines increased throughout the 1990s, thiomersal exposures from vaccines in both Sweden and Denmark – already low throughout the 1970s and 1980s – began decrease in the late 1980s and were eliminated in the early 1990s. The authors concluded that the body of existing data examined was not consistent with the hypothesis that increased exposure to thimerosal-containing vaccines was consistently temporally associated with apparent increase in the rates of autism in young children.”

This reviewer notes that the non-validity of the data reported in the “*Stehr-Green et al. multi-country comparison*” for Sweden has already been rebutted in this reviewer’s discussion of the other studies on Swedish records.

Moreover, the data graphed was limited to the *in-patient* affected individuals (*not* all affected individuals), and to *in-patient* rates in 100,000 *person-years* (*not*, as they should have, the incidence rate in “affected individuals per 100,000 persons”).

Further, the data used in this study has other established (in the discussion of the prior studies) problems including, but, not limited to, the case loss, changing diagnostic criteria, and other database issues.

The Danish database has similar reporting issues including changing criteria and the data used is biased by: **a)** a failure to properly correct/assign the information entered into the database to the correct birth cohort and **b)** a *not* clearly disclosed change in the early 1990s *from only tracking in-patient instances to tracking all patient instances*.

Another problem of the Danish graph is that the data is not reported on a “number of cases per 100,000 individuals in the group” but rather on a number-of-cases basis.

Factually, both the Danish and Swedish data do *not* present a view of the change in the number of cases per 10,000 individuals in the population for a given year versus the level of prior Thimerosal exposure precluding a valid comparison to the California data.

Therefore, one cannot validly compare the graphs because their “y” (response) variables are all in non-comparable units (California’s disease response is in cases *per 10,000 persons*, and Sweden’s is in cases *per 100,000 person-years*, while Denmark’s response is reported in cases, a non-“rate” basis.

Given the preceding realities, the readers are left with the graph of the California data on diagnosed, confirmed, and included DSM autism cases.

This graph clearly shows an increase in autism coupled with an increase in infant exposure level that has driven the incidence rate from about 6 per 10,000 in 1985 to greater than 20 per 10,000 in 1994 (a 3.3-plus-fold increase) for a dose increase from “62.5 mcg” in 1985 to “187.5 mcg” in 1994 (a 3-fold increase in dose).

Thus, contrary to the views of the authors, the only valid data (California) supports “the hypothesis that increased exposure to thimerosal-containing vaccines was consistently temporally associated with apparent increase in the rates of autism in young children.”

“The six papers described above have all used observational data derived from studies of high methodological quality, especially the cohort studies [40-43] to demonstrate the absence of an association which, given the strength of the studies, goes strongly against any causal relationship between thiomersal-containing vaccines and autism or other neurodevelopmental outcomes. First, some of the studies were unable to prove there was no direct relationship between two events – they could only show there was insufficient evidence to show there is a connection. Although this satisfies the pure scientist, it may be harder to convince the public with such an argument. Second, the studies are dependent on the quality of the data. The definitions of the neurodevelopmental abnormalities such as autism have varied over the period that the longitudinal data have been collected, from one centre to another and from country to country. And the popularity of the diagnosis ‘autism’ has changed with time. Physicians and families in many countries are much more aware of autism than ever before, making the diagnosis much more likely to appear in reported data. It is not certain whether or not the rise in reported cases of autism over the last two decades in some countries can be accounted for solely by this phenomenon, or whether there are other factors causing it.”

Since independent reviews by scientists, like this reviewer, who have no financial interest in promoting vaccines or covering up the harm done by Thimerosal in vaccines, have clearly established that the preceding papers are derived from studies that seem to be bereft, for the most part, of any “methodological quality,” this reviewer (and, hopefully, those who read this review and study the basis articles and data) must reject the authors’ rhetoric here because the scientifically sound data analyses clearly do support a strong statistical link between Thimerosal exposure and the risk of neurological harm to the fetus, neonate and young children.

Moreover, *at least for the sound and self-consistent California autism database of diagnosed, confirmed and included DSM autism cases*, studies have clearly established that the majority of the increases seen are *not* caused by changing diagnostic criteria, increased physician or parent awareness, or increased educational and health service availability but by increased exposure. [See: “THE EPIDEMIOLOGY OF AUTISM IN CALIFORNIA – Report to the Legislature on the Principal Findings from The Epidemiology of Autism in California: A Comprehensive Pilot Study” published on-line by the M.I.N.D. Institute, University of California, Davis on Thursday, October 17, 2002. {Note: The complete report is available at [http://www.ucdmc.ucdavis.edu/mindinstitute/newsroom/study\\_final.pdf](http://www.ucdmc.ucdavis.edu/mindinstitute/newsroom/study_final.pdf).}]

Since, *during the late 1980s to the early 2000s*, the US had the highest exposure level and the most consistent definitions for the worst-case mercury poisoning diagnosis, “DSM/CDER type 1” autism, the study findings from a valid US epidemiological would be the most appropriate that can be used, *if not twisted and/or misrepresented*, to estimate the general dose-dependent risks for Thimerosal-preserved vaccines world wide.

Hopefully, all who read this review will pressure the US government to fully open up the VSD to all researchers and require full disclosure of all financial and other conflicts of interests for all those who seek to publish any epidemiological study based on the VSD database so that researchers in all countries may be able to independently assess the relative risk for all possible vaccine-associated adverse reactions and have their findings confirmed, *after they publish*, by other independent researchers.

When, and only when, full independent access is provided to the VSD database for those children born between 1986 and 2007 and valid independent studies are fully conducted, written up, peer-reviewed, published, and openly verified by other independent researchers will the public be provided with valid estimates of the relative risk for various levels of Thimerosal exposure at various times.

#### ***“2.5.7 Geier and Geier, US***

This group of six papers, by the same authors, Geier *et al.* [46-51], are all similar with only minor variations. Because they are outliers and claim to show damaging effects of thiomersal in vaccines, they have generated extremely hostile reactions in the scientific press.”

This reviewer notes that, in violation of the authors’ stated “they are each reviewed in depth,” the six papers by the Geiers are *not* reviewed in any depth but are lumped together and maligned, without documented proof of the claimed weaknesses and deficiencies raised, to justify the dismissal of these papers by the authors of this “expert opinion” article.

Moreover, the “excuse” given for lumping them together, that they “are all similar with only minor variations,” seems to be specious because the Geiers’ papers are, in general, no more similar than the previous six studies that the authors “reviewed” separately.

In addition, the authors’ “they have generated extremely hostile reactions in the scientific press” seems to fly in the face of reality because these papers have been published:

- ❖ In recognized peer-reviewed journals (after apparently more rigorous review than the previous six received),
- ❖ By qualified scientists, the Geiers, who, *unlike the authors of the previous six papers*, received no grant or other financial support from the CDC or other governmental agencies or industry sources and are not directly employed in capacities that would benefit by the minimization of any risk from vaccines, and
- ❖ Without any in-depth *fact-supported* published rebuttals, in journals or online, of any of their findings.

Moreover, *as far as this reviewer can ascertain*, the hostile press reactions “in the scientific press” have been confined to statements published in or by government and/or industry funded or supported individuals or agencies, who seem to be functioning as apologists for the vaccine establishment.

“Each evaluated the effects of mercury from thiomersal-containing vaccines childhood vaccines on the prevalence of childhood neurodevelopmental disorders using weak study designs consisting of descriptions of publicly available data sets with varying and/or uncertain denominator populations.”

Factually, the study designs the Geiers used on the “publicly available datasets” are similar to the CDC-recognized designs that the CDC has previously used and published on similar “publicly available datasets” without receiving similar criticisms.

Given the preceding realities, this reviewer must discount the validity of the authors’ views.

Further, unless the authors believe, or have proof, that the US government's data on the vaccine denominator populations is "uncertain," none of the Geiers' papers used "uncertain denominator populations" because the Geiers' published studies used US-government-supplied population denominators.

In addition, *as long as the population denominators are known*, using "varying ... denominator populations" is *not* a study design weakness *per se*.

Moreover, since at least one of the Geiers' papers (the authors' reference "[50]") used the non-public Vaccine Safety Datalink (VSD) database's data sets, the authors' assertion concerning the use of "designs consisting of descriptions of publicly available data sets" is, at best, less than factually accurate.

With these general points in mind, this reviewer will briefly review each of the Geiers six papers by the year in which they were published.

### 2.5.7.1 Geiers' 2003 papers

#### 2.5.7.1.1 *Geier MR, Geier DA. Thimerosal in Childhood Vaccines. Neurodevelopmental Disorders, and Heart Disease in the United States. J. Am. Phys. Surg. (2003) 8(1):6-11.*

Using the VAERS database and study designs and recognized evaluation procedures like those that have been used in previous epidemiological studies on the VAERS database, in this study the Geiers (current article's reference "[49]") found that there was statistically significant dose-dependent "epidemiological evidence of a link between increasing mercury from thimerosal-containing childhood vaccines and neurodevelopmental disorders and heart disease."

In addition, the Geiers reported:

"In light of voluminous literature supporting the biologic mechanisms for mercury-induced adverse reactions, the presence of amounts of mercury in thimerosal-containing childhood vaccines exceeding Federal Safety Guidelines for the oral ingestion of mercury, and previous epidemiological studies showing adverse reactions from such vaccines, a causal relationship between thimerosal-containing childhood vaccines and neurodevelopment disorders and heart disease appears to be confirmed."

Though this paper generated an uproar in the medical community, no group or individual was willing to submit a *signed* critique for publication in the journal, leading the journal to publish the Geiers' response (*see J. Am. Phys. Surg. 8(3):68-70*) to the Internet-published critique by unnamed persons on the American Academy of Pediatrics (AAP) website with the following editorial note:

*"[Editor's Note: Some vociferous criticisms have been made of the article concerning possible adverse effects of thimerosal published in our spring issue. To date, however, no one has been willing to send a signed letter for publication. Because the critique has been widely circulated by Internet, as in reference 18 below, we offered the authors an opportunity to respond.]"*

For those researchers who do *not* have ready access to the *Journal of American Physicians and Surgeons*, this reviewer has provided a quoted copy of the Geiers' response without the editors' note and the Table 1 data (which seems to be no longer available online) [*see Appendix E*]:

- So that the reader of this review can see that the cogent issues raised by the critique on the AAP website were addressed, and
- Because the Geiers' responses address many of the issues raised about the validity of the findings reported in their other papers.

Finally, this reviewer must note that no in-depth attributed review of the underlying data has been published that refutes the findings of the Geiers and, therefore, *to date*, the possibility of a dose-related link between the level of Thimerosal-containing mercury injected and neurodevelopmental disorders and heart disease must be accepted.

**2.5.7.1.2 Geier MR, Geier DA. Neurodevelopmental disorders after thimerosal-containing vaccines: a brief communication. Exp. Biol. Med. (2003) 228(6):660-664.**

First, the Geiers reported being “initially highly skeptical that differences in the concentrations of thimerosal in vaccines would have any effect on the incidence rate of neurodevelopmental disorders after childhood immunization.”

In spite of their initial skepticism, using VAERS, they found epidemiologic evidence that “associates increasing thimerosal from vaccines with neurodevelopmental disorders.”

Specifically, the Geiers reported their analysis of the VAERS database “showed statistical increases in the incidence rate of autism (relative risk [RR] = 6.0), mental retardation (RR = 6.1), and speech disorders (RR = 2.2) after thimerosal-containing diphtheria, tetanus, and acellular pertussis (DTaP) vaccines in comparison with thimerosal-free DTaP vaccines.”

Similar to the findings by the Verstraeten group when they tabulated the California VSD data by sex, the Geiers found male/female ratios indicating “autism (17) and speech disorders (2.3) were reported more in males than females after thimerosal-containing DTaP vaccines, whereas mental retardation (1.2) was more evenly reported among male and female vaccine recipients.”

The Geiers used age similarity and acute adverse reactions as “controls” to check for evidence of biasing and found little to no evidence of significant biasing between the groups evaluated bias.

For example, they found that the overall adverse reactions were reported in similar-age populations “after thimerosal-containing DTaP ( $2.4 \pm 3.2$  years old) and thimerosal-free DTaP ( $2.1 \pm 2.8$  years old) vaccinations.”

Comparing acute control adverse reactions after thimerosal-containing vaccines to those after the thimerosal-free DTaP vaccines, the Geiers found the relative-risk values were similar for: “deaths (RR = 1.0), vasculitis (RR = 1.2), seizures (RR = 1.6), ED visits (RR = 1.4), total adverse reactions (RR = 1.4), and gastroenteritis (RR = 1.1).”

Though their results clearly supported a probable association between the neurodevelopmental disorders evaluated and the administration of the thimerosal-containing vaccines, the Geiers concluded “additional studies should be conducted to confirm and extend this study.”

Later in 2003, Mann (Clements and McIntyre’s reference “[52]”) attempted to raise questions about this paper, but this reviewer found that most of the “concerns” raised were theoretical and/or definitional and, *except for those that echoed the Geiers’ published caveats about the data*, most of the others could have been answered by Mann’s appropriately querying the VAERS database had he wanted to answer the questions he raised.

After reviewing the Geiers’ paper, and considering Mann’s issues, this reviewer finds that the estimated uncertainties in the RR values for autism, mental retardation, and speech disorders still compel this reviewer to *reject* the *hypothesis* there is *no* Thimerosal effect.

**2.5.7.1.3 Geier DA, Geier MR. An assessment of the impact of thimerosal on childhood neurodevelopmental disorders. Pediatr. Rehabil. (2003) 6(2):97-102.**

After noting that the “prevalence of autism in the US has risen from 1 in approximately 2500 in the mid-1980s to 1 in approximately 300 children in the mid-1990s,” the Geiers, using both VAERS database and case data reported in a 2001 US Department of Education Report, conducted exploratory epidemiological evaluations designed to determine whether or not “mercury from thimerosal in childhood vaccines contributed to neurodevelopmental disorders.”

As was the case in the previous papers, appropriate check control assessments were used to support the validity of the findings of an association between the level of Thimerosal exposure and the subsequent occurrence rate for neurodevelopmental disorders.



This reviewer finds that, *as the Geiers stated*, “The evidence presented here shows that the occurrence of neurodevelopmental disorders following thimerosal-containing childhood vaccines does not appear to be coincidental.”

### 2.5.7.2 Geiers’ 2004 papers

#### 2.5.7.2.1 *DA Geier, MR Geier. A comparative evaluation of the effects of MMR immunization and mercury doses from thimerosal-containing childhood vaccines on the population prevalence of autism. Med. Sci. Monit. (2004) 10(3):P133-P139.*

This is one of the papers that the authors discussed and, in discussing it (authors’ reference “[47]”) and the previous paper (Clements and McIntyre’s reference “[48]”; discussed by this reviewer [reviewer’s “2.5.7.1.3”]), stated:

“One of the papers [47] used as its database the Biological Surveillance Summaries of the Centers for Disease Control and Prevention (CDC), the US Department of Education data sets, and the CDC’s yearly live birth estimates. The others used the Vaccine Adverse Events Reporting System (VAERS), a passive reporting system instituted to provide early warning of possible adverse events to provide early warning of possible adverse events for more rigorous evaluation. The dose-response curves in one of their studies [48] showed increases in odds ratios of neurodevelopmental disorders from both the VAERS and the US Department of Education data closely linearly correlated with increasing doses of mercury from thiomersal-containing childhood vaccines. For overall odds ratios, statistical significance was achieved. Similar slopes and linear regression coefficients for autism odds ratios in VAERS and the US Department of Education data helped to mutually validate each other.”

This reviewer finds that the authors’ discussion of this article is incomplete because it failed to note that, *in addition to finding a dose-related correlation between Thimerosal dose and autism rates*, this study by the Geiers also pointed out an association between increased MMR vaccine coverage percentages in the UK and the US, and increased adverse neurological outcomes.

In contrast to the studies “touted” by the authors of the “When science is not enough ...” article being reviewed, the Geiers provided a clear description of the data they used for their studies and its sources.

Further, unlike the authors of the “When science is not enough ...” article being discussed by this reviewer, this reviewer found that the Geiers’ disclosed the characteristics of the datasets used and correctly pointed out that the dataset weaknesses found did *not* significantly affect the validity of the Geiers’ findings.

#### 2.5.7.2.2 *Geier DA, Geier MR. Neurodevelopmental disorders following thimerosal-containing childhood immunizations: a follow-up analysis. Int. J. Toxicol. (2004) 23(6):369-376.*

Except to note that the Geiers, *like the researchers in some of the other studies*, used the ambiguous term “ethylmercury” to describe the nominal mercury amounts in each dose of vaccine administered, this reviewer finds that the Geiers’ conclusions are scientifically sound and that their designs and practices followed those recognized by the CDC as appropriate for evaluating the VAERS database to ascertain possible risks and their magnitude estimates from the adverse events reported (mainly [ $> 95\%$ ] by healthcare professionals) in the VAERS database for the review period the Geiers used in this study.

Fundamentally, this study *confirmed* a strong statistical link between increasing mercury dosing and the increasing risk of autism and other neurodevelopmental disorders for a single vaccine type, DTaP, where both Thimerosal-Preserved and Thimerosal-Free vaccines were administered.



### 2.5.7.3 Geiers' 2005 paper

#### 2.5.7.3.1 DA Geier, MR Geier. *A two-phase epidemiological study of the safety of thimerosal-containing vaccines: a follow-up analysis. Med. Sci. Monit. (2005) 11(4):CR160-CR170.*

Here this reviewer finds that the valid epidemiological study of the VSD database (the Geiers' "Phase two" study) that has few of the alleged "problems" raised by the critics of the VAERS and other data sources used by the Geiers in other studies they have conducted.

