In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 03-584V

(Filed: March 12, 2010)

TO BE PUBLISHED[1]

* *		
FRED KING and MYLINDA KING, parents of Jordan King, a minor,	*	Vaccine Act Entitlement; Causation-in-fact; Thimerosal/Autism Causation Issue.
Petitioners,	*	
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	
* *		

Michael Williams and Thomas Powers, Portland, Oregon, for petitioners.

Lynn Ricciardella, U.S. Department of Justice, Washington, D.C., for respondent.

DECISION

HASTINGS, ***Special Master***.

This is an action in which the petitioners, Fred and Mylinda King, seek an award under the National Vaccine Injury Compensation Program (*see* 42 U.S.C. § 300aa-10 *et seq*.[2]), on account of the condition known as "autism" which afflicts their son, Jordan King. I conclude that the

---

[1]Both parties have filed notices waiving their 14-day "waiting period" pursuant to Vaccine Rule 18(b) and 42 U.S.C. § 300aa-12(d)(4)(B). Accordingly, this document will be made available to the public *immediately*, as petitioners have requested.

[2]The applicable statutory provisions defining the Program are found at 42 U.S.C. § 300aa-10 *et seq*. (2006). Hereinafter, for ease of citation, all "§" references will be to 42 U.S.C. (2006). I will also sometimes refer to the act of Congress that created the Program as the "Vaccine Act."

petitioners have *not* demonstrated that they are entitled to an award on Jordan's behalf. I will set forth the reasons for that conclusion in detail below. However, at this point I will briefly summarize the reasons for my conclusion.[3]

The petitioners in this case have advanced the theory that thimerosal-containing vaccines can substantially contribute to the causation of autism, and that such vaccines did contribute to the causation of Jordan King's autism. However, as to each of those issues, I conclude that the evidence is overwhelmingly contrary to the petitioners' contentions. The expert witnesses presented by the respondent were far better qualified, far more experienced, and far more persuasive than the petitioners' experts, concerning the key points. The numerous medical studies concerning the issue of whether thimerosal causes autism, performed by medical scientists worldwide, have come down strongly against the petitioners' contentions. Considering all of the evidence, I find that the petitioners have *failed* to demonstrate that thimerosal-containing vaccines can contribute to the causation of autism. I further conclude that while Jordan King has tragically suffered from autism, the petitioners have also failed to demonstrate that his vaccinations played any role at all in causing that condition.

I

THE APPLICABLE STATUTORY SCHEME AND CASE LAW

Under the National Vaccine Injury Compensation Program (hereinafter the "Program"), compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations, including showings that an individual received a vaccination covered by the statute; received it in the United States; suffered a serious, long-lasting injury; and has received no previous award or settlement on account of the injury. Finally--and the key issue in most cases under the Program--the petitioner must also establish a *causal link* between the vaccination and the injury. In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table" corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table.[4] If so, the Table Injury is presumed to have been caused by the vaccination, and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B).

In other cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table. In such instances, an alternative means exists to demonstrate

---

[3]For the convenience of the reader, I have attached at the end of this Decision, as an Appendix, a Table of Contents of the Decision.

[4]No Table Injury is alleged in this case.

entitlement to a Program award. That is, the petitioner may gain an award by showing that the recipient's injury was "caused-in-fact" by the vaccination in question. § 300aa-13(a)(1)(A); § 300aa-11(c)(1)(C)(ii). In such a situation, of course, the presumptions available under the Vaccine Injury Table are inoperative. The burden is on the petitioner to introduce evidence demonstrating that the vaccination actually caused the injury in question. *Althen v. Secretary of HHS*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines v. Secretary of HHS*, 940 F.2d 1518, 1525 (Fed. Cir. 1991). The showing of "causation-in-fact" must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); *see also Hines*, 940 F.2d at 1525; *Althen*, 418 F.3d at 1278. Under that standard, the petitioner must show that it is "more probable than not" that the vaccination was a cause of the injury. *Althen*, 418 F.3d at 1279. The petitioner need not show that the vaccination was the sole cause or even the predominant cause of the injury or condition, but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition, and was a "but for" cause. *Shyface v. Secretary of HHS*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). Thus, the petitioner must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury;" the logical sequence must be supported by "reputable medical or scientific explanation, *i.e.*, evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F.3d at 1278; *Grant v. Secretary of HHS*, 956 F.2d 1144, 1148 (Fed. Cir. 1992).

The *Althen* court also provided additional discussion of the "causation-in-fact" standard, as follows:

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury. If Althen satisfies this burden, she is "entitled to recover unless the [government] shows, also by a preponderance of evidence, that the injury was in fact caused by factors unrelated to the vaccine."

Althen, 418 F.3d at 1278 (citations omitted). The *Althen* court noted that a petitioner need not necessarily supply evidence from *medical literature* supporting the petitioner's causation contention, so long as the petitioner supplies the *medical opinion* of an expert. *Id*. at 1279-80. The court also indicated that, in finding causation, a Program factfinder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Id*. at 1280.

Since *Althen*, the Federal Circuit has addressed the causation-in-fact standard in several additional rulings, which have affirmed the applicability of the *Althen* test, and afforded further instruction for resolving causation-in-fact issues. In *Capizzano v. Secretary of HHS*, 440 F.3d 1317, 1326 (Fed. Cir. 2006), the court cautioned Program factfinders against narrowly construing the second element of the *Althen* test, confirming that circumstantial evidence and medical opinion,

sometimes in the form of notations of treating physicians in the vaccinee's medical records, may in a particular case be sufficient to satisfy that second element of the *Althen* test. Both *Pafford v. Secretary of HHS*, 451 F.3d 1352, 1355 (Fed. Cir. 2006), and *Walther v. Secretary of HHS*, 485 F.3d 1146, 1150 (Fed. Cir. 2007), discussed the issue of which party bears the burden of ruling out potential non-vaccine causes. *DeBazan v. Secretary of HHS*, 539 F.3d 1347 (Fed. Cir. 2008), concerned an issue of what evidence the special master may consider in deciding the initial question of whether the petitioner has met her causation burden. In *Andreu v. Secretary of HHS*, 569 F. 3d 1367 (Fed. Cir. 2009), the court again emphasized the importance of the impressions of a vaccinee's treating physicians, and cautioned special masters against requiring too high a standard for establishing causation. Finally, in *Moberly v. Secretary of HHS*, 592 F. 3d 1315, 1322 (Fed. Cir. 2010), the court clarified that the "preponderance of the evidence" standard, utilized to decide causation issues in Vaccine Act cases, is the same as the traditional tort standard of "preponderant evidence," meaning that the petitioner need not provide "conclusive" proof of causation, but must demonstrate more than a "possible" or "plausible" causal link.

Another important aspect of the causation-in-fact case law under the Program concerns the factors that a special master should consider in evaluating the *reliability* of expert testimony and other scientific evidence relating to causation issues. In *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), the Supreme Court listed certain factors that federal trial courts should utilize in evaluating proposed expert testimony concerning scientific issues. In *Terran v. Secretary of HHS*, 195 F.3d 1302, 1316 (Fed. Cir. 1999), the Federal Circuit ruled that it is appropriate for special masters to utilize *Daubert*'s factors as a framework for evaluating the reliability of causation-in-fact theories presented in Program cases. One of the factors listed in *Daubert* is whether the scientific theory "has been subjected to peer review and publication." 509 U.S. at 593. The Court noted that while publication does not "necessarily" correlate with reliability, since in some instances new theories will not yet have been published, nevertheless "submission to the scrutiny of the scientific community is a component of 'good science,'" so that the "fact of publication (or lack thereof) in a peer reviewed journal thus will be a relevant, though not dispositive, consideration in assessing the scientific validity" of a theory. *Id*. at 593-94.

A second important factor listed in *Daubert* is the issue of "general acceptance." The Court stated that a "reliability assessment does not require, although it does permit, explicit identification of a relevant scientific community and an express determination of a particular degree of acceptance within that community. * * * Widespread acceptance can be an important factor in ruling particular evidence admissible, and a known technique which has been able to attract only minimal support within the community * * * may properly be viewed with skepticism." 509 U.S. at 594 (citations and internal quotation marks omitted).

II

FACTS

The following facts are taken from Jordan's medical records, and are not in dispute.

A. Jordan's early period [5]

Jordan King was born on September 29, 1997. (Ex. 11, p. 1.) The medical records of his mother's pre-natal care indicate an uncomplicated pregnancy. (Ex. 11, pp. 2 and 7.) The labor that

---

[5]Both parties have filed numerous documents in this case. Petitioners have filed, on various occasions, exhibits numbered 1 through 35. I will refer to those exhibits as Ex. 1, Ex. 2, etc. Respondent has filed, on various occasions, exhibits designated as Ex. A through Ex. AAA. I will refer to those exhibits as Ex. A, Ex. B, etc. In addition, in conjunction with the evidentiary hearing held in May of 2008, both parties also filed other exhibits, separately numbered, as "Petitioners' Trial Exhibits" and "Respondent's Trial Exhibits." I will refer to those as P. Trial Ex. 1, R. Trial Ex. 1, etc.

In addition, "Tr." references will be to the pages of the *corrected* transcript of the evidentiary hearing held on May 12 through May 30, 2008. In this regard, I note that because of the importance of this case to many pending autism claims, the parties agreed to a transcript correction process. The original transcript was filed with this court, in multiple volumes, on July 1 to July 8, 2008. The parties then listened to the digital audio recording of the hearing, and agreed upon an extensive set of corrections to the original transcript. After that review process was complete, the respondent filed with this court, on October 7, 2008, a compact disc containing the parties' agreed corrections. The court reporter was instructed to make those changes, and then a "Revised and Corrected" transcript, containing the parties' corrections, was filed, again in multiple volumes, on October 21 to 24, 2008. Accordingly, "Tr." citations are to the pages of the "Revised and Corrected" transcript. (Also, references to the *Dwyer* transcript are to the revised and corrected version of that transcript.)

I also note that due to the large amount of medical literature filed by the parties in this case, the parties have devised a special system of citation to those documents. Each party has compiled a "reference list" of articles. Petitioners have styled their list as the Petitioners' Master Reference List ("PML"), and respondent's list has been dubbed the Respondent's Master List of Articles ("RML"). The PML now contains 761 items, while the RML contains 523 items. Petitioners filed a compact disc containing items 1 through 664 of the PML on May 6, 2008. Additional compact discs containing additional items added to the PML were filed on August 4, 2008, April 3, 2009, and July 6, 2009. Respondent filed compact discs containing the items of the RML on March 21, April 29, May 23, and October 7, 2008.

Finally, I note that when documents were filed electronically in this case, electronically-generated page numbers appear in the upper-right-hand corner of those documents. However, such electronically-generated page numbers often do not correspond exactly to the page numbers of the exhibits as originally numbered by parties. In this opinion, I will refer to the pages of the expert reports and other exhibits as *originally numbered*, usually at the bottom of the pages.

resulted in Jordan's birth was complicated by the mother's fever of 101°, but was not otherwise remarkable. The records of Jordan's visits to the pediatrician during his first two years of life indicate that his health appeared relatively normal during that period. (Ex. 2, pp. 24-34.) Those records show a few mild illnesses, but mostly normal examinations, with Jordan meeting typical early developmental milestones. Jordan's most significant illness during that period occurred at age 16 months, when he experienced a severe episode of fever, vomiting, and diarrhea that lasted several days. This resulted in an emergency room evaluation on February 6, 1999, at Providence Medical Center, where he received a diagnosis of "viral syndrome." (Ex. 3, pp. 77-78.) In late June and early July of 1999, Jordan suffered a "fever for 3-4 days, as high as 105°," accompanied by vomiting, coughing, and weight loss. (Ex. 2, p. 25.) The medical records also show that Jordan often suffered from diarrhea during much of his infancy. (None of the expert witnesses in this case, however, have opined that either Jordan's chronic diarrhea, or his above-described illnesses in February and June/July 1999, have any relevance to the causation issues in this case.)

Jordan received the typical infant vaccinations during his first two years of life. His initial hepatitis B vaccination was administered in the hospital shortly after his birth. (Ex. 11, p. 4; Ex. 3, p. 31.) On December 1, 1997, at the age of two months, Jordan received several vaccinations, including diphtheria-tetanus-acellular pertussis ("DTaP"), polio ("IPV"), hemophilus influenza ("Hib"), and his second hepatitis B inoculation. (Ex. 3, p. 31; Ex. 2, p. 34.) On February 4, 1998, at his four-month examination, Jordan received his second DTaP, IPV, and Hib vaccinations. (Ex. 3, p. 31; Ex. 2, p. 33.) On April 10, 1998, Jordan's third DTaP, Hib, and hepatitis B vaccinations were administered. (Ex. 3, p. 31.) Jordan received measles/mumps/rubella ("MMR") and varicella vaccinations on October 2, 1998. (Ex. 3, p. 31.) On October 29, 1999, Jordan received his third IPV, as well as his fourth DTaP and Hib vaccinations. (Ex. 3, p. 31.)

A number of those vaccinations--*i.e.*, the DTaP, hepatitis B, and Hib vaccinations--contained a mercury-based preservative known as "thimerosal," which will be discussed at length below.

B. Symptoms and diagnosis of autism

The first indication in the medical records of a developmental problem was recorded on October 25, 1999, when Jordan was 25 months of age. Jordan's pediatrician wrote on that date that Jordan had "no language" at that time, although he had previously used single words. (Ex. 2, p. 23.) The pediatrician recommended that Jordan be evaluated for "possible autism." (*Id.*)

On January 11, 2000, Jordan underwent an examination by a speech and language pathologist, which revealed that he was significantly delayed in language and social skills. (Ex. 7, pp. 10, 15.) "PDD spectrum" was listed as a possible diagnosis. (Ex. 7, p. 10.) Additional evaluations during the following weeks, on January 25, 2000 (Ex. 8, pp. 100-05), February 2, 2000 (Ex. 8, p. 106), February 9, 2000 (Ex. 8, pp. 168-69), February 11, 2000 (Ex. 1, pp. 15-16), and March 13, 2000 (Ex. 8, pp. 84-92), confirmed that Jordan had severe developmental deficits and autism. Subsequent evaluations a few months later, on August 21, 2000 (Ex. 16, pp. 1-2) and August 28, 2000 (Ex. 8, pp. 56-60), again confirmed the diagnosis of autism.

III

BACKGROUND: THE CONTROVERSY CONCERNING VACCINES AND AUTISM, THE "OMNIBUS AUTISM PROCEEDING," AND THE PROCEDURAL HISTORY OF THIS CASE

This case concerning Jordan King is one of more than 5,000 cases filed under the Program in which it has been alleged that a child's disorder known as "autism," or a similar disorder, was caused by one or more vaccinations. A brief history of the controversy regarding vaccines and autism, along with a history of the development of the 5,000 cases in this court, will follow.

A. Autism described

The terms "autism" and "autistic spectrum disorder" ("ASD") have been used to describe a set of developmental disorders characterized by impairments in social interaction, impairments in verbal and non-verbal communication, and stereotypical restricted or repetitive patterns of behavior and interests. (RML 255,[6] pp. 32-33.) Those terms are essentially synonymous with the term "pervasive developmental disorder" ("PDD"), commonly used in medical diagnoses. (*Id*.) The PDD category is further subdivided into five subcategories: autistic disorder, childhood disintegrative disorder ("CDD"), Asperger's Syndrome, Rett's Syndrome, and "pervasive developmental disorder not otherwise specified" ("PDD-NOS"). (RML 255, p. 32.) In this Decision, I will use the terms "autism," "autistic," and "autism spectrum disorder" interchangeably, to refer to the *entire group* of disorders within the broad PDD category. (The specific term "autistic disorder," on the other hand, will be used to refer to the *first specific subcategory* of PDD listed above. (RML 255, p. 33, fn. 3.))

Autism is a condition that is usually recognized during a child's first few years of life, sometimes during the first year, but sometimes not until later years. (RML 255, p. 33.) Autism can vary widely in severity. For some, the condition can be extremely severe and devastating, rendering the autistic individual completely unable to care for himself or herself.

B. Increase in diagnoses, and inception of controversies about potential vaccine causation

Autism was first described in a medical journal by Dr. Leo Kanner in 1943.[7] In recent years, the rate of *diagnosis* of autism has increased dramatically. (RML 255, p. 35.) It is unclear, however, whether the *actual incidence* of autism-- that is, the rate at which new cases occur during a given period of time--has truly changed during that time period. Some experts have suggested that the incidence of the condition is, in fact, substantially on the increase, perhaps due to environmental

---

[6]Institute of Medicine, IMMUNIZATION SAFETY REVIEW: VACCINES AND AUTISM (The National Academies Press 2004). (RML 255.)

[7]Leo Kanner, *Autistic Disturbances of Affective Contact*, 2 NERVOUS CHILD 217 (1943). (RML 270.)

factors. Other experts argue that the increase in diagnoses does *not* represent a real increase in the incidence of the condition, resulting instead from a broadening of the diagnostic criteria for autism, improved recognition of autism, and other factors. (RML 255, p. 35; Ex. M, paras. 65-68.)

In any event, there is no doubt that at this time autism is a relatively common condition, in this country and throughout the world. For example, one survey of studies in the United States around 2002 found that the prevalence rate of autism in this country--that is, the proportion of the population that suffers from autism at a particular time--was about 1 out of 152 children.[8]

Because of the recent increase in diagnoses of autism and the increased public awareness of the condition, some have asked whether environmental factors may have caused an increase in autism. Relevant here are two different theories that have become prominent during the last ten years, in which it is theorized that *childhood vaccinations* may be causing or contributing to autism. First, one controversy arose in 1998 when British physician Dr. Andrew Wakefield and colleagues published an article raising the possibility that the measles-mumps-rubella ("MMR") vaccine might be causing autism. (RML 255, p. 40.) Second, beginning in 1999, a theory emerged that a mercury-based preservative used in a number of childhood vaccinations, known as "thimerosal," might be causing autism. (RML 255, p. 37.)

The emergence of those two controversies led to a large number of claims filed under the Program, each alleging that an individual's autism, or a similar disorder, was caused by the MMR vaccine, by thimerosal-containing vaccines, or by both. To date, more than 5,000 such cases have been filed with this court, and most of them remain pending.

C. The Omnibus Autism Proceeding

1. Inception of the Omnibus Autism Proceeding

To deal with this large group of cases involving a common factual issue--*i.e.*, whether these types of vaccinations can cause autism--the Office of Special Masters (OSM) conducted a number of informal meetings in 2002, including both attorneys who represent many of the autism petitioners, and counsel for the Secretary of Health and Human Services, who is the respondent in each of these cases. At those meetings, the petitioners' representatives proposed a special procedure by which the OSM could most efficiently process the autism claims. They proposed that the OSM utilize a two-step procedure: first, conduct an inquiry into the *general causation issue* involved in these cases--*i.e.*, whether the vaccinations in question can cause autism and/or similar disorders, and if so in what

---

[8]Centers for Disease Control and Prevention, *Prevalence of Autism Spectrum Disorders -- Autism and Developmental Disabilities Monitoring Network, 14 Sites, United States, 2002*, 56 Morbidity and Mortality Weekly Report 12 (Feb. 9, 2007). (PML 586.) (See also Tr. 3636.)

I note also that some more recent studies have found even higher prevalence rates, but those studies were not filed into the record of this case.

circumstances-- and then, second, apply the evidence obtained in that general inquiry to the individual cases. They proposed that a team of petitioners' lawyers be selected to represent the interests of the autism petitioners during the course of the general causation inquiry. They proposed that the proceeding begin with a lengthy period of discovery concerning the general causation issue, followed by a designation of experts for each side, an evidentiary hearing, and finally a ruling on the general causation issue by a special master. Then, the evidence concerning the general causation issue, obtained as a result of the general proceeding, would be applied to the individual cases.

As a result of the meetings discussed above, the OSM adopted a procedure generally following the format proposed by the petitioners' counsel. On July 3, 2002, the Chief Special Master, acting on behalf of the OSM, issued a document entitled the *Autism General Order #1*.[9] That order set up a proceeding known as the Omnibus Autism Proceeding (hereinafter sometimes the "OAP"). In the OAP, a group of counsel selected from attorneys representing petitioners in the autism cases, known as the Petitioners' Steering Committee ("PSC"), was charged with obtaining and presenting evidence concerning the *general issue* of whether those vaccines can cause autism, and, if so, in what circumstances. The evidence obtained in that general inquiry was to be applied to the individual cases. *Autism General Order #1*, 2002 WL 31696785 at *3, 2002 U.S. Claims LEXIS 365 at *8.

The *Autism General Order #1* assigned the initial responsibility for presiding over the Omnibus Autism Proceeding to the undersigned. In addition, I was assigned responsibility for all of the *individual* Program petitions in which it was alleged that an individual suffered autism or a similar neurodevelopmental disorder as a result of MMR vaccines and/or thimerosal-containing vaccines. The individual petitioners in the vast majority of those cases requested that, in general, no proceedings with respect to their *individual petitions* be conducted until after the conclusion of the OAP concerning the *general* causation issue.[10] The plan has been that once the OAP concerning

---

[9]The *Autism General Order #1* is published at 2002 WL 31696785, 2002 U.S. Claims LEXIS 365 (Fed. Cl. Spec. Mstr. July 3, 2002). I also note that the documents filed in the Omnibus Autism Proceeding are contained in a special file kept by the Clerk of this court, known as the "Autism Master File." An electronic version of that File is maintained on this court's website. This electronic version contains a "docket sheet" listing all of the items in the File, and also contains the complete text of most of the items in the File, with the exception of copies of published medical literature that are withheld from the website due to copyright considerations or due to § 300aa-12(d)(4)(A). To access this electronic version of the Autism Master File, visit this court's website at www.uscfc.uscourts.gov. Select the "Vaccine Info" page, then the "Autism Proceeding" page.

[10]Individual petitioners have always had the option to "opt out" of the OAP at any time. In other words, any petitioner who did not want to await the outcome of the OAP could opt to present his own evidence concerning causation to a special master, and obtain a prompt ruling concerning his own causation claim. A few petitioners have voluntarily dismissed their claims. A few others, acknowledging that they do not have evidence demonstrating causation, have asked that a special master file a "ruling on the record," resulting in rulings denying the claims. To date, however, none of the petitioners in the OAP have presented their own *substantive causation evidence*, aside from

the *general* causation issue has concluded, the Office of Special Masters would then deal specifically with the *individual* cases.

In a document filed into the Autism Master File on January 11, 2007, the Chief Special Master made procedural alterations to the Omnibus Autism Proceeding. He added two additional Special Masters, Denise Vowell and Patricia Campbell-Smith, to preside over the OAP along with myself. Since that time, we three special masters have *jointly* resolved *procedural* issues in the OAP, such as discovery motions. The *individual* Program petitions, on the other hand, have been divided among the three special masters. (Under the statutory scheme, a "decision" in an individual Program case is to be issued by a *single* special master. § 300aa-12(d)(3)(A).)

At the inception of the OAP in 2002, the plan was that the PSC would engage in an initial period of discovery, then proceed to a "general causation" hearing in mid-2004. The PSC, however, requested several delays of the "general causation" hearing, in order to pursue additional discovery, and to wait for the results of certain studies. During the years 2002 through 2006, the petitioners made very extensive discovery requests. Ultimately, pursuant to those discovery requests, about 218,000 pages of documents, from the files of a number of government agencies, were supplied to the PSC.

In a document filed into the Autism Master File on July 18, 2006, the PSC proposed that a "general causation" hearing be conducted in June of 2007. Subsequently, in an oral presentation during an OAP status conference held on December 20, 2006, and in a written proposal filed on January 9, 2007, the PSC altered that request in two major respects. First, the PSC proposed that their "general causation" evidence be divided into *three separate theories*: (1) that the *combination* of the MMR vaccine and thimerosal-containing vaccines can cause autism; (2) that thimerosal-containing vaccines *alone* can cause autism; and (3) that the MMR vaccine *alone* can cause autism. Second, the PSC proposed that the PSC utilize a "test case," to be tried in June of 2007, in order to present the PSC's first general causation theory.

2. Plan adopted for hearing the petitioners' causation theories

In response to the PSC's proposal, after discussion at a number of telephonic conferences with counsel from both the PSC and respondent, the three special masters developed a plan for hearing the PSC's theories and evidence. The three special masters agreed that the PSC could, as the PSC desired, divide its "general causation" evidence into three theories, and present the evidence concerning the first theory by utilizing the case of Michelle Cedillo as a "test case" in June of 2007. (See Autism Update filed January 19, 2007, in the Autism Master File.) However, the PSC was also instructed to choose two *additional* "test cases" falling within the same "general causation" theory. The PSC would present its general causation evidence concerning the first theory, along with all evidence specific to the particular case of Michelle Cedillo, in June of 2007. Then, over the next

---

the petitioners in the six "test cases" described below at p. 11 fn.11.

several months, the PSC would present its case-specific evidence concerning the two *additional* test cases. Each of the three special masters would then resolve one of the three test cases. (*Id*.)

Thereafter, under the plan that the three special masters adopted, a similar "test case approach" would be applied to each of the *other two* "general causation" theories of the PSC. That is, the PSC would designate three test cases as to each theory, and the three cases as to each theory would be decided separately by the three special masters. Eventually, however, the PSC elected to present only *two* theories.[11]

3. Execution of Omnibus Autism Proceeding plan to date

Since adopting the general plan described above for hearing the petitioners' causation theories, the three special masters have put that plan into practice. This *King* case has been a major part of that plan.

First, in 2007 lengthy evidentiary hearings were held in three test cases concerning the PSC's *first* "general causation" theory, that the MMR vaccine and thimerosal-containing vaccines can *combine* to cause autism. On February 12, 2009, decisions were issued concerning those three "test cases." In each of those three decisions, the petitioners' causation theories were rejected. I issued the decision in *Cedillo v. Secretary of HHS*, No. 98-916V, 2009 WL 331968 (Fed. Cl. Spec. Mstr. Feb. 12, 2009). Special Master Patricia Campbell-Smith issued the decision in *Hazlehurst v. Secretary of HHS*, No. 03-654V, 2009 WL 332306 (Fed. Cl. Spec. Mstr. Feb. 12, 2009). Special Master Denise Vowell issued the decision in *Snyder v. Secretary of HHS*, No. 01-162V, 2009 WL 332044 (Fed. Cl. Spec. Mstr. Feb. 12, 2009). Each of those three decisions has since been reviewed and affirmed by a judge of this court. *Cedillo*, 89 Fed. Cl. 158 (2009) (Judge Wheeler); *Hazlehurst*, 88 Fed. Cl. 473 (2009) (Judge Wiese); *Snyder*, 88 Fed. Cl. 706 (2009) (Judge Sweeney). (The *Cedillo* and *Hazlehurst* decisions are now on appeal to the U.S. Court of Appeals for the Federal Circuit.)

Second, in late 2007 the PSC selected three "test cases" concerning the PSC's *second* theory of "general causation," the theory that the thimerosal-containing vaccines alone can substantially contribute to the causation of autism. This *King* case was one of the three selected. In late 2007 and 2008, the parties presented their evidence concerning that second theory of "general causation," filing a vast amount of material. (See discussion of the scope of that evidence at pp. 15-16 below.) Much evidence was filed in the form of written expert reports and medical literature articles. Then, additional evidence was presented during evidentiary hearings held in May and July of 2008. On May 12 through 30, 2008, a hearing was held in which both parties filed extensive evidence

[11] Apparently the PSC eventually concluded that the evidence that might have been presented as a third theory has already been presented as part of the PSC's *first theory*, in the *Cedillo*, *Hazlehurst*, and *Snyder* cases. (See the "Notice" filed by the PSC into the Autism Master File on August 7, 2008.) Thus, the current plan for the OAP calls for a total of only *six* "test cases," three for the PSC's first theory, and three for the second theory.

concerning the "general causation" theory, and also evidence concerning the "specific causation" issues in both this *King* case and the case of *Mead v. Secretary of HHS*, No. 03-215V. On July 21 and 22, 2008, the parties presented additional evidence, mainly relating to the "specific causation" issue in the third test case, *Dwyer v. Secretary of HHS*, No. 03-1202V.

All three of the OAP special masters were present during *all* of those 2008 hearings. All three listened to and participated in the questioning of the expert witnesses who presented the general causation evidence. The role of each special master was to fully evaluate all of the "general causation" evidence, and then to apply that evidence to the *specific* test case assigned to that master. (I was assigned the *King* case; *Mead* was assigned to Special Master Campbell-Smith; *Dwyer* was assigned to Special Master Vowell.[12])

Since the conclusion of the evidentiary hearings in those three test cases, the parties have filed extensive post-hearing briefs in all three cases.

It is also important to emphasize that because the three cases were tried as "test cases," each involving both "general causation" and case-specific evidence, the evidentiary records regarding "general causation" in the three cases have necessarily "spilled over" into one another. The parties have agreed that all "general causation" evidence filed into the record of *any* of the three cases may be utilized in the other cases. Thus, copies of the "general causation" evidence from each case have been introduced into the case files of the other two cases.

---

[12]It is important to understand the roles of the three special masters who have jointly presided over the Omnibus Autism Proceeding since January of 2007. The three of us have worked together closely on *procedural* matters in the OAP, such as developing a general schedule for the petitioners' three theories of causation, acting upon the PSC's motions for general discovery relating to the OAP, etc. For example, we jointly issued a ruling on a discovery motion (see Ruling filed into the Autism Master File on May 25, 2007), and jointly issued a number of procedural orders concerning the time for filing documents into the OAP.

However, when it comes to deciding cases, it is clear under the statute that a ruling in an *individual case* is to be made by a *single special master*, based on the record of that individual case. § 300aa-12(d)(3)(A). Accordingly, it should be understood that in deciding the three "test cases" under the PSC's second theory of causation, each special master has *independently* analyzed the evidence of that master's own case and is ruling *independently*. While the "general causation" evidence is common to the three cases, each of us has analyzed that common evidence independently of the other two; each has reached his or her own conclusion.

We did agree that we would issue our rulings concerning the "entitlement" issues in the three cases on the same day. That will enable any courts hearing any appeals from our decisions to have the benefit of reading the analyses of *three different* special masters concerning the *general* causation evidence. The *analyses* reflected in the three rulings, however, were undertaken *separately* and independently.

4. Note concerning usage of an "omnibus proceeding"

The Omnibus Autism Proceeding is not the first time that a special master of this court has utilized an "omnibus proceeding" in order to process a large group of Program cases. On several previous occasions, when faced with multiple cases involving a common issue of "general causation," special masters of this court have worked with petitioners' counsel and respondent's counsel to devise special procedures to more efficiently process the cases. Those situations have been described as "omnibus proceedings."

It is important to understand that the use of an "omnibus proceeding" does not change the fact that *each individual petition is decided individually, on its own merits*. The Vaccine Act contains no provision for "class action" suits, or for any type of adjudication of more than one petition at a time. In each prior "omnibus proceeding," each individual case involved in the proceeding ultimately ended with its own "decision," voluntary dismissal, or other *case-specific* disposition of the case. An "omnibus proceeding," rather, is simply a device to *organize the presentation of evidence*, in cases with common "general causation" issues, in order to avoid duplication of effort. For example, if 100 individual petitioners each rely on Dr. Smith for his theory that Vaccine A can cause Disease B, Dr. Smith might need to repeat the same "general causation" testimony at 100 different hearings. But by using an "omnibus proceeding," opposing counsel and a special master may agree that it makes more sense to have Dr. Smith present that "general causation" testimony *once*, and then have the transcript of that testimony available to be introduced into the records of the other 99 cases. Moreover, in practice, it may happen that after Dr. Smith presents his testimony in the first case and that case is decided, the parties in many of the other 99 cases may then *settle* those cases, without the need for a trial in each case.