Yet Clements and McIntyre apparently deliberately failed to address this issue or to discuss the general agreement of the valid epidemiological outcomes observed in all of the datasets evaluated (VAERS, VSD, and the combined data from the Biological Surveillance Summaries of the Centers for Disease Control and Prevention (CDC), the US Department of Education data sets, and the CDC's yearly live birth estimates) clearly established that there is a probable strong statistical link between mercury exposure from "Thimerosal-containing" vaccines and autism and other neurodevelopmental disorders.

Turning to the Geiers' article, this reviewer finds that their "**Summary**":

- " **Background:** Thimerosal is an ethylmercury-containing preservative in vaccines. Toxicokinetic studies have shown children received doses of mercury from thimerosal-containing vaccines (TCVs) that were in excess of safety guidelines. Previously, an ecological study showing a significant association between TCVs and neurodevelopmental disorders (NDs) in the US was published in this journal.
- Material/Methods:** A two phased population-based epidemiological study was undertaken. Phase one evaluated reported NDs to the Vaccine Adverse Event Reporting System (VAERS) following thimerosal-containing Diphtheria-Tetanus-acellular-Pertussis (DTaP) vaccines in comparison to thimerosal-free DTaP vaccines administered from 1997 through 2001. Phase two evaluated the automated Vaccine Safety Datalink (VSD) for cumulative exposures to mercury from TCVs at 1-, 2-, 3-, and 6-months-of-age for infants born from 1992 through 1997 and the eventual risk of developing NDs.
- Results:** Phase one showed significantly increased risks for autism, speech disorders, mental retardation, personality disorders, and thinking abnormalities reported to VAERS following thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines. Phase two showed significant associations between cumulative exposures to thimerosal and the following types of NDs: unspecified developmental delay, tics, attention deficit disorder (ADD), language delay, speech delay, and neurodevelopmental delays in general.
- Conclusions:** This study showed that exposure to mercury from TCVs administered in the US was a consistent significant risk factor for the development of NDs. It is clear from these data and other recent publications linking TCVs with NDs that additional ND research should be undertaken in the context of evaluating mercury-associated exposures and thimerosal-free vaccines should be made available."

accurately reflect the epidemiological studies and findings derived from these apparently well-designed, properly executed and thoughtfully reviewed studies.

"The weaknesses in design of this group have been extensively critiqued."

While this reviewer agrees with the authors' observation, this reviewer notes that these researchers and unidentified critics to whom the authors refer have deliberately overlooked the strengths in the design of these studies.

"The American Academy of Paediatrics considered that the associations between thiomersal-containing vaccines and autism suggested by these studies using data from VAERS were invalid because of numerous conceptual flaws, omissions of fact, inaccuracies, and misstatements [103]."

First, this reviewer must note that the criticisms raised in reference "[101]" were:

- Unsigned, and

- Only raised for one paper (this reviewer's "2.5.7.1.1 Geier MR, Geier DA. Thimerosal in Childhood Vaccines. Neurodevelopmental Disorders, and Heart Disease in the United States. *J. Am. Phys. Surg.* (2003) **8**(1):6-11" [the authors' reference "[49]"]), and,
- Therefore, do not, *per se*, apply to any of the other cited papers published by the Geiers.

This lack of general applicability is particularly obvious in the cited papers where the Geiers used datasets from other sources.

Furthermore, this reviewer finds that the Geiers' published reply to the unsigned allegations posted on the website of the American Academy of Pediatrics (AAP) more than adequately rebutted the cogent issues raised and that, reacting to the AAP's posted self-serving criticisms, the Geiers' subsequent papers explicitly address the cogent issues and point out that the designs, studies, and presumptions used are the same as or similar to those routinely used and published by the epidemiologists in the CDC studying similar vaccine issues.

"Mann [52] pointed out a number of methodological flaws, including the potential bias due to the different time periods of the observation, the incorrect calculation of attributable risk and failure to use incidence rates in the calculation of relative risk. To appropriately measure incidence in those 'exposed' and 'unexposed' to thiomersal-containing vaccine, one would need to follow vaccinated children forward in time after receiving one or the other immunisation to see what proportion in each group developed neurodevelopmental disorders. Instead, the authors compared the proportion of immunised children for whom a perceived connection between vaccination and autism was reported for thiomersal-containing DTaP vaccine versus thiomersal-free vaccine in the VAERS database. This does not amount to a true comparison of incidence rates, since there may have been numerous cases of developmental disorders for which no association with vaccine was suspected and were therefore not reported."

Again, these comments, taken from "Mann [52]" only apply to one of the Geiers' cited papers (the authors' reference "[46]" [this reviewer's "2.5.7.1.2 Geier MR, Geier DA. Neurodevelopmental disorders after thimerosal-containing vaccines: a brief communication. *Exp. Biol. Med.* (2003) **228**(6):660-664])."

Moreover, many of the "issues" raised by Mann were recognized and addressed by the Geiers in that paper or were hypothetical issues that lack substance in light of:

- The reality of the rise in neurodevelopmental disorders in the US that seem to parallel the rise in the amount of mercury that was administered and, based on the California data, to decline when the mercury administered declined.
- The fact that both urban (Chicago's Homefirst Health Services' unvaccinated patients) and rural (Pennsylvania's Amish) US populations of unvaccinated children have a near-zero incidence for autism whereas the general rate for autism in US population groups vaccinated with Thimerosal-containing vaccines is on the order of 1 in 150 (males only) to 1 in 250 (all children) in children 3 to 18 years of age.

Apparently, *like many in the healthcare establishment*, the authors here *cannot* bring themselves to see the harm caused by their profession's allowing mercury in vaccines and other drugs as well as the massive social and financial burdens that their unjustified actions have created and are creating for the public.

"Thus these six papers, the only ones to suggest an association between thiomersal and autism and other developmental disorders, have flawed design and analysis. Despite this, they are frequently quoted by those against the use of the preservative as proving their case."

While, as is the case with all epidemiological studies, this reviewer agrees that these six papers only "... suggest an association between thiomersal and autism and other developmental disorders," but that, *contrary to the authors' views*, the Geiers' papers not only do *not* "have flawed design and analysis" but also have designs and analyses that are more scientifically sound than those published in the first six studies.

## **"2.6 Official organisational reports**

Many Western governments or organisations have issued reports to their constituencies about thiomersal. Without exception, these official reports have summarised scientific findings and expressed their view that thiomersal is, overall, safe to use in vaccines. Some reports have placed qualifications on their endorsements. However, all official reports cannot be attributed the same level of integrity. First, early reports were made in the absence of data available later. The 2001 report was undertaken by independent experts under conditions of extreme rigour. Not all official reports examined the data with such intensity."

Since governments share responsibility for the harm, *if any*, caused by:

- a. permitting Thimerosal-containing vaccines to be used without the requisite proofs of safety and
- b. *when faced with evidence of harm attributable to permitting Thimerosal-containing drugs to be used*, continue to permit the use of such,

this reviewer is *not* surprised that government reports would, *without scientifically sound proof of safety*, simply declare "thiomersal is, overall, safe to use in vaccines" with "qualifications on their endorsements" to "cover" their positions.

What is surprising is that these authors chose to include such self-serving and less-than-science-based reports in their article.

### **"2.6.1 National Academies of Science (US)**

To address the uncertainty regarding the effects of low-level exposure to methyl mercury and the lack of consensus between various US agencies, the US Congress solicited the independent advice of the National Academies of Science (NAS) National Research Council. The National Research Council's findings, release in July 2000, concluded that the 'Environmental Protection Agency's reference dose is scientifically justifiable for protecting the health of the vast majority of Americans' [53]. Because of limited understanding of the difference between methyl and ethyl mercury at the time, this report sadly did not further the discussion about the safety of thiomersal."

What this reviewer finds sad is the authors' failure to point out in this article that recent studies [r4], *published in mid-2005*, have found that the basis criteria upon which this 2000 report rests were *not* valid.

In light of the findings reported in [r4], the "'Environmental Protection Agency's reference dose'" should be reduced by a factor of 2, at least, and, more probably, by a factor of 10 or more.

Hopefully, after carefully reviewing [r4], the authors will update their opinion to reflect the lack of validity of current "'Environmental Protection Agency's reference dose'" should they find that the US Environmental Protection Agency has, as yet, elected to ignore the findings reported in [r4].

### **"2.6.2 The Institute of Medicine (US)**

The Institute of Medicine's Immunisation Safety Review Committee reviewed 'Thimerosal – Containing Vaccines and Neurodevelopmental Disorders' in 2001 [54]. The committee was unable to conclude from the existing evidence whether thiomersal did or did not cause neurodevelopmental

disorders. The committee nonetheless called for the removal of thiomersal from vaccines, recommending the use of thiomersal-free DTaP, Hib and HepB vaccines in the US. They recommended that full consideration be given by appropriate professional societies and governmental agencies to removing thiomersal from vaccines administered to infants, children, or pregnant women in the US.”

In 2004, with much more information to base their comments on, the eighth report of the US Immunisation Safety Review Committee went much further. It found that the body of epidemiological evidence favoured the rejection of a causal relationship between thiomersal-containing vaccines and autism. The report also found that potential biological mechanisms for vaccine-induced autism that had been generated were only theoretical. They did not, however, recommend reversal of any of the previous decisions about removing thiomersal from vaccines [55].”

Since the FIOA-disclosed transcript of this IOM committee’s first (12 January 2001) closed-door meeting clearly indicates that the IOM was instructed by the CDC not to find any link between Thimerosal and autism, this reviewer and the authors should reject any of their reported findings because it is apparent that that IOM committee was limited to reaching outcomes favorable to the their client’s (the CDC’s) position on the issues the IOM was to “independently” review.

Moreover, to date, the CDC has refused to provide a copy of the “charging” instructions that it gave to the IOM to those seeking it under FOIA.

Given the preceding realities, this reviewer is compelled to reject the findings reported by the cited IOM committee because it is obvious that the findings reported have been prejudiced by the instructions given to the IOM by the CDC when the CDC contracted for these studies.

***“2.6.3 Joint Statement of the American Academy of Family Physicians, The American Academy of Pediatrics, the Advisory Committee on Immunization Practices and the US Public Health Service (US)***

Following a joint statement in 1999 indicating a goal of removing the vaccine preservative thiomersal as soon as possible from vaccines routinely administered to infants, a joint statement of the American Academy of Family Physicians, The American Academy of Pediatrics, the Advisory Committee on Immunization Practices and the US Public Health Service was published in June 2000 [104]. They recommended continuation of the current policy of moving rapidly to vaccines which were free of thiomersal as a preservative. Until an adequate supply of vaccine was available, use of vaccines which contained thiomersal as a preservative was acceptable. This statement reflects the incomplete understanding of the time, and is no longer scientifically adequate. New studies have demonstrated the fears driving this statement were largely unfounded.”

Contrary to the authors’ view here, the “new” scientifically sound experimental (non-epidemiological) studies have clearly demonstrated that Thimerosal should *not* be a component in any medicine, including vaccines, because clear CNS-toxic effects have been demonstrated at “Thimerosal” levels of about 0.02 ppm (and Thimerosal-derived “inorganic mercury” levels that are even lower) and metabolic pathway studies have found non-reversible adverse “Thimerosal” (ethylmercurihydroxide) and “Thimerosal-metabolite” (“inorganic mercury”) effects, *at sub-ppm levels of exposure to “Thimerosal” and mercuric ion*, on key metabolic pathways as well as adverse immune and autoimmune effects.

***“2.6.4 Committee on the Safety of Medicines, UK***

Two studies in the UK [40,41] prompted a statement by the Committee on the safety of medicines to reinforce their advice of 2001 that there was no evidence of neurological adverse effects caused by thiomersal in vaccines. The ‘balance of benefits and risks of thiomersal-containing vaccines therefore remain overwhelmingly positive.’ [105]”

#### **2.6.5 World Health Organization**

WHO’s Global Advisory Committee on Vaccine Safety made regular reports on its deliberations as the committee maintained a review of current research. Its deliberations have often be based on prepublication study results and represent the most authoritative information and current assessment of the situation. Its findings have been consistently in favour of continuing to use thiomersal in vaccines [56]. Other reports from the WHO were also supportive of continuing its use in vaccines [57,58].

#### **2.6.6 The European Agency for the Evaluation of Medicinal Products**

The European Agency for the Evaluation of Medicinal Products issued a statement in March 2004 [106] concluding no association between vaccination with thiomersal-containing vaccines and specific neurodevelopmental abnormalities. While encouraging the continued use of these vaccines, the agency promoted reducing exposure to mercury, and where possible, the development of vaccines without thiomersal or with the lowest possible levels.”

#### **2.6.7 STIKO (Germany)**

Germany had largely removed thiomersal from vaccines by 2004, in line with reducing the overall exposure to mercury to children [59].”

Other than to remind the reader that the reporting organizations are responsible for permitting the Thimerosal exposure in the first place and, therefore, have serious conflict-of-interest issues to overcome, this reviewer only notes that the reality in the EU seems to be that the industrial countries in the EU have, *for the most part*, moved rapidly to Thimerosal-free and reduced-Thimerosal vaccines

#### **“2.6.8 National Advisory Committee on Immunisation (Canada)**

By 2002, Canada had removed thiomersal in vaccines delivered to infants < 6 months of age in the routine immunisation schedule. In 2003, the National Advisory Committee on Immunisation recommended that vaccines that did not contain thiomersal as a preservative should be used preferentially in infants to reduce any unnecessary exposure to mercury and to maintain public confidence in vaccine programmes. They affirmed that because the risk of any health effect from thiomersal in vaccines had never been substantiated, and because, compared to the real risk of infection from inadvertent contamination of vaccine, the risk of thiomersal-related health effects was negligible, vaccines containing thiomersal should not be withheld if they were needed [60,61].”

This reviewer would again remind the reader that the Canadian “National Advisory Committee on Immunisation” recommendations are being made by a governmental committee that is responsible for permitting the Thimerosal exposure and, therefore, also has serious conflict-of-interest issues to overcome.

#### **“2.7 Other reviews**

The authors identified 32 additional articles [61-92] published since 1999 that reviewed available data on the impact of receiving a vaccine containing on autism or other neurodevelopmental abnormality. In all, nine reviews covered the issues in-depth, but did not present any new data or particularly novel ways of analyzing existing data. The remainder were reviews of mercury metabolism and the need to reduce mercury exposure, in general, including in vaccines. Although these views of acknowledged experts in the field varied considerably, the papers did not add substantially to the body of knowledge derived from the original papers above [40-45].”



### **“3. Benefits of using thiomersal**

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The benefits of maintaining thiomersal as a preservative are immense, enabling the continued use of hundreds of millions of doses per year of liquid vaccines that are part of the global effort to control vaccine-preventable diseases in industrialised and developing nations. Without a preservative, multi-dose liquid preparations of vaccine are vulnerable to bacteriological contamination that can result in death or serious illness to the recipient. Although 2-phenoxyethanol has been used as a preservative, its effects are less bactericidal than thiomersal and manufacturers have not been inclined to switch. There is, then, no compound waiting to take the place of thiomersal in the vaccine industry. And if there were, there is always the possibility that any replacement preservative might have adverse reactions that could be hard to identify in the short-term. Even withdrawing thiomersal from a vaccine has major implications on the regulation of vaccine production [93] – the vaccine would have to be reclassified and would need field trials and control authority clearance; always a costly and time-consuming business.”

Basically, the authors’ “immense” benefits boil down to maintaining the *status quo* is easier/cheaper for the vaccine industry and continues to protect the government and the healthcare establishment from criticism for their past/continuing actions/inactions.

Since studies reported in the 1940s and 1950s have clearly established that the 100-ppm level of Thimerosal is *not* bactericidal and, in the 1970s, multiple exposure to the 1000-ppm level is potentially lethal to humans, this reviewer has problems with the authors unsubstantiated “Although 2-phenoxyethanol has been used as a preservative, its effects are less bactericidal than thiomersal and manufacturers have not been inclined to switch.”

This reviewer has those problems because there are US vaccines that use 2-phenoxyethanol (DTaP [(Infanrix; GlaxoSmithKline {GSK}), Hepatitis A [Havrix; GSK], Hepatitis A/Hepatitis B [Twinrix; GSK]) or 2-phenoxyethanol plus phenol (IPV [IPOL; Aventis Pasteur {AP; now, sanofi-pasteur}] and DTaP [Daptacel; AP]) as the “preservative” for a given vaccine.

Moreover, recently approved “no Thimerosal” vaccines, like Aventis’ “no Thimerosal” doses of their Fluzone influenza vaccine (licensed by the US FDA in December of 2004), and GSK’s new Boostrix® “dtap” vaccine and AP’s new Adacel® “dtap” vaccine (that were approved in 2005), contain a significant level of 2-phenoxyethanol, indicating that this compound was used, *at a minimum*, as a sterilant in some phase of the manufacturing processes for these vaccines and that, *contrary to the authors’ statement*, some vaccine manufacturers have been “inclined to switch” to 2-phenoxyethanol.

Further, given that the lifetime costs for one DSM autism case exceed \$ 2,000,000 dollars US, this reviewer hopes that the authors can see that even IF Thimerosal in vaccines is linked to only 10% of the autism cases (and the current estimate is that the linkage is to somewhere between 75% and 96+% of those diagnosed in the US with DSM or “CDER type 1” autism), THEN preventing the use of Thimerosal in vaccines, after 1968, would have saved in excess of \$ 64,000 million (64 billion) in today’s US dollars).

Thus, rather than focusing on the costs to change, which are in the low millions, this reviewer suggests that the authors need to consider the lifetime costs of not changing, which, for the estimated 1 in 6 to 1 in 7 (depending on which estimate you believe) who have been adversely impacted by being injected with Thimerosal-Preserved vaccines and other drugs, are, *for the US children harmed*, currently estimated to exceed the current GDP for the US.

#### **“4. Discussion**

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The thiomersal controversy began in an unexpected way with the sudden realisation that guidelines for methyl mercury had been exceeded in infant vaccines.”

Contrary to the authors’ view, the “thiomersal controversy” has existed from the 1930s, when the compound began to be used in medicines.

If the authors read the 1948 paper by Morton *et al.* [r24], they should see that the research at the time clearly indicated that Thimerosal was *not* suitable for use in vaccines and that it was much more toxic to human cells than it was to bacteria.

In the 1970s, *based on recent reports*, Eli Lilly found that Thimerosal was toxic at 1 ppm and then, *though a major vaccine manufacturer at the time*, “abruptly” exited the vaccines business.

Further, based on the Merck memo, the “realization” that the “guidelines for methyl mercury had been exceeded in infant vaccines” had actually come in/before 1991 and it was *not* as “sudden” as the authors assert.

“After initial concerns that infants may be at risk from mercury in vaccines came the realisation that insufficient was known about the toxicology of ethyl mercury, despite a wealth of knowledge being available about methyl mercury. The published literature on the subject was limited to case histories of thiomersal applied topically in doses vastly exceeding anything in vaccines.”

This reviewer notes that the maximum nominal level of Thimerosal in topicals (0.1%) is only ten times the 100-ppm nominal level of Thimerosal in vaccines.

Factoring in the more-frequent, but unspecified amounts, implicated in the deaths associated from topical application of a 0.1% Merthiolate tincture and this reviewer’s personal experience that the amount applied to a wound is typical on the order of 0.1- to 0.2- mL, the authors’ “in doses vastly exceeding anything in vaccines” translates into overall doses in a 2-week period that are only 10 to 15 times that a baby receives by the age of two. – significantly more, but *not* “vastly” more.

Moreover, the toxic threshold for Thimerosal in tissues had clearly been established to be below 1 ppm in the 1950s by Engley [r26].

“Epidemiologists and bench scientists soon began publishing papers that brought to light the difference between the toxicological profile of ethyl and methyl mercury, and the evidence for the preservative’s safety in vaccines.”

In general, epidemiological studies are *not* appropriate for determining differences “between the toxicological profile of ethyl and methyl mercury.”

Moreover, such studies *cannot* prove safety but rather only estimate the probability that some adverse outcome is associated with (linked to) the Thimerosal injected.

Given the preceding, this reviewer suggests that the authors rework this sentence and include the post-1980 toxicology *in vitro* and *in vivo* studies (which they seem to have overlooked or missed) that elucidate the biochemical processes that are poisoned by “Thimerosal” (ethylmercurihydroxide) and Thimerosal’s metabolite (“inorganic mercury”) and/or the harm caused by Thimerosal in animals studies at animal levels below 5 ppm.

“However, although scientists contemplated safety studies well done, the public remained unconvinced.”

Contrary to the authors’ statement, this reviewer, a scientist, knows that the requisite

(required by law [21 CFR Sec. 610.15(a)]) safety studies for Thimerosal to be used as a preservative in a vaccine have either never been conducted (or have been conducted by some firm and, because the results proved Thimerosal was unsafe for use as a vaccine preservative, never been reported to the US FDA).

Moreover, the US government's studies into the acute, chronic and long-term toxicity of Thimerosal at vaccine levels, though finally scheduled in 2000, have *not* been conducted (they were placed on hold in 2001).

“A number of circumstances since 1999 conspired to create an environment of public distrust. The half dozen studies that were regarded as methodologically flawed by main-stream scientists were quoted extensively in the lay press.”

Since the peers that reviewed the Geiers' papers are recognized as mainstream scientists and did *not* find the “flaws” that unnamed individuals (authors' reference “[103]”) and Mann (authors' reference “[65]”) claimed were present, this reviewer finds that the authors' “were regarded as methodologically flawed by main-stream scientists” is, at best, a misrepresentation of how true mainstream scientists regard the Geiers' studies.

Because:

- The studies in question were peer-reviewed and published in recognized journals,
- Their findings pointed to a possible cause for autism and some other neurodevelopmental diseases for which mainstream medicine had, in 50+ years, failed to find a cause, and
- Independent experimental *in vitro* and *in vivo* studies have elucidated the mechanisms by which both “Thimerosal” (ethylmercurihydroxide) and “ethylmercurihydroxide's mercury-containing metabolite” (inorganic mercury) poison various critical metabolic pathways in the human body,

the media, lay or otherwise, was, and is, more than justified in reporting the Geiers' findings.

Moreover, *without finding any proof of a cause for autism and many other “symptom defined” or “causeless” neurological disorders*, apologists for Thimerosal in medicine, *as the authors appear to be*, continued to attack the Geiers' studies rather than to conduct the requisite safety studies required to prove that Thimerosal in vaccines was safe for ***all*** who receive said vaccines (or even to demand the requisite experimental safety studies be conducted).

“Pressure groups lobbied hard for the removal of the chemical from vaccines on the grounds that it exceeded levels defined by some public health authorities and caused conditions such as autism.”

In addition to the grounds the authors have raised, *as a member of one of those US pressure groups*, this reviewer and many of the others with whom he is acquainted have lobbied hard and formally petitioned the US FDA for the removal of Thimerosal from vaccines until its use as a preservative has been proven safe in the appropriate battery of safety studies (which FDA officials admit have never been submitted to the agency or conducted by the appropriate governmental health institute charged with conducting such) as *per* US law.

“Although some commentators have proposed that some of the symptoms of autism resemble some of the symptoms of mercury, it is understandable that the public might conclude autism is a form of mercury poisoning. However, experts such as Nelson and Bauman [72] disagreed, pointing out that the clinical and neuropathological differences between autism and mercury poisoning greatly outweigh the similarities, which are limited to non-specific symptoms, such as anxiety, depression and irrational fears. Such expert conclusions offer strong evidence against the biological plausibility of causation.”

This reviewer finds that the work of Nelson and Bauman seems to ignore most of the published similarities between autism and mercury poisoning and suggests that the authors study the tables in **Appendix B** of the “Comparison Of: The Characteristics of ‘Autism’ To Those Of Mercury Poisoning” in the article “**Thimerosal (49.55% mercury) Causes Mercury Poisoning III — Rebuttal To Dr. Orenstein’s Views**” ([http://www.mercury-freedrugs.org/docs/051101\\_Thimerosal\(49.55\\_%20Hg\)CausesHgPoisoning\\_III\\_DrOrensteina.pdf](http://www.mercury-freedrugs.org/docs/051101_Thimerosal(49.55_%20Hg)CausesHgPoisoning_III_DrOrensteina.pdf)) posted on the CoMeD web page <http://www.mercury-freedrugs.org/docs/>.

Hopefully, *after completing the suggested study*, the authors will see the similarities between the symptoms associated with autism and those associated with mercury poisoning are such that autism is an obvious “form” of mercury poisoning.

Contrary to the authors’ view, *given the problems with the “expert conclusions” alluded to by the authors, the validity of the alternative toxicity/toxicological articles referenced by this reviewer and the Geiers findings and the articles they cite that support “the biological plausibility of causation,”* the “strong evidence” actually points to “the biological plausibility of causation.”

“Public reaction was in contrast to that of the scientific community. The deliberations of many august medical bodies concluded that there was no causal association between the receipt of thiomersal (mercury)-containing vaccines and autism. However attractive the hypothesis may have appeared, any similarity between the two conditions has been shown to be coincidental. A vocal minority of the public continues to disagree.”

This reviewer finds that the authors’ “scientific community” seems to consist of those in the vaccine establishment who are wedded to promoting the use of vaccines regardless of the health costs to the public.

Moreover, the authors’ “The deliberations of many august medical bodies concluded that there was no causal association between the receipt of thiomersal (mercury)-containing vaccines and autism” is empty rhetoric because the “august bodies” cited reached no such conclusion – at best, they concluded that there was insufficient evidence to prove that injecting Thimerosal-preserved vaccines into neonates, babies and young children causes autism.

Similarly, the authors’ “However attractive the hypothesis may have appeared, any similarity between the two conditions has been shown to be coincidental” is simply the authors’ unsupported rhetoric, which ignores the evidence from, or cited in, the Geiers’ studies as well as the toxicological evidence cited by this reviewer.

Since this reviewer is a scientist who is a member of that vocal minority, this reviewer agrees with the authors that, *as they should*, “A vocal minority of the public continues to disagree.”

“But if thiomersal does not cause autism, what does? Courey [94] states that the epidemiology of the autistic spectrum disorders is changing. A clear increase in prevalence has been noted during the past two decades. What is less clear is the cause for the increase. Multiple factors appear to be responsible. The preponderance of evidence suggests most of the rise in incidence and prevalence is related to changes in diagnostic criteria and greater awareness on the part of both professionals and parents. Proposed theories of causation, which also seek to explain the increase in prevalence, have not been substantiated. Further research is needed to better determine the incidence and prevalence of these disorders and their aetiology.”

This reviewer finds that the authors’ statements here are simply rhetoric designed to justify why, after having more than 60 years to find the cause of autism and more than 40 years to conduct the required US safety studies (as per 21 CFR Sec. 610.15(a)), the Establishment has:

- Failed to find the cause of autism,
- Knowingly refused to conduct and/or submit the requisite safety studies to prove that 100-ppm Thimerosal is safe to use as a vaccine preservative, and
- Continued to employ the same “there is no proof” mantra used by the asbestos and tobacco industries

while knowingly *not* conducting the experimental studies that would unequivocally prove (or disprove) that repeatedly injecting Thimerosal-Preserved vaccines into neonates, babies and young children mercury poisons some of those so treated to the point that they exhibit the set of symptoms associated with DSM/CDER Type 1 autism.

“In the meantime, epidemiology and toxicology need to focus on ensuring all possible evidence is examined that might add further light on thiomersal and its safety record.”

Hopefully, the medical establishment will heed the authors’ implicit admonition and increase the funding for the toxicological studies required to answer the question of autism’s cause and prove what is the maximum safe level of Thimerosal in a vaccine or other drug.

“Pregnancy and the newborn period may represent unique dynamics of exposure due to the sensitivity of the newborn brain to mercury, and to the low body mass that, in effect, increases the concentration of the preservative. Maternal vaccine-derived thiomersal is the most likely source of prenatal mercury exposure to ethyl mercury (i.e., from influenza vaccine or tetanus toxoid), and is normally limited to a maximum of two or three doses during pregnancy.”

This reviewer finds that the authors have overlooked the Thimerosal in Thimerosal-Preserved RhoGAM (on average, 21 µg of Thimerosal per dose) and BayRho (on average, 35 µg of Thimerosal per dose). [See <http://www.fda.gov/cber/blood/mercplasma.htm>.]

Since it has been reported that up to 50 % of those diagnosed with DSM autism in the US have Rh-negative mothers [even though Rh-negative pregnant women are only about 15 % of the US population], it would appear that “Rho” products could have been a contributing factor to the autism risk prior to the time, in the US, when the last of the “Thimerosal Preserved” RhoGAM batches released to the US market should have expired (mid-2003) *unless*, to save money, Thimerosal-Preserved product from other markets where such legally continued to be distributed was used on US citizens.

Thus, in addition to the authors’ sources of prenatal fetal Thimerosal and their putative “normally limited to a maximum of two or three doses during pregnancy,” prior to 2004, an Rh-negative mother could have received from one to, *in the cases where periodic blood spotting occurs*, six-plus “Rho” prenatal injections leading, *in the worse case*, to a *nominal* mercury load to the pregnant woman of up to 285 micrograms of mercury.

“The same blood and brain distribution dynamics can be expected to apply for maternal doses as for infant exposure, except that the mother’s body mass is much greater than the infant’s and the tissue concentrations proportionately much less. Given the same levels of exposure, adults are at much lower levels of risk because of increased body mass. It would seem sensible to minimise exposing the fetus to maternally-derived sources of mercury, including thiomersal-containing vaccines.”

While the authors’ statement is generally true, the distribution dynamics are altered because it has been reported that the dynamics lead to higher levels in the fetus than in the mother.



However, this discussion ignores the effect of impaired excretion on the outcomes observed. Case studies have shown that children with autism and one or both of their parents often have impaired excretion for mercury and other heavy metals.

Thus, *in addition to exposure*, excretion is a critical variable in determining the degree to which any dose or dosing pattern causes the form of mercury poisoning diagnosed as autism.

This hereditary or induced (some antibiotics and other drugs temporarily block excretion) excretion variability helps to explain why injecting identical doses with the same dosing regimen into different individuals does *not* lead to identical or near identical outcomes.

While increased body mass is protective in adults, one's life history of mercury ingestion from food and the number and size of dental fillings contribute some amount to the "inorganic mercury" that recent studies have found to accumulate in the brain and the heart to the point that the added doses from vaccines may be sufficient to trigger persistent adverse symptoms and/or adult mercury-linked diseases (e.g., Alzheimer's disease), because the half-life of bound "inorganic mercury" in the brain and other organs is decades (e.g., its half-life in the brain is estimated to be between 20 and 30 years).

"The question remains incompletely answered whether or not the infant birth dose of thiomersal-containing hepatitis B vaccine (the only thiomersal-containing vaccine currently offered to high-risk infants) is a risk for the newborn. At the moment, most HepB vaccines available for developing countries contain thiomersal, even if they are mono-dose preparations. The WHO is now promoting animal model studies to evaluate this aspect [95]."

On the basis of the nominal amount (25 µg Thimerosal; 12.5 µg of mercury) and the infants' approximate weight range (1 kg to 5 kg), the infant dose in a Thimerosal-Preserved Hep B vaccine translates into a 12.5 µg of mercury/kg of baby for a 1-kg neonate to 2.5 µg of mercury/kg of baby for a 5-kg neonate.

Since the current EPA daily recommended maximum daily intake level for mercury from fish is:

- a. a limit with little or no safety factor, based on the recent review studies that found the original intake values were overestimated and the harmful effects underestimated, and
- b. 0.1 µg of mercury/kg of body,

it is, or should be, obvious that the birth dose of a Thimerosal-Preserved Hep B exceeds the EPA recommended daily maximum by a factor of 25 to 125 times.

Moreover, given the fact that, *in "normal" adults eating a fish diet*, only about 20% of the mercury in the fish is absorbed, the effective excess for the injected Thimerosal is more than 125 to 625 times the EPA level for daily mercury intake.

Given the high excess factors and the fact that, in the recent baby monkey studies, a significant portion of the "Thimerosal" injected (ethylmercurihydroxide) is effectively deposited in the monkey's brains as "inorganic mercury" (which has been shown, in other studies, to be toxic to growing neurons at levels below 0.02 ppm), it should be a "no brainer" that such a dose is toxic to some degree to those neonates to whom it is given.

Moreover, because excretion is a critical variable for injected Thimerosal, the animal model will have to be one that has, or can be easily induced to exhibit, impaired ethylmercurihydroxide and "inorganic mercury" excretion. {See: Haley's recent paper [r5] for studies supporting this reality.}

Hopefully, the authors will accept the reality of this reviewer's preceding comments and proceed accordingly.

## **“5. Conclusions**

Recent work on the toxicological profile of methyl and ethyl mercury has revealed significant differences in these compounds’ metabolism in the human body. Ethyl mercury does not accumulate like methyl mercury, but is actively excreted.”

This reviewer finds that, *as he has established*, the authors’ statement are misleading since the metabolism of “Thimerosal” (effectively, ethylmercurihydroxide in the vaccine formulation) in the brain (and apparently the heart) generates “inorganic mercury” which, in the brain, has an estimated half-life of 20 – 30 years and, based on Burbacher *et al.* (the authors’ reference “[34]”), this “inorganic mercury” accumulates at a rate 2 to 3 times higher than in the same-dosing amounts in the methylmercurihydroxide oral-dosing case].

Moreover, *even in this small study*, the levels of “inorganic mercury” accumulated in the baby monkeys’ brains varied by more than an order of magnitude (**see** Figure 7 of Burbacher *et al.*, authors’ reference “[34]”).

“With some exceptions that we have discussed above, thiomersal has been shown by science to be safe as a preservative for use in vaccines administered to infants, children and non-pregnant adults.”

When pressed in testimony before US congressional committees on the issue of the proven safety of Thimerosal for use as a preservative in vaccines (as required from 1968 by the Title 21 of the Code of Federal Regulations {CFR} Section 610.15(a)), US FDA officials from the Center for Biologics Evaluation and Research have repeatedly testified that the requisite studies to prove Thimerosal’s safety for use as a preservative have *not* been conducted.

Thus, in the US, the legal answer is there requisite proof of safety does *not* yet exist and, though scheduled in 2000, the government project to properly assess the safety of Thimerosal for use as a preservative in vaccines has been on hold since 2001.

Based on the preceding realities, government, academic, and industry scientists have, to date, knowingly failed to prove that the use of Thimerosal as a preservative in vaccines is safe.

“A relatively small number of epidemiological studies have been undertaken to clarify this issue.”

This reviewer again reminds the authors that epidemiological studies *cannot* settle the issue of safety since they can only assess the statistical possibility of the risk of an adverse relationship.

“The results are convincing that it does not cause neurodevelopmental problems in vaccine recipients.”

Again, for the reasons previously stated, the authors are mistaken because, among other things, scientifically sound epidemiological studies can only estimate the possibility of a link between cause “A” and effect “B”; they cannot address, *what is obviously the case here*, subpopulations who have increased susceptibility to the adverse effects of Thimerosal.

Moreover, the epidemiological studies the authors have cited to support their assertions have all been proven to be fundamentally and deliberately flawed while the studies the authors discounted have been shown to be fundamentally sound and to support the evidence of a link between the Thimerosal dose and autism and other neurodevelopmental disorders.]

“The outlying papers that would contradict this statement have been discussed – they lack rigorous scientific method, despite being quoted frequently by advocates against the preservative.”

Other than the authors' rhetoric and that of those who have attacked the papers that present a dissenting view, no proof has been published to substantiate any of the significant claims made against the Geiers' peer-reviewed and published papers.