For example, I myself presided over an "omnibus proceeding" concerning the "general causation" issue of whether the rubella vaccine can cause chronic arthropathy. I met with counsel representing petitioners whose cases involved that "general causation" issue, and respondent's counsel. Those counsel developed evidence concerning the general causation issue, filed expert reports and medical literature, and then presented oral testimony from the experts at an evidentiary hearing. Based upon that evidence, I filed a published opinion concluding that the rubella vaccine *can* cause chronic arthropathy under certain circumstances, if a case meets certain criteria. *In re Ahern*, No. 90-1435V, 1993 WL 179430 (Fed. Cl. Spec. Mstr. Jan. 11, 1993). Based on that opinion, most of the pending or later-filed cases involving that general causation issue then resolved *without* the need for an individual, case-specific trial. For example, in 70 such cases the parties reached a settlement affording compensation to the petitioner, based upon the similarity of those petitioners' situations to the criteria outlined in the *Ahern* opinion. In 52 other cases, the petitioner either voluntarily dismissed the petition or abandoned prosecution, apparently in light of the fact that the petitioner's case *did not* fit within the stated criteria. In only 31 cases was I required to make a formal ruling concerning whether the petitioner was entitled to an award, and even those cases involved either no trial or a limited trial, because the "general causation" evidence from the omnibus proceeding was available for application to those individual cases. (Ten of those 31 cases were resolved in favor of a petitioner, *e.g.*, *Long v. Secretary of HHS*, No. 94-310V, 1995 WL 470286

(Fed. Cl. Spec. Mstr. July 24, 1995), while in 21 such cases the claim was denied, *e.g.*, *Awad v. Secretary of HHS*, No. 92-79V, 1995 WL 366013 (Fed. Cl. Spec. Mstr. June 5, 1995).) Thus, the rubella/arthropathy "omnibus proceeding" turned out to be a highly successful procedural device. Each individual case was ultimately resolved on its *own merits*, but they were resolved far more efficiently than if we had needed a full-blown trial, with multiple expert witnesses, in each case.[13]

Other "omnibus proceedings" have utilized a "test case" approach. That is, the "general causation" evidence is presented in the context of an evidentiary hearing concerning one *individual case*, and the special master decides the test case. After that decision, the other cases involving the same general causation issue may then settle based on the outcome of the test case, and/or the general causation evidence developed in the test case may be "imported" into the records of the other cases, facilitating the decisions in those cases.[14]

In summary, the important point to note, concerning the OAP and other "omnibus proceedings" that have been used in the Program, is that, even when an "omnibus proceeding" is utilized, *each individual case will still ultimately be resolved individually*, according to the facts and circumstances of that individual case. The "omnibus proceeding" is simply a *procedural tool* that is employed to add efficiency to the process of presenting evidence and evaluating that evidence.

5. Additional procedural history of this King case

Petitioners filed their Program petition in this *King* case on March 14, 2003, and the case was assigned to my own docket on that date. The petitioners utilized the "short-form" autism petition, thereby indicating the desire that case-specific proceedings in this case be deferred indefinitely, pending the outcome of the Omnibus Autism Proceeding. (*See* the Notice Regarding Omnibus Autism Proceeding, filed by the petitioners on April 3, 2003.) Accordingly, at the petitioners' request, during the following four years I did not conduct case-specific proceedings in this case.

As explained above (p. 10), in January of 2007 the Chief Special Master added two additional special masters to the OAP, and the pending autism cases were then divided among the three special masters. As part of that process, on February 22, 2007, this case was reassigned from my docket to the docket of Special Master Campbell-Smith. In late 2007, however, as noted above, this case was

---

[13]In fact, during the above-described 2002 meetings which resulted in the Omnibus Autism Proceeding, it was the *petitioners'* representatives who proposed that the rubella/arthropathy "omnibus proceeding" be used as a model for organizing the autism cases.

[14]Note that the outcome of a "test case" is not formally "binding" on any other case. The parties in subsequent cases are free to submit additional "general causation" evidence that was not presented in the test case. (That is certainly true with respect to these autism test cases.) Thus, a "test case" will be most useful in fostering the settlement or other resolution of additional cases if the parties do a comprehensive job of presenting all of the available "general causation" evidence concerning the causation issue in question. (It appears to me that the parties to this *King* case and the companion *Mead* and *Dwyer* cases have, in general, done such a comprehensive job.)

selected by the Petitioners' Steering Committee (PSC) as one of the three "test cases" for the PSC's *second theory* of general causation. Accordingly, to ensure that one of the three "test cases" was assigned to each of the three OAP special masters, this case was reassigned to my docket on December 18, 2007.

Both parties then filed numerous documents in preparation for the evidentiary hearing in this case. Petitioners filed extensive medical records of Jordan, and an expert report of Dr. Elizabeth Mumper, in December of 2007. Additional medical records, and numerous expert reports for both parties, were filed in early 2008.

A three-week evidentiary hearing, as previously noted, was held in May of 2008, and both parties thereafter filed lengthy post-hearing briefs.[15] Further, as described above, the parties in this case agreed that I should consider the "general causation" evidence from the *Mead* and *Dwyer* cases in resolving this *King* case. Accordingly,"general causation" evidence from *Dwyer* was formally introduced into the record of this case, on a compact disc, via my Order of October 5, 2009. (Because this *King* case and the *Mead* case were tried jointly, all the "general causation" evidence filed in *Mead* was identical to that which was filed in this case, so there was no need to file any evidence from the *Mead* case into the file of this case.)

6. The scope of the record

Finally, I note that much time has passed since the conclusion of the evidentiary hearing in this case in May of 2008. However, two major factors should be recognized.

First, the completion of the combined three-week evidentiary hearing in this *King* case and the *Mead* case in May of 2008 did *not* mark the end of the presentations by the parties relevant to this case. Some additional "general causation" expert testimony was presented during the evidentiary hearing in the *Dwyer* case in July of 2008. Then, the parties' process of *briefing* this case extended into July of 2009.

Second, the evidentiary record, based upon which I have decided this case, is massive. This record far exceeds any evidentiary record that I have seen in other Program cases, with the exception of the record in the three test cases concerning the PSC's *first theory* of autism causation. A few statistics may give a flavor of the amount of material involved. The parties filed a total of 26 expert reports in this *King* case and the companion *Mead* and *Dwyer* cases. At the evidentiary hearings, 17 expert witnesses testified during the combined *King/Mead* hearing, and two during the *Dwyer* hearing. The hearing transcripts totaled more than 3200 pages for the *King/Mead* hearing, plus more

---

[15]Those post-hearing briefs will be cited as follows:

Petitioners' Post-Hearing Brief, filed on April 5, 2009----------cited as P-1.
Respondent's Post-Hearing Brief, filed on June 2, 2009----------cited as R-1.
Petitioners' Reply to the Respondent's Post-Hearing Brief, filed on July 12, 2009---------cited as P-2.

than 300 pages in *Dwyer*.[16] And the petitioners filed more than 1000 pages of Jordan King's medical records in this *King* case alone.

In addition, the amount of *medical literature* filed into the records of the three cases was staggering. In the three cases, the parties filed more than 1200 medical journal articles, medical textbook excerpts, or other items of medical literature (even after excluding from the count those documents that were filed in more than one case). Some of those items were extremely lengthy. (*E.g.*, RML 6, 617 pages; RML 255, 199 pages; PML 443, 342 pages.) The total number of pages of those documents runs well into the tens of thousands of pages. And most of those documents are densely packed with technical information.

Further, the material involved here is extremely complex as well. The medical records, expert testimony, and medical literature involve many different subspecialties of biology and medicine, including neurology, immunology, molecular biology, toxicology, genetics, and epidemiology.

In sum, the massive nature of the evidentiary record, along with the complexity and variety of the scientific issues involved, necessitated the lengthy time period spent in preparing this Decision.

IV

ISSUES TO BE DECIDED

As noted above, the petitioners in this case do not contend that Jordan suffered a "Table Injury." Their contention, instead, is one of "causation-in-fact," also known as "actual causation." The petitioners and their expert witnesses contend that Jordan's autism was caused, at least in substantial part, by the thimerosal-containing vaccines that he received during his early months of life. Petitioners' overall causation theory[17] in this case can be summarized as follows. (See

---

[16]The transcripts of the *King/Mead* hearing and the *Dwyer* hearing contain gaps in pagination. For example, volume one of the *King/Mead* transcript ends at p. 287, while volume two begins at p. 351. Pages 288 through 350 do not exist. Accordingly, while the last page of the *King/Mead* transcript is numbered as page 4374, in fact there are only 3281 pages of actual text in that transcript.

[17]In science, the words "theory" and "hypothesis" may have different meanings. A "hypothesis" is an idea or supposition that is *proposed* to explain an event or phenomenon. (Tr. 1978-80; *Dorland's Illustrated Medical Dictionary* 899 (30th ed. 2003) (hereinafter *Dorland's*).) The term "theory," on the other hand, can be used in science to describe a doctrine or set of principles that has been *developed*, based on *observations*, to explain a set of data. (Tr. 1979-80; *Dorland's* at 1893.) Thus, the term "theory" may imply a doctrine that has been developed and supported by *evidence*, in contrast to a "hypothesis" that is merely an untested *idea*.

In this strict scientific nomenclature, then, the petitioners in this case technically are

especially P-1, pp. 11-14.) Petitioners contend that once the thimerosal in the thimerosal-containing vaccines that Jordan received during his first years of life entered his body, the mercury contained in the thimerosal, known as "ethylmercury," separated from the other component of thimerosal (thiosalicylate), and some of that ethylmercury made its way into his brain. (P-1, p. 18.) Once in the brain, the ethylmercury converted into another form of mercury, "inorganic mercury," and that inorganic mercury triggered a process of "neuroinflammation," including "oxidative stress," in Jordan's brain. (P-1, pp. 12, 19.) The neuroinflammation impaired and disrupted Jordan's brain function, resulting in his autistic symptoms. (P-1, pp. 12-13.)

The petitioners contend that such an autism causation process has occurred in many children. They do not argue that the thimerosal is the *sole* cause of the autism in such cases, but that the thimerosal *substantially contributes* to the causation of autism, in individuals who for genetic reasons are especially *susceptible* to that causation process. (P-1, p. 13.) They contend that this causation process occurs in individuals who suffer from a particular subcategory of autism known as "regressive autism." (P-1, pp. 13-14.)

Respondent's experts strongly disagree with the contentions of the petitioners' experts. Respondent's experts argue that there is no good evidence to indicate that thimerosal-containing vaccines ever play any role in causing autism, and that all of the many competent epidemiologic studies done around the world have uniformly found *no association* between thimerosal-containing vaccines and autism. Those experts also see no reason to conclude that thimerosal-containing vaccines played any role in causing *Jordan King's* own autism.

In the following sections of this Decision, I will discuss the different parts of petitioners' theory. In section V, I will explain that petitioners failed to demonstrate any merit in their "general causation" theory; that is, they failed to demonstrate that thimerosal-containing vaccines *can* contribute to the causation of autism. In section VI, I will explain that petitioners failed in their attempted "specific causation" showing in this case; that is, they failed to demonstrate that thimerosal-containing vaccines likely[18] *did* substantially contribute to the causation of *Jordan's own autism*. In section VII, I will explain how my previously-stated analysis of petitioners' factual contentions fits within the context of the legal test set forth in *Althen v. Secretary of HHS*, 418 F. 3d 1274 (Fed. Cir. 2005). Finally, in section VIII, I will set forth some concluding comments.

---

presenting "hypotheses" concerning causation, not "theories." However, in ordinary everyday use of the English language, the word "theory" is often used to describe what a scientist would call a "hypothesis." Moreover, the parties to this case have usually referred to the petitioners' "theory" or "theories" concerning causation. Accordingly, in this Decision, I will also refer to petitioners' "theory" or "theories" concerning causation.

[18]It is the *petitioners' burden* to demonstrate that it is "more probable than not" that the vaccination was a substantial factor in causing Jordan's autism. *See* § 300aa-13(a)(1)(A). Under that standard, the existence of a fact must be shown to be "more probable than not." *In re Winship*, 397 U.S. 358, 371 (1970) (Harlan, J., concurring).

It may be noted that I could have elected *not* to discuss and resolve, in this Decision, *all* of the issues raised by petitioners in this case. For example, as I will discuss below, petitioners' expert Dr. Kinsbourne explained that while he believes that mercury in the brain could cause autistic behavior, he does not know *how much* mercury it would take to cause such a process; he relies on another of petitioners' experts, Dr. Aposhian, for the opinion that thimerosal-containing vaccines could result in *enough* mercury in the brain to produce such a process. For reasons that I will explain in detail below, I have rejected Dr. Aposhian's opinion. Therefore, since I have rejected one of the *assumptions* upon which Dr. Kinsbourne based his causation opinion, the foundation for Dr. Kinsbourne's opinion has disappeared, and, therefore, there is no strict necessity that I evaluate the soundness of Dr. Kinsbourne's opinion in *other* respects. Nevertheless, I have chosen to include a full evaluation of Dr. Kinsbourne's analysis, for the purpose of providing guidance for the other pending autism cases.

In other words, I have attempted in this Decision to provide a complete analysis of *all* of the petitioners' major causation contentions raised in this case, whether strictly necessary for resolution of this case or not, in order to provide guidance for the remaining autism cases.

V

PETITIONERS HAVE NOT DEMONSTRATED THAT THIMEROSAL-CONTAINING VACCINES *CAN* CONTRIBUTE TO THE CAUSATION OF AUTISM

A. Introduction

As noted above, the petitioners in this case have attempted to make the "general causation" showing that thimerosal-containing vaccines *can* contribute to the causation of autism, in individuals who for genetic reasons are especially *susceptible* to that causation process. After fully considering that contention, I must reject it. I find that the petitioners' evidence offered in support of that contention is not persuasive, and that the respondent's evidence offered in contradiction to that contention is quite persuasive.

1. Thimerosal in vaccines

Thimerosal is a compound consisting of mercury and another component, thiosalicylate, that has been used in vaccines, and in other biological and pharmaceutical products, since the 1930s. (RML 255, p. 36; PML 87, p. 1.) It is used, in very small amounts, as a preservative in multi-dose vials of vaccine, in order to prevent fungal and bacterial contamination. (RML 255, pp. 36-37.) Thimerosal has been used in more than 30 vaccines licensed in the United States. (*Id*. at 37.) During the 1990s, it was used in a number of vaccines given to infants in the United States, including the

vaccines for diphtheria/tetanus/pertussis ("DTP"), diptheria/tetanus/acellular pertussis ("DTaP"), hemophilus influenza ("Hib"), and hepatitis B.[19] (*Id*.)

Jordan King received thimerosal-containing vaccines on a number of occasions. He received hepatitis B vaccinations on September 29, 1997, December 1, 1997, and April 10, 1998. (Ex. 3, p. 31.) He received DTaP vaccinations on December 1, 1997, February 4, 1998, April 10, 1998, and October 29, 1999. (*Id*.) And he received Hib vaccinations on December 1, 1997, February 4, 1998, April 10, 1998, and October 29, 1999. (*Id*.)

2. Petitioners' theory summarized

As noted above, the petitioners' overall "general causation" theory in this case can be summarized as follows. (P-1, pp. 11-14.) Petitioners note that the thimerosal in thimerosal-containing vaccines, received by infants during their early months of life, after entering the body breaks down into its component parts, one of which is ethylmercury; some of that ethylmercury then makes its way into the brain and is converted into inorganic mercury.[20] (P-1, p. 12.) They contend that such inorganic mercury can, in susceptible individuals, trigger a process of "neuroinflammation," including "oxidative stress," in the infant's brain. (*Id*.) The neuroinflammation, they contend, can impair and disrupt the infant's brain function, resulting in autistic symptoms. (P-1, pp. 12-13.)

The petitioners contend that such an autism causation process has occurred in many children. They do not argue that the thimerosal is the *sole* cause of the autism in such cases, but that the thimerosal *substantially contributes* to the causation of autism, in individuals who for genetic reasons are especially susceptible to that causation process. (P-1, p. 13.) They contend that this causation process occurs in individuals who suffer from a particular subcategory of autism known as "regressive autism." (P-1, pp. 13-14.)

3. Respondent's argument, and points in dispute, summarized

Certain parts of petitioners' general causation theory are *not* disputed by respondent. There is no dispute about the following points. Thimerosal, as contained in a thimerosal-containing vaccine, is a combination of two substances, thiosalicylate and a form of mercury known as "ethylmercury." (RML 255, p. 36; PML 182, p. 14.) Once thimerosal enters a vaccinee's body, it

---

[19]Between 1999 and 2002, thimerosal was phased out of most of the vaccines commonly given to infants in the United States. (RML 255, pp. 37-39.) However, thimerosal remains in some influenza vaccines, which are sometimes given to infants. (*Id.* at 38, Table 1.)

[20]To describe this form of mercury that remains in the brain, the experts in this case sometimes used the term "inorganic mercury" and sometimes used the term "mercuric mercury." Actually, "mercuric mercury" is a specific subcategory of "inorganic mercury." (Tr. 155.) For simplicity's sake, I will use the term "inorganic mercury."

quickly breaks down into its component parts, so that the mercury portion of the thimerosal is now in the form of ethylmercury, no longer bound to the thiosalicylate. (PML 87, p. 1; PML 182, p. 15; Tr. 173-74.) Nor is it disputed that some of that ethylmercury can enter the brain, and can eventually be converted to another form of mercury, "inorganic mercury," in the brain. (Tr. 234-35.)

There is also no dispute that mercury, in certain forms and at certain doses--much higher doses than the amounts contained in thimerosal-containing vaccines--can be harmful to humans. Further, there is no dispute that evidence of neuroinflammation has been found in the brains of some autistic children, by a credible group of medical researchers.

However, while acknowledging the accuracy of these small parts of the petitioners' overall causation theory, the respondent's experts strongly dispute many other elements of the petitioners' theory. Respondent's experts explained that all humans have some amount of mercury in their brains from a number of non-vaccine sources, without harm, and those experts argued that there is no evidence that the *extremely small* amounts of mercury in thimerosal-containing vaccines would make any significant difference in the overall amount of mercury in a child's brain, or can cause any harm to the brain.

Respondent's experts also pointed out what they believe to be many gaps, inaccuracies, and errors in the individual parts of the petitioners' theories, and in the testimony offered by each of the petitioners' expert witnesses. For example, respondent's experts explained that while evidence of neuroinflammation has been found in the brains of some autistic children, medical researchers have as yet not discovered whether such inflammation plays a role in *causing* autism. Those experts also argued that there is no evidence that *inorganic mercury* in the brain causes neuroinflammation, and that even if inorganic mercury in the brain could cause autism, the evidence shows that infants have substantially more inorganic mercury in the brain from *other sources* than from the very small amounts of mercury in thimerosal-containing vaccines.

Respondent's experts also pointed out that the petitioners' theory seems unlikely in light of certain basic scientific understandings about the causation of autism, including the facts (1) that autism is very strongly genetic in origin, (2) that the only established non-genetic factors in causing autism are *prenatal* exposures, and (3) that autopsy studies indicate that the abnormal features of autistic brains are features that of necessity would arise during the *early prenatal* period. Respondent's experts argued further that when, on occasions in the past, mercury exposure (involving much greater amounts of mercury) has been harmful to the human brain, the actual symptoms involved have been nothing like autism.

Respondent's experts also stressed that the theory that thimerosal-containing vaccines can contribute to the causation of autism has been addressed by many "epidemiologic" studies performed by researchers around the world, and that all of the competent studies have found *no association* between thimerosal-containing vaccines and autism.

All of those points raised by respondent's experts will be discussed in detail below.

4. Organization of my analysis

I have organized my discussion of the petitioners' "general causation" theory in this case as follows. In part B of this section V, I describe the expert witnesses for both sides who have provided the principal evidence concerning this "general causation" issue. In part C, I describe the primary reasons for rejecting the petitioners' overall "general causation" argument, as presented by their principal expert Dr. Kinsbourne. In parts D, E, and F, I describe the flaws in the testimony of petitioners' additional experts, Dr. Aposhian, Dr. Deth, and Dr. Mumper. Next, part G discusses the issue of the *epidemiologic studies* concerning thimerosal and autism, in which section I analyze the testimony of the petitioners' epidemiologic expert, Dr. Greenland. In part H, I explain that my conclusion is supported by reports of numerous distinguished medical groups. Finally, in part I, I summarize my conclusion concerning the petitioners' "general causation" theory.

B. Qualifications and experience of the experts

Before discussing the primary reasons for rejecting the petitioners' overall "general causation" theory, I will describe the qualifications and experience of the expert witnesses who testified for both parties in this case, and set forth my evaluation concerning the relative qualifications of those experts.

1. Petitioners' experts

a. Dr. Marcel Kinsbourne, M.D.

The petitioners' primary expert concerning "general causation" was Dr. Marcel Kinsbourne, a medical doctor who has a distinguished background in pediatric neurology. Dr. Kinsbourne obtained his medical degree in 1955 from Oxford University in Britain, and is a member of the Royal College of Physicians of London. (Ex. 26, p. 1.) He has had a number of appointments to teach, research, and/or provide clinical treatment at Oxford University, the Harvard Medical School, the Massachusetts General Hospital, and other distinguished institutions. (*Id*.) He was chief of the pediatric neurology division at the Duke University Hospital. (*Id*.) He served for ten years as the director of the Behavioral Neurology Department at the Eunice Kennedy Shriver Center in Massachusetts. (Tr. 773; Ex. 26, p. 1.) In his practice, Dr. Kinsbourne has had extensive involvement with autism, attention deficit disorder, and other disorders of mental development. (Tr. 770-71.) He has authored a chapter concerning developmental disorders in seven editions of the MENKES TEXTBOOK OF CHILD NEUROLOGY, including a section about autism. (Ex. 26, p. 2; Tr. 773-74.) He has authored or co-authored over 400 medical and scientific articles, textbook chapters, books, and monographs. (Ex. 26, p. 2.) He has served on the editorial boards of many scientific and medical journals. (Ex. 26, p. 2.)

b. Dr. H. Vasken Aposhian, Ph.D.

The petitioners' expert in toxicology, Dr. H. Vasken Aposhian, has had a long and distinguished career as a Ph.D. researcher and academic in toxicology issues. He received his Ph.D.

in physiological chemistry from the University of Rochester in 1953, and has held academic positions at the Vanderbilt University School of Medicine, the Stanford University School of Medicine, and the Tufts University School of Medicine, among other institutions. (Ex. 25, p. 37.) Since 1975, he has been a professor of pharmacology, and later molecular and cellular biology as well, at the University of Arizona School of Medicine. (*Id*.) Dr. Aposhian has published more than 200 peer-reviewed scientific articles. (Tr. 139.) He has been employed as a consultant concerning heavy metal toxicity by the Environmental Protection Agency, the National Institute for Environmental Health Services, the National Institutes of Health, and many international agencies. (Ex. 25, pp. 39-40.)

c. Dr. Richard Deth, Ph.D.

Dr. Richard Deth has had a long career as a Ph.D. university professor and researcher in pharmacology. He received his Ph.D. in pharmacology from the University of Miami in 1975, and obtained post-doctoral training at the University of Leuven in Belgium. (Ex. 23, p. 1; Ex. 30, p. 1.) He has taught pharmacology at Northeastern University since 1976, advancing to a full professorship in 1987. (Ex. 30, p. 1.) He served as director of that university's pharmacy program for four years, and as chairman of its department of pharmaceutical sciences for two years. (Ex. 30, p. 2.) As a pharmacological researcher, he has published more than 60 peer-reviewed scientific articles and book chapters. (Ex. 23, p. 1.) His laboratory research has focused on autism-related issues for about five years. (Tr. 497.)

d. Dr. Elizabeth Mumper, M.D.

Dr. Elizabeth Mumper is a medical doctor who has practiced pediatrics for more than 25 years. Dr. Mumper received her medical degree in 1980 from the Medical College of Virginia. (Ex. 29, p. 1; Tr. 1191-92.) She completed her residency in pediatrics at the University of Virginia in 1983, and served as Chief Resident there from 1983-84. (Ex. 29, p. 2.) She has held medical teaching positions at the University of Virginia and the Virginia College of Osteopathic Medicine. (Ex. 29, p. 2.) Beginning in the year 2000, when she established a private medical practice known as Advocates for Children, she further specialized in the treatment of pediatric neurodevelopmental and behavioral disorders. (Ex. 13, p. 1; Tr. 1190-91.) She has been the medical director of the Autism Research Institute since 2005. (Ex. 13, p. 1.) In 2007, she founded the Rimland Center, a treatment and research facility for neurodevelopmental disorders. (Tr. 1194.)

e. Dr. Sander Greenland, Ph.D.

Dr. Sander Greenland has outstanding credentials as a Ph.D. expert in epidemiology. He received his doctorate in public health, with a major in epidemiology, in 1978 from the UCLA School of Public Health. (Ex. 31, p. 1; Ex. 24, p. 2.) He has taught epidemiology at the UCLA School of Public Health since 1979, attaining a full professorship in 1989. (Tr. 73-74; Ex. 31, p. 1.) He holds professional certifications as a Fellow of the American Statistical Association and the Royal Statistical Society. (Ex. 31, p. 2.) Numerous government agencies and private corporations

have employed him as a consultant, including the National Institute of Environmental and Health Sciences (NIEHS), the Environmental Protection Agency (EPA), the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), and the World Health Organization (WHO). (Ex. 24, p. 3.) He has served as an editor or referee for numerous scientific and medical journals. (Ex. 24, pp. 3-4.) He has published more than 500 scientific articles, abstracts, letters, and book chapters. (Ex. 24, p. 3.) He is co-author of the textbook MODERN EPIDEMIOLOGY, which is used for instruction at many universities.[21] (Tr. 73; Ex. 24, p. 1.)

2. Respondent's experts

a. Dr. Michael Rutter, M.D.

Dr. Michael Rutter has more than 50 years of experience as a medical doctor, including extraordinary experience in the area of autism. Dr. Rutter received his medical degree at the University of Birmingham, England, in 1955. (Ex. HH, p. 1.) He specialized in neurology, pediatrics, and general medicine, obtaining the British equivalent of board certification in internal medicine (1958), and then in psychological medicine (1961). (Ex. GG, p. i.) He also holds the British equivalent of a Ph.D. in psychology, and board certification in that discipline. (Tr. 3236-37.) Dr. Rutter participated in the early development of standardized methods for assessing children with autism. (Tr. 3242.) He also pioneered in the use of epidemiology to study psychiatric problems in childhood. (Ex. GG, p. i.) His clinical practice, although decreased in recent years, involved diagnosing and treating hundreds of children with autism, and following their progress through adolescence and adulthood. (Tr. 3243.) During the course of his career, he has published more than 400 articles and more than 200 book chapters about child psychiatry and development, and he has authored more than 40 books concerning psychiatry and the genetic component of psychiatric problems. (Tr. 3245.) He is a member of the editorial board of numerous psychiatric and psychological journals. (Tr. 3246.)

b. Dr. Robert Rust, M.D.

Dr. Robert Rust is a medical doctor specializing in pediatric neurology, with a long history of treating patients with autism. Dr. Rust received his medical degree from the University of Virginia in 1981, then completed an internship and residency specializing in pediatrics at the Yale University School of Medicine. (Ex. JJ, pp. 2-3.) He holds board certifications in pediatrics, and in neurology with special qualification in child neurology. (Tr. 2352.) He has been a medical faculty

[21]I note that in the *Dwyer* case the petitioners filed a report of another expert, Dr. John F. Haynes, Jr., M.D., a board-certified medical toxicologist. (*Dwyer* Ex. 15.) Dr. Haynes' extremely brief report states that it is "offered in the individual vaccine injury compensation claim of Colin Dwyer," and indicates the opinion that the thimerosal-containing vaccines administered to Colin Dwyer resulted in his autism. (*Id*. at 2.) The report, however, offers only a few sentences of very vague and unpersuasive explanation concerning *why* Dr. Haynes holds that opinion. Thus, while I examined the report, I find that it offers no credible support for the petitioners' "general causation" argument in this case.

member at the Washington University School of Medicine, the University of Wisconsin School of Medicine, the Harvard Medical School, and the University of Virginia School of Medicine. (Ex. JJ, pp. 3-4.) He was the director of the Child Neurology Training Program at Boston Children's Hospital and Harvard Medical School from 1997 to 1999. (Ex. JJ, p. 4.) In 2003, he became director of the Child Neurology Training Program at the University of Virginia School of Medicine. (Ex. JJ, p. 4.) During each of his academic assignments, Dr. Rust practiced as a pediatric neurologist in hospitals and clinics affiliated with the university medical school. (Ex. JJ, p. 4.) During the course of his career, he has been involved with treating many hundreds of children with autism, and he still manages 80 to 100 such cases today. (Tr. 2355.) He serves on the editorial boards of several scientific journals, including *The Journal of Child Neurology* and *Pediatric Neurology*, while serving as a reviewer for many others. (Tr. 2352-53.) His area of research includes autism, epilepsy, and pediatric degenerative conditions. (Tr. 2354.) He has published more than 50 peer-reviewed articles, and more than 50 book chapters and reviews, concerning pediatric neurology. (Tr. 2353.)

c. Dr. Eric Fombonne, M.D.

Dr. Eric Fombonne is a medical doctor specializing in psychiatry who has extensive experience in treating autistic children, and considerable experience in the epidemiologic study of autism. Dr. Fombonne received his medical degree from the University of Paris in 1978. (Ex. N, p. 1; Ex. M, para. 2.) He specializes in psychiatry, including sub-specialties in child and adolescent psychiatry, receiving the French equivalent of board certification in that field. (Ex. N, p. 1; Tr. 3608-09.) His interest in autism research commenced in 1984, as planner for a national epidemiologic survey of childhood psychiatric disorders in France. (Tr. 3610; Ex. M, para. 4.) He has academic and clinical experience since then in both Britain and Canada. (Ex. N, pp. 6-8; Ex. M, paras. 4-9.) He has been head of the division of child and adolescent psychiatry at McGill University in Montreal, and director of the department of psychiatry at the Montreal Children's Hospital. (Ex. N, p. 7; Tr. 3614.) Dr. Fombonne has published about 170 scientific articles, four books, and 34 textbook chapters concerning childhood developmental disorders. (Tr. 3621; Ex. M, para. 14.) He has worked in the field of autism since 1986, including a substantial clinical practice for many years focusing on the evaluation and treatment of autistic children. (Tr. 3609, 3619-20.) He is Co-Director of the Autism Spectrum Disorders Clinic in Montreal. (Ex. N, p. 7.) He has been involved in developing the diagnostic criteria utilized internationally in diagnosing autism. (Tr. 3617-18.) He regularly reviews research papers for numerous professional journals, and served nine years as associate editor of the *Journal of Autism and Developmental Disorders*. (Ex. M, para. 12.) He has been involved in the design, execution, and analysis of ten epidemiologic studies concerning autism, involving patients in five different countries. (Ex. M, para. 8.)

d. Dr. Catherine Lord, Ph.D.