Furthermore, the Geiers studies used the same general designs and methods that the CDC has itself used in other epidemiological studies and, in one case, the Geiers, using the VSD, confirmed the validity of their VAERS findings with their VSD epidemiological studies.

Based on the preceding findings, this reviewer must reject the authors' unsubstantiated assertion that the Geiers' studies "lack rigorous scientific method."

"Although evidence in support of thiomersal's safety is persuasive, the scientific community should remain open to credible scientific work that improves our understanding further."

Based on the body of evidence presented by this reviewer and the failure of the manufacturers and the government to conduct the appropriate scientifically sound acute, chronic, and long-term safety required to prove that 100-ppm levels of Thimerosal in vaccines are safe for all (as required by law), this reviewer must conclude that "the evidence in support of thiomersal's safety":

- a. is lacking and
- b. *based on the existing credible in vivo and in vitro experimental test evidence*, points to a sub-ppm level as the safe level for Thimerosal in vaccines.

Until such time as the safe level for Thimerosal in vaccines for use in humans and animals is unequivocally established, this reviewer recommends a 0.01-ppm level because it has been reported that, in 1971, Lilly researchers found toxicity at the 1-ppm level and, *for highly toxic bio-accumulative chemicals, like Thimerosal*, a safety factor of 100 is appropriate in the absence of the appropriate scientifically sound toxicology studies that have unequivocally established a safe level.

"But the public in Western nations has not all together agreed with the scientists."

This reviewer notes that, like this reviewer, some of that "public" of which the authors speak are also "scientists" who strongly disagree with the authors' views.

"This has resulted in pressure groups demanding that the offending thiomersal be removed from vaccines. At least in the US, the response of the government has been to switch wherever possible to mono-dose presentations that do not need a preservative."

For early childhood vaccines, the reality is that the use of Thimerosal as a preservative in vaccines has been banned in Russia from the late 1980s and, in Denmark and Sweden, phased out in the early 1990s. In the UK, Thimerosal has been phased out, starting in 2004, when the 5-in-1 vaccines was phased in for childhood immunization.

"As a result, concern there about thiomersal is fading."

As a US scientist involved in this issue, this reviewer finds that the authors are again mistaken not only because of the millions of American children who have suffered lifelong harm but also because Thimerosal-Preserved vaccines, including the influenza vaccines, continue to be given to children from < 6 months to 18 years of age as well as to the elderly, where Thimerosal-Preserved influenza jabs have been linked to a subsequent increased risk of Alzheimer's.

"Although authorities in the US were initially alarmist, their responses quickly became one of damage control."

Based on the records (obtained under the Freedom of information Act (FOIA) from the illegally-closed-to-the-public meetings (1999 meeting on Thimerosal in the Lister Hill Auditorium on the Bethesda, Maryland campus of the US National Institutes of Health and the 2000 meeting on vaccines and neurodevelopmental disorders at the Simpsonwood retreat in Georgia), US authorities have been engaged in “damage control” since 1999 and the true extent of the harm caused and the risks of harm have been systematically understated.

“Messages emanating from there now assure parents not so much by saying there is proof that thiomersal is safe, but more saying that thiomersal has been removed from children’s vaccines by producing them in mono-dose presentations that do not need preservatives.”

This reviewer disagrees with the authors’ view that the parents are being assured, because the messages “emanating from” the US officials are *not* factually accurate and ignore at least three important realities:

- More than a million US children have been severely harmed,
- Some Thimerosal-Preserved vaccines and other drugs are still being given to children and pregnant women, and
- The majority of the influenza vaccine doses approved for use in children 6 months to 4 years of age are still “Thimerosal Preserved.”

“Thus, the American public is reassured that their children will not receive vaccines that may contain mercury.”

As a member of the American public, this reviewer has *not* been reassured because there are at least 18 US-licensed vaccines that: **a)** contain some level of Thimerosal and **b)** are, *without valid proof of appropriate toxicological safety*, licensed for administration to children.

“Whether or not thiomersal is actually safe has become irrelevant because it is hardly used.”

The authors are wrong; the million-plus US children that have apparently been severely harmed by mercury poisoning by Thimerosal in drugs administered to their mothers while pregnant and to themselves after birth are *not* irrelevant.

In the US, the current estimate is that the today’s lifetime cost of caring for just the DSM autism cases is more than two trillion US dollars (> \$ 2,000,000,000,000.00).

Moreover, many in the US, including this reviewer, are concerned about the harm being caused in those countries where Thimerosal-Preserved vaccines are still being widely used.

“Although this scenario works well in the US, it is potentially devastating for much of the world. The conflicting messages from the US of ‘safe’ and ‘we have removed it’ could easily backfire on developing nations who continue to promote widespread use of vaccines containing thiomersal in their national immunisation programmes.”

Since both messages, “safe” and “we have removed it,” are *not* factually true, and Denmark, France, Russia, Sweden, the UK, the US and ... have, in general, stopped using Thimerosal-Preserved vaccines for routine childhood immunization, it would seem to this reviewer that there is a growing consensus in the developed countries that Thimerosal-preserved vaccines should *not* be given to anyone.

The only major players pushing Thimerosal-Preserved vaccines are the vaccine makers, medical professionals, and governmental agencies, including the WHO, who use, or have used, such vaccines, and/or promote, or have promoted, the use of Thimerosal-Preserved vaccines, and who, as a result, have much to lose if Thimerosal-Preserved vaccines were found *not* to be safe.

“There is a real danger that this controversy may result in the loss to the world of thiomersal as a preservative, simply from popular pressure. In reality it would be impossible to cease overnight using thiomersal and maintain the supply of vital vaccines. It may eventually be possible to restructure vaccine manufacture to produce presentations that are mono-dose and, therefore, would not need a preservative. However, this would need expensive field trials of reformulated vaccines and would take years, even if fast-tracked. The result would be a range of mono-dose vaccines that would be much more expensive and would require greatly expanded cold chain and storage facilities.”

This reviewer is bemused by the simplistic picture the authors paint here – a picture that blatantly ignores the real danger that when the US public finds out that the healthcare establishment have been knowingly engaged in poisoning their children (not only for the short-term profit from the vaccines administered but also to sicken these parents and their children so that the healthcare establishment’s long-term profits from mitigating the harm caused would increase) not only will any who are, or were, responsible for causing the harm, including death, or responsible for not preventing these criminal practices be tried for crimes against humanity and those convicted given life imprisonment or, if they are licensed healthcare professionals, life-time sentences to care for those that their actions have harmed with only subsistence wages but also all the businesses involved will be seized by nations everywhere and hopefully operated by the seizing governments as not-for-profit companies with all gross profits being used to pay for the harm caused until the last child severely damaged by Thimerosal-Preserved vaccines dies (about a century from now).

Hopefully, the public will *not* let the “healthcare” establishment “bury” those harmed by Thimerosal-containing medicines like they have allowed it to “forget” those, diagnosed with “Pink Disease,” who, if they survived their childhood mercury poisoning, were permanently harmed by the “harmless” Calomel-laced teething (soothing) powders given to them by their well-meaning parents.

“Nonetheless, the next decade will likely see a global drift towards (a) single dose vaccine preparations and (b) vaccine delivery by technologies other than the conventional needle and syringe. This shift will be driven predominantly by safety considerations, including (but not only) the thiomersal issue [96].”

Hopefully, for vaccines, the next decade will also see:

- ❖ A return to truly preventive and curative medicine with a move away from long-term treatment for all but the most severe chronic conditions
- ❖ The honest disclosure of
  - The true incidence of adverse events,
  - Risks of long-term harm, and
  - The probable level and persistence of protection for each vaccine,
- ❖ Simple inexpensive titer-check tests to verify immunity,
- ❖ The rejection of those vaccines whose long-term negatives and costs do *not* justify their use as a “panacea” for a given disease,
- ❖ The end to mandatory vaccination for all but the most serious diseases where the proven long-term benefits clearly outweigh the development, licensing, procurement, administration and adverse reaction costs,
- ❖ General postponement of vaccination until the child’s immune system approaches maturity (between 2 and 3 years of age), and



- ❖ A holistic approach to childhood immunization that emphasizes breastfeeding (preferably until the natural weaning occurs when the mothers' milk supply "dries up") and sound hygiene, nutrition and lifestyle education as important adjuncts to sound vaccination policies.

"The thiomersal debate represents an example of pressure groups speeding up (it had already started) a change in public policy relating to vaccines despite reassuring scientific evidence."

In this reviewer's view, the "thiomersal debate" in the US represents an example of the vaccine maker's knowing failure to comply with the binding vaccine regulations as amended in 1968 (21 CFR Sec 610.15(a)) and the US FDA's ongoing failure to enforce compliance thereto.

Had the responsible parties acted as the law requires, the unequivocal proof of the safe level for Thimerosal in any vaccine would have been established in the late 1960s preventing tens of millions of children from being harmed to the point they exhibit one or more of the clinical symptoms of mercury poisoning and millions of children from being harmed to point that they are diagnosed with DSM autism.

This reviewer finds that most of the "reassuring scientific evidence" touted by the authors and the healthcare establishment is *not* reassuring to any scientist who understands the flaws and limitations in epidemiological studies falsely purported to support the safety of Thimerosal-Preserved vaccines.

In addition, the medical establishment's case has *not* been helped by apologists who not only admit to lying to the public about the risks and benefits associated with a given vaccine but also claim that their lies are for the public's good as well as by those who make obviously specious remarks about vaccine safety and stubbornly refuse to admit their remarks are *not* accurate.

"The conclusions are clear – the once compliant public in the West no longer trusts to the same degree scientists or public servants who implement public policy. They want their say. Scientific evidence of safety is not now the only factor in ensuring acceptance of a vaccine by the public. So far, the effect is less marked in developing countries where health imperatives are different. In addition, the public is not so well informed and pressure groups are not yet so active. It is only a matter of time before this changes."

At least the authors recognize the reality that the public trust has declined even though they did *not* recognize that that trust has been and is being betrayed by those who influence, devise or implement public policy as well as by those in the healthcare establishment who treat the public's health as a commodity to be manipulated to maximize the healthcare establishment's profit with little or no regard for the true health of the public.

Moreover, the people not only want their say but also want the healthcare system to revert to a system where:

- The true health of the public is put before the healthcare establishment's profits, and
- The *only* mission of the government's regulation of all facets of healthcare is to protect and cost-effectively promote the public's long-term physical and mental health.

## **"6. Expert opinion**

The overwhelming weight of scientific opinion rejects the hypothesis that neurodevelopmental abnormalities are causally related to the use of thiomersal in vaccines."

However, what is needed is proof that Thimerosal at 100 ppm is safe to all those who are administered Thimerosal-Preserved vaccines.

This not only has *not* been done but also *cannot* be done because, if nothing else, Thimerosal has been shown to cause anaphylaxis and severe seizures in some who are administered Thimerosal-Preserved vaccines.

“A particularly important study from Denmark showed the incidence of autism continued to increase after thiomersal was withdrawn.”

As this reviewer and others have reported, the authors’ “important study from Denmark” is flawed because increases in reporting rates (caused by a widening of the scope of those tracked in the database) were knowingly improperly considered as increases in incidence rate and the database had case loss and other reporting changes that adversely affected its usability as well as other problems that its authors attempted to mask by reporting their findings in incidents per 100,000 person years.

Given the problems found in the database used and the reporting of the findings, this study does *not* support the authors’ statement that “the incidence of autism continued to increase after thiomersal was withdrawn.”

“It is difficult for science to come closer than this in proving that thiomersal does not cause autism. There are some outlying reports that continue to provide ammunition for those who remain skeptical. Although such results should be noted, their number and quality is such that they do not deflect from the strength of the conclusions from the vast majority of high quality, thoughtful research that confirms the preservative’s safety. Thiomersal is safe as a vaccine preservative, and should continue to be used in settings where accessibility and cost require that multi-dose vials of vaccine are available.”

The authors’ views here remind me of the parable of the blind men and the elephant, because, given their omissions of key references and information, they seem to be blind to:

- the overall toxicity of Thimerosal, and its in-solution hydrolysis product, ethylmercurihydroxide, and
- the fact that the long-term poison to the brain is the bound “inorganic mercury” trapped there, and *not* the transitory levels of either ethylmercurihydroxide or “methylmercurihydroxide,” which are short-term toxins

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- Those in SafeMinds, including Lyn Redwood, Sally Bernard, and Mark Blaxill, whose help in getting copies of the FOIA-disclosed documents they uncovered to me has been an invaluable aid in understanding the workings of the Verstraeten group and the IOM committee that addressed a few of the safety issues for Thimerosal in vaccines, and
- The other representatives of CoMeD who, along with the Geiers, helped fashion the Citizen Petition to the FDA (**see** FDA Public Docket 2004P-0349; a copy of the posted petition can be found on the CoMeD documents web page, <http://www.mercury-freedrugs.org/docs/>) asking that the FDA enforce the law and comply with the applicable statutes governing the use of Thimerosal in vaccines and other drug products and preparations.

Finally, this reviewer affirms that he has received no direct or indirect remuneration for this review and does *not* have any financial interest in this review.

Thus, this appraisal is entirely a *pro bono* effort on the part of this reviewer.

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### Affiliation

C John Clements<sup>†1</sup> MD, MSc, FAFPH & Peter B McIntyre<sup>2</sup>

<sup>†</sup> Author for correspondence

<sup>1</sup> Associate, Centre for International Health, The Macfarlane Burnet Institute for Medical Research and Public Health Ltd, GPO Box 2284, Commercial Road, Melbourne, VIC 3004, Australia; FAX: +61 3 9282 2144; E-mail: john@clem.com.au

<sup>2</sup> Director, National Centre for Immunisation Research and Surveillance of Vaccine-Preventable Diseases, Children's Hospital at West mead and University of Sydney, Sydney, NSW, Australia; E-mail: PeterM@chw.edu.au”

This reviewer notes that, *given their job titles*, both of these authors have “obvious” built-in conflicts of interest.

In addition, Clements also advises the WHO on vaccine policy, an additional prejudicing conflict that has seemingly blinded this author to the obvious toxicity of Thimerosal in Thimerosal-Preserved vaccines.

Hopefully, the reader, *after studying this review and the papers cited*, will begin to understand not only the depth of the authors' conflicts but also the global scope of the harm that allowing/continuing to allow the use of Thimerosal in medicine *without* the scientific toxicological proofs of safety required by the applicable US drug statutes and laws has caused/is causing to those who are susceptible to being mercury-poisoned by Thimerosal.

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## Appendix A

### Calomel (86.96% mercury by weight; mercurous chloride) poisoning and “pink disease” – Heather’s story

(Source: [http://www.bionatural.com.au/upload/Pink\\_Disease\\_Heathers\\_Profile.doc](http://www.bionatural.com.au/upload/Pink_Disease_Heathers_Profile.doc))

“Pink Disease Support Group  
Mrs. Heather Thiele  
PO Box 134  
Gilgandra  
NSW 2827  
Email [hmthiele@hwy.com.au](mailto:hmthiele@hwy.com.au)

My name is Heather Thiele (nee Kemp) and I was born on 11th June 1949, the first born of twins. I was born at Bacchus Marsh Victoria, Australia. I weighed 6lbs 3oz at birth and was a healthy, thriving baby, until I reached the age of nine months when I started to teethe. I had rather large teeth and was suffering with cutting them. To soothe my gums and relieve my distress, my mother used the commonly used teething (or soothing as they were also known as) powders readily available over the counter in corner stores and chemists throughout the country of Australia, and other English speaking countries at the time. These were sold in little paper wrappers and were advertised at the time in women’s magazines as ‘guaranteed harmless’. (I have copies of such magazines.) The teething powder was rubbed on the gums or the tongue of the suffering infant. My mother used Steedman’s brand, but other available brands were Fishers, Bayley’s and Ashton’s & Parson’s.

Immediately, I became lethargic, sensitive to noise, light and touch, lost my appetite and consequently lost weight alarmingly. My mother carried me on a pillow, because I would scream if she touched me. She put blankets at the windows and would only take me outside at night. I lost muscle tone and I found it hard to hold my head up or sit, and although I was on the verge of walking, I became like a floppy doll. The skin on the soles of my feet and palms of my hands became bright pink and began to peel off. I started to chew at my hands, so my mother made me cotton mittens to cover them. I could not tolerate anything woolen or rough in my clothing. My mother started dressing me in my older brother’s bigger shirts used as ‘nightgowns’, so that my fitted clothes did not irritate me. I would scream if placed in a bath, so my mother started ‘washing’ me with olive oil and cotton wool. I would rock myself from side to side in my pram or cot, and bashed my head against the walls. Nothing seemed to pacify me, and I would go for days without sleep. My mother says my cry was more like the whimper of a frightened animal, and could last for periods of 24 hours or more, without a break. My hands turned ‘puffy’ and it was this edema, along with the photophobia and pink extremities, that the doctor used to diagnose the condition as ‘pink disease’. He said the symptoms were too classic and dramatic to suggest any other diagnosis. The medical professionals of the time knew a name for this condition (medical term being acrodynia), but did not know the cause or treatment.

I started to convulse and developed pneumonia regularly. I would recover from one bout to go down with another. I had to be half sat up with pillows all the time to drain my chest of fluid. Many a time the doctor would visit in the morning and comment that he did not think I’d survive the night. He gave my mother little hope for my survival, as so many babies with these symptoms were dying in the district. He treated 19 babies in the area over some months, and I was the only one to live. Many of the babies seemed to get worse in hospital, so he encouraged my mother to nurse me at home. My mother was determined to ‘pull me through’. I am convinced I am alive today only because of my mother’s dedicated nursing. She had my twin brother and three older children to



raise at the time. The doctor suggested to my mother that she give me a dummy (or pacifier) for me to suck on. She had not used one before with her three older children and she found I would suck the medicine or a little liquid glucose off the dummy if it were offered. At one stage, the only food I would eat was a half-set jelly (jello). Of course, I lost weight alarmingly. I looked like a little skinned rabbit, according to my older sister.