Dr. Catherine Lord is a Ph.D. psychologist with very extensive experience in treating autistic children and in studying autism. Dr. Lord received her Ph.D. in psychology from Harvard University

in 1976. (Ex. X, p. 1.) Since then, she has engaged in the clinical practice of child psychology, and has taught child psychology at a series of universities and medical schools in the United States, Canada, and Britain. (Ex. X, pp.1-2.) She is board-certified in clinical psychology. (Tr. 3536.) She served from 1993 to 2001 as director of the Developmental Disorders Clinic at the University of Chicago. (Ex. X, p. 2.) Since 2001, Dr. Lord has been the director of the University of Michigan Autism and Communication Disorders Center, while serving as a professor in the departments of psychology and psychiatry. (Ex. X, pp.1-2.) Throughout her career, her primary research activity has been the long-term study of children with autism, in order to develop diagnostic criteria to quantify their behavioral deficits. (Ex. W, pp. 1-2; Tr. 3544-47.) She has played a leading role in creating the standardized clinical assessment instruments and questionnaires that are used to diagnose autism. (Ex. W, p. 2; Tr. 3538-39, 3548-52.) She is one of four scientists comprising the strategic planning committee for autism research for the National Institutes of Health. (Tr. 3537-38.) Dr. Lord has special experience concerning the phenomenon of "regression" in autism, and has participated in the development of diagnostic criteria for autistic regression. (Tr. 3447-48.) During more than 30 years of practice as a clinician and researcher, she has participated in the diagnosis and treatment of more than 4000 autistic patients, with ages ranging from 12 months to 56 years. (Tr. 3541-44.) She has published more than 125 peer-reviewed articles related to child development and psychology, nine books, and 61 book chapters. (Tr. 3552-53.) She also serves on the editorial boards of six child psychology or autism-related journals, and as a reviewer for many others. (Tr. 3553-54.)

e. Dr. Jeffrey Brent, M.D., Ph.D.

Dr. Jeffrey Brent is a medical doctor with impressive credentials in the specialty of medical toxicology. He received a Ph.D. in biochemistry in 1976, and a medical degree in 1980. (Ex. H, p. 4; Ex. G, p. 1.) He has served at the University of Colorado in a number of medical and academic positions. (Ex. H, p. 1-3; Ex. G, pp. 1-2.) He is one of only about 350 board-certified medical toxicologists in the United States. (Tr. 1797.) He has published over 200 peer-reviewed articles, book chapters, and abstracts. (Tr. 1787.) He has served as an editor for several professional toxicology journals, and as a peer-reviewer for many other medical and scientific publications. (Ex. H, p. 7; Ex. G, pp. 5-6.) In his private practice, Dr. Brent frequently treats patients suffering from mercury toxicity. (Tr. 1792-95.)

f. Dr. Thomas Kemper, M.D.

Dr. Kemper is a medical doctor specializing in neuropathology, who has personally performed some of the most important research into the pathology of the autistic brain. Dr. Kemper received his medical degree at the University of Illinois School of Medicine in 1958. (Ex. V, p. 1.) He has been a member of the medical school faculty at both the Harvard Medical School and the Boston University School of Medicine, lecturing in neurology, anatomy, pathology, and neuropathology. (Ex. V, p.1; Tr. 2794.) He also maintained a clinical practice as a neuropathologist at the Boston City Hospital until about 2002. (Tr. 2793-94.) Dr. Kemper has published about 170 scientific articles, including about 30 concerning autism. (Tr. 2795.) He has been a reviewer for

many medical and neuropathology journals. (Tr. 2795-96.) He has devoted a considerable portion of his career to the study of the neuropathogenesis of autism. (Tr. 2799.) He and a colleague, Dr. Margaret Bauman, performed some of the pioneering research concerning the pathology of the autistic brain, publishing their first article in 1985. (Tr. 2797-98; see Bauman and Kemper articles listed in Ex. V.)

g. Dr. L. Jackson Roberts, M.D.

Dr. L. Jackson Roberts is a medical doctor who has specialized in internal medicine and pharmacology, and who has impressive experience in the area of "oxidative stress," an area emphasized by the petitioners' expert Dr. Deth. Dr. Roberts received his medical degree from the University of Iowa in 1969, and became board-certified in internal medicine. (Tr. 2154.) In 1975 he commenced his specialization in clinical pharmacology. (Ex. DD, p. 2.) Since that time, he has conducted research and taught at Vanderbilt University, becoming a full professor of pharmacology and medicine in 1986. (Ex. DD, p. 2.) His research has focused primarily on oxidative stress and oxidative injury. (Ex. CC, p. 2.) He has published over 340 articles, abstracts, and book chapters, among which more than half are devoted to oxidative stress. (Tr. 2160.) He holds seven patents, four of which relate to oxidative stress, and several others are pending. (Ex. DD, p.6.)

h. Dr. Steven Goodman, M.D., Ph.D.

Dr. Steven Goodman is a medical doctor with impressive credentials in the area of epidemiology. Dr. Goodman received his medical degree from New York University in 1981, and was board-certified in pediatrics. (Tr. 3065-66; Ex. P, p. 2.) He also holds a master's degree in biostatistics and a Ph.D. in epidemiology from the Johns Hopkins School of Public Health. (Ex. P, p. 1; Ex. O, p. 2.) He is currently a professor at the Johns Hopkins School of Medicine, where he devotes his time to epidemiology, and is the director of the division of biostatistics in the department of oncology. (Tr. 3066, 3069.) He is a former member of the Institute of Medicine Committee on Immunization Safety, in which capacity he reviewed the evidence concerning the thimerosal/autism controversy, and helped produce two reports on that subject in 2001 and 2004. (Ex. O, pp. 1-2.) He has published more than 100 scientific articles, reviews, and book chapters, including many with a focus on epidemiology and clinical research. (Tr. 3069-70; Ex. O, p. 2.) He is also editor of the journal *Clinical Trials: Journal of the Society for Clinical Trials*, and senior statistical editor for *Annals of Internal Medicine*. (Ex. O, p. 3.)

i. Dr. Patricia Rodier, Ph.D.

Dr. Patricia Rodier is a Ph.D. psychologist with extensive research experience concerning both autism and mercury toxicity. Dr. Rodier received her Ph.D. in psychology from the University of Virginia in 1970. (Ex. EE, p. 1.) She has taught psychology at both the University of Virginia and the University of Rochester. (Ex. FF, p. 1.) She has researched extensively concerning the development of the human nervous system, leading to the publication of more than 60 scientific articles. (Tr. 2911-13.) She is a reviewer for multiple scientific journals concerning toxicology,

autism, psychobiology, genetics, and psychiatry. (Tr. 2913-14.) Some of her experiments at the University of Rochester involved studying the sensitivity of human infants to methylmercury while in the womb, and she has also researched and published articles about autism since the 1980s. (Tr. 2914-15, 2917.) For the last ten years, she has been the director of two research projects funded by the National Institutes of Health focusing on genetic studies and treatments for autism, which involves managing 30 to 40 investigators with Ph.D.s or medical degrees. (Tr. 3007-08.)

j. Dr. Jeffrey Johnson, Ph.D.

Dr. Jeffrey Johnson is a Ph.D. pharmacologist with excellent credentials in that discipline. Dr. Johnson received his Ph.D. in molecular and environmental toxicology from the University of Wisconsin in 1992. He has served on the pharmacology faculty at the University of Kansas Medical Center and the University of Wisconsin School of Pharmacy. (Ex. R, p. 1.) The primary focus of his research is neurodegenerative diseases. (Tr. 2199.) His resume lists more than 60 peer-reviewed scientific publications (Ex. R, pp. 6-9), and he is a frequent reviewer for medical journals (Tr. 2200).

k. Dr. Dean Jones, Ph.D.

Dr. Dean Jones is a Ph.D. biochemist with important credentials concerning the "oxidative stress" issue raised in this case. Dr. Jones received his Ph.D. in Medical Biochemistry at the University of Oregon Health Sciences Center in 1976. (Ex. S, p. 1.) He has taught biochemistry at the Emory University School of Medicine since 1979, where he is a Professor of Medicine. (Ex. T, p. 1.) Over the course of his career, he has published more than 325 peer-reviewed scientific articles, reviews, and book chapters. (Tr. 2696.) At least 100 of his original research publications focus on oxidative stress and sulfur metabolism. (Tr. 2696-97.) He currently directs two laboratories that investigate clinical biomarkers and oxidative stress. (Tr. 2695-96.) He is a regular reviewer for several scientific journals. (Tr. 2694.)

l. Dr. Richard Mailman, Ph.D.

Dr. Richard Mailman is a Ph.D. researcher with an impressive background in neuropharmacology and neurotoxicology, who provided testimony relevant to the issues raised by Dr. Deth's presentation. Dr. Mailman received a Ph.D. in physiology and toxicology from North Carolina State University in 1974. (Ex. BB, p.1; Tr. 1975.) Since 1978 he has conducted research and taught psychiatry, pharmacology, neurology, and medical chemistry at the University of North Carolina School of Medicine. (Ex. BB, p. 2.) His scientific research has been funded by the National Institutes of Health for 28 years. (Ex. AA, p.1; Ex. BB, p. 4.) The results of his research have been published in more than 170 peer-reviewed articles and more than 50 textbook chapters and reviews. (Tr. 1977; Ex. BB, pp. 5-21.) He has served on the editorial boards of ten scientific journals, and reviews articles for many others. (Ex. AA, pp. 1-2; Tr. 1977.)

m. Dr. Manuel Casanova, M.D.

Dr. Manuel Casanova is a medical doctor specializing in psychiatry and neuropathology. He received his medical degree in 1979, and is board-certified in neurology. (Ex. I, pp. 1-2.) He has served as a professor of psychiatry and neurology and as a researcher at the Medical College of Georgia. (Ex. J, pp. 2-4.) He is a peer-reviewer for many scientific and medical journals. (*Id*. at 7-8.) He has published more than 150 peer-reviewed scientific articles, as well as numerous book chapters and other scientific writings. (*Id*. at 20-61.) His publications include several very important articles describing abnormal formations in the brains of autistic children. (See articles described at Ex. I, pp. 6-10.) Dr. Casanova filed an expert report, but did not testify orally. His expert report did offer additional support for my conclusions stated at p. 39 below, but, because he did not testify orally, his evidence has played only a minor role in my resolution of this case.

n. Dr. Bennett Leventhal, M.D.

Dr. Bennett Leventhal is a medical doctor specializing in child psychiatry, who has very extensive experience in diagnosing and treating autistic children and in teaching about autism. (*Dwyer* Tr. 206-16.) He was a co-author of an important autism diagnosis protocol, has published more than 120 peer-reviewed articles on child psychiatry and autism, and is a reviewer for a number of medical journals. (*Dwyer* Tr. 217-20.) Dr. Leventhal provided an expert report and hearing testimony only in the *Dwyer* case, not in this *King* case.[22] (*Dwyer* Ex. CC; *Dwyer* Tr. 205-289.)

3. The respondent's experts have far superior qualifications and experience.

As set forth below, after comparing the qualifications and experience of the experts of the two parties, I conclude that those of the respondent's experts [23] are *far superior* to those of the petitioners' experts.

a. Primary experts

First, concerning the *overall general causation issue* in this case--*i.e.*, whether it is likely that thimerosal-containing vaccines contribute to the causation of autism--the principal witnesses for

---

[22]I note that based upon some answers that he gave in his hearing testimony in *Dwyer*, Dr. Leventhal, in approaching causation issues, may have been requiring a higher level of proof, closer to scientific certainty, rather than the "more probable than not" standard that is applicable concerning Vaccine Act causation issues. Accordingly, his testimony has not played any significant role in my analysis of this case. However, he certainly is a well-qualified and knowledgeable expert in his specialty area, so I have cited his testimony as *additional* support concerning a few *specific* points that were established by the respondent's experts in this case.

[23]Respondent originally filed expert reports of two additional experts, Drs. Magos and Clarkson. (Exs. K, Y.) However, respondent eventually elected to withdraw those reports, and those reports have played *no role* in my analysis of this case.

respondent certainly have superior credentials. The petitioners' primary witness concerning general causation, Dr. Kinsbourne, to be sure, is a medical doctor with impressive credentials in pediatric neurology, a field highly relevant to autism, a neurologic disorder. Dr. Kinsbourne did publish two articles concerning autism during the 1980s. (Tr. 773, 910.) Moreover, Dr. Kinsbourne has written, for an important neurologic textbook, a chapter on developmental disorders, with a section concerning autism. (Tr. 773, 848.) However, those credentials concerning autism pale in comparison to those of respondent's principal witnesses on "general causation," especially those of Drs. Fombonne, Rutter, Rust, and Lord. Dr. Rust, like Dr. Kinsbourne, is a pediatric neurologist, and Drs. Fombonne and Rutter are psychiatrists--autism is considered a psychiatric as well as a neurologic disorder. Dr. Lord is a Ph.D. psychologist, a member of the psychology discipline that also does much of the day-to-day diagnosis and treatment of autism.

In terms of clinical experience with autistic children, all four of these principal experts of respondent have *far more experience* than Dr. Kinsbourne in treating autistic patients, particularly in recent years. Dr. Kinsbourne acknowledged that he has not had an active clinical pediatric practice, treating autistic children or any other children, for the past 18 years. (Tr. 910.) In contrast, Dr. Rust has had an extensive clinical practice treating many autistic patients since the mid-1980s, and continuing to the present day. (Tr. 2355.) Dr. Fombonne has maintained, from the 1980s to the present, a substantial clinical practice focusing specifically on autistic children. (Tr. 3619-20.) Dr. Lord has had a very active clinical practice for over 30 years to the present, participating in the diagnosis of over 4,000 autistic children. (Tr. 3541-44.) And Dr. Rutter has had a clinical career of more than 40 years involving extensive diagnosis and treatment of autism, and still maintains a clinical practice involving autistic patients, though substantially reduced in recent years. (Tr. 3243-44.)

Moreover, even more important is the contrast between Dr. Kinsbourne and respondent's principal witnesses in terms of *intensive focus*, *study*, *and research concerning autism*. While Dr. Kinsbourne did *not* testify that autism has been a particular focus of his medical career, Drs. Fombonne, Rutter, and Lord obviously have made the study of autism a primary object of their very long research and clinical careers. A review of their résumés and testimony makes it plain that all three of those experts have spent much of their careers in an intense focus upon autism. (Ex. M, paras. 1-14; Ex. N; Ex. W, pp. 1-2; Ex. X; Ex. GG, pp. i-ii; Ex. HH; Tr. 3236-49, 3535-58, 3607-25.) All three, for example, have been important figures in the development of the standardized methods and criteria for diagnosing and assessing children with autism. Drs. Rutter and Fombonne have been leading participants for many years in the *epidemiologic* study of autism, while Dr. Lord has also been the principal investigator in a major epidemiologic study of autism. Indeed, a review of their resumes and testimony indicates that Drs. Fombonne, Rutter, and Lord are among the *leading* experts concerning autism in the medical community. In contrast, nothing in the record of this case indicates that Dr. Kinsbourne has even a remotely comparable background in the study of autism.

b. Expertise concerning specific topics

In addition, concerning virtually all of the important *specific topics* of the expert testimony in this case, the credentials of the respondent's experts are distinctly superior.

For example, concerning the topic of *autopsy studies* of autism, and the lessons that can be learned about the causation of autism from such studies, respondent offered evidence from Dr. Kemper and Dr. Casanova. Dr. Kemper is clearly one of the leading experts in this area, in which he has participated since the early 1980s, as he and his colleague Dr. Baumann performed some of the pioneering research concerning the autistic brain. (Tr. 2997-98.) Similarly, Dr. Casanova has published several important articles describing abnormal features of the autistic brain. (See articles described at Ex. I, pp. 6-10.) Petitioners offered no experts with comparable experience.

Concerning the general topic of *toxicology*, the petitioners' expert, Dr. Aposhian, certainly has impressive experience and credentials, as reflected in the description of his experience set forth above. However, the respondent's corresponding expert, Dr. Brent, has even more impressive qualifications to opine in this area. Dr. Brent, unlike Dr. Aposhian, is a *medical* doctor. Further, Dr. Brent is a *medical toxicologist*, which means that he has specific and extensive medical training concerning the effects of poisons on the human system. (Tr. 1781-82, 1796-97.) He is one of only about 350 board-certified medical toxicologists in the United States (Tr. 1797), and he has experience in treating patients with actual mercury toxicity (Tr. 1792).

Another important aspect of this case concerned the views of the petitioners' expert Dr. Deth concerning the topic of "oxidative stress" and related issues. Dr. Deth, as set forth above, does have solid credentials as a Ph.D. pharmacologist and academic/researcher. However, the credentials of the five experts of respondent who provided the main analysis of Dr. Deth's arguments--Drs. Roberts, Brent, Jones, Mailman, and Johnson--are even more impressive. Drs. Jones, Mailman, and Johnson all have credentials as Ph.D. researchers similar to those of Dr. Deth in terms of length of experience, but Drs. Jones and Mailman have been far more prolific than Dr. Deth in terms of production of published scientific articles, textbooks, and other publications; Drs. Jones and Mailman have about 325 and about 220 publications, respectively, compared to about 63 for Dr. Deth. (Ex. 23, p. 1; Ex. BB, pp. 5-21; Tr. 1977, 2696.) And Dr. Roberts and Dr. Brent, in addition to highly distinguished academic and publications backgrounds, with about 340 and 200 scientific publications respectively, are also *medical doctors*, unlike Dr. Deth. (Tr. 1782, 1787, 2154, 2160.)

Moreover, it is notable that even in the *specific areas* stressed by Dr. Deth concerning "oxidative stress" and "sulfur metabolism," two of respondent's experts have credentials that are substantially more impressive than those of Dr. Deth. That is, Dr. Jones has authored far more scientific publications regarding these topics than Dr. Deth, since about 200 of Dr. Jones' publications deal with sulfur metabolism, and about 100 of his publications constitute original research articles that address oxidative stress. (Tr. 2696-97.)

And, even more remarkably, Dr. Roberts since 1990 has dedicated his research intensively to the specific area of oxidative stress, with about 180 publications in that area alone. (Tr. 2160.)

As a final example, in the area of *epidemiology*, there is, again, a significant advantage to respondent's experts. To be sure, the petitioners' expert, Dr. Greenland, does have superb credentials as an epidemiologist in *general*, as evidenced by his co-authorship of an important epidemiologic textbook. However, respondent's expert epidemiologist Dr. Goodman also has outstanding credentials as a general epidemiologist. And, more importantly, respondent's experts Dr. Fombonne and Rutter have outstanding credentials in the *specific* area of the epidemiology of *autism*, an area in which Dr. Greenland does *not* claim any special experience.

4. Summary concerning qualifications of experts

Of course, I must stress that the weighing of the relative credentials of the respective parties' experts is *not* necessarily a determinative factor in *any* Vaccine Act case. To the contrary, a Vaccine Act factfinder *need not* automatically adopt the view of the expert or experts with more experience or more striking academic credentials. Sometimes an expert with lesser experience or credentials may offer superior analysis, and may therefore prove to be more persuasive.

In this case, the superiority in expert credentials is certainly *not* the decisive factor in my analysis. In this case, the *testimony* of the respondent's experts, concerning virtually every issue, was simply better explained, more logical, and backed by far greater scientific evidence than that of the petitioners' experts. Accordingly, the outcome of my analysis would be the same *regardless* of the credentials of the experts.

Nevertheless, in this case it is simply noteworthy that respondent's experts, *in addition* to offering more persuasive testimony, also do possess substantially superior experience and background concerning the causation issues in this case.[24]

C. Primary reasons for rejecting petitioners'/Dr. Kinsbourne's overall "general causation" theory

As explained above, the petitioners' primary expert witness concerning their "general causation" case--that is, their *overall theory* that thimerosal-containing vaccines *can* contribute to the causation of autism--is Dr. Kinsbourne. As noted, Dr. Kinsbourne is the only medical doctor presented by the petitioners who attempted to set forth a general theory as to how the thimerosal in

[24]Program decisions have often noted that *one factor* to be considered, in evaluating conflicting expert testimony, is the experience and credentials of the respective experts. *See, e.g., Hopkins v. Secretary of HHS*, 84 Fed. Cl. 530, 541 (2008); *Shepperson v. Secretary of HHS*, No. 05-1064V, 2008 WL 2156748, at *14 (Fed. Cl. Spec. Mstr. April 30, 2008); *Doe 11 v. Secretary of HHS*, No. 99-212V, 2008 WL 4899356, at *7 (Fed. Cl. Spec. Mstr. Oct. 29, 2008), *aff'd* 87 Fed. Cl. 1 (2009).

thimerosal-containing vaccines might possibly contribute to the causation of autism.[25] Therefore, the *petitioners'* overall causation theory is essentially *Dr. Kinsbourne's* overall causation theory.

To be sure, as will be seen below (see especially pp. 32-33), even Dr. Kinsbourne failed to provide an opinion vouching for the validity of *parts* of petitioners' overall theory, leaving those parts essentially *unsupported* by *any* expert testimony of a medical doctor. Nevertheless, in the following pages, I will sometimes refer to "Dr. Kinsbourne's theory" of general causation or "petitioners' theory" of general causation to mean the same thing--*i.e.*, to mean the *overall* causation theory suggested by Dr. Kinsbourne, and adopted by the petitioners in this case as their causation theory.

Thus, in the next 22 pages, I will articulate and explain the most important reasons for rejecting the petitioners', and Dr. Kinsbourne's, overall causation theory.

1. Dr. Kinsbourne's opinion supports only <u>part</u> of petitioners' general causation theory.

One important point is that, very significantly, Dr. Kinsbourne did *not* actually state the opinion that thimerosal-containing vaccines *can* contribute to the causation of autism. His opinion is much more limited than that. He indicated that his role, as an expert in this proceeding, was merely to suggest a "mechanism"[26] by which *inorganic mercury*, in the brain of a child, *might*

---

[25]Petitioners' experts Dr. Greenland, Dr. Aposhian, and Dr. Deth did attempt to provide support for petitioners' theory as to certain specific points, but they are not medical doctors, and they did not, in any event, offer an *overall* general causation theory. Petitioners' expert, Dr. Mumper, on the other hand, is an M.D., and her testimony did generally indicate her view that thimerosal *can* contribute to the causation of autism, since she testified that thimerosal-containing vaccines likely *did* contribute to the autism of Jordan King, as well as the autism of William Mead and Colin Dwyer. However, as will be discussed in detail below, Dr. Mumper did not provide any *significant explanation* as to *why*, in general, she believes that thimerosal-containing vaccines can contribute to causing autism. Her testimony, rather, was presented specifically for the purpose of stating the "specific causation" conclusion that thimerosal-containing vaccines likely *did* contribute to the causation of the autism of Jordan King, William Mead, and Colin Dwyer, and she generally did not attempt to provide evidence concerning the "general causation" issue.

[26]To be sure, it is *not* the burden of the petitioners to demonstrate the "mechanism" by which thimerosal-containing vaccines could contribute to autism. *Knudsen v. Secretary of HHS*, 35 F. 3d 543, 549 (Fed. Cir. 1994). In other words, in some Vaccine Act cases a petitioner might be able to provide sufficient evidence that Vaccine A can cause Injury B, via evidence such as "challenge-rechallenge" evidence or epidemiologic studies, *without* demonstrating the causal *mechanism*. However, where, as here, the petitioners do offer evidence concerning a mechanism of injury, it is appropriate for the special master to evaluate that evidence. Indeed, in some cases evidence of a plausible mechanism could be an important part of a successful causation showing.

In this case, however, the petitioners simply have not offered persuasive evidence of *any* type that thimerosal-containing vaccines can contribute to the causation of autism. And the "mechanism"

possibly provoke a reaction by the brain's immune system, producing "neuroflammation" which could disrupt the child's brain function and thereby result in autistic behavior. (*E.g.*, Tr. 842, 886; Ex. 26, pp. 3, 24.)

Thus, Dr. Kinsbourne's opinion, even if persuasive, would provide only limited support to the petitioners' overall "general causation" theory. That is, Dr. Kinsbourne is merely opining that *some amount* of inorganic mercury in the brain, from *whatever* source, could prompt a neuroinflammatory condition, which could result in autistic behavior. He expressly does not claim to know *how much* inorganic mercury it would take to cause such a neuroinflammatory condition; or, *how much* inorganic mercury would be delivered to a child's brain by a childhood course of thimerosal-containing vaccines; or whether the amount of inorganic mercury sent to the brain by a typical course of thimerosal-containing vaccines would be *enough* inorganic mercury to provoke the type of neuroinflammatory response that he proposes. (*E.g.*, Tr. 859-72, 888-90, 944-45.) Dr. Kinsbourne expressly leaves it to *another expert*, the petitioners' toxicologist Dr. Aposhian (who is not a medical doctor), to make the determinations concerning *how much* inorganic mercury in the brain it would take to prompt the neuroinflammatory response, and whether a typical course of thimerosal-containing vaccines would direct a *sufficient amount* of inorganic mercury to the brain to provoke such a response. (*E.g.*, 859-60, 862-63, 866-67, 871, 886, 888-90.)

Thus, even if I were to find Dr. Kinsbourne's testimony to be *completely convincing*--which I certainly do not--that still would *not* be sufficient to demonstrate that thimerosal-containing vaccines can contribute to the causation of autism. The petitioners' additional witness, Dr. Aposhian, would still need to offer persuasive evidence that the typical course of thimerosal-containing vaccines would deliver a *sufficient amount* of inorganic mercury to the brain to cause such a process. And, for reasons set forth below (pp. 66-69), I conclude that Dr. Aposhian failed completely to make a persuasive case on that point.

Therefore, to repeat, because Dr. Aposhian has been unable to offer persuasive testimony concerning *his* part of the petitioners' theory, then Dr. Kinsbourne's theory, even if found to be completely convincing, would still not provide significant support to the petitioners' overall causation theory.

2. Dr. Kinsbourne testified only that his theory was "possible," not that it was "probable."

Second, it is noteworthy that even concerning his very limited proposition that some unknown amount of mercury in the brain might result in autistic behavior, Dr. Kinsbourne's testimony was extremely tentative. Not only did he acknowledge that his theorized process was certainly not scientifically proven, but he also could not say even that his theory was "probable" or "likely." To the contrary, Dr. Kinsbourne was careful to state that his theory was "possible," that

---

evidence of Dr. Kinsbourne has proved to be no more persuasive than any of the petitioners' other causation evidence.

it "might" or "could" be true, or that his theory was one theory, among many, that is worthy to be "considered."

For example, in his written report, Dr. Kinsbourne explained that he was setting forth a "viable candidate mechanism" to explain how mercury in the brain might contribute to autism. (Ex. 26, p. 17.) The word "candidate" indicates that he was offering the theory as one of *several possible* theories. He added that his theory was "medically reasonable," not that it was medically probable. (*Id*.)

In his oral testimony, Dr. Kinsbourne again was careful to stress the tentative nature of his opinion. He stated that thimerosal, because it is a source of mercury that might enter the brain, should be "considered" as a "potential" contributor to autistic behavior. (Tr. 779.) He stated that mercury in the brain, from whatever source, "should be considered" for a list of items that "might" cause neuroinflammation in the human brain. (Tr. 812.) Repeatedly, he stated that mercury in the brain "could" cause neuroinflammation. (Tr. 814, 867.) He remarked that the question of whether thimerosal-containing vaccines could cause neuroinflammation was a question "worth taking seriously." (Tr. 868.) He noted that "I have to consider mercury as one of the multiple possible causes" of neuroinflammation in autistic patients. (Tr. 871.) He stated that mercury is a "potential" cause of neuroinflammation. (Tr. 886.) He emphasized that he was offering a "possible mechanism." (Tr. 4111.)

At one point, after a question concerning the "conclusion" of his report, Dr. Kinsbourne stated that "no, I didn't reach a conclusion. I've told you that what I was offering was a mechanism of injury in general causation." (Tr. 886.)

It is noteworthy that in his written report, Dr. Kinsbourne, in summarizing his opinion, broke the aspects of his opinion into several sentences. (Ex. 26, p. 24.) He began by stating that it is his opinion, "to a reasonable degree of medical probability," that a series of thimerosal-containing vaccines can result in an accumulation of inorganic mercury in the brain. (*Id*.) It is hardly surprising that he could describe *that initial part* of his theory as "medically probable," since it is *undisputed* by respondent's experts that some of the mercury in thimerosal can end up as inorganic mercury in the brain. In the rest of his summary paragraph, however, Dr. Kinsbourne did *not* give opinions to the level of "medical probability." In contrast, he stated only that such mercury in the brain "may" trigger an inflammatory response in some children. (*Id*.) Dr. Kinsbourne then stated, in the following paragraph, that it is "medically reasonable to consider" thimerosal-containing vaccines as a possible causative factor in an individual case of "regressive autism." (*Id*.)

Thus, the fact that the petitioners' primary expert concerning "general causation" can state only that the major elements of his theory are "possible," not "probable," is a reason to be cautious about the reliability of that theory.

3. No medical doctor testified that thimerosal-containing vaccines can contribute to causing autism, while providing an overall explanation as to why such causation might occur.

As demonstrated above, Dr. Kinsbourne never opined that thimerosal-containing vaccines *can* contribute to the causation of autism. (See pp. 32-33 above.) And even concerning those *parts* of petitioners' overall "general causation" theory for which Dr. Kinsbourne did provide testimony, he could state only that his theorized mechanism was "possible," not that it was "probable." (See pp. 33-34 above.)

Therefore, it is important to note, *no medical doctor* testified that thimerosal-containing vaccines *can* contribute to the causation of autism, while providing an overall explanation as to *why* such causation might occur.

This point becomes evident by summarizing the testimony of each of the petitioners' five expert witnesses in this case. Dr. Kinsbourne, as explained above, strictly limited his testimony, and did *not* testify that thimerosal-containing vaccines can contribute to causing autism. Dr. Aposhian and Dr. Deth did opine that thimerosal-containing vaccines can contribute to causing autism, but neither is a medical doctor. Dr. Mumper, on the other hand, is a medical doctor, and her testimony did generally indicate her view that thimerosal *can* contribute to the causation of autism, since she testified that thimerosal-containing vaccines likely *did* contribute to the autism of Jordan King. However, as will be discussed in detail below, Dr. Mumper did not provide any *significant explanation* as to *why*, in general, she believes that thimerosal-containing vaccines can contribute to causing autism. (Moreover, as will also be discussed in detail below, the testimony of Drs. Aposhian, Deth, and Mumper was not persuasive in any event.) Finally, Dr. Greenland, also a non-physician, gave testimony limited to a certain theoretical epidemiologic point, and he did not indicate an opinion, either way, as to whether thimerosal-containing vaccines can contribute to the causation of autism.

Therefore, it is significant to note that, after years of assertions by the Petitioners' Steering Committee that thimerosal-containing vaccines can contribute to causing autism, when it came time for the attorneys of the Petitioners' Steering Committee to finally present their best evidence for that causation assertion, the petitioners were unable to supply the testimony of *even one* medical doctor who was willing *both* to opine that it is probable that thimerosal-containing vaccines *can* contribute to causation autism, and to provide a general explanation of *why* that might be the case. It seems to me that the failure of the petitioners to present the testimony of any such medical doctor speaks volumes concerning the merit of their overall "general causation" theory.

4. Dr. Brent's points

Respondent's expert Dr. Brent, as noted above, has impressive credentials as a medical toxicologist. Dr. Brent made several related but distinct points that strongly contradict petitioners' general causation theory.

Dr. Brent did not dispute that mercury can be toxic to humans in some circumstances, depending on its form and the amounts involved. However, he explained that virtually all substances can be harmful if given in large enough doses, so that the key to whether a substance will be harmful in a particular setting is the "dose"--*i.e.*, the amount given. (Tr. 1799-80; Ex. G, pp. 13-14.) His testimony stressed that there is no reason to think that the very small amounts of mercury contained in thimerosal-containing vaccines would be of harm to infant brains.

Dr. Brent explained that all humans, like all animals, have small but measurable amounts of mercury in their brains from natural sources, including airborne sources and, chiefly, dietary sources, and those small amounts do *not* harm the individuals, as long as they stay below a certain threshold. (Tr. 1802-05.) Dr. Brent explained that autopsy studies have shown that normal human brain mercury levels are in the range of two to 30 or 40 parts per billion, averaging about 15 parts per billion. (Tr. 1818, 4335.) The amount of mercury that American infants would get from their typical course of thimerosal-containing vaccines in the first months of life, he said, would add only about two to three parts per billion. (Tr. 1818-19, 1810-11.) And studies have shown that there is no observed effect of mercury on the human brain until the brain mercury level reaches at least 150 to 200 parts per billion, perhaps higher. (Tr. 1819-20, 1885; RML 294, p. 701, figure 9.) Therefore, Dr. Brent explained, there is no reason to think that the very small amounts of mercury reaching the brain as a result of thimerosal-containing vaccines would cause any type of harm.[27] (Tr. 1823, 1885.)

Dr. Brent's second important point concerned the *type* of neurological problems known in the past to be caused by mercury, which involved mercury exposures involving much greater amounts of mercury than contained in thimerosal-containing vaccines. Dr. Brent explained that in such instances, the symptomatology involved was *nothing like autism*. (Ex. G, pp. 9-11.)

---

[27]Dr. Brent in his oral testimony did not explain exactly how he calculated the figure of two to three parts per billion. However, in his supplemental report that he filed after the hearing (in response to Dr. Aposhian's post-hearing supplemental report), Dr. Brent indicated that the calculation was derived in part by using data from the Burbacher infant monkey study (discussed at pp. 65-66 below). (See Ex. PP, p. 5. In fact, that page indicated that in his updated post-hearing calculation Dr. Brent arrived at a slightly lower figure, of 1.2 parts per billion (see sentence in bold).) Petitioners have not refuted these parts-per-billion estimates of Dr. Brent, and his calculation approach indicated in the supplemental report appears basically sound to me. However, I note that an argument could possibly be made that Dr. Brent slightly erred in his calculation, by failing to take into account the fact that during the 1990s thimerosal was administered to human infants in several stages over a six-month period during which the infants' weight gradually increased, whereas Dr. Brent based his calculation only on the infants' weight at six months of age. I do not reach a firm conclusion as to whether Dr. Brent's figure of two to three parts per billion was slightly inaccurate for that reason. But even if he did slightly err in that regard, the error would *not* change the basic analysis. Even if the mercury from thimerosal-containing vaccines in the first six months of life contributed five or even ten parts per billion of mercury to an infant's brain, rather than two to three parts per billion, there would still be no harmful effect. That is, as explained above, studies have shown that there is no observed effect of mercury on the human brain until the brain mercury level reaches at least 150 to 200 parts per billion, perhaps higher. (Tr. 1819-20, 1885; RML 294, p. 701, figure 9.)

Dr. Brent also pointed out that there are certain islands--the Seychelles and the Faroe Islands--in which the people consume far more seafood than typical human populations, and, as a result, have far higher levels of mercury in the brain. Yet those populations do *not* experience greater rates of autism. (Tr. 1819-22, 1897-99.)

These points of Dr. Brent were not refuted by petitioners, and offer strong reasons to doubt the petitioners' causation theory.

5. Studies of toxic effects of mercury contradict petitioners' theory.

Four more of respondent's experts also testified, as did Dr. Brent, that in prior instances in which mercury exposure has led to neurotoxicity, the neuropathological findings and the symptoms were *quite different* from those of autism.

Dr. Kemper, the neuropathologist, explained that the neuropathological findings in cases of neurotoxicity from mercury are quite distinct from the neuropathological findings in autism. (Ex. U, pp. 8-9; Tr. 2840-45.) He noted that while mercury in toxic amounts is known to destroy specific types of neurons in particular parts of the brain--specifically the visual cortex, the auditory cortex, the motor cortex, and the sensory cortex--no such destruction has been observed in autopsies of autistic brains. (Ex. U, p. 8; Tr. 2840-41.) He stated that in mercury toxicity cases, in the brain granule cells are destroyed while Purkinje cells are relatively preserved, but that is the exact opposite of what is observed in autism. (Tr. 2842; Ex. U, pp. 8-9.) Dr. Kemper also explained that autism and mercury toxicity affect *different* parts of the cerebellum portion of the brain. (Ex. U, pp. 8-9.)

Dr. Kemper further testified that the *clinical* symptoms of mercury neuroxicity, including sensory neuropathy, loss of visual field, and ataxia, are not observed in autism. (Tr. 2844-45.) He added that while autistic children typically experience abnormally large head growth in the early months of life, that is inconsistent with the experience with mercury toxicity, which would make brains (and thus heads) *smaller*. (Tr. 2840; Ex. U, pp. 4-6.)

Similar testimony was presented by Dr. Rodier, who has considerable research experience concerning autism. Dr. Rodier further explained how the symptoms of mercury poisoning are very different from those of autism. (Ex. EE, pp. 3-4; Tr. 3012-17.)

Dr. Casanova, another medical doctor with extensive experience in the neuropathology of autism, reiterated one of Dr. Kemper's points, that the larger-than-normal brain of autistics in their early months of life *contrasts* with the experience in mercury toxicity, which causes smaller brains. (Ex. I, pp. 8-9.)

Finally, Dr. Rust, the neurologist, also pointed out that the pathology and symptoms of autism differ considerably from those found in instances of mercury neurotoxicity. (Ex. II, pp. 3-4, 13.)

In sum, in prior instances in which mercury exposure has led to neurotoxicity, the neuropathological findings and the symptoms were quite different from those of autism. This fact adds another reason to be skeptical of the petitioners' theory advanced in this case.

6. Petitioners' theory seems improbable in light of accepted scientific understandings concerning the causation of autism.

It is certainly true that there is still very much about the causation of autism that medical scientists do not yet understand. However, it is also true that the issue of the causation of autism has been studied intensively for many years, and much has been learned. Respondent's experts argued that petitioners' general causation theory advanced in this case seems improbable in light of certain accepted scientific understandings concerning the causation of autism. For the reasons set forth below, I find that argument to be persuasive.

a. Three basic scientific understandings concerning the causation of autism

Three basic points concerning the causation of autism, which are well-accepted and not disputed by the petitioners in this case, are relevant here. The first basic point is that there is a *very strong genetic component* to the causation of autism. (RML 255, pp. 33-34, 127; Ex. M, paras. 53-55; Ex. GG, para. 14; Tr. 3272-75, 3777.) This understanding of the strong genetic component of autism results from numerous medical studies. Family studies show that when a person has autism, members of that person's family are much more likely to also suffer from autism than nonrelated persons (at least 10 times more likely). (RML 255, p. 34; Ex. M, para. 53.) Twin studies show that among *fraternal* twins, who share 50% of their genes, if one twin has autism, the second twin will have a chance of having autism of about five percent, which is substantially higher than the risk of an average person; but among *identical* twins, who share 100% of their genes, the chance of the second twin having autism would be much greater, about 70%. (RML 255, p. 34; Ex. M, para. 54.) Taken together, the family and twin studies indicate clearly that autism is strongly genetic in character.

In this regard, however, there are two important qualifications. First, the evidence indicates that while autism is *strongly* genetic, it is not *exclusively* genetic. For example, even among identical twins, who share 100% of their genes, in a small percentage of instances one twin experiences autism and the other does not, indicating that non-genetic factors may play at least some role in some cases. Secondly, it must be stressed that at this time scientists are able to identify a *particular gene* (or set of genes), as the cause of the autism, in only a small percentage of the cases of autism, perhaps 5 to 20%. (Tr. 851, 2376, 2531, 3266; Ex. M, para. 47.) While the family and twin studies described above certainly indicate that many other cases of autism must have genetic origins, at this time it is not possible to pinpoint *which* other specific cases have genetic origins.

The second basic point is that some specific *non-genetic* factors have been identified and accepted as factors in causing autism, but those consist of exposures during the *early prenatal* period. (RML 255, p. 33; Ex. M, para. 58; Tr. 3019.) Specifically, *in utero* exposure to thalidomide,

valproic acid, misoprostol, ethanol, and rubella virus infection have been found to increase the risk of autism. (RML 255, p. 33; Ex. M, para. 58; Ex. EE, paras. 14-15; Tr. 3019.) Importantly, the evidence indicates that those exposures cause interference with fetal developmental that takes place at *specific time periods* early in the prenatal period. For example, thalidomide and valproic acid cause damage occurring between 20 and 24 days after conception, while misoprostol and rubella virus infection affect the fetus during the first 12 weeks of gestation. (Ex. M, para. 58; Ex. EE, paras. 15-16; RML 255, p. 33; Tr. 3019.)

The third basic point is that autopsy studies, comparing brains of autistic children to those of non-autistic children, indicate that the autistic brains show a number of different abnormal features that of necessity would have occurred during specific parts of the *prenatal* period, as the unborn child developed. Several different well-qualified experts on behalf of respondent described those findings at length, explaining in detail why development of those abnormal brain features must have occurred during the early prenatal period. (Ex. M, paras. 58, 60-61 (Dr. Fombonne); Ex. I, pp. 3-8 (Dr. Casanova); Ex. EE, pp. 6-7, Tr. 3024-27 (Dr. Rodier); Ex. U, pp. 1-4, Tr. 2810-32 (Dr. Kemper); see also RML 255, pp. 33-34 (Institute of Medicine report).) The petitioners did not provide any evidence to refute that testimony of respondent's experts.

b. The petitioners' argument in this regard

The petitioners in this case do not dispute that genetics plays a large role in the causation of autism. They argue, rather, that it is likely that genetics and thimerosal-containing vaccines can *interact* to result in autism in an individual child. That is, they argue that genetic factors likely make some infants' brains *susceptible* to damage, and then the thimerosal-containing vaccines become the additional factor that causes the individual to become autistic. (P-1, pp. 54-58.)

c. The accepted scientific understandings make petitioners' theory seem unlikely.

i. General discussion

The petitioners are correct that the existing evidence supports the idea that some cases of autism may be a result of a genetic/environmental interaction. That is, the existing evidence indicates, as respondent's witnesses acknowledged, that autism is likely *not 100%* genetically determined. For example, even among identical twins, who share 100% of their genes, the outcomes concerning the existence or the severity of autism are not always exactly the same. Moreover, evidence also indicates, as noted above, that certain environmental exposures during the *early prenatal period* also appear to play a causative role in autism.

However, the petitioners' causation theory at that point takes a *huge leap* from the existing evidence, by asserting that, since it is known that autism is not 100% genetic, and that some *prenatal* exposures seem to contribute to autism, we can therefore infer that the thimerosal-containing vaccines constitute another environmental factor that can contribute to the causation of autism. At that point, the petitioners' argument goes far beyond the existing evidence. Moreover, the three

accepted points concerning the causation of autism, set forth above, make the petitioners' general causation theory seem quite improbable, in two ways. First, we know for certain that *genetic* factors and *prenatal* exposures can contribute to causing autism, while the evidence concerning the possibility of causation by *postnatal* factors is weak, as will be discussed. This point, of course, certainly does not *rule out* the possibility of causation by a particular postnatal factor, such as thimerosal-containing vaccines, but it does make one *cautious* about attributing causation to *any* postnatal factor. Secondly, as noted above, autopsy studies strongly indicate that autism results from abnormal brain development *prior to birth*. That finding is consistent with either genetic causation or causation by early prenatal environmental exposures, but it is *inconsistent* with causation by vaccines that are received after birth.

ii. Possibility of causation by postnatal factors in general

In their post-hearing briefs, the petitioners have pointed to a few items of medical literature suggesting that postnatal factors, *in general*, can contribute to the causation of autism. (P-1, pp. 54-58; P-2, p. 7.) I note also that two of petitioners' experts, Drs. Kinsbourne and Aposhian, briefly discussed the fact that the condition known as "herpes encephalitis" has been proposed as a possible postnatal cause of autism. (Tr. 482-83; 793.) A brief analysis of this area of possible causation by postnatal factors, therefore, is appropriate here.

First, the petitioners are plainly mistaken when they assert that "[r]espondent maintains that the disorders [*i.e.*, autism] are entirely genetic." (P-2, p.7.) Clearly, respondent does *not* take the position that autism is *entirely* genetic. To the contrary, as pointed out above (pp. 38-39), respondent's experts explicitly acknowledge that *prenatal* environmental factors do play a role in causing autism. Nor have respondent's experts asserted that no postnatal factor could *possibly* contribute to autism. Rather, respondent's experts opine only that there is currently no *persuasive* evidence that any postnatal factors play a role (*e.g.*, Ex. M, para. 52; Tr. 2575, 3265-67), and that the above-described autopsy studies, showing brain anomalies in autistics that would necessarily have arisen prenatally, makes it seem *unlikely* that postnatal factors play any significant causal role in autism.

Second, I note that most of the items of medical literature cited by petitioners in their briefs merely indicate that "environmental factors" or "environmental events" might or can affect the causation of autism. Those statements mean little, since there is no dispute that *some* environmental factors--*i.e.*, *prenatal* factors--affect autism. None of the citations, however, contains solid evidence of any *postnatal* factors having a causal effect.[28]

---

[28]Petitioners have also pointed to one study in which evidence of neuroinflammation was observed in rats who received a substance called "terbutaline" soon after birth, and argue that the experiment "suggest[s] that environmental 'triggers' for inflammation and autism are not limited to gestational, *in utero* exposures." (P-1, p. 40--see M.C. Zerrate, et al., *Neuroinflammation and Behavioral Abnormalities after Neonatal Terbutaline Treatment in Rats: Implications for Autism*, 322 J. PHARMACOLOGY & EXPERIMENTAL THERAPEUTICS 16 (2007) (PML 106).) However,

To be sure, it is important to note that medical science does *not* at this time completely understand the causation of autism, and is open to evidence of the *possibility* of postnatal factors playing a causal role. Some scientists are currently exploring the possibility of a causal role of postnatal factors, and perhaps such a role may be confirmed in the future. But in science, general conclusions concerning causation are not usually based upon isolated reports of a single case or a few cases suggesting a causal connection. Rather, as explained above (pp. 38-39), *most* of the existing scientific data concerning the causation of autism, accumulated over decades of research, supports the conclusion that autism is the result of malformation of the brain during the *prenatal period*, as a result of genetic factors and/or prenatal environmental exposures. Therefore, a few items of evidence indicating the *possibility* of postnatal contributions to the causation of autism, while interesting, do not change the strong direction of the large majority of the available data. The balance of the existing evidence still leaves it as simply *unclear* whether postnatal environmental factors *ever* cause autism.[29]

iii. Summary concerning impact of accepted science on petitioners' general causation theory

Considering the existing evidence concerning the causation of autism *as a whole*, I must conclude that such evidence tends to make the petitioners' theory advanced in this case seem *unlikely*. That is, as explained above, first we know for certain that *genetic* factors and *prenatal* exposures can cause autism, while it is as yet *unclear* whether *postnatal* factors play any causal role. Second, the petitioners' theory is *strongly contradicted* by the above-discussed autopsy studies, which indicate that autism is caused by brain malformations occurring *prior to birth*.

In this regard, however, I must raise three *caveats*. First, as noted above, the causation of autism is still not well understood, and we also have the evidence discussed above raising the *possibility* that postnatal factors might play a causal role. Therefore, my point set forth in this section V(C)(6) of this decision is certainly *not* the strongest argument against the petitioners' theory. But this point does add some additional reason to be doubtful of the causation theory advanced by the petitioners in this case.

Second, I want to be clear that, in including this point concerning "accepted" scientific understandings, I do *not* mean to suggest that a petitioner's causation theory must *automatically* be rejected simply because it differs from "generally accepted" medical thinking, or because it goes

---

respondent's expert Dr. Rodier pointed out that rats are developmentally immature compared to humans when born, so that the time when the terbutaline was administered to the rats would actually correspond to administration during *gestation* in humans. (Tr. 3023-24.) Petitioners presented no evidence contradicting Dr. Rodier concerning this point.

[29]For example, a report of the Institute of Medicine concerning the causation of autism (see p. 96 below) stated that "the consensus of most scientific experts is that autism is generally caused by early prenatal exposures * * * or is linked to early developmental genes * * *." (RML 255, p. 33.)

beyond "generally accepted" medical principles. To the contrary, under the applicable case law, a petitioner certainly may advance a new and unproven medical theory, and may *prevail* on a causation issue via such a theory, if the petitioner can supply adequate evidentiary support for that theory. *Capizzano v. Secretary of HHS*, 440 F.3d 1317, 1324 (Fed. Cir. 2006). My point here, rather, is simply that because of the way in which the petitioners' general causation theory diverges from scientifically accepted points, there is reason to be *cautious* in evaluating that theory. (See, e.g., *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 594 (1993) ("'general acceptance' can have a bearing on the [reliability] inquiry").)

Third, I also wish to be clear that I have *not* concluded that Jordan King's own autism was *caused by a genetic defect*. Respondent has *not* alleged that a genetic defect should be considered to be a "factor unrelated to the administration of the vaccine" pursuant to § 300aa-13(a)(1)(B), nor do I so conclude. In this case, the petitioners have *failed*, under part (A) of §300aa-13(a)(1), to show that it is probable that Jordan's vaccinations contributed to the causation of his autism, so that the burden *never shifted* to respondent to demonstrate, under part (B) of §300aa-13(a)(1), that some *other* factor caused his autism. *See*, *e.g.*, *DeBazan v. Secretary of HHS*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). My point in this part V(C)(6) of this decision *has nothing to do* with the "factor unrelated" analysis in part (B) of §300aa-13(a)(1). Rather, my point simply is, once again, that the three above-described points of scientific knowledge concerning the causation of autism make the petitioners "general causation" argument in this case seem *unlikely*.

Finally, I note that it is certainly *not* necessary to resolve, in this case, the general question of whether *any* postnatal environmental factors, other than thimerosal-containing vaccines, can contribute to the causation of autism. That is, even if the evidence showed clearly that *some* postnatal factors can contribute to the causation of autism, that by itself would still do very little to advance the petitioners' general causation case here. The petitioners would still need to demonstrate that a *particular* postnatal factor, thimerosal-containing vaccines, can contribute to the causation of autism. And that they have failed to do.

7. Dr. Kinsbourne's claim to offer his theory as a mechanism only for "regressive autism" is problematic.

Another problematic aspect of Dr. Kinsbourne's theory is the fact that he offers it as a possible cause for a *sub-type* of autism that he calls "regressive autism," rather than as a possible cause for autism *in general*. (Ex. 26, pp. 3, 24; Tr. 842, 901-03.) This aspect of Dr. Kinsbourne's theory does not withstand close inspection.

a. Regression in autism, and "regressive autism," described

Some individuals with autism do not merely fail to develop normally, but actually *lose skills* that they previously demonstrated, in language and related areas, usually sometime during the second year of life. This phenomenon is described as "regression in autism" or "autistic regression." (*E.g.*, Ex. M, pp. 12-13, 33-34; Ex. W, p. 3; Ex. GG, p. 25; Tr. 3558, 3284-85.) There have been various

estimates as to what percentage of autistic individuals experience regression, but many recent estimates have been in the vicinity of 20 to 40 percent. (Ex. GG, p. 25; Ex. M, p. 12; Tr. 3285, 3291, 3310.)

The term "regressive autism" derives from this phenomenon of regression in autism, being used to designate a category of autistics who have suffered a regression. The term has often been used in the context of the allegation that vaccines can cause autism. Proponents of a vaccine/autism connection have argued that autistic children who experience regression should be viewed as suffering from a distinct sub-type of autism, described as "regressive autism," and that this sub-type, as opposed to other sub-types of autism, is likely to result from measles vaccines and/or thimerosal-containing vaccines.

It is not clear from the record of this case whether the term "regressive autism" is typically used outside of the context of the vaccine/autism controversy. Dr. Lord, who has worked in the field of autism research since 1969 (Tr. 3547), and has spent much of her career studying regression in autism since the early 1980s (Tr. 3547), testified that she had never heard the term "regressive autism" until she heard of the allegation that the measles vaccine could cause autism, an allegation that originated only about ten years ago.[30] (Tr. 3578-79). That indicates that use of the term "regressive autism" may be confined to the context of the vaccine/autism allegations. Nevertheless, in this Decision I will at times use the term to refer to the autism of those who have suffered regression, even though I have concluded that the evidence is insufficient to support the proposition that "regressive autism" is really a *distinctive sub-type* of autism. (See discussion at pp. 44-47 below.)

b. Dr. Kinsbourne did not explain why he offers his theory as to "regressive autism" only.

As noted above, Dr. Kinsbourne offers his theory as a possible causal mechanism *only* for a sub-type of autism that he calls "regressive autism," rather than as a possible mechanism for autism *in general*. (Ex. 26, pp. 3, 24; Tr. 842, 901-03.) However, as respondent's experts Dr. Rust and Dr. Rutter pointed out, there is no obvious reason why Dr. Kinsbourne's mechanism would be limited to children who experience regression. (Tr. 2592, 3320.) Dr. Kinsbourne failed to offer an explanation as to why his theory would work only for "regressive autism," and not for all forms of autism. When questioned about that failure, Dr. Kinsbourne again did not offer a reasoned explanation, but stated only that he had not "considered" whether his mechanism would apply to non-regressive autism. (Tr. 903, lines 6-11.) Pressed further, he seemed to acknowledge that his theory might be equally applicable to non-regressive autism. (Tr. 903, line 12, through 904, line 4.)

[30]Similarly, respondent's expert Dr. Fombonne, and respondent's expert in the *Dwyer* case, Dr. Leventhal, testified that the term "regressive autism" did not come into use until Dr. Andrew Wakefield initiated in 1998 the controversy about whether the MMR vaccine can cause autism. (Tr. 3284; *Dwyer* Tr. 224.)

This factor, that Dr. Kinsbourne offered his proposed mechanism only for "regressive autism," yet he cannot even suggest a reason why his proposed mechanism would cause "regressive autism" but not non-regressive autism, is another reason to doubt Dr. Kinsbourne's theory. The question seems to be an obvious one, and it seems extremely dubious that the question never occurred to Dr. Kinsbourne. His failure to provide an answer to that question, when asked, indicates that he simply has no credible answer.

c. Dr. Kinsbourne's theory is inconsistent with the phenomenon of sudden regression.

In addition, Dr. Kinsbourne's theory seems to be inconsistent with the very phenomenon of regression in many autistic individuals. As Dr. Kinsbourne himself indicated, in some individuals such regressions are very "sudden" and "dramatic." (Tr. 902.[31]) Yet Dr. Kinsbourne's testimony also indicated that his theorized neuroinflammation would be the result of a *gradual* accumulation of inorganic mercury in the brain, with the accumulation of more mercury causing greater neuroinflammation. (*E.g.*, Tr. 899, 945.) These aspects of his theory seem inconsistent, with Dr. Kinsbourne failing to explain why a *gradual* build-up of mercury in the brain would result in a *sudden and dramatic* loss of skills in some children with regressive autism. Dr. Rutter, for example, noted that Dr. Kinsbourne's theory fails to account for the phenomenon of sudden regression. (Tr. 3320.)

d. The evidence does not support the idea that "regressive autism" is a distinct sub-type of autism that would have a different set of causes.

Central to the causation theory of the petitioners and Dr. Kinsbourne in this case is the idea that "regressive autism" is a *distinct sub-type*, or "phenotype,"[32] of autism, likely to have a different set of causes than the autism of non-regressive individuals. However, the overall evidence contained in this record indicates that it is unlikely that "regressive autism" should be considered a "phenotype," or distinct sub-type, of autism, likely to differ causally from the autism of those who have not suffered from regression.

Several of respondent's experts, with very impressive credentials and expertise in the study of autism, testified persuasively in this regard. Dr. Lord has spent 40 years in autism research, and

---

[31]Respondent's expert Dr. Rutter also testified that in some autistic children regression involves a "striking and dramatic" loss of skills (Tr. 3313), although he stated that in most cases the regression is "subtle" or "gradual" (Tr. 3313-14).

[32]The experts in this case have at times discussed the issue of whether regressive autism constitutes a separate "phenotype" of autism. Unfortunately, the record of this case does not contain a good definition or explanation of the term "phenotype," but the experts seemed to use the term to mean a sub-type of autism that is genuinely distinct from other types of autism in its *overall characteristics*, rather than merely in a *single* characteristic, such as whether or not a regression was observed. (See, *e.g.*, Tr. 3587-88.) I will use the term "phenotype" in that way.

has intensively studied the phenomenon of regression since the early 1980s. (Tr. 3547.) She opined that there is no "distinct phenotype" of regressive autism. (Tr. 3571, 3586-87; Ex. W, pp. 4-5.) She explained that none of the research into regression supports the concept of such a distinct sub-type. (Tr. 3579.) She noted that studies comparing autistics who have suffered regression, with those who have not suffered regression, do *not* show any significant differences in clinical outcomes between the two groups. (Tr. 3580.) The two groups end up, for example, with similar language skills. (Tr. 3567.) She stated that there is no evidence indicating that the "etiology"--*i.e.*, the causation--of autism is different between regressives and non-regressives. (Tr. 3583.)

Dr. Lord explained that the fact that children suffer regression during the second year of life does *not* mean that such children were previously normal. To the contrary, when the prior lives of such children are retrospectively studied, by examining records or videotapes or other means, it is often found that the child had unrecognized symptoms of autism even prior to the observed regression. (Tr. 3570-71, 3577; Ex. W, pp. 4-5.) Dr. Lord also explained that as additional studies have examined the concept of regression, distinctions have in fact blurred concerning which children have actually suffered regression and which have not. Research has found that "there isn't a cut-and-dried," clear difference between those with regression and those without regression. (Tr. 3577.) She noted that under one definition of regression, almost all children with autism would be considered as having regression. (Tr. 3566.)

Dr. Lord, in fact, was the principal researcher on one particular study, known as the Richler study,[33] that was specifically designed to look at, among other things, whether regression constituted a distinctive phenotype of autism. (Tr. 3573-74.) The study found some minor differences, but no significant differences, between autistic patients who had or had not suffered from regression. (Tr. 3575-77.)

Another expert with outstanding expertise in autism who gave similar testimony was Dr. Rutter. Dr. Rutter, like Dr. Lord, opined that the existing evidence makes it seem doubtful that autistics who suffered regression constitute a "distinctive" group as compared to those who did not. (Tr. 3365.) He indicated that there is no evidence that regressive autism is a distinct form of autism (Tr. 3294), or that autism with regression is any different than autism without regression (Ex. GG, para. 46). He stated that there is no evidence to indicate that regressive autism and non-regressive autism are at all distinct as to *causation*, stating that it is "pure speculation" to suggest that there is a difference as to causation. (Tr. 3291.) He also explained that the fact that a regression occurred does *not* mean that the child was previously normal. (Tr. 3290.)

Similar testimony came from Dr. Rust, a pediatric neurologist with extensive experience in studying autism. Dr. Rust testified that no meaningful biological differences have been identified between autistics with or without regression. (Tr. 2391, 2577.) He noted three different aspects in

---

[33] Jennifer Richler, et al., *Is There a 'Regressive Phenotype' of Autism Spectrum Disorder Associated with the Measles-Mumps-Rubella Vaccine? A CPEA Study*, 36 J. AUTISM & DEV. DISORDERS 299 (2006) (PML 279, RML 397).

which regressive autism could be compared to non-regressive autism--*i.e.*, in familial clustering, electrophysiologic profile, and ensuing course--and explained that no differences have been found between the two groups in those areas. (R. Trial Ex. 8, p. 12; Tr. 2389-91.) He also noted, like Dr. Lord, that when researchers have retrospectively studied groups of children who have suffered regression, it turns out that in most individuals evidence of abnormality that *pre-existed* the regression can be identified. (R. Trial Ex. 8, p. 12; Tr. 2388.)

Dr. Fombonne, another expert with outstanding experience and achievement in studying autism, also provided testimony to the same effect. Dr. Fombonne opined that there is no basis for concluding that regressive autism is a phenotype or distinct sub-type of autism. (Tr. 3813.) Dr. Fombonne noted that, other than the regressions themselves, there is no evidence of any distinction between autistics who have or have not suffered regression.[34] (Ex. M, p. 54; Tr. 3671-73, 3688, 3692.) He explained in detail why, under ordinary principles of distinguishing between disorders in medicine, there is not sufficient evidence to establish regressive autism as a distinct sub-type of autism. (Ex. M, paras. 124-25; Tr. 3813.) Like Dr. Lord, he explained that recent research has blurred the line between regressives and non-regressives. (Ex. M, p. 54; Tr. 3684.)

Dr. Fombonne reiterated that when autistics with regression are retrospectively scrutinized, abnormal development *prior* to the regression can be identified in a majority. (Ex. M, p. 54; Tr. 3685, 3761.) He explained that as autism researchers have become even more skilled in identifying subtle signs of autism, the proportion of individuals retrospectively found to have pre-regression symptoms of autism has grown larger. (Ex. M, p. 54; Tr. 3689, 3762.) In this regard, he also noted that one recent study[35] of abnormal head growth in autistics during the first year of life, prior to any regression, found that such abnormal growth was *equally common* in those with or without subsequent regression. (Ex. M, pp. 54-55; Tr. 3687-88.)

Dr. Fombonne also explained that autistics with regression are as likely as non-regressive autistics to have relatives who suffer from autistic-like features. (Ex. M, para. 121(e).) As Dr. Fombonne suggested, this factor indicates that autism with regression is just as dependent upon genetic factors as non-regressive autism, contradicting the petitioners' theory that regressive autism is a distinct form of autism uniquely affected by the alleged environmental trigger of mercury.

Further, Dr. Fombonne also explained that the Autism Diagnostic Interview, a diagnostic tool commonly used to diagnose autism, does *not* contain a separate subcategory for regressive autism. (Tr. 3767-70.)

---

[34]Even Dr. Kinsbourne eventually acknowledged that there are no general differences in developmental outcome between autistics who have or have not suffered regression. (Tr. 781, 909.)

[35]Sara Webb, et al., *Rate of Head Circumference Growth as a Function of Autism Diagnosis and History of Autism Regression*, 22 J. CHILD NEUROLOGY 1182 (2007) (RML 506).