Unbeknown to my mother at the time, was the fact that the cause of the pink disease was the calomel, mercurous chloride, used in the powders as a preservative. Steedman's powders contained up to 23% by weight of this form of mercury compound. When she was told this many years later, she was horrified that I suffered this condition and its life long effects from something she had given me. I have documented cases of mothers denying they used the powders on their children, and later on admitting that they may have used one or two. It is a very sad part of our story that these parents have had to live with the guilt of using the powders. Some families have been torn apart from this knowledge with children not being able to forgive their parents for doing this.

Word reached the family doctor that a doctor in South Australia had discovered that the pink disease babies were showing a lack of salt in their bodies and recommended a treatment of adding salt to the diet for the pink disease babies. This proved to be not the cause, but one of the symptoms, and the doctor was Dr. Donald Brooke Cheek. I was to contact him in the months before his death from cancer in 1990, and he was pleased that I was doing the work for the pink disease 'babies' in the form of the support group. In the early 1950's the work of Dr. Joseph Warkany of the USA proved that the cause of the pink disease was the calomel in the teething powders and with Dr. Cheek's encouragement, the powders were withdrawn from the market in Australia and the United Kingdom. I have copies of the legislation from each of the states of Australia to ban the use of the mercury compound in the powders. Western Australia was the last to legislate in 1956, but the mercury-powders were still sold in stores for many years after this. I have copies of advertisements for them 'without the harmful calomel' from magazines in 1959. Once the powders were withdrawn from sale, the incidence of pink disease stopped immediately. It is not heard of now. I have a Sydney newspaper which published a warning not to use the powders containing the calomel from July 1st 1874, following the death of a baby with pink disease. Yet it took another 80 years for the incidence of pink disease to stop. It is a shame so many hundreds, even thousands, of babies had to suffer and die because of slow action by the medical profession. I have documented cases of a family having 5 of their 10 children die from suffering pink disease, and many cases of two or three babies in the one family dying. Plus you have to consider the effects that having suffered such a horrific form of mercury poisoning at such an early age in life has had on each and every pink disease sufferer and their families. But, I am getting 'ahead of myself now'.

My mother added salt to my diet, often giving me some on a plate, which I readily stuck my finger in and licked off my hands. Many pink disease sufferers have told me they used to eat salt by the handful, if allowed. I have researched since that mercury does deplete sodium in the body. I was also given vegemite (yeast extract) in a broth, which was not only a source of salt, but also a rich source of vitamin B, which treated the nerve damage of the mercury. The doctor also prescribed a 'grey powder' which was mixed in honey and water as a treatment. In those days (1950) a patient did not question what a medication was, and many pink disease sufferers were given treatment or tonics that they did not know the particulars were at the time. Babies were put into hospitals and the parents weren't allowed to visit even. Many were used as 'guinea pigs' in treatment. The doctors at the time did not know the cause, treatment or history of pink disease.

At the age of 18 months, when I was slowly recovering and starting to catch up with my twin brother in my physical skills, our family moved to the town of Eildon where my father was working on the building of the huge Eildon Weir. There was no town as yet, and my family was living in

sparse conditions in a tent. I became ill again. The doctor treating me offered penicillin as a treatment. I was given needles of this every second day. My mother used to walk through the icy waters of the Eildon River up to her waist to take me to the doctor's facility, one of the few buildings in the town.

Eventually, I began to recover, although I was unwell until I was 7 years of age, when our family moved to the warmer climate of Queensland. I can remember the terrible nightmares I had until this time and being very tired all the time. I was particularly clumsy and very shy as a child. I would sit in the corner of a room, reading a book or playing, and be quite unaware of all that was going on around me. (Not a mean feat when you think that by this time, I had another two brothers, also twins, and baby sister, making our family of 10.) I did well at school only because I used to study so hard at all I did. As I write this in June 2001, I can say that I have always lacked spatial judgment and fine motor skills. I have trouble judging 'how much of this would fit into this', doing up things like locks, seat belts, jewelry clasps, double clicking my computer mouse etc. I always say that I do everything in life twice: firstly, the wrong way and secondly, the right way!

During my illness and early childhood, my mother was told that I would not live to reach school age (around five years of age), that I would not live to adulthood, that if I did manage to live I would be sterile etc. She was in constant fear that I would relapse at any time. I have records of pink disease sufferers who were told that their hair would fall out when they reached 14, that they would be sterile and many other horrific things. The sterility claim was not far off the mark as mercury damages the cilia in both female and male genital tracks. Young's Syndrome in men has sterility as one of its symptoms. I had no difficulty falling pregnant at age 18, but could not conceive naturally after that until 10 years later, and have two healthy children. Because of our family incidence of twins, I was reluctant to seek any fertility treatment.

I suffered pneumonia bronchitis and asthma in April 1952 (34 months of age) and nearly died. I suffered severe measles in March 1953 and chicken pox on both my 1st and 2nd birthdays. The second dose was very severe. I suffered German measles in October 1952, and had constant bouts of pneumonia. I suffered pneumonia on my 3rd, 4th and 5th birthdays. My mother had begun to dread my birthdays! I am amazed that I never developed bronchiectasis, as over 23% of pink disease sufferers did. I must have had amazingly strong lungs. I have never smoked in adulthood, nor drank alcohol. I have always led a healthy life preferring natural foods to processed ones.

In recent months I have studied the effects of another form of mercury sensitivity/poisoning in the autism spectrum disorders children who had Thimerosal in childhood vaccinations, and I have been interested and alarmed at our similarities in symptoms. I can relate to their inability to make eye contact when talking to people (I can remember being yelled at by a teacher when I was eight years of age: 'Look at me when I talk to you, you ignorant child'). I can relate to their feeling of detachment from what is happening around them. I have often felt as if I was on the 'outside of life looking in.' I can relate to their sensitivity to touch, noise and light. I have severe pain especially around my ribs in the connective tissue (costal chondritis) and cannot bear to be hugged by anyone. If I bump my leg against a piece of furniture, it really pains for days afterwards. I have no sense of direction. If I park my car, it doesn't end up anywhere near where it should be. I have a rope hanging down from the carport roof to show where I should park the car, but still can't get it right! My husband gets so frustrated with me. I go around turning down the sound on the TV and turning off lights in the house. As a child, my father would yell at me sitting as he thought it was 'in the dark' reading. He would tell me I'd send myself blind! Even now, I own a coffee lounge with a bright fluorescent light over the stove as well as a light in the ceiling and I turn off the stove light as soon as I am in the shop on my own every afternoon. I often wear my tinted glasses inside of a day to stop the glare. When I have my field vision tests on my eyes, my ophthalmologist tells me he can see the scarring on my retinas, which indicates heavy metal damage. I can feel nauseated

when I am in a crowd of people, or if I am in a group of screaming children at a party e.g. I still rock myself when I am distressed or worried. I have definite patterns of repetition and order in many things that I do. Sometimes I wonder if these are more of a survival mechanism than an actual symptom of a disorder. I am so used to thinking out in advance the easiest way to do things so that I don't do mistakes, that I have quite a reputation for being very organized. The same people and friends, who compliment me for being organized in my life and ways, don't appreciate that this is the ONLY way I can cope with life! I have maintained a rather stubborn streak in my personality and a good sense of humour which both help at times!

When I go to type out words, they get mixed up. 'That' is typed as 'hatt' for example. I am OK if I write by hand. I cannot do things like shuffle cards, do up seat belts, do up jewelry clasps etc. When I am interrupted in a task or speech, I lose all track of where I was up to before the interruption. I find it hard to remember books and articles I have just read. I have to make notes and go back to the article time and time again to remember the basic thoughts of the article. However, I am marvelous at remembering dates. I am terrible at remembering people's names and faces. Recently, I was with my daughter and kept calling her by my grand-daughter's name, and telling her to put something into the car when I meant shopping basket. I recently saw a program on TV about the recognition of faces. It discussed how certain people with brain damage could not recognize even familiar faces after car accidents etc. It was the part of the brain that connected current faces with a memory of a face, before the accident that was damaged. I thought at the time that this is what I have problems with.

Some of my problems seem to 'come and go' in intensity, but I notice they are worse when I am stressed. I own a café, and when we get busy I have to literally 'check' myself and 'go down a gear' in my actions, and really concentrate on taking orders etc. I will take an order down as three black coffees and one white, when it should be the other way around. I constantly have to double check orders so that I don't make mistakes. Both my husband of many years and my staff get very cranky with me when I make mistakes, and this adds to my frustration. I think pink disease people must be very frustrating to live with. I have noticed many of us have had more than one marriage and many are now divorced and living on their own. I know I prefer my own company than being with a crowd or even a couple of people.

I also have no strength in my arms, when holding things above my shoulders, or stacking things onto shelves. I am a hopeless swimmer for this reason. This seems to be common amongst pink disease people. Another thing I have noticed is that I have had what I might describe as 'hot flushes' all my life. Even as a child when I made a mistake or was embarrassed, I'd flush in the face and come out in a hot flush over my body. I have never been good at speaking in front of an audience or being the centre of attention. I do not self promote myself. I find I do not attempt to do some things, like fill sauce bottles in my shop, as I know I will spill the sauce and waste it. I go and do something else that I am good at instead. Sometimes I do things, like a jig saw puzzle or cross-stitch, just to prove to myself that I can do it. In spite of all this, I feel I have a good self-esteem, in that I know now why I make mistakes and have accidents etc, whereas I consider some other people rather ignorant of their shortcomings. At least I have an excuse!

At this stage let me state that I am not medically qualified in any manner. I am not even a nurse. I am simply a victim of mercury poisoning who has been looking for answers most of her life. Because our condition is not obvious, we are forgotten, ignored and dismissed, even by our closest family members, but especially by the medical profession. We do not have any obvious signs of our disabilities, and look quite 'normal'. Most of us seem to be rather determined, intelligent and hard working, so we do not draw attention to the daily struggle we have to function in this world. The only signs I have physically of having pink disease are the strongly rigged finger nails and skin pigmentation around my neck as if I have a rash. Others really have to spend a day or so with me

to see that I do have problems performing normal every day tasks. I will go to open a door and have to take two or three attempts to grab the door knob etc. Or I will go to place a plate on a shelf, and miss the shelf completely, grazing my knuckles. I often have bruises on my body from bumping into things and I don't remember doing it.

I have mentioned only the things I do not have in common with other members of my family, as I do appreciate that some things, like a tendency to suffer arthritis, are genetic. I am one of eight children and have a large extended family. No other members of my family have the problems and issues I have mentioned.

In 1989, I started to investigate the possibility that there may be other pink disease sufferers left alive in Australia. I had never met another survivor in my life until then, and often wondered if my mother was really telling the truth about it all. If I mentioned it to a younger doctor, he would say 'no, never heard of that one'. It was not in any of the modern baby health books. When I would go horse riding, my feet would go numb and I had always had all these other things happening, like drifting when I walked, stumbling, getting things back to front when I typed etc.

I went to one doctor, who told me I was 'menopausal and to get in and do a decent day's work.' This was at a time that I was working a 10 hour day in our family business (as I still do). He accused me of being a hypochondriac. I was devastated, and went into my shell a bit further emotionally. I then had occasion to attend another doctor for an accident I had had, due to my clumsiness, and I mentioned pink disease. He casually said, 'Yes, that was such a terrible thing. So many babies died and so many left with problems. You know it was mercury poisoning, don't you?' I literally burst into tears of relief there and then!

I wrote a small two line letter to a popular Women's magazine in Australia, the New Idea, asking if there were any other pink disease 'people' out there. I thought I might get about six letters back. Within weeks, I had over 200 people write to me. The magazine was amazed at the response. Many of the people thought they were the only ones left alive in Australia, as I had. I had people ring me up in tears. From that first letter, I formed a support group with my own funding and in my 'spare' time. It grew to over 2,000 noted cases, varying from one line 'I had pink disease in 1944, and nearly died', to detailed letters and tapes. During 1999, I realized that the support group had taken over my life. My family life, finances and personal energy were all badly affected. I had spent thousands of dollars of my personal money on the project and felt guilty that my family had not benefited from this. I am of rather humble finances and had even put myself into debt over it all. I decided to give up the work, and wrote to the over 800 people I had been mainly the free newsletter to advise them so. One of our members offered to set up a web page and continue on in a small way with email newsletters, but was unable to do the postal ones.

A reporter from a Sydney newspaper wished to do a story on why I had to give up the work. She thought that by doing so, some medical body may 'take on' our cause. This did not happen, of course, and all I achieved was to find a further 130 'new' pink disease people to add to my list! But, the reporter discovered Sallie Bernard of the Coalition for SAFE MINDS as a person of 'interest'. From there, we have established a working relationship, by email and post.

The other member who was maintaining the website and following up on a health survey she had compiled some years previous, Diane Farnsworth suggested that she and I could do the support group together, and thus share the workload. We decided to charge a small annual fee for membership to cover the newsletter costs as from January 2001. I am handling this money as treasurer. Diane has now taken over the majority of the workload and is doing the co-ordination of the group including the newsletters, continuing on with research and maintaining the website. We are currently only posting out the postal newsletters and updates to financial members, and this

has dropped the number down to just under 300 members. I have kept all records of non-financial members, along with those who have died at the time or since, moved address or stopped being interested in the group for some reason. I have over 2,000 noted cases in Australia altogether.

I had terrible teeth, which, when they finally erupted were black and crumbly in the gums. I had them taken out and never filled, they were so bad. I am grateful for this, as I have never had a mercury/amalgam filling in my mouth because of this! I had a full set of dentures by age 16. Many other pink disease people had excessive cavities and gum/teeth disorders. I had gingivitis when I had the pink disease also. The scenario of having suffered pink disease followed by another mercury exposure in amalgam fillings horrifies me! Many pink disease people have had their amalgams removed and replaced, with an improvement in health (once they realized what caused pink disease).

This is another thing: many, many pink disease people did not know it was mercury poisoning/sensitivity until I told them. I did not know until 1989, myself. The doctors at the time did not know why we had pink disease and when they did realize, did not inform anyone. They just stopped putting the calomel in the powders!

We are also terrible 'form filler inners'. We tend to put things in the wrong place when filling in forms, which is getting to be a more frequent problem in this world. I even signed my wedding certificate in the wrong place. I notice that every second membership form filled in by support group members has a mistake on it.

Also, I have bad skin reactions (itching and burning sensation and red flare in skin) to many chemicals and cosmetics. I cannot wear eye shadow or makeup as my skin actually blisters. I find I do not use any perfumes, make ups, medications etc without checking for any form of mercury. I check every medication I can for mercury. Recently, I was prescribed eye drops by my doctor who knows I have a mercury sensitivity only to find the preservative was mercuric nitrate!

I suffered from bad migraine headaches from 1974 until 1989. I put them down to stress or hormonal changes. Then I realized I got them whenever I was involved with the horses outside for daylong periods (when I went with my husband to a horse endurance ride, or went to pony club with my children). I then also realized that my hat was an Akubra brand, when is made of felt, which in turn is made from rabbit skin fur being soaked in mercurous oxide! I gave the hat away, bought a straw hat, and have never had a migraine since!

I honestly feel I have angels looking after me, as I have often had incidences where I have avoided mercury. When I was 16 years old, my parents told me that I could leave school, if I could get a job. I applied for many, including one as a dental nurse, which would have involved grinding the mercury/amalgams in a bowl by hand (without any protection in those days). I did not get that position, and it was not until 1989, that I realized the implications if I had! Then in 1977, we were thinking of buying a business in town, the dry cleaning business. The owner changed his mind to sell to us, and the couple he ended up selling it to both ended up with health problems from the chemicals used.

Over the years, I have tried to get medical and government organizations interested in our case, to no avail. I have literally boxes of copies of letters I have sent out to such people, with many of them remaining not answered. It appears to me that most people consider the pink disease story as something that children 'got' years ago, like measles, and it had no long-term effects. It is a long forgotten story to everyone but the people who suffered it or maybe a parent who watched a child fade away from the condition or its complications. I have letters from mothers whose babies died with pink disease in hospital and they weren't even told where the baby's body went. These



parents have grieved all their lives for these children. Many mothers in particular, as it was often the mothers who nursed the babies in those days (first half of last century), still talk of the terrible struggle they had to bring their babies through pink disease or the heartbreak they suffered when their babies died. The doctors at the time did not know the cause and many mothers were told it was a venereal disease their husbands brought back from the wars, or the baby was 'spoilt' or they were overanxious. Many parents had their first baby suffering pink disease and were so traumatized; they did not have any other children! And then there is the guilt many mothers feel on learning it was the teething powders that caused pink disease. My own mother feels guilty, but is also proud that I am doing the work for the pink disease people now.

One thing I have learnt to do is to not use the term 'pink disease' or acrodynia, the correct medical term, for my condition when discussing it with others. I now say I had 'a form of mercury poisoning', as I find people now can relate to that better. I have learnt my capabilities in life and stick to those things. I'd rather do something I know I can do well, than try new things. I will continue to endeavour to educate all that 'should know better' about the long forgotten pink disease children and what we have endured. I feel strongly that I was meant to survive so I can make this my 'purpose in life'.

Heather Thiele (nee Kemp)"

## Appendix B

**Thimerosal (49.55% mercury by weight) causes the form of mercury poisoning called autism**

(Source: <http://www.altcorp.com/DentalInformation/notcrackpot.htm>)

### **“The Not-So-Crackpot Autism Theory**

By ARTHUR ALLEN

November 10, 2002

<http://www.nytimes.com/2002/11/10/magazine/10AUTISM.html?ei=1&en=99d1b535fa33bba3&ex=1037894857>

<http://www.nytimes.com/2002/11/10/magazine/10AUTISM.html?ex=1037894857&ei=1&en=99d1b535fa33bba3>

Neal Halsey says that vaccinologists have no choice but to take the thimerosal threat seriously.

Neal Halsey's life was dedicated to promoting vaccination. In June 1999, the Johns Hopkins pediatrician and scholar had completed a decade of service on the influential committees that decide which inoculations will be jabbed into the arms and thighs and buttocks of eight million American children each year. At the urging of Halsey and others, the number of vaccines mandated for children under 2 in the 90's soared to 20, from 8. Kids were healthier for it, according to him. These simple, safe injections against hepatitis B and germs like haemophilus bacteria would help thousands grow up free of diseases like meningitis and liver cancer.

Halsey's view, however, was not shared by a small but vocal faction of parents who questioned whether all these shots did more harm than good. While many of the childhood infections that vaccines were designed to prevent -- among them diphtheria, mumps, chickenpox and polio -- seemed to be either antique or innocuous, serious chronic diseases like asthma, juvenile diabetes and autism were on the rise. And on the Internet, especially, a growing number of self-styled health activists blamed vaccines for these increases.

Like all medical interventions, vaccines sometimes cause adverse reactions. But unlike pills, vaccines come packaged with high expectations, which make them particularly vulnerable to public criticism. Vaccines don't cure people, and they are administered to healthy children, which gives them few opportunities for good press. When they work, nothing happens. When vaccinated children become ill, their parents are grief-stricken and often enraged, even if vaccines aren't proved to be at fault. All of this puts public-health advocates like Halsey on the defensive. Most attacks on vaccines, they say, are based on hysteria, bad science and dubious politics.

Halsey, 57, has green eyes, a white beard that makes him look like a ship's captain and an air of careful authority. As chairman of the American Academy of Pediatrics committee on infectious diseases from 1995 through June 1999, he often appeared in the media administering calm reassurance. 'Many of the allegations against vaccines,' Halsey said in one interview, 'are based on unproven hypotheses and causal associations with little evidence.'

And then suddenly in June 1999, during a visit to the Food and Drug Administration, a squall appeared on the horizon of Halsey's confidence. Halsey attended a meeting to discuss thimerosal, a mercury-containing preservative that at the time was being used in several vaccines -- including the hepatitis B shot that Halsey had fought so hard to have administered to American babies. By the time the dust kicked up in that meeting had settled, Halsey would be forced to reckon with the hypothesis that thimerosal had damaged the brains of immunized infants and may have contributed to the unexplained explosion in the number of cases of autism being diagnosed in children.

That Halsey was willing even to entertain this possibility enraged some of his fellow vaccinologists, who couldn't fathom how a doctor who had spent so much energy dismantling the arguments of people who attacked vaccines could now be changing sides. But to Halsey's mind, his actions were perfectly consistent: he was simply working from the data. And the numbers deeply troubled him. 'From the beginning, I saw thimerosal as something different,' he says. 'It was the first strong evidence of a causal association with neurological impairment. I was very concerned.'

The investigation into mercury vaccines was instigated in 1997 by Representative Frank Pallone Jr., a New Jersey Democrat whose district includes a string of shore towns where mercury in fish is one of many environmental concerns. Pallone, who had been pressing the government to re-evaluate its overall guidelines on mercury toxicity, attached an amendment to an F.D.A. bill requiring the agency to inventory all mercury contained in licensed drugs and vaccines.

The job of adding up the amount of mercury in vaccines and assessing its risk fell to Robert Ball, an F.D.A. scientist, and two F.D.A. pediatricians, Leslie Ball, Robert's wife, and R. Douglas Pratt. Thimerosal, which is 50 percent ethyl mercury by weight, had been used as a vaccine preservative since the 1930's in the diphtheria-tetanus-pertussis shot, known as D.T.P., and it was later added to some vaccines for hepatitis B and haemophilus bacteria, which by the early 1990's had become routine immunizations for infants.

The F.D.A. team's conclusions were frightening. Vaccines added under Halsey's watch had tripled the dose of mercury that infants got in their first few months of life. As many as 30 million American children may have been exposed to mercury in excess of Environmental Protection Agency guidelines -- levels of mercury that, in theory, could have killed enough brain cells to scramble thinking or hex behavior.

'My first reaction was simply disbelief, which was the reaction of almost everybody involved in vaccines,' Halsey says. 'In most vaccine containers, thimerosal is listed as a mercury derivative, a hundredth of a percent. And what I believed, and what everybody else believed, was that it was truly a trace, a biologically insignificant amount. My honest belief is that if the labels had had the mercury content in micrograms, this would have been uncovered years ago. But the fact is, no one did the calculation.'

Making matters worse, the latest science on mercury damage suggested that even small amounts of organic mercury could do harm to the fetal brain. Some of the federal safety guidelines on mercury were relaxed in the 90's, even as the amount of mercury that children received in vaccines increased. The more Halsey learned about these mercury studies, the more he worried.

'My first concern was that it would harm the credibility of the immunization program,' he says. 'But gradually it came home to me that maybe there was some real risk to the children.' Mercury was turning out to be like lead, which had been studied extensively in the homes of the Baltimore poor during Halsey's tenure at Hopkins. 'As they got more sophisticated at testing for lead, the safe level marched down and down, and they continued to find subtle neurological impairment,' Halsey says. 'And that's almost exactly what happened with mercury.'

Halsey was beginning to think that it would be prudent to limit thimerosal-containing vaccines and urge pediatricians to use thimerosal-free shots when possible. But his decision inflamed some of his peers. After all, although the thimerosal data was worrisome to Halsey, the available science offered no clear proof that the preservative posed a genuine danger to children when given in parts per million. Moreover, it wasn't clear that there were enough thimerosal-free vaccines available for diseases like pertussis and hepatitis B. Should an unproven fear justify the cessation of a procedure that protected children from proven dangers?

Halsey looked into the matter further and found only complexity. In the medical literature, most cases of acute mercury poisoning result from doses hundreds or thousands of times higher than what infants received with thimerosal-laden vaccines. And although the thimerosal levels in vaccines exceeded the E.P.A.'s guidelines for methyl mercury, thimerosal contained ethyl mercury, a compound that behaves somewhat differently in the body. The E.P.A. based its guidelines on a series of studies of 917 children born in 1987 in the Faeroe Islands, a windswept North Atlantic archipelago, to women who ate methyl-mercury-tainted whale meat. The Faeroes children, whose umbilical cord blood averaged four times the E.P.A.'s daily 'safe' dose -- which was 0.1 micrograms per kilo -- exhibited small but measurable neurological deficits seven years later. They had slower reaction times and diminished attention spans and their word choice and memorization were less keen than those of their classmates who had been exposed to less mercury, according to Philippe Grandjean, a Danish researcher who leads the continuing Faeroes study and teaches at Boston University.

During most of the 90's, many American 6-month-olds received a total of 187.5 micrograms of ethyl mercury through vaccination. While the Faeroes children were exposed to mercury as developing fetuses, and therefore were more vulnerable than the vaccinated American infants, the American babies included about 60,000 each year who had already been exposed to high mercury levels because their mothers had eaten a lot of contaminated fish. What's more, hundreds of thousands of Rh-negative pregnant women and their unborn Rh-positive babies received additional thimerosal each year through injections designed to keep the mothers' immune systems from attacking the fetuses.

The Faeroes studies, though they dealt with methyl mercury, unnerved Halsey. Other researchers were troubled, too. George Lucier, a toxicologist who led a 1998 White House review of mercury's dangers, went so far as to say it was 'very likely' that thimerosal had damaged some children. There was precious little data to back up that precise suspicion -- and little to dismiss it -- because of the lack of toxicology research on ethyl mercury.

On July 7, 1999, at Halsey's urging, the American Academy of Pediatrics and the Public Health Service released a statement urging vaccine manufacturers to remove thimerosal as quickly as possible and advising pediatricians to postpone giving most newborns the birth dose of the hepatitis B vaccine. The decision, which helped to create vaccine shortages and led some babies to become infected with hepatitis B, outraged some senior vaccine experts. Walter Orenstein, director of the National Immunization Program at the Centers for Disease Control and Prevention, would charge that the rush to remove thimerosal-containing vaccines was 'precipitous.' Stanley Plotkin, a renowned vaccine developer, said that it was fruitless to try to soothe vaccination critics. 'If antivaccinationists did not have mercury, they would have another issue,' he said at one meeting. 'One cannot prevent them from making hay regardless of whether the sun is shining or not.'

In Halsey's view, however, thimerosal wasn't simply a bone for rabid vaccine opponents to gnaw on. In the middle of that hectic summer he took a vacation in Maine. Canoeing on a lake, he came across posters that advised fishermen to 'protect your children -- release your catch.' Halsey took that message to heart. If the government was warning people against eating fish with mercury, he asked his colleagues, 'does it make sense to allow it to be injected into infants?'

Although other vaccinologists criticized Halsey, many of his colleagues rallied around him. 'Neal put kids ahead of the vaccination program, which was gutsy,' says Lynn Goldman, a former E.P.A. official who has been on the Hopkins faculty since 1999 and worked with Halsey on thimerosal. 'It would have been easier for him to line up on the other side.'

Few scientists believe that the spike in autism could have been caused solely by the thimerosal in vaccines, but in October 2001, a vaccine-safety committee at the starchy Institute of Medicine confirmed that it was 'biologically plausible' – though by no means proved – that thimerosal could be related to neurodevelopmental delays in some children. The committee recommended that thimerosal be removed from vaccines and called for extensive research to determine any damage it had caused.

Halsey's fellow researchers were right about one thing. Antivaccine advocates immediately seized upon the thimerosal theory, and Halsey became something of an unwilling hero to the vaccine-safety advocates with whom he had so often sparred. In fact, thousands of parents with autistic children have responded to the Institute of Medicine report by filing lawsuits. Michael Williams, who has won millions in toxic tort settlements from pharmaceutical companies, was among the first lawyers to sue vaccine manufacturers, on behalf of William Mead, a 4-year-old Portland, Ore., boy with autism. Williams also filed a separate class-action lawsuit with William's healthy older sister, Eleanor, as lead plaintiff, demanding that vaccine makers also pay for studies to determine thimerosal's effects on millions of children who might have lower I.Q.'s or other less obvious signs of mercury poisoning. Past studies have shown that mercury's effects vary tremendously from person to person, presumably because of genetic differences in the body's capacity to protect delicate organs from it.

'In order to win the Eleanor lawsuit you need to establish liability, but I don't think that is going to be that hard,' Williams said in a recent chat in his Portland office. 'Organic mercury is a very serious neurotoxin.'

Williams embodies the vaccine establishment's worst fear about Halsey's course of action – which is that taking the precautionary step of eliminating thimerosal would be read as an admission of fault. 'The agenda was set by the lawyers and the antivaccine activists,' a source close to a number of manufacturers complained to me. 'The scientists responded to it scientifically, and that put them behind the eight ball right away. You had Neal Halsey running around saying: 'We've got to do something! We've got to show we're concerned!''

Paul Offit, a vaccinologist at the Children's Hospital of Philadelphia, takes it a step further. 'In some instances I think full disclosure can be harmful,' he says. 'Is it safe to say there is zero risk with thimerosal, when it is remotely possible that one child would get sick? Well, since we say that mercury is a neurotoxin, we have to do everything we can to get rid of it. But I would argue that removing thimerosal didn't make vaccines safer – it only made them perceptibly safer.'

For Halsey, thimerosal injury is a possibility that must be addressed – but by science, not by the courts. The scientific agenda, however, is already deeply politicized. From the start, the C.D.C.'s efforts to examine the possibility of thimerosal damage became snarled in acrimony. Critics of the vaccination system don't trust the C.D.C., which monitors evidence of adverse reactions to vaccines through the Vaccine Safety Datalink, a computerized set of 7.5 million medical records. Safe Minds, an advocacy group of parents who believe that their autistic children were damaged by thimerosal, has used the Freedom of Information Act to obtain documents showing that as early as December 1999 the C.D.C. had reason to believe that thimerosal caused developmental delays in some children. It was far from conclusive evidence, but vaccine critics charged that the C.D.C. tried to play it down. One of those critics was Dan Burton, a Republican congressman from Indiana, who says he firmly believes that his grandson's autism is a result of vaccines. 'I'm so ticked off about my grandson, and to think that the public-health people have been circling the wagons to cover up the facts!' Burton fumed at a June hearing. 'Why, it just makes me want to vomit!'



What comes through in an examination of the documents uncovered by Safe Minds is less a coverup than an impression of scientists anxiously watching over their shoulders as they work. One document, for example, records comments made by Robert Brent, a Philadelphia pediatrician who served as a consultant for the thimerosal study. 'The medical-legal findings in this study, causal or not, are horrendous,' Brent said. 'If an allegation was made that a child's neurobehavioral findings were caused by thimerosal-containing vaccines, you could readily find a junk scientist who would support the claim with a reasonable degree of certainty. But you will not find a scientist with any integrity who would say the reverse with the data that is available. ... So we are in a bad position from the standpoint of defending any lawsuits if they were initiated.'

More research is in the works. The C.D.C. is setting up a study of neurodevelopmental effects based in part on the Faeroe Islands model. The N.I.H. is financing studies of thimerosal metabolism in animals and children. (An early University of Rochester study was reassuring: it indicated that children eliminate thimerosal much more quickly than expected.)

Clearly, a lot is riding on this research, and pressure is being brought to bear on both sides. Can the vaccine authorities accept a positive answer? Can the vaccine opponents accept a negative one? 'No one wants to think that harm might have been done,' Halsey says. "I don't want to think harm might have been done.'

American children still receive up to 20 vaccines in the first two years of life. The first symptoms of autism often appear between the ages of 12 and 24 months. Most autism experts say that the two facts are coincidental, but as a major California study recently confirmed, autism is being diagnosed in numbers far higher than ever before, suggesting that a nongenetic cause may be partly to blame. In some children, the behavioral traits of autism present themselves along with physical problems like sensory dysfunction and motor disorders that have rough correlates in the mercury-poisoning literature. For some parents, thimerosal provides a grand unifying theory that squarely points the finger at the government and vaccine makers.

During much of the 20th-century, children suffered from an ailment called pink disease, which caused peeling skin on the extremities as well as regressive behavior. In 1948, a keen-eyed Cincinnati pediatrician named Josef Warkany noticed a common risk factor in these children: they had all been given teething powders containing calomel, a mercury derivative. Only about 1 in 500 children whose parents gave them calomel got pink disease – suggesting that a constitutional vulnerability to mercury was part of the clinical picture. Soon after the powders were taken off the market, pink disease disappeared.

Autism is a global phenomenon that was first reported in America in 1943, long before the potential dangers of thimerosal vaccines were raised. Removing the preservative won't – even in the best case – eliminate the illness. But scientists estimate that the current rate of autism in its various forms might be as high as 1 in 500. If the autism trend begins to recede now that thimerosal has been removed, it could certainly suggest a cause. If it does decline, we might have Neal Halsey to thank. If it doesn't, his colleagues in the vaccine establishment may blame him for stoking an irrational protest from the public.

Halsey, who still heads the Hopkins Institute for Vaccine Safety, which he was a founder of in 1997, is on the fence. 'I don't believe the evidence is convincing now that there has definitely been harm done by thimerosal,' he says, absently stroking his balding head. But to keep the vaccine program on a steady keel, Halsey says, the public-health authorities simply must follow through with the studies and face the consequences without flinching. If there is damage, he says, 'there should be some kind of compensation, though I don't know how.' He pauses, and sighs. 'I empathize with families of children with these disorders. How are you going to put dollar values on that?'

“Arthur Allen lives in Washington and is working on a history of vaccination.

Neal Halsey M.D., Professor, Director  
International Health  
Hygiene w5515  
nhalsey@jhsph.edu  
Phone: 410.955.6964  
Fax: 410.502.6733

#### Research

My primary research and teaching effort is directed toward the prevention of infectious diseases with the safest vaccines possible. I have conducted or participated in epidemiological studies of vaccine-preventable diseases and phase I, II, and III vaccine trials of hepatitis B, hepatitis A, inactivated polio virus, pertussis, Haemophilus influenzae type B, tetanus, Lyme disease, rotavirus, Argentina Hemorrhagic Fever, and influenzae vaccine viruses. The control of measles has been a particular focus of interest and I support the ongoing measles and poliomyelitis eradication efforts. My interest in vaccine safety stems from experience with vaccine-associated paralytic poliomyelitis, increased mortality after high-titer measles vaccines, and differences in response to acellular and wholecell pertussis vaccines. On-going studies include: persistent poliovirus excretion in immunodeficient children, evaluation of Lyme disease vaccine in children, evaluation of alternative injection devices, and the safety of preservatives and adjuvants in vaccines.

#### Keywords

International Health, prevention of infectious diseases with the safest vaccines possible, epidemiological studies of vaccine-preventable diseases and phase I, II, and III vaccine trials of hepatitis B, hepatitis A, inactivated polio virus, pertussis, Haemophilus influenzae type B, tetanus, Lyme disease, rotavirus, Argentina Hemorrhagic Fever, and influenzae vaccine viruses

Institution: The Johns Hopkins University  
Division: Bloomberg Sch of Public Health  
Department: Intl Health - Div of Disease Cntl  
Title: PROFESSOR  
Campus: East Baltimore Campus  
Campus/Office Address: HYGIENE 5515  
Affiliation: Faculty  
Office Phone: (410) 955-6964  
Office Fax: (410) 502-6733  
Email: nhalsey@jhsph.edu

Institution: The Johns Hopkins Medical Institutions  
Division: The Johns Hopkins Hospital  
Department: PEDIATRICS  
Title: Act Staff Full Time  
Campus: East Baltimore Campus  
Affiliation: Staff  
Office Phone: (410) 955-6964  
Email: nhalsey@jhsph.edu  
Additional Titles: Professor, Div of Disease Control (SPH)  
Joint Appointment, Pediatrics (SOM)  
Active Staff, Pediatrics (JHH)”

## Appendix C

### *“Safe Minds Analysis of Denmark Autism Registry October 2003”*

(Source: [http://www.safeminds.org/research/docs/Hviid\\_et\\_alJAMA-SafeMindsAnalysis.pdf](http://www.safeminds.org/research/docs/Hviid_et_alJAMA-SafeMindsAnalysis.pdf))

#### **“Analysis of the Danish Autism Registry Data Base in Response to the Hviid *et al* Paper on Thimerosal in JAMA (October, 2003)**

Sallie Bernard, Safe Minds, 14 Commerce Drive, PH, Cranford, NJ 07016,  
sbernard@safeminds.org, 970 429-1460

#### **KEY FINDINGS**

A large percentage of diagnosed autism cases are lost from the Danish registry each year. In the ten years preceding 2000, 815 cases were lost, more than the 710 remaining in the registry in 2000. The vast majority of those lost cases would represent older children in the 2000 registry. Since the relative risk of the Hviid study is based on finding fewer older thimerosal-exposed children than younger unexposed children, the validity of their conclusion exonerating thimerosal in autism is questionable. More likely, the finding is a result of missing records rather than true lower incidence rates among the exposed group.