Next, Dr. Kemper, a neuropathologist who did the pioneering work in examining autistic brains via autopsy, added important testimony concerning this subject from the neuropathologic perspective. Dr. Kemper explained that one recent study[36] autopsied brains of autistics both with and without regression, and found no pathological differences. (Tr. 2801, 2853-54.) He knows of no evidence of differences in brain pathology between regressive and non-regressive autism cases. (*Id*.)

Finally, Dr. Leventhal, respondent's expert in the *Dwyer* case who also has extensive experience with autism, also testified that regressive autism does not constitute a distinct phenotype of autism. (*Dwyer* Tr. 224-25.)

In sum, the above-described six experts, all with solid credentials in studying autism, provided strong testimony to the effect that the available evidence *does not* support the idea that "regressive autism" is a distinct sub-type of autism that would be likely to have a different set of causes. Neither Dr. Kinsbourne, nor any of the petitioners' experts, offered any persuasive evidence to the contrary. I found this testimony of the respondent's experts to be quite persuasive. I find that, based on the overall evidence in the record, there is no reason to conclude that the factors causing autism with regression would be any different from those causing autism without regression. This, then, is another reason to doubt the validity of Dr. Kinsbourne's and petitioners' causation theory.

e. Summary concerning "regressive autism"

In sum, another severe problem with Dr. Kinsbourne's and petitioners' causation theory is their attempt to offer it as a possible cause *only* for "regressive autism," and not for autism in general. Dr. Kinsbourne could offer no explanation for this proposed limitation of his theory. This limitation is inconsistent with the phenomenon of *sudden* regression in some cases. And the theory is inconsistent with the extensive evidence that makes it very *unlikely* that regressive autism is a distinct sub-type of autism that would be likely to have different causes than other forms of autism. This problem, thus, is *another* factor that casts grave doubt on the petitioners' causation theory.[37]

8. The fact of a regression does not indicate an environmental cause for the autism.

In his expert report, Dr. Kinsbourne suggested that because children with autistic regression "lapse into autism in the second year of life," that suggests that there must have been a "triggering event" at about that time that caused the autism and/or the regression. (Ex. 26, p. 9.) He later

---

[36]Diana Vargas, et al., *Neuroglial Activation and Neuroinflammation in the Brain of Patients with Autism.* 57 ANNALS NEUROLOGY 67 (2005) (PML 69).

[37]Curiously, in one section of their main post-hearing brief, the petitioners, inconsistently with the rest of their briefs, seem to abandon their focus on "regressive autism," and temporarily focus their argument on a hypothetical *subset* of regressive autism that they label "clearly regressive autism." (P-1, pp. 52-54.) I will address petitioners' argument concerning "clearly regressive autism" at pp. 88-94 of this Decision, below.

reiterated in his oral testimony that the occurrence of a regression suggests an "environmental factor" as the cause. (Tr. 902.) The testimony of respondent's experts, however, refuted this aspect of Dr. Kinsbourne's reasoning.

Respondent's experts testified that even when signs of autism are first recognized during a child's second year of life, that does *not* provide evidence that some *environmental factor* played any type of causal role in the autism. In this regard, those experts noted that, as explained above (see p. 38), there is a strong genetic component to autism, and that a number of disorders that are indisputably genetic in origin, such as Huntington's disease and Rett's syndrome, do not manifest themselves until long after birth. (*E.g.*, Tr. 3288-90, 3292-93 (Dr. Rutter); Ex. M, paras. 39-40 (Dr. Fombonne).) As the experts explained, some genes are innately "programmed" so that they will automatically be "expressed" or "turned on" at a certain age, sometimes many months or even decades (*e.g.*, Huntington's disease) after birth, *independent* of any environmental factors. Similarly, Dr. Rodier explained that it is scientifically established that a pre-existing abnormality ("lesion") of the nervous system can result in a regression later on in life, without an intervening event. (Tr. 3031-32.)

Respondent's experts, therefore, refuted Dr. Kinsbourne's suggestion that the appearance of autistic symptoms during the second year of life, in an individual with "regressive autism" or any other type of autism, would indicate that the individual's autism must have resulted at least in part from an environmental cause. This apparent reasoning of Dr. Kinsbourne is simply contrary to the scientific evidence regarding many genetic disorders.

9. It is not clear whether neuroinflammation plays a causal role in autism.

One major part of Dr. Kinsbourne's causation theory is his conclusion that neuroinflammation is a *causal* factor in autism. Dr. Kinsbourne is correct that certain recent research indicates that neuroinflammation has been found to be *present* in the brains of a number of autistic individuals. The problem is, however, that medical researchers in that area do not yet understand whether that observed neuroinflammation is a *cause* of autism or an *effect* of autism.

Specifically, Dr. Kinsbourne relies heavily on recent work of a research group at the Johns Hopkins University, including Dr. Carlos Pardo and Dr. Diana Vargas. That group published two articles in 2005, with Vargas listed as the lead author in one, and Pardo as the lead author in the second.[38] The first article described the group's examination of brain tissue from autopsies of 11 persons who suffered from autism, finding evidence of neuroinflammation in that brain tissue. (PML 69.) The second article included a further discussion of the neuroinflammation found in those same autopsies (PML 72, p. 491), and discussed the potential implications of that finding (PML 72, pp. 491-493).

---

[38] Diana Vargas, et al., *Neuroglial Activation and Neuroinflammation in the Brain of Patients with Autism,* 57 ANNALS NEUROLOGY 67 (2005) (PML 69); Carlos Pardo, et al., *Immunity, Neuroglia and Neuroinflammation in Autism*, 17 INT'L REV. PSYCHIATRY 485 (2005) (PML 72).

Respondent's experts do *not* dispute that the Pardo/Vargas group found neuroinflammation in the autistic brains. However, they argue that there is no sound basis for Dr. Kinsbourne's assumption that such neuroinflammation in autistic brains plays a *causal* role in autism. Dr. Rust, a pediatric neurologist who has specialized in inflammatory illnesses of the central nervous system (Tr. 2482-83), testified that it is not clear from the Pardo/Vargas studies whether the observed inflammation plays a *causal* role in the autism, or instead is an *effect* of autism, a part of the body's response to the autism. (Tr. 2490-93, especially 2493 lines 2-6; R. Trial Ex. 8 at 71-73.) Similarly, Dr. Kemper, a specialist in neuropathology and neurology, also provided testimony indicating that, based on the Pardo/Vargas articles, one cannot conclude that the observed neuroinflammation played a *causal* role in the autism. For example, Dr. Kemper explained that the microglial activation, a key marker of neuroinflammation observed in the autopsied brains, might be a *beneficial* process or a "neuroprotectant," rather than a cause of autism. (Tr. 2851.) Further, Dr. Rutter, who has studied autism intensely for more than 40 years, stated that based on the neuroinflammation found in the Pardo/Vargas studies, it is *not* reasonable to conclude that neuroinflammation can play a *causal* role in autism. (Tr. 3415.) He explained that there is simply not sufficient evidence to determine what relevance those neuroinflammation findings have concerning the causation of autism. (Tr. 3336-37, 3338-39, 3357-58.)

Moreover, an analysis of the Pardo/Vargas articles themselves demonstrates the point that those articles are *not* a sound basis for Dr. Kinsbourne's conclusion that the observed neuroinflammation is a *cause* of autism. Nowhere in those articles do the authors state the conclusion that the neuroinflammation is a *cause* of autism. To the contrary, in their discussion of the "implications" of their findings of neuroinflammation in the autopsies, Drs. Vargas and Pardo state clearly that "the precise role of neuroinflammation in the pathogenesis and natural history of autism is still uncertain." (PML 72, p. 492.) They state that while certain factors "suggest that microglial activation and neuroinflammation *may* play a role in processes of injury * * *, however, there is also recent evidence that neuroinflammation may be associated with repair processes and regeneration." (*Id*., emphasis added.) In that latter sentence, in other words, Drs. Pardo and Vargas indicated that it is unclear whether the neuroinflammation process plays a role in *causing* autism, or instead plays a *beneficial* ("repair * * * and regeneration") role. As an additional example, at another point in the same article, Drs. Vargas and Pardo wrote that the observed neuroinflammation responses "may" have a role as a "direct effector of injury," or may have a role, on the other hand, as a "neuroprotectant." (PML 72 at 490.)[39] (Note also that both Dr. Rust and Dr. Kemper similarly interpret those Pardo and Vargas statements as *neutral* concerning the issue of whether neuroinflammation plays a causal or a beneficial role--*see* Tr. 2493, 2851.)

Further, Dr. Pardo himself supplied a letter for this Vaccine Act proceeding, in order to clarify his opinion concerning this point. (Ex. LL.) Dr. Pardo stated that it "is important to clarify the notion [obviously referring to Dr. Kinsbourne's "notion"] that neuroinflammatory responses

[39]Further, Drs. Pardo and Vargas specifically warned practitioners *against* initiating "immunomodulatory" treatments of autistic persons based on the assumption that neuroinflammation was *causing* autism. (*Id*. at 492, second column.)

* * * are directly associated with injury. At present, we are not able to conclude that these neurological reactions are deleterious for the central nervous system." (Ex. LL, p. 2.) Dr. Pardo then added that, as indicated in the article quoted above, it is possible that, to the contrary, the neuroinflammation may represent "repairing processes"--*i.e.*, a *beneficial* process. (*Id*.) Dr. Pardo then summarized that "it is erroneous to assign," as Dr. Kinsbourne does, "an exclusive deleterious or injury effect of those neurological responses in the CNS [central nervous system]." (*Id*.) In sum, Dr. Pardo's letter confirms that the Pardo/Vargas authors themselves do *not* claim to know whether neuroinflammation plays a causal role in autism.[40]

In addition, another of respondent's experts, Dr. Johnson, a neurotoxicologist, explained that neuroinflammation is a common feature observed in many neurologic disorders, but such neuroinflammation is usually considered to be a *result* of the disorder, not a *cause* of the disorder. (Tr. 4315-16.) His opinion is that, in autism, neuroinflammation does *not* likely contribute to *causing* the condition. (Tr. 2249.) Similarly, Dr. Rutter opined that it is unlikely that neuroinflammation contributes to causing autism. (Tr. 3339.) Dr. Kemper offered the same opinion. (Tr. 2860-61.)

In sum, I conclude that, based on the currently available evidence, while it is *possible* that neuroinflammation may play a causal role in autism, there is not a sound basis for concluding, as Dr. Kinsbourne does, that it is *certain* or even *probable* that neuroinflammation causes autism. To the contrary, based on the available evidence it simply is *unknown* whether neuroinflammation plays such a causal role.[41]

10. Even if neuroinflammation causes autism, there is no credible evidence that the thimerosal in thimerosal-containing vaccines could cause autism.

Even if it were demonstrated (which it was not) that neuroinflammation *can* contribute to causing autism, to prevail in a particular Program case a petitioner would still need to demonstrate

---

[40]Further, Dr. Pardo's letter stated specifically that "these findings"--*i.e.*, the findings of neuroinflammination in the Pardo/Vargas study--"are inconsistent with the hypothesis of a potential toxic effect on astrocytes by neurotoxins or toxic material." (Ex. LL, p. 1.) This statement, thus, seems to indicate that Dr. Pardo himself *specifically rejects* Dr. Kinsbourne's theory in this case that the function of astrocytes in the brains of autistic children is being adversely affected by a "neurotoxin"--*i.e.*, mercury from thimerosal-containing vaccines.

[41]As petitioners pointed out (P-1 at 37-38), another researcher, Dr. Eric Courchesne, commented on the Vargas/Pardo work and speculated upon the *possibility* that the neuroinflammation observed in the Pardo/Vargas work *might* explain some of the pathologic features seen in MRI images of the brains of autistic children. (*See* Eric Courchesne, et al., *Autism at the Beginning: Microstructural and Growth Abnormalities Underlying the Cognitive and Behavioral Phenotype of Autism*, 17 DEV. & PSYCHOLOGY 577, 589 (2005) (PML 104).) But Courchesne's article, like the Pardo/Vargas articles discussed above, did not indicate a *conclusion* that neuroinflammation plays a causal role in autism.

that the neuroinflammation in that particular child's brain resulted from the *thimerosal in vaccines*. However, Dr. Kinsbourne acknowledged that neuroinflammation could be caused by *many different agents* other than thimerosal. He pointed to three major categories of potential causes of neuroinflammation: viruses, toxins, and neurodegenerative diseases. (Tr. 810-12.) Thus, even according to Dr. Kinsbourne himself, thimerosal is only one of many potential *toxins*, and, thus, only one of a great many potential *causes*, of neuroinflammation in an autistic child. But Dr. Kinsbourne did *not* explain how, in any particular case, one could say with any degree of probability that it was *inorganic mercury*, rather than one of the viruses, toxins, or other potential causes, that caused the child's neuroinflammation. As Dr. Kinsbourne acknowledged, simply by looking at the inflammation in a child, one could *not* determine the *cause* of the inflammation. (Tr. 810--"when you look at the inflammation you can't tell what the cause was.") This, in my view, is another huge problem with the petitioners' overall causation theory, which the petitioners do not address, much less solve.

Moreover, even if one could somehow demonstrate--which seems exceedingly unlikely--that an individual's autism resulted from neuroinflammation caused by *inorganic mercury* in the brain, even *that* showing would still not demonstrate that the autism resulted from *thimerosal*. Rather, the record of this case demonstrates that a typical breast-fed infant will receive, from breast-feeding alone, *substantially more* mercury (in the form of methylmercury which, like the ethylmercury in thimerosal, can be converted into inorganic mercury inside the child's body) than is contained in all of the vaccines usually received by an infant during the first six months of life. (Tr. 1805; Ex. G, p. 29.[42]) Thereafter, most children, after weaning from breast-feeding, will then ingest even more mercury from food. (Tr. 1804-05, 1847-48, 1964.) Thus, even if it were demonstrated that inorganic mercury in the brain could contribute to autism, the petitioners would still have failed to show that the inorganic mercury *from vaccines*, as opposed to the significantly *larger* amounts of inorganic mercury received by a child via *foods* and other sources of methylmercury, caused any child's autism, much less any *particular* child's autism.

In other words, as Dr. Brent framed the issue, if the small amounts of inorganic mercury from *thimerosal-containing vaccines* could cause autism, why wouldn't many more children get autism as a result of their *substantially greater* exposure to inorganic mercury from dietary sources? (Tr. 1964, 1967.) If thimerosal-containing vaccines are causing autism by delivering small amounts of mercury, why wouldn't human breastmilk, seafood, and other dietary sources be causing even more autism, since those substances deliver *substantially greater* amounts of mercury to children? (Tr. 1940-41, 1972.) And why wouldn't children from islands where an extraordinary amount of seafood

[42]In his expert report, Dr. Brent cited a medical article in support of his assertion that a typical infant receives more mercury from breastfeeding than the child would receive from a full schedule of thimerosal-containing vaccines. (Ex. G, p. 29.) I have reviewed that article. Rejane Marques, et al., *Hair Mercury in Breast-Fed Infants Exposed to Thimerosal-Preserved Vaccines*, 166 EUROPEAN J. PEDIATRICS 935 (2007) (RML 324). The article does support Dr. Brent's assertion, and petitioners have not submitted any evidence contradicting that assertion.

is consumed, causing elevated mercury brains levels much higher than those of most humans, have higher levels of autism? (They do not.) (Tr. 1819-22, 1897-99.)

11. Other problems with Dr. Kinsbourne's theory

The testimony of respondent's experts also cast doubt on Dr. Kinsbourne's general causation theory in other respects.

a. Dr. Kinsbourne's reliance on the Aschner articles is misplaced.

As part of his theory that inorganic mercury in the brain might cause autism by prompting neuroinflammation, Dr. Kinsbourne theorized an impairment of the function of certain brain cells known as "astrocytes," so that the astrocytes could not properly perform their role of mopping up ("uptaking") a substance known as glutamate. In that regard, he relied upon two articles by Aschner and colleagues.[43] (P-1 at 34-35; Ex. 26, p. 16; Tr. 815-22.) Those articles, however, do not provide support for Dr. Kinsbourne's and petitioners' causation theory in this case, for several reasons pointed out by respondent's experts. Those Aschner articles did indicate, as Dr. Kinsbourne noted, that exposure to mercury can reduce glutamate uptake by astrocytes. However, as both Dr. Johnson and Dr. Brent pointed out, those statements in the Aschner articles were based upon experiments involving amounts of mercury *far greater* than the amounts of inorganic mercury that could be delivered to infant brains by thimerosal-containing vaccines. (Tr. 4325, 4331-36.)

In addition, the Aschner experiments were conducted *in vitro*, meaning that the astrocyte cells were removed from a living being and studied in a laboratory setting; thus, as Dr. Brent testified, the results cannot reliably predict what happens when astrocytes *in a living brain* are exposed to inorganic mercury. (Tr. 4335-36; see also Tr. 4348-49, 1824-25.) Further, Dr. Johnson also stated that the studies described in the Aschner articles indicated that the result of such disturbed astrocyte function would be significant *death* of brain neurons, which is inconsistent with Dr. Kinsbourne's theory, which does not involve significant neuronal death. (Tr. 4326, 4328-29.)[44]

---

[43]Michael Aschner, et al., *Methylmercury Alters Glutamate Transport in Astrocytes*, 37 NEUROCHEMISTRY INT'L 199 (2000) (PML 568); Michael Aschner, et al., *Involvement of Glutamate and Reactive Oxygen Species in Methylmercury Toxicity*, 40 BRAZILIAN J. MED. & BIOLOGICAL RESEARCH 285 (2007) (PML 570).

[44]In support of his neuroinflammation theory, Dr. Kinsbourne also relied on an article by Lopez-Hurtado. *See* Edith Lopez-Hurtado and Jorge J. Pietro, *A Microscopic Study of Language-Related Cortex in Autism*, 4 AM. J. BIOCHEMISTRY & BIOTECCHNOLOGY 130 (2008) (PML 446). (*E.g.*, Ex. 26, p. 13; Tr. 805-10.) Respondent's experts, however, argued that the Lopez-Hurtado study should not be considered scientifically reliable. Dr. Kemper testified that the methods used by Lopez-Hurtado were substandard (Tr. 2856-58), so faulty that, in his view, the article would not have been accepted for publication in a "reputable" medical journal (Tr. 2858). Dr. Kemper noted further that the journal in which the article was published is not carried by the Harvard Medical School Library, the second largest medical library in the country, and that he had never before read

Further, Dr. Brent also argued persuasively that the amount of inorganic mercury required to significantly affect glutamate uptake by astrocytes would be *far above* the amount that could come from thimerosal-containing vaccines. (Tr. 4335-37.)

b. The process theorized by Dr. Kinsbourne would result in neuronal death.

Another problem with Dr. Kinsbourne's theory, according to respondent's experts, is that if autistic brains were in fact plagued by a constant state in which the astrocyte cells failed to adequately control intercellular glutamate levels, as Dr. Kinsbourne proposes, the end result would be substantial death of brain neurons. Dr. Johnson so testified. (Tr. 2246-47, 2255, 4321, 4328-29.) Yet there is no evidence that neuronal death is a feature of autism.

Dr. Rust made the same criticism of Dr. Kinsbourne's theory. Dr. Rust stated that if the astrocytes became dysfunctional as Dr. Kinsbourne suggests, "the neurons will not be able to function" (Tr. 2507), "neuronal function will diminish and then stop" (Tr. 2507), and eventually "neurons will not survive" (Tr. 2411). (See also Tr. 2410-11, 2501-02, 2506-07.) Yet, again, there is no evidence of neuronal death in autism.

I find that this point by respondent's experts was persuasive, and that this point was not effectively rebutted by Dr. Kinsbourne or any of the petitioners' experts.

c. Dr. Kinsbourne's theory is inconsistent with the improvement commonly seen in autism.

Another aspect in which Dr. Kinsbourne's theory is inconsistent with what is known about autism concerns the fact that children with autism often *improve* at some point. Dr. Lord, the psychologist who has studied autism for about 40 years, including nearly 30 years of studying regression in autism, testified that most children with autism experience improvement to some extent, including children who have experienced regression in autism. (Tr. 3568.) Dr. Rust, also with extensive experience in autism, similarly testified that autistic children commonly improve,

---

an article in that journal. (Tr. 2854-55.) Dr. Johnson also criticized the Lopez-Hurtado study, pointing out a substantial problem with the study's statistical analysis. (Tr. 4317-20.) And Dr. Rust, too, found the Lopez-Hurtado study to be of dubious validity. (Tr. 2487-89.)

In light of the outstanding qualifications of Drs. Kemper, Johnson, and Rust, along with my impression that the testimony of those witnesses was knowledgeable and credible in general, I credit this testimony that the Lopez-Hurtado study was severely flawed. This point is not an important one, however, since respondent's experts do *not* dispute that the Pardo/Vargas group *has* found evidence of neuroinflammation in autistic patients. The more important questions, of course, are whether such neuroinflammation plays a *causal* role in autism (the answer to that question is unknown, as discussed above), and whether the thimerosal in thimerosal-containing vaccines likely plays a role in *causing the neuroinflammation* (the answer is that there is no good reason to think so, as also discussed above).

often at the age of four or five years. (Tr. 2512-13.) Dr. Kinsbourne's theory, however, involving persistent neuroinflammation by inorganic mercury that accumulates and remains in the brain, is inconsistent with this common phenomenon of improvement of autistic symptoms, as Dr. Rust pointed out. (Tr. 2512-13--"I don't know how that [improvement] can be accounted for in [Dr. Kinsbourne's] hypothesis.") To the contrary, as Dr. Rust also noted, if Dr. Kinsbourne's theory were true one would expect to see *progressive deterioration* of such individuals over a lifetime, which is not the case. (Tr. 2502-03, 2511-12.) That would be true because most people would continue to get additional amounts of inorganic mercury into their brains throughout their lifetimes from sources other than thimerosal, especially from methylmercury via food sources such as fish. (*E.g.*, Tr. 152-53, 1804-05, 1847-48, 1964.)

d. Dr. Kinsbourne's theory has not been submitted for publication.

Another factor inducing skepticism concerning Dr. Kinsbourne's causation theory is the fact that his theory has not been submitted for publication and peer review. (Tr. 1475.) Rather, Dr. Kinsbourne developed his theory, as to how thimerosal-containing vaccines might contribute to autism, in the months prior to the evidentiary hearing in this case, for purposes of this litigation. For example, in June of 2007, less than a year prior to the evidentiary hearing in this case, Dr. Kinsbourne acknowledged, during his testimony in the *Cedillo* case, that as of that time he had not considered the issue of whether thimerosal-containing vaccines could contribute to autism. (Tr. 914-15, 931-32.) Dr. Kinsbourne has also acknowledged that he developed his theory in early 2008, just prior to the filing of his expert report in this case on April 21, 2008. (Tr. 932; Ex. 26.)

Of course, the fact that a theory has been developed for litigation purposes certainly does not mean that the theory should automatically be rejected. A special master must still carefully consider the evidence for the theory and evaluate the theory. However, the fact that a theory appears to have been developed for litigation purposes certainly is a valid reason for giving that theory very close scrutiny. *See*, *e.g.*, *Daubert v. Merrell Dow Pharmaceuticals*, 43 F. 3d 1311, 1317 (9th Cir. 1995).

12. Summary concerning primary reasons for rejecting petitioners' overall causation theory

In the previous pages, I have set forth the *primary* reasons for rejecting the petitioners' overall causation theory, as proposed by Dr. Kinsbourne. In the pages to follow, I will next discuss the testimony of petitioners' experts Dr. Aposhian, Dr. Deth, and Dr. Mumper, and explain why I conclude that the testimony of those experts was also flawed, as they discussed *particular aspects* of the petitioners' general causation theory.

D. Flaws in Dr. Aposhian's testimony

A second witness of the petitioners concerning "general causation" was Dr. Aposhian, the toxicologist. Dr. Aposhian indicated his own view that thimerosal-containing vaccines can contribute to the causation of autism, and offered testimony in support of several specific parts of

the petitioners' overall causation theory. Concerning most of those specific areas of Dr. Aposhian's testimony, respondent replied to Dr. Aposhian primarily with the testimony of Dr. Brent, the medical toxicologist.

With respect to the general topic of toxicology, Dr. Aposhian certainly has substantial experience and credentials, as reflected in the description of the expert witnesses set forth above (pp. 21-22). However, Dr. Brent has even more impressive qualifications to opine in this area. Dr. Brent, unlike Dr. Aposhian, is a medical doctor. Further, Dr. Brent is a *medical toxicologist*, which means that he has specific and extensive *medical* training concerning the effects of poisons on the human system. (Tr. 1781-82, 1796-97.) He is one of about 350 board-certified medical toxicologists in the United States (Tr. 1797), and he has experience in treating patients with actual mercury toxicity (Tr. 1792).

In addition, I found the oral testimony of Dr. Brent to be substantially more cogent than that of Dr. Aposhian. Dr. Brent was much better able to discuss the relevant studies, explain his views, and to respond to questions.

In his expert report and his lengthy hearing testimony, Dr. Aposhian specifically addressed a number of different topics. I will discuss each of those topics, in turn, below. As to each of those areas, I found that the testimony of Dr. Brent, and/or that of another of respondent's witnesses, was much more persuasive than that of Dr. Aposhian.

1. Assertions concerning "genetic hypersusceptibility" and "mercury efflux disorder"

Part of petitioners' overall theory seems to be the proposition that there may exist a group of people, who, unlike most humans, are genetically "hypersusceptible" to mercury, leaving them vulnerable to immune system damage when exposed to ethylmercury. Dr. Aposhian's testimony asserted this "genetic hypersusceptibility" theory. (Ex. 25, pp. 7-9; Tr. 276, 393-94, 409.) Dr. Aposhian also testified that autism in some individuals may be a result, at least in part, of a "mercury efflux disorder," meaning that the child is unable to excrete mercury as efficiently as most children do, resulting in a build-up of mercury in the body that damages the function of the body's cells, including cells in the brain. (Ex. 25, pp. 24-25; Tr. 216-234, 396-402.) After consideration, however, I conclude that the evidence strongly contradicts both the "genetic hypersusceptibility" and "mercury efflux disorder" assertions of petitioners and Dr. Aposhian.

Initially, I note that because Dr. Aposhian's reports and testimony in both this case and the *Cedillo* case have at times been somewhat vague, it was not always clear whether his theories about "genetic hypersusceptibility" and "mercury efflux disorder" were separate or overlapping theories. However, later in his hearing testimony in this case, Dr. Aposhian indicated that they are two parts of the same theory--*i.e.*, that those who are "genetically hypersusceptible" are the same as those who, as a result of that alleged genetic anomaly, have a "mercury efflux disorder." (Tr. 231, lines 11-18; Tr. 393-94.) In any event, whether the two assertions are analyzed separately or together, I find no merit in either theory.

a. "Genetic hypersusceptibility" theory

Concerning the "hypersusceptibility" theory, neither Dr. Aposhian nor any other of petitioners' experts pointed to any *scientific research*[45] that even suggests that such "hypersusceptibility" exists. Rather, Dr. Aposhian seems to be merely *speculating* when he suggests that such a "hypersusceptibility" phenomenon *might* explain why only a small percentage of the children who are exposed to thimerosal end up with autism. Dr. Brent testified that the theory amounts to pure speculation, with no evidence at all to support it. (Ex. G, pp. 14-16, 50-52; Tr. 1801-02.) He testified that medical science has *never* identified a human subpopulation more susceptible than the general population to any type of mercury, despite the fact that in previous instances when medical science has found particular subpopulations to be especially vulnerable to specific substances, medical science has been readily capable of identifying and characterizing such vulnerabilities. (Ex. G, p. 15; Tr. 1802.)

As an alleged example of human hypersusceptibility to mercury, Dr. Aposhian relied upon an analogy to a condition known as "acrodynia" or "Pink Disease." (Ex. 25, pp. 8-9, 19-20.) Acrodynia was caused, between 1850 and 1950, by infants' exposure to a form of mercury known as mercurous chloride, in teething powders. Dr. Brent testified, however, that acrodynia was not an example of hypersusceptibility to mercury, but was more likely to have been a *dose-related* condition. That is, he explained that studies of acrodynia showed that those who suffered the disease had been exposed to *particularly high levels* of mercurous chloride; this indicates that acrodynia was

---

[45]Of course, as a matter of law, there is no *requirement* that a petitioner support his medical theory, or any individual part thereof, with medical literature. *Capizzano v. Secretary of HHS*, 440 F.3d 1317, 1329 (Fed. Cir. 2006); *Althen v. Secretary of HHS*, 418 F.3d 1274, 1279-80 (Fed. Cir. 2005). In appropriate circumstances, medical opinion plus circumstantial evidence can be enough, without medical literature support, to demonstrate causation- in- fact. *Capizzano*, 440 F.3d at 1325; *Althen*, 418 F.3d at 1279-80. However, in considering a medical theory, support for that theory from medical literature in peer-reviewed journals may be a positive factor, while a lack of such support for such theory in medical literature may, in some circumstances, be considered a factor raising doubt about the validity of the theory. (See the cases cited at pp. 94-95, below.)

In this case, as to the "genetic hypersusceptibility" theory of petitioners, the *main* reason that I have rejected it is that Dr. Aposhian's reasoning concerning the theory was unpersuasive, while Dr. Brent's reasoning was convincing. The absence of medical literature support for the theory is simply an *additional* point casting doubt upon the theory.

This pattern will prove to be true concerning a number of aspects of petitioners' causation theories presented in this case. With respect to each of those theories, the *main* reason to reject the theory is that the testimony of the respondent's witnesses was substantially more persuasive. Where appropriate, I may also note that the petitioners' expert failed to point to any literature supporting the theory. Such a lack of support, however, is, in every instance, only *one factor* in the rejection of the theory. I do not mean to suggest, concerning any point, that there is a *requirement* of literature support, or that a lack of literature support *by itself* condemns a theory.

suffered by children that were *exposed to more mercury*, rather than by children who happened to be *more susceptible* to mercury.[46] (Ex. G, pp. 51-52.)

b. "Mercury efflux disorder" theory

Concerning Dr. Aposhian's "mercury efflux disorder" assertion, Dr. Brent again testified persuasively that there is no merit to the theory. (Ex. G, pp. 41-50; Tr. 1834-52.) He noted that such a disorder is not recognized by the medical community.[47] (Ex. G, p. 50.) In support of his theory, Dr. Aposhian relied on a number of studies, but Dr. Brent effectively demonstrated that those studies offer no credible support to Dr. Aposhian.

i. Hair studies

For example, Dr. Aposhian relied on two hair studies, the Holmes study[48] and the Hu study.[49] (Ex. 25, pp. 24-25; Tr. 219-20, 426-33.) In the Holmes study, the investigators measured the mercury levels in the hair of autistic children and non-autistic "control" children, and found lower levels in the autistics, which led them to theorize that autistics may have a problem in excreting mercury. Dr. Brent, however, testified that the results and conclusions of the Holmes study failed to make sense for a number of reasons. (Ex. G, pp. 41-46; Tr. 1837-40.) Among those reasons was the fact that the mercury levels found in the hair of the autistic individuals tested by Holmes actually were within the *normal range* of what accepted testing indicated would be present in the hair of U.S.

---

[46]I also note that a committee of the Institute of Medicine analyzed the available evidence concerning the theory that such a genetic hypersusceptibility to mercury might exist. (RML 255, pp. 138-39.) (For a full description of the Institute of Medicine and the reports issued by that body that are relevant to this case, see pp. 96-99 below.) The committee concluded that it could find "no corroborating data" to support such theory. (RML 255, p. 139.)