Another approach to analyzing the trend data that avoids the above methodological bias by comparing same-age groups, has found a 2.3 times higher number of autism cases among 5-9 year olds exposed to thimerosal relative to 5-9 years old given thimerosal-free vaccines. Using this methodology, the incidence among the unexposed group is approximately 1 in 1,500, which is much lower than the US and UK rates. The incidence of autism in the thimerosal group is estimated to be 1 in 500, similar to US and UK rates, and 3 times higher than the unexposed group.

The Denmark registry has a number of inconsistencies and has experienced large changes to its record keeping practices over the years, making trend analysis difficult. Interpretation of the data is subject to bias which may be hard to detect. Analysis of this data set should be conducted by independent researchers unconnected with the promotion of vaccine programs.

#### **METHODS**

Safe Minds obtained a copy of a data set of the Danish Registry for autism cases, referred to here as the Registry Data Set.<sup>1</sup> The data set shows the number of cases in the registry for the years 1980 to 2002. For each registry year, the number of cases are broken down by age bands in 5 year increments, i.e., 0-4 year olds, 5-9 year olds, 10-14 year olds, etc. The total Danish population for each age band for each registry year, as well as the number of new autism cases added per year, are also provided.

Safe Minds analyzed this data set in light of the results and conclusions stated in the Hviid *et al* paper on thimerosal and autism appearing in the October 2003 issue of JAMA<sup>2</sup>. The Hviid study uses the 2000 registry to examine the rate of autism and exposure to thimerosal in vaccines among those born 1990-1996. Safe Minds compared their findings with the actual Registry Data Set, as well as with other published studies conducted recently by Danish investigators using the same registry.<sup>3,4,5,6</sup>

#### **RESULTS**

##### **Loss of Records from the Registry**

Review of the total cases by registry year (Registry Data Set, tab “Total Both Sex”) shows that the registry does not retain all the cases which are entered into it. As illustrated in Table 1 below, for the registry year 1995, there are 97 cases in the 5-9 year old cohort. This same cohort, as it grows older, becomes the 10-14 year old cohort five years later in the 2000 registry. Yet now the number

of cases for this group has fallen to 75 children, a decline of 22 cases or nearly a quarter (23%) of the original 1995 cases.

**Table 1. Comparison of Case Counts  
for a Single Age Cohort in Two Registry Years,  
1995 & 2000**

Age Group	1995	2000
0-4 year olds	73	156
5-9 year olds	97	257
10-14 year olds	36	75

Since autism is considered a life long disorder, and very few cases in the registry are in older age groups who are likely to die, any case that is entered into the registry should remain there. The exceptions might be rare instances where a misdiagnosis occurs, but this situation is not common to autism. Thus, removal of these cases is probably due to administrative error. It means that these autism cases still exist, but they are not being recorded.

In order to determine the extent of the artificial removal of diagnosed cases from the registry, we calculated the number of cases removed for each year for the ten year period leading up to 2000, or from 1991 to 2000. For each of these years, we took the number of new cases added to the registry for that year, as shown on the Registry Data Set "New Both Sex" tab, and added it to the number of previous year's cases which already existed in the registry. We compared this total of new plus existing cases to the number of cases shown in the registry for that year. We did this calculation for the total number of cases in the registry for a given year, that is, all age bands combined. The results of this analysis are shown in Table 2 below.

It is easily seen that a large number of cases are regularly dropped from the registry. For several years the proportion lost amounts to one fourth of the cases (e.g., 1993). For the registry year 2000, on which the Hviid *et al* analysis is based, 23% of the cases (211 of 921) were dropped from the data set. On a cumulative basis, between 1991 and 2000, 815 cases were eliminated, more than the total number of cases remaining in the data base in 2000.

**Table 2. Number of Diagnosed Cases Dropped from the Registry Each Year**

Year	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000
# Total Cases Reported	100	108	137	168	250	385	451	507	562	673	710
# New Cases	N/A	46	73	91	136	156	130	140	168	237	248
# New +Previous Year's Cases	146	181	228	304	406	515	591	675	799	921	
# Dropped Cases*	38	44	60	54	21	64	84	113	126	211	

\*Represents the difference in reported cases vs real (new + previous) cases.

As removed cases accumulate each year, for any given registry year, proportionately more of the removed cases would have fallen in the older age groups, since with each successive year, the removed case gets older. As a result, the main impact of case removal is a bias in the registry toward more accurately counting younger age cohorts while undercounting older age groups. The relative risk of the Hviid study is predicated on finding fewer cases in the older thimerosal cohort and more in the younger non-thimerosal groups. Given the problem of case elimination in the registry, their analysis is flawed and any conclusions drawn from it are greatly weakened if not invalidated.

### **Reanalysis using alternative methodology**

An alternative method of analyzing case rate trends avoids the bias demonstrated previously of older patients being removed from the data set. This method compares cohorts of the same age but in different registry years. One registry year would be comprised only of those children who received thimerosal-containing vaccines. The other registry year would be comprised of those who

only received thimerosal-free formulations. Since the average age of diagnosis is 4.7 years,<sup>2</sup> the most stable age group to analyze is the 5-9 year olds.

The only registry year available which is exclusively comprised of children 5-9 years old who were entirely exposed to thimerosal-free vaccines is the 2002 registry. For the thimerosal-exposed registry year, we choose the 1992 registry, because several events in Denmark affecting the population of the registry eliminated the choice of other possible registry years:

- (1) Prior to 1992, records for a large clinic in Copenhagen were not included in the registry. This clinic accounted for 20% of autism cases.<sup>5</sup> It would therefore be preferable to choose a registry year from 1992 on.
- (2) In 1993, the Danish health system changed from using ICD-8 codes to ICD-10 codes for diagnostic purposes.<sup>5</sup> A number of seminars were held regarding this switch, which may have inflated the diagnosis and reporting of autism cases.<sup>5</sup> In fact, an increase in cases can be seen in the 1993 and 1994 registry years for many age groups.<sup>1</sup> Therefore, it would be preferable to avoid these two years for analysis.
- (3) In 1995, autism out patient records were added to the registry, which previously only contained in patient records. In a previous paper,<sup>4</sup> Danish researchers stated that 6.9% of the cases in the 1999 registry were in-patients and 93.1% were out patients.

The addition of out patients greatly expanded the number of records in the registry. It would be preferable to avoid the early years of changeover to the expanded data base. In choosing 1992 as our analytic year, we would need to adjust for the absence of outpatient records in the data set. There are 38 cases of autism in the 5-9 year olds in the 1992 registry. We can estimate that the 38 cases in 1992 only represent 6.9% of the total diagnosed cases actually existing in Denmark for this age group. We can estimate the total cases by dividing 38 by 0.069, which equals 551 cases. The 2002 registry contains 239 5-9 year olds. This is the group that received no thimerosal. The 1992 group represents 551 cases, and it received thimerosal. The 1992 group has 2.3 times the number of cases as the 2002 group, suggesting that the removal of mercury was followed by a steep decline in autism incidence.

### **Incidence**

If we look at the 2002 registry for the 5-9 year olds, the 239 cases represent an incidence of 68 per 100,000, which equates to 1 in 1,470, or approximately 1 in 1,500, as shown in Table 3. This is 3-6 times lower than the numbers being reported in the US and UK for core autism (1 in 250 and 1 in 500 respectively)<sup>7,8</sup> If we look at the estimated 551 cases for 1992 among 5-9 year olds, the rate is 204 per 100,000, which equates to an incidence of 1 in 500. This is much closer to the rates observed in the US and UK. We would expect to see a slightly lower rate in Denmark relative to the US because the Danish thimerosal dose amount and timing of administration was slightly less and later than in the US, while these practices were comparable to those in the UK.

**Table 3. Number of Autism Cases and Autism Incidence for 5-9 Year Olds, 1992 vs. 2002 Registry Years**

	<b>1992 Registry 5-9 Year Olds</b>	<b>2002 Registry 5-9 Year Olds</b>
# of Autism Cases*	551	239
Population of Age Group – All of Denmark*	270164	341804
Incidence	1 in 500	1 in 1470

*\*1992 numbers are adjusted for missing outpatient records. 2002 numbers are from Registry Data Set. Population counts are from Registry Data Set.*

### **Volatility of the Denmark Registry Data**

It has been pointed out that the Denmark registry experienced a number of key changes in the 1990s which affected the number of cases in the data set. These changes included the addition of outpatient records, conversion from ICD-8 to ICD-10 diagnoses with accompanying educational seminars, loss of diagnosed cases from the records, and the addition of records from the Copenhagen clinic.

Another example worth noting which illustrates how variable the data set can be with just minor shifts in the study population observed, can be seen through a comparison of the Madsen *et al* (2002) MMR study<sup>4</sup> and the Hviid *et al* Thimerosal study<sup>2</sup> cohorts. Madsen *et al* used the 1999 registry and within it, examined children born in 1991-1998, a total of 8 years. The autism case count was 316, or 40 cases per year on average. Hviid *et al* used the 2000 registry and within it, examined children born in 1990-1996, a total of 7 years. The autism case count was 440, or 63 cases per year.

The increase from the 40 cases of the Madsen *et al* 1999 registry to the 63 cases of the Hviid *et al* 2000 registry is 59%, which is very large for just a single year shift. The lower count for the 1999 registry group is even more surprising given that this study sample extends into the more recent birth years (1997, 1998), when there was no thimerosal and supposedly the autism rates were going up, at least according to the *JAMA* authors.

One reason for this discrepancy, of course, is that for 3 years of the Madsen *et al* MMR study cohort (birth years 1998, 1997, 1996) the children were too young to be fully diagnosed. So the question arises as to why this age group was chosen to analyze the impact of the MMR vaccine on autism rates. The point is that depending on what birth cohorts from the registry an investigator chooses, and what registry year he or she chooses to study, very different results can be produced and significant bias can be introduced.

### **Conflict of interest**

The authors of the *JAMA* paper work for Statens Serum Institut, which is the manufacturer and promoter of vaccines in Denmark. *JAMA* did not disclose to its readers that the authors have a financial conflict of interest in the outcome of the study, contrary to standard medical and scientific journal practice.

A more honest and productive approach to examining the Denmark registry data set would entail having independent researchers unconnected to vaccines investigate the data.

### **CONCLUSIONS**

The Hviid *et al* finding of lower autism rates with thimerosal exposure is likely due to errors in record keeping in the registry data set. Another approach to analyzing the same data, which adjusts for lack of outpatient records, has found a 3-fold increase in autism incidence with thimerosal exposure. The Denmark autism registry has large variability in the nature of its records and utilization of the data set for epidemiological analysis is prone to bias. Use of this data to investigate the role of vaccines in autism should be conducted by researchers unconnected to vaccine manufacture or promotion.

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## Appendix D

### **“Safe Minds Analysis of Madsen et al. September 2003”**

(Source: <http://www.safeminds.org/research/docs/Blaxill-DenmarkAutismThimerosalPediatrics.pdf>)

#### **“Danish Thimerosal-Autism Study in *Pediatrics*: Misleading and Uninformative on Autism-Mercury Link”**

“Mark Blaxill, Director, Safe Minds  
September 1, 2003”

“A report by Madsen *et al.* published by the American Academy of Pediatrics in their journal *Pediatrics*<sup>1</sup> claims to provide evidence against a link between autism rates and the mercury in thimerosal, a preservative used in childhood vaccines. Unfortunately, the study analysis is full of flaws and inaccuracies, invalidating the conclusions regarding thimerosal. The study adds little of value to the scientific literature on autism and mercury.

Thimerosal has been causally linked to autism and other neurodevelopmental disorders.<sup>2,3</sup> Madsen *et al.* claim to refute such a link by analyzing Danish psychiatric records to assess rates of autism. They compare the number of newly recorded autism cases prior to 1992, when thimerosal-containing vaccines were used, with those after 1992, when such vaccines were no longer produced in Denmark. The authors claim to observe a rise in autism rates after removal of thimerosal, and thus conclude that thimerosal plays no role in the etiology of autism. An in-depth analysis of the report reveals three major problems with the analysis and methodology.

1. The report provides information on autism rates in Denmark that is distorted and misleading. These distortions allow the authors to make assertions about a rising trend in autism “incidence” in the 1990s that has no basis in fact. The report’s claims are based on the following distortions:
  - Autism counts were first based on hospitalized, inpatient records and then changed in the middle of the study period to add in outpatient records. This new outpatient registry was introduced in 1995. Therefore, their purported increases after 1994 can be explained entirely by the registration of an existing autism population that did not require hospitalization. The authors minimize this discrepancy and do not adjust for it in their chart (Figure 1), yet in a prior study using the same Danish data,<sup>4</sup> outpatients exceeded the inpatients by a ratio of 13.5 times, and represented over 93% of total cases. This huge gap clearly invalidates their inpatient data, the corresponding time period from 1970-94, and any evidence for a rising trend of autism in Denmark. The authors claim that inpatient admissions were rising also, but the “data [were] not shown”. They did not explain this omission, the only bit of credible data in their possession, since it compared equivalent populations.
  - Additional discrepancies in the autism case counts make the trend assessment unreliable. After 1992, the registry added in patients from a large Copenhagen clinic, which accounted for 20% of the case load in Denmark.<sup>5</sup> The patients from this clinic were excluded prior to 1992. Their inclusion in subsequent years would drive apparent increases in rates from 1992-1995 that was yet another form of registration effect.
  - The diagnostic category used by the Danish psychiatric system changed after 1993 from “psychosis proto-infantis” of ICD-8 to “childhood autism” of ICD-10. Psychosis proto-infantis (code 299) is a category that has never been used in published autism surveys outside of Denmark. ICD-8 contained another, clearly more suitable code, 295.8 for “infantile autism”, which provided diagnostic criteria similar to current criteria used in ICD-10 and DSM-IV. The *Pediatrics* report mentions the diagnostic change in passing but fails to

quantify its effect. In another paper using the same inpatient registry,<sup>6</sup> two of the investigators in the *Pediatrics* report note that the psychosis proto-infantilis category includes *inpatient* cases that do not fulfill the criteria for autism (which would further reduce the value of this case finding tool), while also noting that outpatient cases of autism in Denmark would not be captured.

- The autism trend data are described as an “incidence study”, a marker of quality in an epidemiological analysis. But the report is in no way a proper incidence study. It relies instead for its definition of the “incidence” of autism on the date when cases were entered into the new registry of outpatients. Many of these children were between 7-9 years old, and most were over 4 years old, when recorded as part of an increasing “incidence” trend. Yet the onset of autism must occur, by definition in the diagnostic criteria, before three years of age. Recording an “incidence” event at, say, seven years of age is clearly incorrect. Yet the authors record many such events to report an increase in registrations (especially after 1994) that they misleadingly describe as increasing incidence. The most widely used approach to assessing autism trends is to use year of birth as the “incidence time.” This approach was used, for example, in the California Autism Epidemiology Report by Byrd *et al.*<sup>7</sup> Madsen *et al.* clearly have this information as part of their data set but chose not to report it. Failure to report the birth cohort incidence means that this study’s autism rates cannot be fairly compared with incidence levels observed in other countries.
- A recent study<sup>4</sup> from the same group reported Danish autism rates for children born in the 1990s of 6 per 10,000. This falls below the rates of autism reported in the U.S. (over 30 per 10,000) by more than 80%.<sup>8,9</sup> While emphasizing their illusory increase, the authors never mention that their rates are actually quite low. Although our estimates confirm that these Danish rates are very low in the 1990s compared to the U.S. or the U.K.,<sup>10</sup> the authors fail to provide the most basic statistics that might enable a full comparison with other reports. These crucial omissions suggest a clear bias toward elevating the perception of Danish autism rates later in their study period.
- The report also estimates inpatient rates for the pre-1993 “psychosis proto-infantilis” at well below 1 per 10,000. If these were true rates for autism, these would be among the lowest rates measured anywhere in the world at any time period. This low rate would also contradict the single published survey of autism rates from Denmark, which indicated an autism rate of over 4 per 10,000 as far back as the 1950s.<sup>11</sup> Normally, authors cite relevant studies in their introductory or discussion sections, but Madsen *et al.* fail to mention this study, as they fail to comment on the unusually low autism rates for the earlier years of their study period.

There are only three proper conclusions that one can draw about the autism rates in Denmark based on available data. 1) The rates in the 1990s are low compared to the U.S. and U.K. and possibly stable with respect to trend. 2) The 1990s Danish autism rates are similar to rates in the 1950s. 3) There are still no published, usable data about Danish autism rates in persons born between 1960-90.