[47]Of course, petitioners are *not* required to demonstrate that any of their medical theories are *recognized* or *accepted* by the medical community. *Capizzano*, 440 F.3d at 1325. A new theory can be shown to be probable, via expert testimony and circumstantial evidence, even though *not* recognized generally. *Id*. However, whether a theory has found acceptance in the medical community can be *one factor*, to be weighed along with other factors, in determining whether a theory is reliable or probable. *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 594 (1993) ("'general acceptance' can yet have a bearing on the [reliability] inquiry. Widespread acceptance can be an important factor ***, [while a] 'known technique which has been able to attract only minimal support within the community' *** may properly be viewed with skepticism") (citations omitted).

[48]A.S. Holmes et al., *Reduced Levels of Mercury in First Baby Haircuts of Autistic Children*, 22 INT'L. J. TOXICOLOGY 277 (2003) (PML 237).

[49]Lin-Wen Hu et al., *Neutron Activation Analysis of Hair Samples for the Identification of Autism*, 89 TRANSACTIONS AM. NUCLEAR SOCIETY 681 (2003). (PML 16.) Dr. Aposhian referred to this study as the "MIT study." (Tr. 222.)

children. (Ex. G, p. 42; Tr. 1838-39.) Dr. Brent explained that the Holmes investigators' conclusion, that the autistic children had *abnormally low* levels of mercury in their hair, was caused by the fact that the non-autistic children used as "controls" in the study, for some unexplained reason, had hair mercury levels about *15 times the normal rate* found in a previous huge study of American children's hair. (*Id*.) Dr. Brent found that this unexplained deviation from the prior accepted hair mercury level data made the Holmes study extremely suspect.

Dr. Brent also discounted the Hu study, the other hair study which Dr. Aposhian had described as supporting the Holmes study. Dr. Brent noted the Hu study involved only three autistic individuals, an insufficient number to provide any significant evidence. Further, two of those individuals had been under treatment for heavy metal detoxification, making them unsuitable for providing any worthwhile evidence. (Ex. G, p. 43; Tr. 1839-40.) And the third individual, like the autistic children in the Holmes study, actually had a hair mercury level in the range that would be *expected* in an average American child. (*Id*.)

Dr. Brent explained further that when other groups of researchers[50] performed studies similar to the Holmes study, all found *no significant differences* in the hair mercury levels between the autistics and controls studied.[51] (Ex. G, pp. 44-45; Tr. 1840.)

---

[50]*See* J.B. Adams, et al., *Analyses of Toxic Metals and Essential Minerals in the Hair of Arizona Children with Autism and Associated Conditions, and Their Mothers,* 110 BIOLOGICAL TRACE ELEMENT RESEARCH 193 (2006) (RML 2); Patrick Ip, et al., *Mercury Exposure in Children with Autistic Spectrum Disorder: Case-Control Study*, 19 J. CHILD NEUROLOGY 431 (2004) (PML 275); Janet K. Kern, et al., *Sulfhydryl Reactive Metals in Autism*, 70 J. TOXICOLOGY & ENVTL. HEALTH 715 (2007) (RML 274); Abdullahi Fido & Samira Al-Saad, *Toxic Trace Elements in the Hair of Children with Autism*, 9 AUTISM 290 (2005) (RML 138). (A fifth study, by Williams et al., was cited in Dr. Brent's report (Ex. G, p. 44), but never filed into the record of this case. I have not relied upon that study.)

[51]Petitioners presented evidence that one of the studies cited by Dr. Brent, the Ip study, may have contained a statistical flaw. (Tr. 196-98, 221, 226.) I need not resolve that issue, however, since petitioners did not attempt to refute the validity of the other studies cited by Dr. Brent, and since the two studies relied upon by *petitioners* in this regard clearly *were* flawed.

Further, in a supplemental report filed after the evidentiary hearing, Dr. Aposhian also relied upon another hair study, by Adams. (J.B. Adams, et al., *Mercury in First-Cut Baby Hair of Children with Autism Versus Typically-Developing Children*, 90 TOXICOLOGICAL & ENVTL. CHEMISTRY 739 (2008).) Dr. Brent, however, in a responsive supplemental report, persuasively explained why that Adams 2008 study actually contradicts the Holmes study in important respects, and does not provide significant support for petitioners' "mercury efflux disorder" theory. (Ex. PP, pp. 12-13.)

I note that Adams 2008 hair study was listed as PML 667 on the petitioners' master list, but the article has not been filed into the record of this case. (In fact, items 666 through 670 of the Petitioners' Master Reference List have not been filed into the record. However, the Laurente article, PML 668, was filed as Petitioners' Trial Ex. 11.)

ii. Adams tooth study

Dr. Aposhian also relied on a 2006 tooth study by Adams.[52] (Ex. 25, p. 24; Tr. 229-30, 420-26.) In that study, the researchers purported to find that mercury levels in *teeth* of autistic children were greater than in non-autistic controls. That finding, they asserted, indicated that autistic children have difficulty excreting mercury. Dr. Brent, however, opined that Dr. Aposhian's reliance on the Adams study was misplaced. Dr. Brent testified that the study was small, that there were problems with the study's statistical methodology, and that evaluation of mercury levels in teeth was a questionable technique, since teeth are *not* a normal excretory organ for mercury. (Ex. G, pp. 46-47; Tr. 1836-37.) Further, Dr. Brent explained, Adams neglected to account for the variability of mercury content in different *types* of human teeth. (Ex. G, p. 47; Tr. 1836.)

iii. Bradstreet chelation study

Dr. Aposhian also heavily relied upon the Bradstreet 2003 study.[53] (Ex. 25, p. 25; Tr. 223-24, 433-44.) Dr. Brent, however, criticized that study as well. In the Bradstreet study, urinary mercury excretion was measured in groups of autistic children and non-autistic "control" children, after the subjects underwent a process known as "chelation." The authors reported higher mercury concentrations in the urine of the autistic subjects, concluding therefrom that autistic children have a decreased ability to excrete mercury in the absence of chelation. Dr. Brent, however, explained that the study suffered from many methodological and conceptual errors. (Ex. G, pp. 47-50; Tr. 1840-44.) As one example, he noted that urinary excretion following chelation has been shown to be an *inaccurate* measure of mercury body burden. (Ex. G, p. 48.) He also noted that the way in which the controls were selected for the study was problematic. (Ex. G, p. 48; Tr. 1841.) Additionally, Dr. Brent testified that the study authors made a major mistake in failing to measure the urinary mercury levels in individual subjects *prior* to chelation (Ex. G, p. 48; Tr. 1843), and even Dr. Aposhian acknowledged that in doing such a study he would have "insisted" on getting pre-chelation measurements (Tr. 435). Dr. Brent described problems with the statistical methodology that the study authors used. (Ex. G, pp. 48-49; Tr. 1842.) He also noted that the Bradstreet 2003 study was published in a medical journal not recognized by the National Library of Medicine. (Tr. 1840-41.) Finally, Dr. Brent noted that another research group performed a study similar to Bradstreet's, and published it in a "more legitimate" medical journal. (Tr. 1844.) That study,[54] in

---

[52]James Adams & Jane Romdalvik, *Mercury, Lead and Zinc in Baby Teeth of Children with Autism Versus Controls*, 70 J. TOXICOLOGY & ENVTL. HEALTH 1046 (2007) (PML 138).

[53]Jeff Bradstreet, et al., *A Case-Control Study of Mercury Burden in Children with Autistic Spectrum Disorders*, 8 J. AM. PHYSICIANS & SURGEONS 76 (2003) (PML 244).

[54]Sarah E. Soden et al., *24-Hour Provoked Urine Excretion Test for Heavy Metals in Children with Autism and Typically Developing Controls, A Pilot Study*, 45 CLINICAL TOXICOLOGY 476 (2007) (RML 458).

contrast to Bradstreet's, found *no difference* between autistic children and controls in urinary mercury levels after chelation. (*Id*.)

iv. Porphyrin studies

In the portions of his expert report and hearing testimony concerning the "mercury efflux disorder" issue, Dr. Aposhian also provided brief and vague discussions about articles by Woods[55] and by Nataf[56] concerning testing of urinary porphyrins, suggesting that those articles supported his "mercury efflux disorder" theory. (Ex. 25, p. 8; Tr. 230-31, 383-92.) Dr. Brent, however, explained that there is no evidence that urinary porphyrin profiles provide any data relevant to theories of mercury neurotoxicity. (Ex. G, pp. 52-53; Tr. 1849-50.) Dr. Brent noted that urinary porphyrin profiles are not utilized by toxicologists as tests for mercury toxicity. (Tr. 1849-50.) Further, on cross-examination, even Dr. Aposhian admitted that he does not know whether urinary porphyrin profiles provide any information concerning the level of mercury in the *brain*. (Tr. 392.)

c. Summary concerning "genetic hypersusceptibility" and "mercury efflux disorder" theories

I find that Dr. Brent's testimony concerning these issues was persuasive, and that the testimony of Dr. Aposhian was not. I conclude that the Holmes, Hu, Adams, and Bradstreet studies[57] are of doubtful reliability,[58] and that the contrary studies cited by Dr. Brent provide better evidence. I conclude that the Woods and Nataf articles also provide no significant support to Dr. Aposhian's theory. Accordingly, after analysis of all of the evidence in this regard, I conclude that there is no

---

[55]James S. Woods, et al., *The Association Between Genetic Polymorphisms of Coproporphyrinogen Oxidase and an Atypical Porphyrinogenic Response to Mercury Exposure in Humans*, 206 TOXICOLOGY & APPLIED PHARMACOLOGY 113 (2005) (PML 45).

[56]Robert Nataf, et al., *Porphyrinuria in Childhood Autistic Disorder: Implications for Environmental Toxicity*, 214 TOXICOLOGY & APPLIED PHARMACOLOGY (2006) (PML 65).

[57]It is noteworthy that when the Holmes investigators found allegedly *low* levels of mercury in the hair of autistic children, they found that to be supportive of the "mercury efflux disorder" theory, but when the Bradstreet and Adams groups found allegedly *high* levels of mercury in urine and teeth of autistics, they also found that to be supportive of the same theory.

[58]I note that a committee of the Institute of Medicine specifically reviewed the Holmes and Bradstreet studies, and pointed out problems with both studies. (RML 255, pp. 132-34.) Further, another of respondent's experts, Dr. Rutter, also criticized the Holmes, Adams, and Bradstreet studies. (Ex. GG, paras. 70-72.) He also testified that he has seen no good evidence for the "hypersusceptibility" contention. (Tr. 3311-12.)

merit to the "genetic hypersusceptibility" and "mercury efflux disorder" theories proposed by Dr. Aposhian and the petitioners.[59]

2. Dr. Aposhian's "six pillars"

In his report, Dr. Aposhian stated that his opinion that thimerosal-containing vaccines might contribute to the causation of autism was based primarily upon six items of evidence (Ex. 25, pp. 24-25), which were later described as Dr. Aposhian's "six pillars" (*e.g.*, Tr. 420). Respondent's experts, however, analyzed those six items, and testified that those items do *not* provide persuasive support to the petitioners' causation theory.

Dr. Aposhian's first three pillars (Ex. 25, pp. 24-25) have already been discussed above: (1) the Adams tooth study, (2) the Holmes and Hu hair studies, and (3) the Bradstreet chelation study, along with the Nataf porphyrin study. As noted above, Dr. Brent testified persuasively that those items do *not* provide credible support for the petitioners' causation theory. I will discuss Dr. Aposhian's other three pillars below.

a. Chelation as an allegedly effective treatment

As his fourth pillar, Dr. Aposhian stated that chelation, using a substance known as DMSA, has been the "most beneficial treatment for autism," apparently implying that this alleged treatment success supports the theory that autism can be caused by mercury. (Ex. 25, p. 25.) Although Dr. Aposhian never fully explained this point, his theory in this regard seems to be that since chelation is designed to cause the excretion of mercury, if an autistic person has improved after chelation, that indicates that mercury had been contributing to the autistic symptoms. (*E.g.*, Ex. Tr. 25, p. 25.)

Dr. Brent, however, testified persuasively that this argument of Dr. Aposhian again is without merit. (Ex. G, p. 40; Tr. 1845.) Dr. Brent stressed that there has never been a published study showing that chelation therapy, in fact, has any benefit for autistic individuals. (*Id*.) Dr. Rust provided similar testimony. (Tr. 2398, 2453.) Dr. Brent noted further that it is well established--including support by a study in which Dr. Aposhian himself was an author[60]--that chelation, in

---

[59]Dr. Aposhian presented essentially the same contentions concerning "genetic susceptibility" and "mercury efflux disorder" in the cases concerning the petitioners' *first* theory of causation in the Omnibus Autism Proceeding, as described above (p. 11). However, Special Master Vowell and Special Master Campbell-Smith, as well as myself, found no merit in those contentions, in the resulting decisions. See *Snyder v. Secretary of HHS*, 2009 WL 332044, at *66-71 (Fed. Cl. Spec. Mstr. Feb. 12, 2009); *Hazlehurst v. Secretary of HHS*, 2009 WL 332306, at *60-71 (Fed. Cl. Spec. Mstr. Feb. 12, 2009); *Cedillo v. Secretary of HHS*, 2009 WL 331968 at *20-23 (Fed. Cl. Spec. Mstr. Feb. 12, 2009).

[60]H. Vasken Aposhian, et al., *Vitamin C, Glutathione, or Lipoic Acid Did Not Decrease Brain or Kidney Mercury in Rats Exposed to Mercury Vapor*, 41 J. TOXICOLOGY CLINICAL TOXICOLOGY

particular chelation using DMSA, does not remove mercury from the *brain*; thus, since petitioners' theory is that it is mercury in the *brain* that causes autism, the theory that chelation could relieve autistic symptoms by removing mercury is simply not logical.[61] (Ex. G, p. 40.)

b. Hornig study

Dr. Aposhian's fifth pillar was a study of mice by Hornig and colleagues,[62] in which, according to Dr. Aposhian, "mice exposed to mercury after birth develop enlarged brains and autistic-like symptoms." (Ex. 25, p. 25.) Dr. Brent, however, testified that Dr. Aposhian's description of the study was erroneous. (Ex. G, p. 39.) More importantly, Dr. Brent explained that another research group, led by Berman,[63] in response to the Hornig study, attempted to replicate the Hornig experiment using more detailed and sophisticated techniques, but arrived at different results, casting doubt on the results of Hornig's study. (Ex. G, p. 39; Tr. 1845-46.) Further, respondent's expert Dr. Johnson, with considerable expertise in pharmacology and toxicology, also testified that the Berman study was far superior to the Hornig study. (Ex. Q, p. 2.) Indeed, Dr. Aposhian himself, in light of the Berman study, backed away from his reliance on the Hornig study. (Tr. 449-50.)[64]

c. Courchesne article

Dr. Aposhian's sixth pillar was a citation to an article by Courchesne and colleagues,[65] which, according to Dr. Aposhian, provided evidence of "postnatal loss of brain cells in autism." (Ex. 25,

---

339 (2003) (RML 12).

[61]Dr. Deth suggested that chelation removing mercury from non-brain tissue might *indirectly* benefit the brain, thereby improving autism. (Tr. 579-80.) This testimony, however, was not well-explained, and I did not find it to be persuasive.

[62]M. Hornig, et al., *Neurotoxic Effects of Postnatal Thimerosal Are Mouse Strain Dependent*, 9 MOLECULAR PSYCHIATRY 833 (2004) (PML 15).

[63]The study that could not replicate the Hornig study was Robert F. Berman, et al., *Low-Level Neonatal Thimerosal Exposure: Further Evaluation of Altered Neurotoxic Potential in SJL Mice*, 101 TOXICOLOGICAL SCIENCES 294 (2007) (RML 42).

[64]In his supplemental post-hearing report, Dr. Aposhian also offered one sentence suggesting that a study by Laurente supports the Hornig study. (Ex. 33, p. 6.) (*See* Jonny Laurente, et al., *Neurotoxic Effects of Thimerosal at Vaccines Doses on the Encephalon and Development in 7 Days-Old Hamsters*, 68 ANALES FACULTAD MEDICINA LIMA 222 (2007). A copy of the Laurente study was filed as Petitioners' Trial Ex. 11.) Dr. Brent persuasively explained in his responsive report, however, why the Laurente study is flawed. (Ex. PP, p. 14.)

[65]Eric Courchesne, et al., *Autism at the Beginning: Microstructural and Growth Abnormalities Underlying the Cognitive and Behavioral Phenotype of Autism*, 17 DEV. & PSYCHOLOGY 577, 584 (2005) (PML 104).

p. 25.) Respondent's expert Dr. Kemper, however, effectively rebutted Dr. Aposhian's single-sentence suggestion in this regard.

Dr. Kemper, as explained above, is a medical doctor specializing in neuropathology, who has been one of the pioneers and leading experts in studying the brains of autistic individuals. Accordingly, he is far more qualified to interpret the Courchesne article than Dr. Aposhian, who is not a medical doctor. Dr. Kemper testified that Dr. Aposhian erred in concluding that the Courchesne article described a "postnatal loss" of brain cells in autistic children. (Tr. 2834-35.) Dr. Kemper explained that at the page of the Courchesne article cited by Dr. Aposhian (page 584), the authors were merely describing the fact that in the autopsied autistic brains the number of Purkinje neurons, a specific type of neuron (brain cell), was substantially lower in autistic brains than in brains of non-autistics. (Tr. 2834; PML 104, p. 584.) This reduced number of neurons, however, did *not* indicate a *postnatal* loss of brain cells. (Tr. 2834.) Rather, as the work of Dr. Kemper himself and other autism researchers has clearly established, the Purkinje cells either failed to form, or were lost, during the *prenatal* brain development process. (Tr. 2834-35; see also Ex. U, p. 3; Tr. 2812-20.)

I have examined the page of the Courchesne article in question, and I find that Dr. Kemper's interpretation of that article is persuasive. Thus, I conclude that Dr. Aposhian's reliance on the Courchesne article was clearly misplaced.

3. Adult monkey study articles

In his hearing testimony, Dr. Aposhian also indicated that he based his opinion concerning general causation in part upon a series of articles describing experiments involving adult monkeys, published in the 1990s by a research group including Drs. Charleston, Vahter, and Burbacher. (Tr. 161-69, 202-04, 207-08.) Petitioners in their briefs also rely heavily on those articles (P-1 at 24-28), asserting that those articles provide "direct evidence" that "low-dose, chronic exposure" to mercury can "trigger neuroinflammation" (P-1 at 28).

After consideration of those articles,[66] however, I conclude that the petitioners' and Dr. Aposhian's reliance on them is misplaced.

It is true that in the experiments described in the Charleston/Vahter articles, the adult monkeys were exposed to daily doses of mercury for months-long periods, and experienced microglial activation, a possible indicator of neuroinflammation. However, those studies do not support a contention that exposure of primates to the *amount of mercury contained in thimerosal-containing vaccines* would cause neuroinflammation. Rather, Dr. Brent explained that the daily mercury doses which those monkeys were administered meant that over a period of time those monkeys were exposed to *far more* mercury than human infants would receive from an ordinary course of thimerosal-containing vaccines over a similar period.[67] (Tr. 1863-72, 1888, 1892-93, 1919, 1921, 1932, 1935-36.)

Moreover, Dr. Brent also pointed out that while the studied monkeys eventually were found to have been suffering neuroinflammation, the monkeys were *behaviorally normal*, not showing any signs of behavior similar to autism in humans. (Tr. 1886, 1891-92, 1932, 1935.) This point further contradicts the petitioners' theory that inorganic mercury can cause neuroinflammation leading to autistic behavior.

---

[66]Marie Vahter, et al., *Speciation of Mercury in the Primate Blood and Brain Following Long-Term Exposure to Methyl Mercury*, 124 TOXICOLOGY & APPLIED PHARMACOLOGY 221 (1994) (PML 60); Jay S. Charleston, et al., *Increases in the Number of Reactive Glia in the Visual Cortex of Macaca Fascicularis Following Subclinical Long-Term Methyl Mercury Exposure*, 129 TOXICOLOGY & APPLIED PHARMACOLOGY 196 (1994) (PML 33); Jay S. Charleston, et al., *Autometallographic Determination of Inorganic Mercury Distribution in the Cortex of the Calcarine Sulcus of the Monkey Macaca Fascicularis Following Long-Term Subclinical Exposure to Methylmercury and Mercuric Chloride,* 132 TOXICOLOGY & APPLIED PHARMACOLOGY 325 (1995) (PML 32); Marie Vahter, et al., *Demethylation of Methyl Mercury in Different Brain Sites of Macaca Fascicularis Monkeys During Long-Term Subclinical Methyl Mercury Exposure*, 134 TOXICOLOGY & APPLIED PHARMACOLOGY 273 (1995) (PML 64); Jay S. Charleston, et al., *Changes in the Number of Astrocytes and Microglia in the Thalamus of the Monkey Macaca Fascicularis Following Long-Term Subclinical Methylmercury Exposure*, 17 NEUROTOXICOLOGY 127 (1996) (PML 116).

[67]Dr. Aposhian suggested that the adult monkeys received only a "low" dose of mercury, since the study referred to the dose as a "subtoxic" dose. (*E.g.*, Tr. 162.) The use of the word "subtoxic" or "subclinical" to describe the dose that the adult monkeys were regularly receiving, however, does *not* mean that the dose was very low, comparable to the dosage contained in thimerosal-containing vaccines; rather, it simply means that the dosage was low enough that it did not cause *immediately noticeable* harm to the monkeys. (Tr. 1935-36.) The "subtoxic" term does *not* contradict Dr. Brent's convincing testimony that the daily mercury doses which those monkeys were administered meant that over a period of time those monkeys were exposed to *far more* mercury than human infants would receive from an ordinary course of thimerosal-containing vaccines over a similar period. (Tr. 1863-72, 1888, 1892-93, 1919, 1921, 1932, 1935-36.)

4. Burbacher infant monkey study

In his expert report, Dr. Aposhian relied upon a study involving infant monkeys, described in an article by Burbacher and colleagues in 2005.[68] (Ex 25, pp. 20-21.) Petitioners in their post-hearing brief also seem to put high reliance on that article. (P-1, pp. 23-24.) The Burbacher article analyzed what happens to mercury in infant monkeys when it is administered in equal amounts either as methylmercury or ethylmercury, and found that ethylmercury (the type of mercury in thimerosal-containing vaccines) converts into inorganic mercury in the brain faster than does methylmercury. Both Dr. Aposhian and petitioners are vague concerning exactly what significance this finding of Burbacher has for their overall causation theory. But they seem to imply that this finding somehow supports a conclusion that the inorganic mercury in a typical infant's brain, after the infant received a course of thimerosal-containing vaccines, would be comprised in greater part from ethylmercury (from thimerosal-containing vaccines) than from methylmercury. A careful analysis of the evidence, however, demonstrates that this suggestion by petitioners is mistaken.

In this regard, I note first that, as Dr. Brent pointed out, Dr. Aposhian was mistaken in his assumption (see Tr. 28) that the dosing schedule of ethylmercury in the Burbacher study was designed to duplicate the doses of ethylmercury that human infants received from thimerosal-containing vaccines during the 1990s. Instead, the doses were *substantially higher*[69] than human infants would receive. (Tr. 1808, 1810, 1863-70.) Further, Dr. Brent indicated that it is erroneous to assume, as Dr. Aposhian did, that all of the ethylmercury from thimerosal-containing vaccines that gets into the brain would stay there and be converted into inorganic mercury; rather, the Burbacher study showed that much of the ethylmercury that got into the monkeys' brains actually left the brain. (Tr. 1812-13.)

Dr. Brent also noted that the fact that, in the Burbacher study, ethylmercury converted into inorganic mercury at a *faster rate* than methylmercury, does not mean that ultimately a *greater percentage* of ethylmercury than methylmercury ends up converting to inorganic mercury in the brain. He explained that when the brains of the monkeys were studied at the end of the Burbacher experiment, there was a large amount of methylmercury, still in the form of methylmercury, in the brains. He opined that most of that methylmercury likely would later have been converted into inorganic mercury, and thus would have remained in the brain. (Tr. 1812-15, 1874, 1884, 1911-12.) Thus, Dr. Brent's interpretation of the Burbacher study is that, contrary to the petitioners' suggestion, if primates are given equal amounts of ethylmercury and methylmercury, in fact a greater percentage

---

[68]Thomas Burbacher, et al., *Comparison of Blood and Brain Mercury Levels in Infant Monkeys Exposed to Methylmercury or Vaccines Containing Thimerosal*, 113 ENVTL. HEALTH PERSPECTIVES 1015 (2005) (PML 26).

[69]Dr. Brent stated that the Burbacher infant monkey doses were about *three times* as great as the human dosage would be. (Tr. 1808, 1810.) If Dr. Brent's calculation in that regard was slightly inaccurate for the reason set forth above at p. 36 fn. 27, then the monkey dosage might have been only about 2 ½ times greater. But even if that is true, the basic point would remain that the monkey dosage was substantially greater than the human dosage.

of *methylmercury* ultimately will end up in the brain as inorganic mercury. (Tr. 1879, 1882-84, 1911-12, 1969-71.)

Accordingly, after full analysis I conclude that the Burbacher 2005 infant monkey study does *not* support the petitioners' general causation theory in this case.

5. Failure to explain relationship to regression

Dr. Aposhian offered his opinion in support of the petitioners' *general causation* theory in this case, which is, as discussed above (p. 42), that thimerosal-containing vaccines can contribute to the causation specifically of "regressive autism." However, Dr. Aposhian never limited his theory to regressive autism, and never explained why his theory would be specifically applicable to autism with regression, rather than to autism in general. When specifically asked about whether this theory was limited only to regressive autism, Dr. Aposhian acknowledged that he had never thought about that question (Tr. 408), and was unable to suggest any reason why his theory would apply only to regressive autism (Tr. 409). As will be discussed below (pp. 79-96), the epidemiologic studies show clearly that thimerosal-containing vaccines are not a significant cause of autism *in general*. Therefore, Dr. Aposhian's failure to suggest why his causation theory would affect only those with autistic *regression* is yet another reason to doubt the reliability of his testimony as alleged support for the petitioners' overall general causation theory in this case.

6. Amount of thimerosal necessary to trigger neuroinflammation process

Finally, the petitioners rely on the testimony of Dr. Aposhian concerning one more issue, one that is vital to their overall causation theory. As noted above, the petitioners' primary expert concerning "general causation," Dr. Kinsbourne, explained that he does not know *how much* inorganic mercury it would take to cause the neuroinflammatory condition that he theorizes; or *how much* inorganic mercury would end up in a child's brain as a result of a childhood course of thimerosal-containing vaccines; or whether the amount of inorganic mercury in the brain as a result of typical course of thimerosal-containing vaccines would be *enough* inorganic mercury to provoke the type of neuroinflammatory response that he proposes. (*E.g.*, Tr. 859-72, 888-90, 944-45.) Dr. Kinsbourne expressly left it to another expert to make the determinations concerning *how much* inorganic mercury in the brain it would take to prompt the neuroinflammatory response, and whether a typical course of thimerosal-containing vaccines result in a *sufficient amount* of inorganic mercury in the brain to provoke such a response. (*E.g.*, 859-60, 862-63, 866-67, 871, 886, 888-90.) Petitioners, accordingly, attempted to plug that gap in the testimony of Dr. Kinsbourne with the testimony of Dr. Aposhian.

I conclude, however, that Dr. Aposhian's testimony in this regard was *not* persuasive, and was substantially outweighed by the contrary testimony of Dr. Brent.

First, I note that when he testified during the evidentiary hearing in this case, Dr. Aposhian did *not* say how much inorganic mercury from thimerosal-containing vaccines it would take to trigger the neuroinflammatory process that petitioners theorize as a possible cause of autism. On

cross-examination, he was specifically asked about that issue on two occasions. He first acknowledged that he did not know how much (Tr. 262), and later stated that "I'm not saying how much you need" (Tr. 369). After Dr. Aposhian's testimony concluded, however, Dr. Kinsbourne testified for petitioners, and, as noted above, stated that he, too, did not know how much inorganic mercury it would take to cause the theorized neuroinflammatory process. Therefore, faced with this gap in their theory of proof, petitioners filed a post-hearing supplemental report of Dr. Aposhian.[70] In that supplemental report, Dr. Aposhian offered a calculation concerning how much inorganic mercury that he believes would end up in a child's brain as a result of the course of thimerosal-containing vaccines administered to American children during the 1990s. He then opined that in "some infants" a sufficient amount of inorganic mercury would be deposited in the brain to trigger the theorized neuroinflammatory process. (Ex. 33, p. 7.)

Respondent replied to Dr. Aposhian's supplemental expert report with a supplemental expert report of Dr. Brent. (Ex. PP.) Dr. Brent stated that Dr. Aposhian's supplemental report was "replete with incorrect statements, poorly researched science, incorrect calculations, and, hence, invalid conclusions." (*Id*., p. 1.)

Dr. Brent pointed out several important flaws in Dr. Aposhian's analysis. For example, he explained that Dr. Aposhian erred when he borrowed a figure from a certain 1990 medical article for the "distribution ratio" of mercury between the brain and blood. (Ex. PP, pp. 5-7.) Dr. Brent stated that Dr. Aposhian erred in this regard, first, in using a blood-to-brain "distribution ratio" calculated for *methylmercury*, to calculate what the distribution ratio would be for *ethylmercury*, a different form of mercury. (Ex. PP, p. 5 and p. 6 paras. 1, 4.) Dr. Aposhian also erred because the distribution ratio that he used was based on old and questionable data (Ex. PP, p. 6, para. 2), and because that distribution ratio was calculated for *adult* humans (Ex. PP, p. 6, para. 3). Further, Dr. Aposhian erred in an aspect of his calculation in which he compared brain-to-blood distribution ratios between humans and monkeys, by using an inappropriate distribution ratio for monkeys. (Ex. PP, p. 6, para. 3.)

Dr. Brent also noted a lack of logic in Dr. Aposhian's approach. Dr. Brent argued that if Dr. Aposhian's methodology and calculations were correct, then, in light of the fact that most humans ingest substantial amounts of methylmercury from dietary sources, most humans would have brain mercury levels in the range of many hundreds or even thousands of parts per billion. (Ex. PP, p. 7.) However, as noted above (see p. 36), typical brains of humans in Western societies have been shown to contain an amount in the range of two to 40 parts per billion of mercury. (Ex. PP, p. 7; Tr. 1818-19, 1810-11, 4335.)

Another example of Dr. Aposhian's faulty logic, even if one accepted his flawed calculations, is his conclusion that a few children--he calls them the "highest outliers"--might end up receiving,

---

[70]Dr. Aposhian's supplemental report was first filed into the record in this case as an attachment to petitioners' motion filed on July 28, 2008. The same report was later filed again, with the exhibit number 33, on April 1, 2009.

as a result of thimerosal-containing vaccines, as much as 44.7 nanograms of inorganic mercury per gram of brain tissue ("44.7 ng/g"). (Ex. 33, p. 5; see also Ex. PP, pp. 9-10, in which Dr. Brent traces Dr. Aposhian's calculations.) Dr. Aposhian opines that such a level of inorganic mercury in the brain could trigger the petitioners' theorized neuroinflammatory process. Dr. Brent pointed out in response, however, that Dr. Aposhian's theory that levels of inorganic brain mercury of 60 ng/g or below--equal to 60 parts per billion or below--could trigger autism is "completely contrary to the scientific evidence." (Ex. PP, p. 8.) As Dr. Brent points out, in island populations made up of heavy fish-eaters, brain mercury levels of up to several hundred parts per billion are common, yet the rate of autism is no greater than in other human populations. (*Id*.)

In his responsive report, Dr. Brent also makes other detailed criticisms of Dr. Aposhian's methodology, calculation process, and overall logic. (Ex. PP, pp. 1-12.)

After a full consideration of the supplemental reports of both Dr. Aposhian and Dr. Brent, I again find Dr. Brent's arguments to be substantially more persuasive. I find that Dr. Aposhian has *completely failed* to demonstrate that the small amount of inorganic mercury, that would end up in the brain of a child who received a full course of thimerosal-containing vaccines during the 1990s, could cause the type of neuroinflammatory process that the petitioners and Dr. Kinsbourne theorize.

Finally, I note that while Dr. Aposhian attempted--and failed--to demonstrate that the amount of inorganic mercury resulting from a course of thimerosal-containing vaccines could *by itself* provoke brain inflammation, in the last line of his supplemental report, as well as in a few places in his oral testimony, Dr. Aposhian seemed to suggest an alternative approach. That is, he suggested that because children do end up with inorganic mercury in the brain as a result of other sources such as diet, perhaps the *additional* amount of inorganic mercury in the brain as a result of thimerosal-containing vaccines might "push some kids over the toxic threshold." (Ex. 33, p. 7; see also Tr. 365-66, 369, 396.)

However, Dr. Aposhian never attempted to explain or develop this "threshold" suggestion. He never stated what amounts of inorganic mercury he expected to be in a typical infant brain from non-vaccine sources, nor did he explain why the amounts resulting from thimerosal-containing vaccines might push some children over some unspecified hypothetical threshold.

Moreover, certain testimony from Dr. Brent strongly contradicts any "threshold" suggestion by Dr. Aposhian. As previously noted, Dr. Brent explained that normal human brain mercury levels are in the range of two to 40 parts per billion, averaging about 15 parts per billion, while the amount of mercury that would end up in the brain of an American infant from a typical course of thimerosal-containing vaccines during the 1990s would add only about two to three parts per billion.[71] (Tr. 1810-11, 1818-19, 4335.) And, as noted above, in island populations made up of heavy fish-eaters, brain mercury levels of up to *several hundred* parts per billion are common, yet the rate of autism

[71] As noted above (p. 36, fn. 27), the figure of two to three parts per billion might possibly be slightly low, but any such small error would not affect the general analysis.

is no greater than in other human populations. (Ex. PP, p. 8.) In light of that testimony of Dr. Brent, which the petitioners have not persuasively refuted, it seems extremely unlikely that, even taking into account infants' other mercury exposures, the small amounts of additional inorganic mercury resulting from thimerosal-containing vaccines would increase any infant's brain mercury level by enough to cause autism, or any other harm.

7. Summary concerning Dr. Aposhian

For the reasons set forth above, as to each of the specific topics addressed by Dr. Aposhian, I find that the testimony of Dr. Brent, and/or that of another of respondent's witnesses, was much more persuasive than that of Dr. Aposhian. I find that Dr. Aposhian's testimony did not supply any credible support to the petitioners' general causation theory.

E. Flaws in Dr. Deth's testimony

Petitioners' third witness concerning general causation was Dr. Deth, a Ph.D. pharmacologist. Dr. Deth indicated his view that thimerosal-containing vaccines can contribute to causing autism, and attempted to buttress the petitioners' general causation case by stating his opinion that the mercury from thimerosal-containing vaccines can contribute to "oxidative stress" in brain cells. Dr. Deth theorized that such oxidative stress would disrupt brain cell function in several ways, including impairing the production of "glutathione," impairing the process of "methylation," and impairing the function of a "neurotransporter" known as EAAT-3. (*E.g.*, P-1, p. 46; Ex. 23, pp. 4-7.) He proposed that these effects could disrupt brain function, thereby contributing to the appearance of autistic symptoms.

Respondent, in response to Dr. Deth, relied largely on five experts, Dr. Mailman, Dr. Roberts, Dr. Jones, Dr. Johnson, and Dr. Brent. In this regard, I note that while Dr. Deth does have solid credentials in the area of pharmacology, respondent's corresponding experts have qualifications and experience that are substantially *more* impressive. As noted above (p. 30), Drs. Jones, Mailman, and Johnson all have credentials as Ph.D. researchers similar to those of Dr. Deth in terms of length of experience, but Drs. Jones and Mailman have been far more prolific than Dr. Deth in terms of production of published scientific articles, textbooks, and other publications. And Dr. Roberts and Dr. Brent, in addition to having highly distinguished academic and publication backgrounds, are also *medical doctors*, unlike Dr. Deth.

Further, even in the *specific areas* stressed by Dr. Deth concerning "oxidative stress" and "sulfur metabolism," two of respondent's experts have credentials that are substantially more impressive than those of Dr. Deth. That is, Dr. Jones has had far more scientific publications regarding those topics than Dr. Deth, since about 200 of Dr. Jones' publications deal with sulfur metabolism, and about 100 of his publications constitute original research articles that address oxidative stress. (Tr. 2696-97.) And, even more remarkably, Dr. Roberts since 1990 has dedicated his research to the specific area of oxidative stress, with about 180 publications in that area alone. (Tr. 2160.)

Moreover, after fully considering the reports and testimony of all of the expert witnesses who testified concerning this topic, I found the arguments of respondent's witnesses to be substantially more persuasive than those of Dr. Deth. The opinions of respondent's experts appeared logical, and well-grounded in scientific research. Dr. Deth, on the other hand, did not explain his opinion well, and relied heavily on questionable *in vitro* experiments and on his own laboratory's work, part of it unpublished.[72]

I have divided my discussion concerning Dr. Deth's testimony into several sections below.

1. General problems with Dr. Deth's theory

"Oxidative stress" is a phenomenon that occurs at the molecular level. Molecules are made up of atoms, which, in turn, are made up of subatomic particles, including electrons which typically exist in pairs. (Tr. 2167-69.) When an atom loses an electron, leaving an unpaired electron, such loss is known as "oxidation;" when an atom regains a missing electron, that is known as "reduction." (*Id*.) The oxidation and reduction processes take place frequently in nature, but when there is an imbalance between oxidation and reduction, with an excess of oxidation, that is known as "oxidative stress." (Tr. 2170; Ex. S, p.6.) Dr. Deth's theory, as noted above, is that the inorganic mercury from thimerosal-containing vaccines causes oxidative stress in brain cells, which contributes to autistic symptoms. Respondent's experts, on the other hand, opined that there is no merit to Dr. Deth's theory.

Respondent's experts Dr. Roberts, Dr. Jones, and Dr. Johnson explained that every human being regularly experiences oxidative stress, which is a natural process that occurs from many

---

[72]In their post-hearing briefs, petitioners attempt to portray the theories presented by Dr. Kinsbourne and Dr. Deth as parts of a unified general causation theory. (*E.g.*, P-1, p. 12, final paragraph.) And it is true that the two presentations were similar in the sense that both theorize that the inorganic mercury that enters the brain as a result of thimerosal-containing vaccines can disrupt the function of brain cells, thereby causing autistic symptoms. However, it is noteworthy that the two experts propose *distinctly differing mechanisms* by which the alleged brain cell dysfunction is caused. As noted above, Dr. Kinsbourne posits a "neuroinflammation" process, in which the mercury triggers an immune reaction from microglial cells, the actions of the microglial cells disrupt the glutamate-mopping function of the astrocyte cells, and the resulting glutamate excess leads to a persistent state of "overarousal" of the brain. Dr. Deth, on the other hand, theorizes that the mercury causes "oxidative stress" and disrupts brain function by lowering the production of glutathione in the brain, turning off the activity of "methionine synthase," shutting down the "methylation" processes necessary for proper neuronal function, and impairing the pathway of the "D-4 dopamine receptor." (*E.g.*, P-1, pp. 12, 47.) The specifics of Dr. Deth's proposed mechanism, thus, are very different from Dr. Kinsbourne's proposed mechanism.

In fact, *neither* of the two experts' proposed mechanisms was persuasive, for reasons set forth above. The fact, however, that the proposed mechanisms of the petitioners' two primary "general causation" experts are so different, is simply one a*dditional* reason to be skeptical concerning the validity of the petitioners' overall "general causation" theory in this case.

causes, including ordinary diet and exercise.[73] (Ex. CC, p.4; Ex. Q, p.7; Tr. 2170-71, 2185-86, 2741-42.) Those experts explained that the occurrence of oxidative stress does *not* mean that damage has been done to the human body. (Tr. 2172, 2176, 2186, 2195-96.) To the contrary, oxidative stress can have a *protective* effect for the human body, by instigating the body's protective mechanisms. (Tr. 2171-73, 2186; Ex. S, p.7.) In fact, the benefit of exercise for a human is that the exercise causes a modest oxidative stress, Dr. Roberts testified. (Tr. 2171-72.) Drs. Johnson, Roberts, and Jones noted that since all humans constantly experience oxidative stress from many different sources throughout their lives, if Dr. Deth's causation theory were correct, then everyone would be autistic. (Ex. Q, p.7; Ex. CC, p. 4; Ex. S, p2.)

In detailing his proposed causation process, Dr. Deth stated that in the brain the inorganic mercury from thimerosal-containing vaccines would cause oxidative stress by triggering a reduction of the levels of a substance known as glutathione, thereby disturbing the brain's "sulfur metabolism." (Ex. 23, pp. 3-4; Tr. 508-14.) Dr. Jones, however, explained that the body's amount of glutathione and its capacity to make glutathione are great, so that the small amount of inorganic mercury generated by thimerosal-containing vaccines simply would be far too small to have any significant effect on glutathione levels and sulfur metabolism. (Tr. 2706-08, 2712, 2714-15, 2717-19, 2738-39; Ex. S, p.9.) For example, he stated that the cumulative mercury dose from a normal (1990s) six-month course of thimerosal-containing vaccines would cause no more of an effect on the body's glutathione level than would be caused by drinking a four-ounce glass of milk. (Tr. 2713-14.) He explained further that even if the entire amount of thimerosal contained in a full six-month course of thimerosal-containing vaccines was administered to an infant at one time, the resulting depletion in the person's glutathione would be so slight that it would take the body less than one minute to replace the glutathione. (Tr. 2718-19.)

Moreover, Dr. Johnson testified that while Dr. Deth proposed that oxidative stress leads to neuroinflammation and autism, in all diseases of the brain known to involve oxidative stress and neuroinflammation, the disease progresses to eventual neuronal cell loss and death--yet that does not happen in autism. (Ex. Q, pp.3-4; Tr. 2246-48.) In addition, Drs. Johnson and Jones pointed to evidence indicating that oxidative stress is more likely to be the *effect* of disease, not the *cause* of disease. (Ex. Q, p.8; Ex. S, p.13.)

2. The studies on which Dr. Deth relied do not support his theory.

Respondent's experts also pointed out significant problems with the experiments and studies that Dr. Deth offered in support of his theory.

[73] Dr. Deth himself acknowledged that oxidative stress is a normal process in the human body. (Tr. 3915.)

a. Limits on the usefulness of <u>in vitro</u> experiments

Respondent's experts criticized Dr. Deth's reliance on several *in vitro* studies. They explained that while *in vivo* studies are studies that are done on living humans or other animals, *in vitro* studies are studies in which a cell or other entity is removed from a living being and studied in a laboratory setting. They testified that what happens to a cell in a laboratory when exposed to a chemical might be completely different from the effect that such chemical might have on a similar cell if it was part of a living being. They noted that *in vitro* studies are useful for *generating hypotheses* about toxicity, but that any hypotheses generated by *in vitro* experiments must be considered as purely speculative until *in vivo* testing can be done. (Ex. G, pp. 16-18; Ex. S, pp. 2, 7-9; Ex. CC, pp. 4-6; Tr. 1824-32, 2000-05, 2183-84, 2204-05, 2719, 2724-33.)

b. Chauhan and Ming studies

In his expert report, Dr. Deth relied upon two studies by Chauhan[74] and one by Ming,[75] for the proposition that increased levels of oxidative stress in autistics "has been well-documented." (Ex. 23, pp. 4, 9, 10.) However, Dr. Roberts persuasively criticized Dr. Deth's reliance on those studies. (Ex. CC, pp. 2-3; Tr. 2178-83.) Dr. Roberts, the expert with outstanding experience specifically concerning oxidative stress, explained that all three studies used unreliable measures of oxidative stress. (*Id.*)

c. Dr. Deth's own experiments

Dr. Deth placed great reliance on the results of two *in vitro* experiments performed by his own laboratory. This reliance was also strongly criticized by respondent's experts.

Dr. Deth was the principle author of an article published in 2004, in which the first-named author was Waly.[76] In the experiment described in that article, the investigators exposed human "neuroblastoma" cells to thimerosal *in vitro*, and found that the ability of the cells to produce glutathione was reduced. Dr. Deth relied on that result as support for his theory that the thimerosal in thimerosal-containing vaccines can reduce glutathione in brain cells, thereby causing oxidative stress and, eventually, autism.

---

[74]Abha Chauhan & Ved Chauhan, *Oxidative Stress in Autism*, 13 PATHOPHYSIOLOGY 171 (2006) (PML 48); Abha Chauhan, et al., *Oxidative Stress in Autism: Increased Lipid Peroxidation and Reduced Serum Levels of Ceruloplasmin and Transferrin - the Antioxidant Proteins*, 75 LIFE SCIENCES 2439 (2004) (PML 481).

[75]X. Ming, et al., *Increased Excretion of a Lipid Peroxidation Biomarker in Autism*, 73 PROSTAGLANDINS, LEUKOTRIENES & ESSENTIAL FATTY ACIDS 379 (2005) (PML 124).

[76]M. Waly, et al., *Activation of Methionine Synthase by Insulin-Like Growth Factor-1: A Target for Neurodevelopmental Toxins and Thimerosal*, 9 MOLECULAR PSYCHIATRY 358 (2004) (PML 257).

The criticisms of Dr. Deth's reliance on the Waly study by respondent's experts were persuasive. First, the Waly experiment was an *in vitro* experiment, so that its results do not provide strong evidence concerning what the effects of mercury in a *living brain* might be, for the reason described above. (See p. 72 above.) Indeed, even Dr. Deth and his co-authors of the Waly article acknowledged that it is "obvious that biochemical studies under cultured cell conditions do not replicate the complex *in vivo* environment." (PML 257, p. 368.) Thus, Dr. Deth's heavy reliance on this *in vitro* experiment as justification for his overall causation theory seems highly inappropriate, as respondent's experts testified. (Ex. Q, p. 5, para. 2; Ex. CC, pp. 5-6; Tr. 1827-28.)

Further, there are additional difficulties with the Waly study. Dr. Mailman testified that there were so many faults with the article that, had he been the editor of a medical journal, he would not have accepted the article for publication (Tr. 1999), and later Dr. Deth acknowledged that several journals did reject the submitted article before a fourth journal accepted it (Tr. 3967-68). Among other things, Dr. Mailman explained that the Waly investigators failed to use appropriate experimental "controls." (Ex. AA, p. 6; Tr. 1996-97.) Dr. Mailman, Dr. Johnson, and Dr. Brent also found fault with the Waly investigators' use of "neuroblastoma" cells for the experiment, since such cells are abnormal, so that the experiment could not predict what might happen with *normal* brain cells. (Ex. Q, p. 5, para 1; Ex. AA, p. 6; Ex. G, p. 19; Tr. 1995-96, 2219-20.) Dr. Mailman and Dr. Johnson also noted a number of other specific problems with the techniques and data analysis utilized in the study.[77] (Ex. Q, pp. 5-7; R. Trial Ex. 5, p. 23; Tr. 2016-17.)

Dr. Deth also relied heavily, during his oral testimony, on *unpublished* data from a second series of *in vitro* experiments conducted in his laboratory. Respondent's experts persuasively criticized Dr. Deth's reliance on that unpublished data. Dr. Mailman argued that such unpublished data should be disregarded on the basis of the lack of publication alone, since that data has not been presented to the scientific community for peer-review and analysis. (Tr. 1999-2000.) In that regard, it is noteworthy that, at the evidentiary hearing, Dr. Deth admitted that much of that data was generated in 2006 or early 2007 (Tr. 649-52), yet that data was *not* included or described in any detail in his expert report, which he submitted in August of 2007 (Ex. 23, p. 1).

Moreover, even though respondent's experts had little opportunity to scrutinize Dr. Deth's reported data from his 2006-2007 study, because it was neither published nor included in Dr. Deth's expert report, nevertheless after hearing his oral testimony at the hearing, those experts were able to readily identify a number of substantial problems with the data as described by Dr. Deth. For example, Dr. Johnson identified calculation errors on two of the "slides" on which Dr. Deth presented his data at the hearing, errors that Dr. Johnson found to be evidence of "careless" work. (Tr. 2228-29.) Dr. Johnson also noted that Dr. Deth described his unpublished data as showing an adverse biological effect of thimerosal at a dose that was "100 to 1000 times lower than any other published data." (Ex. Q, p. 4; Tr. 2221-24.) Dr. Johnson found that result to be so vastly different

---

[77]In addition, an Institute of Medicine (IOM) Committee (see p. 96 below) evaluated the Waly study. The IOM committee found that the study did *not* provide support for the proposition that thimerosal can contribute to causing autism. (RML 255, pp. 136-37.)

from previous experiments as to be extremely unlikely, so that "the most likely explanation for [Deth's reported result] is technical error." (*Id*.) Dr. Jones pointed out the same problem. (Tr. 2720-22, 2733-34.) Dr. Jones added that it would not make sense scientifically to accept that unpublished, unscrutinized, highly implausible result reported by Dr. Deth, rather than the *published* results of other laboratories. (Tr. 2734-35.)

Dr. Johnson also pointed out a number of ways in which Dr. Deth's descriptions of his unpublished data at the hearing simply left it unclear how that data was derived, and thus unclear whether there is any validity to that data. (Tr. 2234, 2236-38.)

Indeed, Dr. Deth himself seemed to concede, during his rebuttal testimony after respondent's experts had testified, that Dr. Johnson had raised reasonable doubt about the validity of Dr. Deth's unpublished data. Dr. Deth stated that he would take Dr. Johnson's criticisms of his unpublished data "to heart," and admitted that it was "incumbent" on him to "go back to the lab" and respond to Dr. Johnson by "checking" his own calculations.[78] (Tr. 3921-22.)

In short, the respondent's experts were persuasive in their arguments that the work of Dr. Deth's own laboratory does not provide support for his stated causation theory.

d. James articles

Dr. Deth stated that two articles by James and colleagues constitute the "strongest evidence" supporting his causation theory.[79] (Tr. 583; Ex. 23, p. 9, references 9 and 10.[80]) Dr. Deth relied upon the two articles for the proposition that thimerosal "interferes with cellular production" of glutathione (Ex. 23, p. 6), thereby causing autistics to have insufficient amounts of the glutathione needed to combat oxidative stress. (Tr. 537; see also Pet. Tr. Ex. 3, slide 13.) Respondent's experts argued convincingly, however, that those articles do not offer persuasive support for Dr. Deth's theory.

---

[78]More than 21 months have passed since Dr. Deth made those statements, that he would return to his laboratory and check his data. During that time, however, petitioners have not attempted to submit any supplementary report from Dr. Deth.

[79]Confusingly, Dr. Deth labeled the James articles as his "strongest evidence" only minutes after indicating that his *own* unpublished laboratory work was the "strongest piece of evidence" supporting his theory. (Tr. 582-83.)

[80]S. Jill James, et al., *Metabolic Biomarkers of Increased Oxidative Stress and Impaired Methylation Capacity in Children with Autism*, 80 AM. J. CLINICAL NUTRITION 1611 (2004) (PML 5); S. Jill James, et al., Metabolic Endophenotype and Related Genotypes are Associated with Oxidative Stress in Children with Autism, 141 AM. J. MED. GENETICS Part B (Neuropsychiatric Genetics) 947 (2006) (PML 49).

It is true that the James 2004 study found less glutathione in the blood *plasma* of autistic children, when compared to non-autistic controls. However, James and her co-authors acknowledged in that very article that "attempts to interpret these findings are clearly speculative." (PML 5, p. 1615.) Moreover, Dr. Deth opined that his theorized glutathione decrease and resulting oxidative stress would occur in the *brain*, not in the blood. (*E.g.*, Tr. 622-23; P-1, pp. 16, 45.) Dr. Roberts and Dr. Jones testified that findings of oxidative stress in plasma do *not* indicate oxidative stress in the *brain* (Tr. 2173, 2176-77, 2745-46), and Dr. Deth then agreed, acknowledging that James' test of glutathione levels in plasma "doesn't tell us what the brain concentration is" (Tr. 3986). Accordingly, the 2004 James article provides no support for Dr. Deth's theory that thimerosal-containing vaccines contribute to autism by lowering glutathione levels in the *brain*.

In the 2006 James article, the authors found genetic variations ("polymorphisms") in some autistic children, and speculated that such variations could indicate that autistic children have an increased vulnerability to oxidative stress that might contribute to autistic symptoms. (PML 49, p. 947.) However, again the article's authors cautioned that the findings of their small study "should be considered preliminary until confirmed in larger population-based studies" (*id*. at p. 954), and no such subsequent studies have been published (Tr. 639; Ex. CC, p. 5). Dr. Roberts, the oxidative stress expert, also pointed out other limitations of the James 2006 study. (Ex. CC, p. 5.) Thus, as Dr. Roberts suggested, that article does not provide significant evidence for the proposition that oxidative stress plays a role in autism. (*Id*.) Moreover, even if *oxidative stress* does play some causal role in autism, there would still be no reason to think that the tiny amount of *thimerosal in vaccines* could play any significant role in causing oxidative stress, as shown above.

Accordingly, I conclude that the two cited James articles also do not provide substantial support for Dr. Deth's causation theory.

e. Hornig article

Dr. Deth also relied on the 2004 mouse study by Hornig and colleagues. (Ex. 23, p. 4, reference 26; Tr. 3945-53, 3986-88.) However, Dr. Johnson testified that the quality of the technical work in the Hornig study was poor. (Tr. 2212-14.) Moreover, as discussed above, another research group, led by Berman, attempted to replicate the Hornig experiment using more detailed and sophisticated techniques, but arrived at different results, casting doubt on the results of Hornig's study. (Ex. G, p. 39; Tr. 1845-46.) And Dr. Johnson testified that the quality of the technical work in the Berman study was much better than that in the Hornig study. (Tr. 2214-2218.)

During his rebuttal testimony, Dr. Deth referred to a study by Laurente that he had not mentioned in his report or initial testimony, opining that the Laurente study supported the Hornig study. (Tr. 3948, 3952-53.) However, in a post-hearing expert report, respondent's expert Dr. Brent explained in detail why the Laurente study is flawed. (Ex. PP, p. 14.)

I conclude that, in light of the Berman study, the Hornig study provides no significant support for Dr. Deth's testimony, just as it provided no support for Dr. Aposhian's testimony.

3. Dr. Deth's argument concerning treatment

Dr. Deth also argued that treatments designed to reduce oxidative stress or remove heavy metals from the body have been "reported to bring clinical improvement in autism," thus suggesting that oxidative stress and heavy metals may play a causal role in autism. (Ex. 23, p. 8.) However, the evidence cited by Dr. Deth for this proposition does not support this argument. Dr. Deth cited a 2006 article by Nataf to support this assertion (Ex. 23, p. 8, reference 7[81]), but clinical improvement was *not* assessed in that Nataf study, as Dr. Roberts pointed out. (Ex. CC, p. 6.) A second article cited by Dr. Deth, by Boris and colleagues,[82] was criticized by Dr. Roberts, and the study's own authors acknowledged that the study's limitations reduced the ability to draw any "strong conclusions" regarding whether the treatment was actually beneficial. (Ex. CC, p. 6.)

I conclude that Dr. Deth's brief mention of the treatment point provides no significant evidence for his overall causation theory. See also the discussion concerning treatment below (pp. 108-09).

4. Failure to explain relationship to regression

Dr. Deth offered his opinion in support of the petitioners' *general causation* theory in this case, which, as discussed above (p. 42), is that thimerosal-containing vaccines can contribute to the causation specifically of "regressive autism." However, Dr. Deth never explained why his theory would be specifically applicable to autism with regression, rather than to autism in general. To the contrary, on cross-examination he admitted that his theory would *not* apply only to regressive autism. (Tr. 614.) But, as will be discussed below (pp. 79-96), the epidemiologic studies show clearly that thimerosal-containing vaccines are not a significant cause of autism *in general*. Therefore, Dr. Deth's failure to suggest why his causation theory would affect only those with autistic regression is yet another reason to doubt the reliability of his testimony.

5. Summary concerning Dr. Deth

Each of respondent's five experts who discussed Dr. Deth's theory found it to be without merit. Dr. Johnson, the neuropathologist, opined that Dr. Deth's entire approach to the issue was simply unscientific, and wholly invalid. (Tr. 2238-40, 2247-48.) Dr. Jones, the medical biochemist, explained that the evidence indicates that the small amounts of inorganic mercury from thimerosal-containing vaccines would not have any of the effects proposed by Dr. Deth (Tr. 2756-58), so that there is "no plausibility * * * at all" to Dr. Deth's hypothesis (Tr. 2757). Dr. Mailman, the neuropharmacologist, stated that "the odds of [Dr. Deth's theory] being correct are literally almost

---

[81]Robert Nataf, et al., *Porphyrinuria in Childhood Autistic Disorder: Implications for Environmental Toxicity*, 214 TOXICOLOGY & APPLIED PHARMACOLOGY 99 (2006) (PML 65).

[82]Marvin Boris, et al., *Effect of Pioglitazone Treatment on Behavioral Symptoms in Autistic Children*, 4 J. NEUROINFLAMMATION 3 (2007) (PML 114).

infinitesimal." (Tr. 2005.) Dr. Roberts, the expert with superb experience concerning oxidative stress, summarized that there is no reliable evidence at all that autism is caused by oxidative stress, much less oxidative stress resulting from thimerosal-containing vaccines. (Tr. 2186.) And Dr. Brent, the medical toxicologist, stated that there is "absolutely not" any evidence that thimerosal-containing vaccines induce oxidative stress. (Tr. 1847-48.)

Indeed, even Dr. Deth himself admitted that his theory still awaits testing, is only a "useful starting point" for considering the thimerosal/autism causation issue, and could be "revised or discarded." (Tr. 655, 3990.)

After listening to the testimony of Dr. Deth and respondent's corresponding experts, including the rebuttal testimony of Dr. Deth, I find that the testimony of respondent's experts concerning these issues was persuasive, and the testimony of Dr. Deth was not. In the pages above, I have highlighted some of the areas in which respondent's experts convincingly rebutted specific points raised by Dr. Deth. There were also a number of other specific points concerning which Dr. Deth's presentation was again shown to be erroneous, too numerous to detail here.

In this regard, I note that I am *not* concluding that it is *established* that oxidative stress plays no role in autism. There is at least some evidence indicating that oxidative stress might *possibly* play a role in autism. (See, *e.g.*, the James 2006 study discussed above, or PML 705.[83]) However, based upon the evidence placed into the record of this case, it is *unclear* whether oxidative stress plays *any* role in autism. And there certainly has *not* been a showing that it is probable that oxidative stress plays a *causal* role in autism.

Moreover, even if it were to be assumed that *oxidative stress* does play some type of causal role in autism, there is simply a lack of any persuasive evidence that the *inorganic mercury from thimerosal-containing vaccines* would cause any substantial amount of oxidative stress.

Accordingly, after considering all the evidence in the record concerning this issue, I find that the testimony of respondent's highly-qualified experts was far more persuasive than that of Dr. Deth. I find no credible support for Dr. Deth's theory that thimerosal-containing vaccines can contribute to the causation of autism by causing oxidative stress.[84]

---

[83]S. Jill James, *Oxidative Stress and the Metabolic Pathology of Autism*, Chapter 11 in AUTISM: CURRENT THEORIES AND EVIDENCE (Andrew Zimmerman, ed., Humana Press 2008) (PML 705).

[84]I also note that even if one could somehow credit Dr. Deth's dubious theory that inorganic mercury in the brain can cause oxidative stress and thereby trigger autistic behavior, Dr. Deth's argument would *still* fail to be of help to petitioners, for the same crucial reason discussed in detail above as to Dr. Kinsbourne's theory. That is, as Dr. Brent testified, infants acquire substantially more inorganic mercury in the brain from *other* sources, such as diet, than they would have acquired from a normal American course of thimerosal-containing vaccines during the 1990s. (See pp. 50-51 above.) Thus, even if one could somehow show that a child had autism caused by inorganic mercury

F. Dr. Mumper's view concerning "general causation"

A fourth expert witness of the petitioners was Dr. Elizabeth Mumper, a pediatrician. Petitioners offered Dr. Mumper's testimony in this case solely for the purpose of proving "specific causation" concerning Jordan King's own case; her testimony was also offered for the same purpose in the two other "test cases" as to the petitioners' second general causation theory, the William Mead and Colin Dywer cases. However, in the process of expressing her view that thimerosal-containing vaccines *did* likely contribute to the causation of autism in the three individual cases, Dr. Mumper obviously also indicated her general view that thimerosal-containing vaccines *can* contribute to the causation of autism. Therefore, I include this section in my Decision in order to make clear that I have considered Dr. Mumper's views concerning general causation in my evaluation of the petitioners' general causation theory.

In fairness to Dr. Mumper, I note that, given her designated role in the case as the petitioners' expert concerning *specific* causation, Dr. Mumper was *not asked* to explain her *general* view that thimerosal-containing vaccines can contribute to causing autism. Thus, it is not surprising, and not a criticism of her, that she did not provide such a general explanation in any detail, in either her expert report or hearing testimony. What Dr. Mumper did provide in this regard, rather, was merely a very brief indication that she relies upon the *same general causation* mechanisms proposed by Drs. Deth, Aposhian, and Kinsbourne. For example, in her expert report, Dr. Mumper noted that she was relying on the specific expert reports of Drs. Deth and Aposhian in this case. (Ex. 13, pp. 3, 8-9.) In that same report, she also cited a number of the same medical articles cited by Drs. Deth, Aposhian, and Kinsbourne. (Ex. 13, pp. 4, 6-8.) In her hearing testimony, she again made similar general representations that she was relying upon the "general causation" theories of Dr. Deth, Dr. Aposhian, and Dr. Kinsbourne. (Tr. 1224-29.) She even added that she first came to the belief that thimerosal-containing vaccines might cause autism by reading Dr. Deth's work. (Tr. 1224.)

Accordingly, for purposes of this case, I must assume that Dr. Mumper's general belief that thimerosal-containing vaccines *can* contribute to the causation of autism is derived from the same reasoning explained by Drs. Deth, Aposhian, and Kinsbourne, and relies on the same evidence cited by those three experts. However, for the reasons set forth above, I have found the reasoning of those experts to be severely flawed, and the evidence upon which they rely to be quite unpersuasive.