2. The mercury exposure levels described in Madsen *et al.* are likely to be overstated. The authors describe a level of mercury exposure to Danish infants of 125 micrograms (mcg) by 10 months of age between 1970-92, a period in which they claim (without justification) that autism rates were low. All exposures came from the monovalent pertussis vaccine manufactured by Statens Serum Institut, which, according to the paper, provided the vaccine coverage rates reported therein.
  - These mercury levels of 125 mcg are substantially lower and later than those scheduled in the U.S. in the 1990s, 187.5 mcg by six months.<sup>12</sup>

- The exposure level of 125 mcg requires full compliance by Danish parents. The authors assert coverage rates of over 90% for this schedule, yet a recent report using the same data suggests that completion rates were well below 90%.<sup>5</sup> The authors also fail to provide any information regarding the timing of the actual exposures. Given widespread Scandinavian concern over pertussis vaccine (Sweden banned pertussis vaccines in 1979) it would be surprising if coverage rates were as high as 90% and if on-time schedule compliance was common throughout the 1970-1992 period. Documentation of compliance rates by Statens Serum Institut is needed.
  - These ethyl mercury exposures—at 50 mcg per dose for the 9 week and 10 month injections—are the highest amounts ever described in any single vaccine dose. The authors fail to acknowledge this unusual mercury level and to provide an explanation for why this formulation was so much higher than formulations used in all other countries and by all other manufacturers, which were typically 25 mcg per dose.
3. The context for the early mercury exposures was completely different in Denmark when compared to any other country, and particularly compared to the U.S. and U.K., where autism rates are being watched most closely. The Danish report describes a different world of vaccine exposures and ignores exposures that are present today that were not present in Denmark in the 1970s. Autism onset has been reliably associated with exposure to viruses.<sup>13</sup> In the cases where increasing thimerosal exposures have accompanied autism increases, numerous additional confounders were present that were not present in Denmark.
- Between 1970-92, the only childhood vaccine given in Denmark until 5 months of age was the monovalent pertussis vaccine.
  - In the United States in the 1990s, children were exposed to multiple doses of diphtheria, pertussis, tetanus, polio, hepatitis B and haemophilus influenza B (Hib) vaccines before five months of age.
  - In the United Kingdom, injections before age 5 months included multiple doses of meningitis C, polio, diphtheria, tetanus, Hib, and pertussis vaccines. Increasing autism rates there were accompanied by earlier thimerosal exposures due to schedule changes, new exposures to MMR and Hib vaccines, and stringent on-time compliance procedures.
  - Denmark did not administer thimerosal-containing Rho D immunoglobulin during pregnancy.

In summary, the report by Madsen *et al.* appears to be an attempt to present selectively chosen data that provide support for policy choices in which the authors and their collaborators are involved. Once again, rather than seriously evaluating the autism-mercury hypothesis and carrying out the research agenda specified by the Institute of Medicine<sup>14</sup> in 2001, public health authorities (now teamed with a Danish vaccine manufacturer) have chosen to issue another piece of propaganda masquerading as science, with the only possible outcome being that legitimate research and discussion might be suppressed. We sincerely hope that well-informed scientists and public officials will note the flaws in this report and be motivated to conduct the recommended investigations into the autism-mercury connection, which still await completion.

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## Appendix E

### **“Response to Critics on the Adverse Effects of Thimerosal in Childhood Vaccines”**

(Source: *J. Am Phys Surg* 8(3):68-70)

“The United States is in the midst of a devastating epidemic of neurodevelopment disorders. Statistics from the U.S. Department of Education on autism in children aged 6 to 21 years served by the Individuals with Disabilities Education Act (IDEA) showed an increase from 11,956 cases in 1992-1993 to 97,329 in 2001-2002, an increase of 714 percent.<sup>1</sup> (Data for each state are found in Table 1 appended to the internet posting of this letter at [www.jpands.org](http://www.jpands.org).) Between 9 and 15 percent of all children aged 6 to 17 years were served under IDEA during the 1999-2000 school year.

In light of the threat of this epidemic to the very existence of our society, it is not surprising that our recent article,<sup>2</sup> in which we have shown an epidemiologic link between thimerosal and neurodevelopment disorders, has generated tremendous controversy. We would like to respond to some of the erroneous statements made about our work.

Some object to our use of the Vaccine Adverse Event Reporting System (VAERS) database to conduct an epidemiologic assessment. No database is perfect. Inherent limitations include incomplete reporting, misreporting, and underreporting. We employ various methods to control for these limitations.

As an example, we have evaluated rotavirus vaccine and intussusception, a recognized complication of rotavirus immunization.<sup>3</sup> We determined that, prior to the introduction of rotavirus vaccine, not one case of intussusception had been reported following more than 50 million doses of Diphtheria-Tetanus-whole-cell-Pertussis (DTwCP) vaccines. We then evaluated cases of intussusception reported in 1999 following DTwCP and rotavirus vaccines, which were both administered at 2, 4, and 6 months of age in the U.S. We found that only 4 percent of cases of intussusception were misreported as being associated with DTwCP vaccines, rather than with concurrently administered rotavirus vaccine.

Additionally, we evaluated cerebellar ataxia reported following DTwCP vaccine in comparison to Diphtheria-Tetanusacellular-Pertussis (DTaP) vaccine.<sup>4</sup> A previous report from Japan had shown that cerebellar ataxia was reported with similar frequency following these vaccines. It was hypothesized that popular media reports of the risk of serious neurologic disorders following DTwCP vaccine might cause overreporting to VAERS. However, our results showed virtually the same frequency of reports of cerebellar ataxia following DTwCP and DTaP vaccines (0.29 per million vaccinations vs 0.30 per million vaccinations, respectively), essentially the same rate as was expected based upon the Japanese data, confirming the validity of VAERS reports.

Governmental agencies have previously conceded that the VAERS database may be used for ‘hypothesis proving.’ By using a vaccine control group and the Biological Surveillance Summaries of the CDC, we and others have been able to undertake a statistical epidemiologic assessment of the VAERS, as was previously developed and published by Rosenthal *et al.*<sup>5</sup> from the National Immunization Program (NIP) of the CDC.

Specifically, they reported that, ‘Rates of reported adverse events per 100,000 vaccinations were significantly lower [ $P < 0.001$ ] after administration of diphtheria and tetanus toxoids and acellular pertussis vaccine than diphtheria and tetanus toxoids and pertussis vaccine for the following outcomes: all reports, 2.2 vs 9.8; fever, 1.9 vs 7.5; seizures, 0.5 vs 1.7; and hospitalizations, 0.2 vs 0.9.’ In addition, Sever *et al.*<sup>6</sup> from the Anthrax Vaccine Expert Committee (AVEC), have examined the VAERS database, ‘... to assess the causal relationship between vaccination and reported adverse events ... Six events qualified as serious adverse events, and all were judged to be certain consequences of vaccination.’



The VAERS database provides a perspective regarding adverse events following vaccination that is available by no other means of analysis. More than 200,000 adverse event reports are recorded in the VAERS database following more than one billion doses of more than 30 different types of vaccines administered as part of the U.S. National Immunization Program. No data set will ever be able to provide this much information about the actual clinical effects of such a large number of immunizations of so many different types.

Most epidemiologic studies encounter this problem: 'Several social and medical attributes are associated both with avoidance or delay of vaccination... Studies that fail to control adequately for such confounding factors are likely to underestimate the risks of adverse events attributable to vaccination.'<sup>7</sup> Analyses of the VAERS database using the CDC's methods of comparing one vaccine to another, instead of comparing vaccine recipients to a background population, circumvents this difficulty because equal avoidance or delay of vaccination is likely for both vaccine populations under study.

Our calculation of the instantaneous exposure of U.S. infants to thimerosal from childhood vaccines in comparison to the Federal Safety Guidelines has also been criticized, citing the 2001 Institute of Medicine (IOM) report,<sup>8</sup> which found that the dose to infants from vaccine was only slightly in excess of the Guidelines. The IOM calculated exposure in the first six months (180 days) of life by dividing the dose received in the vaccines by 180. By this method, the infants were barely in excess of the Environmental Protection Agency (EPA) limit of 0.1 mcg of methylmercury/kg/day, but not in excess of the Food and Drug Administration (FDA) limit of 0.4 mcg/kg/day. (Since that report was published, the FDA has lowered its maximal permissible oral dose of methylmercury to concur with the EPA limit.)

Applying the IOM method to a newborn weighing 3 kg, hepatitis B vaccine containing 12.5 mcg of mercury gives a dose 39 times the daily permissible oral intake, and this cannot be hidden by dividing by the child's age (1 day).

We believe the IOM method of calculation to be absolutely erroneous and extremely misleading. By this method, if a 55-year-old man were given a lethal dose of ethylmercury today, the dose averaged over the number of days in his lifetime would not exceed EPA or FDA limits, but he would still be dead.

The FDA and EPA maximal permissible doses for the oral doses of methylmercury are daily instantaneous maximal doses, and the vaccines administered to children are instantaneous exposures to mercury. Thus, the appropriate calculation finds that infants were, when thimerosal was present in childhood vaccines, exposed to instantaneous levels of mercury that were manifold (i.e. in some cases more than 100-fold) in excess of the Federal Safety Guidelines for the oral ingestion of methylmercury.

Some have objected to our applying the Federal Safety Guidelines for the oral ingestion of methylmercury to exposures from injected ethylmercury from thimerosal. The IOM itself uses this comparison. Moreover, injection results in much greater absorption of mercury than does oral ingestion.

Criticism of our estimates of mercury dosage appears to be based on a misunderstanding of the information available from VAERS. The VAERS database states which dose was associated with the adverse event; thus, we were able to determine the approximate amount of mercury that the child had been exposed to from previous immunizations. Because VAERS records the vaccine manufacturer, we could, by reviewing the Physician's Desk Reference (PDR) and the 2001 IOM Report, determine how much thimerosal was present in each vaccine under study. Unfortunately, we were unable to provide the identities of the vaccine manufacturers or the number of doses distributed based upon the Biological Surveillance Summaries of the CDC, which are broken down by manufacturer. The CDC claims that this information is proprietary and required us to agree not to divulge it, as a condition of being given access to these summaries.

Some argue that the CDC's summaries do not accurately reflect the dosages administered to children, but others rely on that data. As Rosenthal *et al.*<sup>5</sup> state: 'The annual numbers of Pertussis-containing vaccine doses administered during the period from 1991 to 1993 were estimated from

the Centers for Disease Control Biologics Surveillance. This surveillance system receives voluntary reports from all manufacturers of doses distributed and doses returned by providers, thereby permitting calculation of net doses distributed, an approximation of doses administered.'

We have also been attacked for our analysis of the data from the Vaccine Safety Datalink (VSD) database because neither the original preliminary VSD study of thimerosal and neurodevelopment disorders nor any of the follow-up expanded studies identified a 'signal' indicating any association between thimerosal and autism. This statement is incorrect regarding the VSD and neurodevelopment disorders.

A complete review of the relevant VSD studies was published in the 2001 IOM report.<sup>8</sup> In a study of 114,966 children in HMO-B, increasing ethylmercury dosage was associated with a statistically significantly increased adjusted risk of any neurodevelopment disorder, stammering, language delay, and speech delay.

In a study that analyzed 15,309 children in HMO-A for only a limited number of types of neurodevelopment disorders, increasing dosage of ethylmercury was associated with a statistically significantly increased adjusted risk of stammering and emotional disturbances.

The IOM then considered information from the Phase II study that was conducted by the CDC group using the Phase I study design in an East Coast HMO (i.e. Harvard Pilgrim of Massachusetts). In this study it was only possible to analyze attention deficit disorder and speech delays. Based upon an examination of 17,500 children, there were no significant differences in risk of these two outcomes associated with receipt of thimerosal-containing vaccines.

In the light of these inconsistent results, the IOM found that the studies were inconclusive with regard to causality. However, further examination shows that IOM was seriously misled by this presentation. A review of the U.S. Department of Education data concerning autism in children 6 to 21 years old shows that the overall prevalence of autism increased by 435 percent from 1992-1993 to 1999-2000. This report shows that California, where the VSD Phase I studies were conducted, had a 422 percent increase in autism during this period, while Massachusetts, where the Phase II study was conducted, had only a 10 percent increase in autism over the same period. A general review of the U.S. Department of Education data shows that every state in the United States, with the exception of Massachusetts, experienced a greater than 100 percent increase in autism, and many states experienced a many thousand percent increase in autism during this period. Thus, the CDC's method was able to show an effect where an effect was present, and returned a negative result in the state with the least increase in autism. Thus, we believe that these CDC studies strongly support a causal relationship between the increasing mercury from thimerosal-containing childhood vaccines and the increase in neurodevelopment disorders.

Our attempts to gain access to the VSD database began before the CDC's press release announcing that the VSD was opened to the public at the end of August 2002. Despite more than 10 months of communication, and our providing the CDC with a cashier's check for about \$3,200 out of our own pockets, we still have not been given access to the VSD database. Moreover, we have been told that outside investigators will have no access to data regarding thimerosal and neurodevelopment disorders until the CDC publishes an analysis of this material – much of which has been in its possession since 1999.

The 2001 U.S. Department of Education Report provides a completely independent source and method that strongly confirms previous epidemiologic assessments.

Some have cast aspersions on the editors and peer reviewers of the *Journal of American Physicians and Surgeons* for publishing our article. This is also a direct assault on major peer-reviewed journals that have previously published articles by us that used similar methods. Additional articles by us are in press.<sup>9,10</sup> Many other authors using a variety of study methods will soon publish papers that confirm and extend our work, such as a study by Baskin *et al.*<sup>11</sup> demonstrating that thimerosal in micromolar concentrations rapidly induces membrane and DNA damage, and initiates caspase-3 dependent apoptosis in human neurons and fibroblasts, and a study by Holmes *et al.*<sup>12</sup> on significantly different mercury levels in the first baby haircuts of autistic children in comparison to normal controls. The association of thimerosal in vaccines and other

medical products with neurodevelopment and other disorders is very real and simply cannot be denied.

We have been criticized for failing to comment on a recent article by Nelson and Bauman,<sup>13</sup> which appeared after our article was written. These authors do not acknowledge several recent epidemiologic studies that have shown an increase in the prevalence of autism from about 1 in 2,500 children in the mid-1980s to about 1 in 150 children by 2002.<sup>14-17</sup> Their arbitrary statement that ethylmercury is not like methylmercury in its effects is without basis, is contrary to published data, and even ignores the conclusion of the 2001 IOM Report regarding the biological plausibility of the relationship between ethylmercury from thimerosal in childhood vaccines and neurodevelopment disorders. Finally, their article is simply a commentary and was published before our epidemiologic data that support the hypothesized relationship.

We are stunned by this assertion in an official statement by the American Academy of Pediatrics (AAP)<sup>18</sup> concerning our article: 'The authors claim falsely that children in the United States in 2003 may be exposed to higher levels of mercury from thimerosal contained in childhood immunizations than any time in the past, when in fact, all routinely recommended infant vaccines currently sold in the United States are free of thimerosal as preservative and have been for more than 2 years.' Regrettably, our comments are true and can be verified by anyone. A simple review of the 2003 PDR indicates that thimerosal is present at 25 mcg per dose (i.e. in full strength) in multidose vials of DTaP vaccine manufactured by Aventis Pasteur, haemophilus influenza Type b (Hib) vaccine manufactured by Wyeth, Td vaccine (recommended for children > 7 years old) manufactured by Aventis Pasteur, and all influenza vaccines (influenza vaccine is now recommended for most children). Additionally, the PDR indicates that Merck makes a pediatric hepatitis B vaccine that contains 12.5 mcg per dose and adult hepatitis B vaccine that contains 25 mcg of mercury per dose. The package inserts of these vaccines also indicate that they still contain the original amounts of thimerosal. In addition, a sequential review of previous PDRs indicates that in 2002 and 2001 there were even more vaccines listed as containing thimerosal.

In a recent interview, Len Lavenda, a spokesman for Aventis Pasteur, stated: 'In March 2001 we stopped all sales of that product [DTaP] in the preservative formulation...The PDR is outdated...The current package insert does not accurately reflect what is being marketed.'<sup>19</sup>

If the assertions by the AAP and Lavenda are true, then vaccines are mislabeled. That is a criminal offense and a situation that cannot be tolerated in medicine. An independent analysis of vaccine content should determine the truth.

There has been much discussion about how we fund our studies. We have never received one penny from anyone to conduct any studies but have funded all of our research out of our own limited resources. Dr. Geier has been paid as an expert witness and as a consultant in hearings before the Vaccine Compensation Act and in civil litigation involving adverse reactions. Similarly, David Geier has been a consultant in hearings before the Vaccine Compensation Act and in civil litigation involving adverse reactions to vaccines. However, as of the acceptance of our three papers on thimerosal and neurodevelopment disorders, we had never received any money from any cases alleging damage from thimerosal.

Assertions that we are anti-vaccine is belied by a review of our publications. We have opposed the current position of the World Health Organization (WHO) that poliomyelitis vaccination can be stopped within the foreseeable future.<sup>20</sup> We have also argued for a need to reintroduce a newly formulated vaccine to combat the alarming 30-fold increased incidence of Lyme disease in the United States from 1982 to 1996.<sup>21</sup>

As Fine and Chen have stated, 'No intervention is entirely without risk...'<sup>7</sup> We as physicians and scientists have an obligation to conduct open and frank discussions about the safety and efficacy of vaccines. We believe that there is no doubt that continued immunizations are critical to our safety and welfare, but we need a concerted effort to improve the safety and efficacy of existing vaccines. Those who apparently have been injured by a vaccination should report their

adverse reaction to the VAERS database and are entitled to rapid, non-litigious, and generous justice before the National Vaccine Injury Compensation Program (NVICP).

Personal assaults on us and on the journals in which we publish, along with denying the existence of the tragic massive autism epidemic, will neither cure the problem, nor will it restore confidence in our much needed vaccine program. Rather, we must admit our past mistakes openly and honestly, and then work to improve current and future vaccines. The first step in this process is the immediate removal of thimerosal from all vaccines, which we predict will result in the end of the autism epidemic.

**Mark R. Geier, M.D., Ph.D.**  
**David Geier**  
Silver Spring, MD"

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