Thus, I acknowledge that Dr. Mumper is a pediatrician of considerable experience, with a creditable academic background, and with very substantial experience in treating autistic children. I find no reason to believe that Dr. Mumper is not sincere in her general view that thimerosal-containing vaccines can contribute to causing autism. And I acknowledge that the mere fact that she holds that general view, given her credentials, is at least *some* evidence in favor of that general view. However, having already thoroughly considered and rejected the *reasoning and evidence* upon which

---

in the brain, via Dr. Deth's proposed mechanism *or* Dr. Kinsbourne's proposed mechanism, one could still not say that the autism was substantially caused by the mercury *from thimerosal-containing vaccines*.

Dr. Mumper seems to rely, I conclude that the evidentiary value of her general opinion is *far outweighed* by the overwhelming evidence to the contrary provided by respondent's experts and the medical literature supplied by respondent.

G. Epidemiology

Numerous medical researchers have studied the issue of whether thimerosal-containing vaccines cause autism. The results of those epidemiologic studies, taken as a whole, add another significant reason to reject the petitioners' "general causation" theory in this case.

1. All competent epidemiologic studies have found no association between thimerosal-containing vaccines and autism.

Epidemiology is the study of the distribution of disease in human populations and the factors that influence that distribution. (Tr. 3625, 3088-89.) It is a branch of medical science that has been very important in studying the environmental causes of diseases. (Tr. 3297.) After the issue of whether thimerosal-containing vaccines might cause autism was raised about 1999, a number of research groups in several countries conducted epidemiologic studies concerning that issue. With the exception of several studies by one suspect research group to be discussed separately below (pp. 86-87), all of the studies *found no evidence of any association*[85] between exposure to thimerosal-containing vaccines and autism.

There have been eight important, competent studies which have looked at the issue of whether the thimerosal-containing vaccines are "associated" with autism--*i.e.*, whether children who received thimerosal-containing vaccines are more likely to be autistic than those children who did not receive thimerosal-containing vaccines. *All* of those studies have *failed* to find any association. (RML 255, pp. 42-55; Ex. M, paras. 91-109; Ex. GG, paras. 76-89; Tr. 3301-06, 3377-86, 3638-59.) I will briefly discuss each of those eight studies, and two additional relevant studies, below.

a. Hviid study

One major study was conducted by Hviid and colleagues concerning the Danish population, and was published in 2003.[86] The Hviid study was an extremely large cohort study which looked at incidence rates of autism in more than 467,000 children born between 1990 and 1996. The study

---

[85]Technically, epidemiologic studies do not address the question of whether Factor A "causes" Condition B, but instead whether the two are "associated." Two factors are said to be "associated" if they occur together more often than would be expected by chance. (*Dorland's* at 167.) If an "association" is found, then medical experts will evaluate other factors to determine if that association is "causal." (RML 169, p. 156.) But if no association is found, then that result casts doubt on (though does not entirely disprove) the proposition that Factor A is a cause of Condition B.

[86]Anders Hviid, et al., *Association Between Thimerosal- Containing Vaccine and Autism*, 290 JAMA 1763 (2003) (PML 238).

took advantage of the fact that thimerosal was discontinued in vaccine production in that country in 1992, so that there were large groups both of children who had received thimerosal-containing vaccines, and those who had not. The study's results were that there was no increased risk of autism among the children who received thimerosal-containing vaccines, in comparison to those who did not. There was no evidence of a "dose-response" effect, meaning that there was no increased risk of autism associated with increased intake of thimerosal. The study was published in a leading medical journal, the *Journal of the American Medical Association*. (RML 255, pp. 42-44; Ex. M, para. 93-94; Ex. GG, para. 81; Tr. 3638-42.)

b. Madsen study

A second study involving Danish data was conducted by Madsen and colleagues, and was published in 2003.[87] This study was similar to the Hviid study noted above in some respects, but looked at data from a much longer time period, from 1971 to 2000. (PML 239; Ex. M, para. 103; Tr. 3647-50, 3742-47; RML 255, p. 53.) The results of the study showed that the incidence of autism in Denmark remained relatively static from 1971 through 1985, with a mild rise in the rate of autism diagnoses in the late 1980s, then a sharp rise beginning in 1990 and continuing throughout the 1990s. (PML 239, p. 605, Figure 1.) That increasing frequency of autism diagnoses, however, had no correlation to the exposure of children to thimerosal, which was contained in Danish infant immunizations until 1992, then eliminated from infant immunizations in that year. (PML 239, p. 604.) To the contrary, the notable result was that the increase in autism diagnoses began during a time period (1985 through 1991) when there was *no change* in the amount of thimerosal given to Danish children, then continued to rise steeply when thimerosal was *eliminated* from infant vaccinations in 1992. The study's authors concluded that the data did not support an association between thimerosal-containing vaccines and the incidence of autism. (*Id*. at 605.)

c. Verstraeten study

Another major study, concerning American children, was conducted by Verstraeten and colleagues and also published in 2003.[88] Verstraeten was another large cohort study, involving well over 100,000 children. The authors recorded the cumulative thimerosal administered to children in vaccines at ages one, three, and seven months, and evaluated whether there was any statistical association between the amount of thimerosal received and the incidence of autism. The study found *no statistical association* between the exposure to thimerosal and autism, whether thimerosal receipt was measured at the one-month, three-month, or seven-month stage. The study was published in the well-respected medical journal *Pediatrics*. (Ex. M, paras. 98-101; Ex. GG, para. 79; Tr. 3301-03, 3377-82, 3642-45; RML 255, pp. 44-52.)

---

[87] Kreesten M. Madsen, et al., *Thimerosal and the Occurrence of Autism: Negative Ecological Evidence From Danish Population-Based Data*, 112 PEDIATRICS 604 (2003) (PML 239).

[88] Thomas Verstraeten, et al., *Safety of Thimerosal-Containing Vaccines: A Two-Phased Study of Computerized Health Maintenance Organization Databases,* 112 PEDIATRICS 1039 (2003) (PML 247).

Some people, associated with the belief that thimerosal-containing vaccines can cause autism, have raised criticisms concerning the Verstraeten study. However, a committee of the Institute of Medicine[89] considered and discounted those criticisms, finding that the Verstraeten study used established epidemiologic procedures, and reached valid results. (RML 255, pp. 47-52.)

d. Stehr-Green study

A fourth important study was published in 2003 by Stehr-Green[90] and colleagues. This study looked at data from three areas: Denmark, which removed thimerosal from pediatric vaccines in 1992; Sweden, where the infant vaccination schedule always included less thimerosal than in Denmark or the United States, and which eliminated thimerosal in 1993; and California, where total thimerosal receipt by infants actually increased in the 1990s due to the introduction of the hepatitis B and Hib vaccinations, and where thimerosal remained in infant vaccinations throughout the 1990s, before being eliminated after 2000. (PML 230, p. 103; Ex. M, para. 104; Ex. GG, para. 87; Tr. 3645-47; RML 255, pp. 54-55.)

The data showed that the diagnoses of autism began to rise in *all three areas* in the 1985-89 period, and that the rate of increase in all three locales accelerated in the early 1990s. (PML 230, p. 101.) This was true even though during the studied period thimerosal exposure was *declining* and eventually eliminated in Denmark and Sweden, while the exposure to thimerosal was *increasing* in the 1990s in California. The study's authors concluded that these results, in which the rates of autism diagnoses were similar in all three areas despite the fact that the pattern of thimerosal exposure was starkly different between the areas, were *inconsistent* with the proposition that thimerosal has any causal link to autism. (PML 230, p. 101.)

e. Andrews study

A study involving British children was published by Andrews and colleagues in 2004, again in the *Pediatrics* journal.[91] That cohort study used data from about 110,000 children born between 1988 and 1997. The authors measured exposure to thimerosal at ages three, four, and six months, and checked whether the amount of exposure to thimerosal at any of those ages was associated with

---

[89]For a discussion of that Institute of Medicine report, see pp. 96-98 below.

[90]Paul Stehr-Green, et al., *Autism and Thimerosal-Containing Vaccines: Lack of Consistent Evidence for an Association,* 25 AM. J. PREVENTIVE MED. 101 (2003) (PML 230).

[91]Nick Andrews, et al., *Thimerosal Exposure in Infants and Developmental Disorders: A Retrospective Cohort Study in the United Kingdom Does Not Support a Causal Association,* 114 PEDIATRICS 584 (2004) (PML 4).

rates of autism. The study found no relationship between exposure to thimerosal and the incidence of autism.[92] (PML 4; Ex. M, paras. 95-96; Ex. GG, para. 78; Tr. 3301, 3650-52.)

f. Fombonne study

A study involving Canadian children was published by respondent's expert Dr. Fombonne, along with several co-authors, in 2006.[93] The study looked at a period of time in which the vaccination schedule in Quebec changed, so that in the early years (1987-91) infants were cumulatively exposed to a medium level (100 to 125 micrograms) of ethylmercury from thimerosal-containing vaccines; during the middle years (1992-95) the exposure became substantially higher (200 micrograms); and during the later years (1996-98) thimerosal was eliminated from the vaccines. The results were that the increase in thimerosal, then the elimination of thimerosal, had *no effect* on the pattern of diagnosis of autism in the studied children. (PML 40; Ex. M, paras. 105-06; Ex. GG, para. 80; Tr. 3655-57, 3748-52.) The authors concluded that their results concurred with those of previous studies, noted above, finding *no association* between thimerosal exposure and autism. (PML 40, p. 148.)

g. Schechter and Grether study

Another study of American children was published by Schechter and Grether in 2008.[94] This study took advantage of the fact that, as noted above, thimerosal was gradually phased out of infant vaccinations in the United States from 1999 to 2002. The authors looked at California data concerning the number of children reported as autistic to the California Department of Developmental Services. Their hypothesis was that if the thimerosal in vaccines was causing a substantial amount of autism, then the number of children seeking services for autism from that department should *decline* in correspondence with the phase-out of thimerosal in vaccines. The results they found, however, were that the numbers of autistic children in California continued to *climb* throughout the years when one would have expected *reduced* numbers under their hypothesis. (PML 432; Ex. M, para. 107; Ex. GG, para. 88; Tr. 3657-59, 3815-17.) The authors concluded that this result was *inconsistent* with the hypothesis that thimerosal had been a primary cause of autism in California. (PML 432, p. 22.)

---

[92]The Institute of Medicine's 2004 report described a then-unpublished study by "Miller," which was soon to be published in the *Pediatrics* journal. (RML 255, pp. 62-64.) That description was of the Andrews study, which was published later that year in *Pediatrics*, with Elizabeth Miller as the second author.

[93]Eric Fombonne, et al., *Pervasive Developmental Disorders in Montreal, Quebec, Canada: Prevalence and Links with Immunizations*, 118 PEDIATRICS 139 (2006) (PML 40).

[94]Robert Schechter & Judith K. Grether, *Continuing Increases in Autism Reported to California's Developmental Services System: Mercury in Retrograde*, 65 ARCHIVES GEN. PSYCHIATRY 19 (2008) (PML 432).

h. Jick and Kaye study

Another study of British children was described by Jick and Kaye in 2004.[95] The authors examined records of children born between 1990 and 1998, and compared a group of autistic children to a set of "control" children matched to the autistic subjects by gender and age. They measured whether there was any difference between the autistics and controls in terms of exposure to thimerosal. The study found no significant difference between the autistics and controls as to exposure to thimerosal. (PML 92; Ex. M, para. 102; Tr. 3652-53.) This finding caused the authors to comment that their results "provide further support for the view that exposure to mercury in vaccines is not the cause of the rising incidence of autism." (PML 92, p. 2723.)

The results of this Jick and Kaye study, then, are quite consistent with the epidemiology studies described above. However, there are two problems with the study that substantially diminish its value. First, the results of the study were not presented in a full-length article in a medical journal, as were those of the other studies listed above. Instead, only a short letter describing the study was published. (See fn. 95 below.) Second, the published letter is followed by a notation indicating that the study's two authors served as consultants to a law firm representing a vaccine manufacturer. If those authors were retained in such a consultant capacity at the time that they conducted the study, that arrangement would call into question the objectivity of the authors.

For those two reasons, then, I accord the results of this study only minimal weight, compared to the other epidemiologic studies described in this section of this Decision.

i. Heron and Thompson studies

Two other studies did not directly address the question of an association between thimerosal and autism, but do provide relevant information.

The first study, involving British children, was published by Heron and colleagues in 2004, again in the *Pediatrics* journal.[96] This study followed 13,000 children in one geographical area from birth to school age, and measured exposure to thimerosal at ages 3, 4, and 6 months, to determine whether the level of exposure to thimerosal was associated with any negative outcomes. The study did not specifically use autism as an outcome, but did note whether each child was designated for special educational needs. The study found no association between exposure to thimerosal and the risk of being designated for special education. (PML 14; Ex. M, para. 97; Ex. GG, paras. 76-77; Tr. 3301, 3382-86, 3654-55.) Dr. Fombonne commented that since autistic children are usually

---

[95]Hershel Jick & James A. Kaye, *Autism and DPT Vaccination in the United Kingdom*, 350 NEW ENG. J. MED. 2722 (2004) (PML 92).

[96]Jon Heron, et al., *Thimerosal Exposure in Infants and Developmental Disorders: A Prospective Cohort Study in the United Kingdom Does Not Support a Causal Association,* 114 PEDIATRICS 577 (2004) (PML 14).

designated for special education, this was another example of a study indicating no relationship between thimerosal exposure and the risk of autism. (Ex. M, para. 97; Tr. 3655.)

Of similar relevance is a study by Thompson and colleagues of American children, published in 2007.[97] The authors measured thimerosal exposure in a group of children, and then evaluated the children for a number of negative neurological outcomes. The measured outcomes did not specifically include autism, but did include several outcomes related to autism, including speech and language measures, and intellectual functioning measures. The study generally found no association between thimerosal exposure and negative neurological outcomes. (PML 192; Ex. M, 108; Tr. 3659-61.) The authors concluded that their results did not support an association between thimerosal exposure and deficits in neuropsychological functioning. (PML 192, p. 1291.)

j. Summary concerning studies listed above

In sum, following the initiation of public concerns that thimerosal in vaccines might be a contributing factor in causing autism, a number of research groups in several countries devised several different types of studies to test that issue. Each of the studies described and discussed above, however, *failed* to find any evidence that thimerosal-containing vaccines are associated with autism, as pointed out by all three of respondent's epidemiologic experts. (Tr. 3300, 3662; Ex. O, pp. 9-10, 14.)[98] To be sure, none of those studies is definitive by itself. While each of the study

---

[97]William W. Thompson, et al., *Early Thimerosal Exposure and Neuropsychological Outcomes at 7 to 10 Years*, 357 NEW ENG. J. MED. 1281 (2007) (PML 192).

[98]I could write many pages describing in detail those studies, discussing the strengths and weaknesses of the different studies, and explaining in detail why certain of the studies seem to be of especially heavy probative value, others somewhat less so. But I do not find it necessary to provide such a lengthy discussion, for two reasons. First, the record of this case contains not only the published articles describing in detail virtually all of those studies, but also some lengthy descriptions and discussions of those studies by well-qualified experts. Respondent's experts Dr. Fombonne and Dr. Rutter, who are extremely well-qualified concerning autism (see discussion at p. 29 above), described those studies in both their expert reports (Ex. M, paras. 93-108; Ex. GG, paras. 76-89) and their hearing testimony (Tr. 3301-06, 3377-86, 3642-64). In addition, several studies are described in detail in a comprehensive report issued by the Institute of Medicine (IOM) in 2004. (See RML 255, pp. 42-55.) (For a discussion of that 2004 IOM Report, see p. 96 below.)

Second, the petitioners in this case for the most part have *not contested* the descriptions and interpretations of those studies by the IOM committee and by Dr. Fombonne. Dr. Greenland did point out the specific limitations of several of the individual studies. (Ex. 24, pp. 12-15; Tr. 88-93.) However, those limitations were acknowledged by Drs. Fombonne and Rutter as well. (Ex. M, paras. 93-108; Ex. GG, paras. 76-89; Tr. 3301-06, 3377-86, 3642-64.) I acknowledge the limitations and weaknesses in each study, as described by the experts, but I conclude that the studies, when *taken together*, provide strong evidence that there is no association between thimerosal-containing vaccines and autism in general. In essence, the petitioners have *not disputed* respondent's argument that the studies described above show clearly that thimerosal-containing vaccines do not play any

approaches has its strengths, each also has acknowledged limitations and weaknesses. However, when all of the studies are considered *together*, the study results are highly important. (*E.g.*, RML 169, p. 156; Tr. 3091, 3300-01, 3385-86, 3419, 3661-62; Ex. O, p. 8; Ex. M, para. 116; Ex. GG, para. 90.) First of all, the studies show that medical researchers have *looked extensively* for any affirmative evidence that thimerosal-containing vaccines can contribute to the causation of autism, but have *failed* to find any such evidence. Therefore, when taken together, the studies make it appear *extremely unlikely* that thimerosal-containing vaccines have played any significant role in the *overall* causation of autism.[99] Of course, it is true that epidemiologic studies cannot prove definitively that Factor A *never* causes Condition B; such a study cannot ever completely rule out the possibility that Factor A causes a *tiny percentage* of the cases of Condition B, a percentage too small for the study to detect. However, when a variety of well-designed studies by different researchers have looked extensively for evidence of an association between Factor A and Condition B, but have found none, not only can one conclude confidently that Factor A does not cause a *significant percentage* of cases of Condition B, but it is also reasonable to interpret those studies as casting *at least some doubt* on the proposition that Factor A *ever* causes Condition B.

In this case, the studies described above, taken as a whole, show very clearly that thimerosal-containing vaccines do not cause any *substantial portion* of the cases of autism in the studied countries. And while those studies cannot completely rule out any possibility that thimerosal-

---

significant causal role in the causation of *autism overall*. Rather, the petitioners have argued that the studies should be considered as *irrelevant* to the issue of whether the thimerosal-containing vaccines contribute to *regressive autism*, or a subspecies of regressive autism that they deem "clearly regressive autism," rather than autism in general.

I have dealt in detail with this "irrelevancy" argument of the petitioners, at pp. 88-94 of this Decision. This footnote simply explains why I have not discussed each of the many individual epidemiologic studies in greater detail in this Decision.

[99]In addition to medical journal articles that publish the results of *individual new studies*, another category of medical articles is that of "review articles." A review article does not publish the results of a new study, but analyzes the results of the existing published studies concerning a certain scientific issue, in an attempt to possibly draw inferences concerning that issue. The record of this case contains three such review articles analyzing the epidemiologic studies concerning the thimerosal/autism causation issue. (Sarah K. Parker, et al., *Thimerosal- Containing Vaccines and Autistic Spectrum Disorder: A Critical Review of Published Original Data*, 114 PEDIATRICS 793 (2004) (RML 368); F. DeStefano, *Vaccines and Autism: Evidence Does Not Support a Causal Association*, 82 CLINICAL PHARMACOLOGY & THERAPEUTICS 756 (2007) (RML 120); Michael Rutter, *Incidence of Autism Spectrum Disorders: Changes Over Time and Their Meaning*, 94 ACTA PAEDIATRICA 2 (2005) (RML 427).) Notably, all three of these articles analyze the epidemiologic evidence in a fashion consistent with that of the *respondent's* epidemiologic experts in this case--*i.e.*, the reviewers found that all of the competently-conducted studies contained *no evidence of an association* between thimerosal-containing vaccines and autism. (Although it should be noted that the third review article was authored by the same Dr. Rutter who served as one of respondent's experts in this case.)

containing vaccines might play some causative role in a *tiny fraction* of autism cases (a fraction too small to be detected by even the largest studies), it seems to me that the failure of so many studies to find any association between thimerosal-containing vaccines and autism at least *casts doubt* upon the proposition that thimerosal-containing vaccines *ever* play a role in causing autism.

2. Studies by the Geiers

As explained above, most of the epidemiologic studies that have addressed the thimerosal/autism causation issue have failed to find any association between thimerosal-containing vaccines and autism, but there have been certain exceptions. Those exceptions were studies published by the research team of Dr. Mark Geier and his son David Geier. (Ex. M, para. 111; RML 255, pp. 51-52, 55-62.[100]) To be sure, the petitioners in this case have *not* cited or relied upon those Geier studies in their post-hearing briefs, because, as I will discuss below (p. 88), the petitioners argue that *all* of the epidemiologic studies done to date are *irrelevant* to the petitioners' causation theory in this case. However, since I find that the epidemiologic studies *are* of relevance, I have found it reasonable to examine those Geier studies, to see if they afford any significant counterweight to the many contrary studies discussed above.

After careful consideration, I conclude that the Geiers' studies *cannot* be given any weight. A number of those studies were considered by the Institute of Medicine (IOM) committee that fully

---

[100]The Geier and Geier studies that I reviewed were the following: David A. Geier & Mark R. Geier, *An Assessment of the Impact of Thimerosal on Childhood Neurodevelopmental Disorders*, 6 PEDIATRIC REHABILITATION 97 (2003) (RML 185); David A. Geier & Mark R. Geier, *A Comparitive Evaluation of the Effects of MMR Immunization and Mercury Doses from Thimerosal-Containing Childhood Vaccines on the Population Prevalence of Autism*, 10 MED. SCI. MONITOR 133 (2004) (RML 186); David A. Geier & Mark R. Geier, *A Two-Phased Population Epidemiological Study of the Safety of Thimerosal-Containing Vaccines: A Follow-Up Analysis*, 11 MED. SCI. MONITOR 160 (2005) (RML 187); David A. Geier & Mark R. Geier, *An Evaluation of the Effects of Thimerosal on Neurodevelopmental Disorders Reported Following DTP and Hib Vaccines in Comparison to DTPH Vaccine in the United States*, 69 J. TOXICOLOGY & ENVTL. HEALTH 1481 (2006) (RML 188); David A. Geier & Mark R. Geier, *An Assessment of Downward Trends in Neurodevelopmental Disorders in the United States Following Removal of Thimerosal from Childhood Vaccines*, 12 MED. SCI. MONITOR 231 (2006) (RML 189); David A. Geier & Mark R. Geier, *A Meta-Analysis Epidemiological Assessment of Neurodevelopmental Disorders Following Vaccines administered from 1994 through 2000 in the United States*, 27 NEUROENDOCRINOLOGY LETTERS 401 (2006) (RML 190); David A. Geier & Mark R. Geier, *A Case Series of Children with Apparent Mercury Toxic Encephalopathies Manifesting with Clinical Symptoms of Regressive Autistic Disorders*, 70 J. TOXICOLOGY & ENVTL. HEALTH 837 (2007) (RML 192); David A. Geier & Mark R. Geier, *A Prospective Assessment of Porphyrins in Autistic Disorders: A Potential Marker for Heavy Metal Exposure*, 10 NEUROTOXICITY RESEARCH 57 (2006) (RML 193); Mark R. Geier & David A. Geier, *Thimerosal in Childhood Vaccines, Neurodevelopment Disorders, and Heart Disease in the United States,* 8 J. AM. PHYSICIANS & SURGEONS 6 (2003) (RML 194); Mark R. Geier & David A. Geier, *Neurodevelopmental Disorders After Thimerosal-Containing Vaccines: A Brief Communication*, 228 EXPERIMENTAL BIOLOGY & MED. 660 (2003) (RML 195).

studied the entire thimerosal/autism causation issue in 2004. (RML 255, pp. 51-52, 55-62.) That committee concluded that the studies were so flawed as to be "uninterpretable," and that the studies contributed nothing meaningful ("noncontributory") concerning the causation issue. (RML 255, pp. 52, 58, 61, 62.) The committee noted that the studies were based on databases that themselves had "significant limitations" (*id*. at 57), and that the studies had "serious methodological problems" (*id*. at 57) or "serious methodological limitations" (*id*. at 61). The committee added that the Geiers' articles describing their analytical methods were "not transparent" and omitted "important details," so that it was impossible to evaluate the studies. (*Id*. at 58, 62.) Other specific deficiencies in the studies were also discussed, including the fact that the Geiers incorrectly used several epidemiologic terms and measures. (*Id*. at 59 n. 18; 60 n. 19; 60 n. 20.)

In addition, Dr. Fombonne agreed with the IOM's criticisms of the Geier studies, and testified that the Geier studies in general failed to use accepted epidemiologic methods. (Tr. 3664-65.) Dr. Rutter was critical of the Geier studies as well. (Ex. GG, paras. 67-68.) Further, petitioners' *own expert* witness concerning epidemiology, Dr. Greenland, *agreed* with the criticisms of the Geier articles, acknowledging that those studies are "deficient in methodology." (Tr. 122-23.) And none of the expert witnesses for the petitioners vouched for the reliability of the Geier studies.

I have reviewed the published Geier studies discussed in the 2004 IOM report, and I agree with the analysis of those studies set forth in that IOM report. Further, I have reviewed the additional studies published by the Geiers since the 2004 IOM report, and find that those studies suffer from the same type of flaws as the earlier Geier studies. That view includes a study published in 2008 by the Geiers, along with Young as a third author.[101] Two of respondent's experts, Drs. Fombonne and Rutter, testified that that 2008 study was again deeply flawed, and those experts provided a number of specific examples of deficiencies in the study. (Tr. 3387-94, 3423-24, 3665-68, 3753-60.) And, again, none of the petitioners' experts testified in support of that 2008 Young, Geier, and Geier study.

In summary, I conclude that all of the Geier epidemiologic studies are *not* reliable, and cannot be accorded any weight.[102]

---

[101]Heather A.Young, David A. Geier, Mark R. Geier, *Thimerosal Exposure in Infants and Neurodevelopmental Disorders: An Assessment of Computerized Medical Records in the Vaccine Safety Datalink,* 15 J. NEUROLOGICAL SCI. 110 (2008) (PML 665).

[102]In addition, the 2004 Institute of Medicine report noted the existence of an ecological study submitted to that committee by Blaxill, which also purported to find an association between thimerosal-containing vaccines and autism. (RML 255, p. 64; RML 48.) The IOM committee, however, found that the study had deficiencies which rendered it "uninformative" concerning the thimerosal/autism causation issue. (*Id*.)

3. The petitioners' argument that the epidemiologic studies are "irrelevant"

As noted above, the petitioners have not disputed respondent's argument that the epidemiologic studies show that thimerosal-containing vaccines have *not* played any significant causal role in the causation of *autism overall*. Rather, the petitioners argue that the studies are relevant only in regard to *autism in general*, and, should be considered as *irrelevant* to the issue of whether thimerosal-containing vaccines might possibly contribute to causing autism in a *subgroup* of regressive autism that they theorize to possibly exist, which they label "clearly regressive autism." The petitioners argue that because "clearly regressive autism" would be a narrow subset of autism, and because the epidemiologic studies have not specifically addressed the issue of whether thimerosal-containing vaccines cause "clearly regressive autism," the epidemiologic studies are therefore *irrelevant* to their theory advanced in this case. (P-1, pp. 52-54.) In this regard, petitioners rely upon the testimony of their epidemiology expert, Dr. Sander Greenland. I will first describe the point that Dr. Greenland made, then explain why his point does not materially advance the petitioners' "general causation" argument.

a. Dr. Greenland's point regarding "clearly regressive autism"

As noted above, the petitioners' expert in epidemiology, Dr. Greenland, has superb credentials as an epidemiologist. (See pp. 22-23 above.) And Dr. Greenland certainly did convincingly make one point on petitioners' behalf--*i.e.*, that the epidemiologic studies concerning the thimerosal/autism causation issue do not mathematically *rule out the possibility* that receipt of thimerosal-containing vaccines could be associated with a very narrow subset of autism that he theorizes to exist, and that he labels as "clearly regressive autism."

Dr. Greenland's testimony may be summarized as follows. Dr. Greenland noted that there are limitations to each of the epidemiologic studies described at pp. 79-84 above. (Ex. 24, pp. 12-15; Tr. 89-93.) However, he did not dispute that those epidemiologic studies have not detected any association between thimerosal-containing vaccines and any form of autism. (Ex. 24, p. 1; Tr. 124.) Nor did he dispute that those studies, taken as a whole, are incompatible with the proposition that thimerosal-containing vaccines are associated with *autism in general*. Dr. Greenland argued, rather, that the studies do not mathematically *rule out the possibility* that thimerosal-containing vaccines *might* be associated with some hypothetical very small *subgroup* of autism. Dr. Greenland explained that it is a mathematical possibility that thimerosal-containing vaccines might have no association with most forms of autism, but have a substantial association with a *very small subgroup* of autism. If that were the case, he said, then the epidemiologic studies discussed above would not have been able to detect that association with the small subgroup. (Ex. 24, pp. 6-7; Tr. 90-91, 94-96, 116, 121, 125-26.)

Dr. Greenland acknowledged that his argument in this regard is purely one of mathematical, statistical *possibility*. (Tr. 130, 135.) He acknowledged that nothing in any epidemiologic studies even suggests that such an associated subgroup might actually exist. (Tr. 128-31, 134-35.) He

merely argued that statistically, the studies do not *rule out* that possibility. (*E.g.*, Tr. 94-96, 116, 121, 125-26.)

Further, Dr. Greenland added a suggestion as to a hypothetical subgroup of autism that might be a small enough subgroup so that its association with thimerosal-containing vaccines would not have been detectable in the existing studies. Dr. Greenland did *not* state that *regressive autism* would be a small enough subgroup so that its association with thimerosal-containing vaccines would have gone undetected.[103] Rather, he suggested the possible existence of a *subset* of regressive autism, to which he gave the name "clearly regressive autism." He noted that when children with regressive autism are retrospectively studied, by techniques such as analysis of videos, it turns out that in most such children evidence of subtle pre-regression abnormality is found. However, in some children, no evidence of pre-regression abnormality is found. Dr. Greenland proposed that the latter group, constituting perhaps 28% or less of the "regressive autism" group, be considered as a separate subgroup of autism, to which he gave the name "clearly regressive autism."[104] He suggested that *if* thimerosal-containing vaccines caused autism only in that very small "clearly regressive" group, but did not affect the causation in all other persons with autism, then that causal association of thimerosal-containing vaccines with "clearly regressive autism" would *not* have been detected in the epidemiologic studies. (Ex. 24, pp. 6-7, 16; Tr. 90-91; 94-96, 116, 121, 125-26.)

Again, in this regard Dr. Greenland was careful to state that he is merely suggesting a mathematical, statistical *possibility*. (Tr. 130, 135.) He is not a medical doctor, and he does not claim to have any particular knowledge concerning autism. He does not have any idea whether the "clearly regressive" group actually differs causally in any way from other autistic individuals. (Tr.

---

[103]Petitioners in their brief misconstrue Dr. Greenland's testimony in this regard. They state that Dr. Greenland "testified that Dr. Fombonne was incorrect when Dr. Fombonne argued that 'regressive autism is common enough to be detectable in available studies.' *King Tr.*, p. 78." (P-1, p. 53.) However, that summary does not accurately represent the point actually made by Dr. Greenland at p. 78 of the transcript of this case. Dr. Greenland at that point of his testimony did *not* dispute the contention that an association between thimerosal-containing vaccines and *regressive autism* would be detectable in the epidemiologic studies. Rather, Dr. Greenland on that page was merely reiterating his point that if there was an association between thimerosal-containing vaccines and the *smaller subset* of "clearly regressive autism," such an association with the *smaller subgroup* might have gone undetected.

[104]The petitioners in their brief seem to suggest that respondent's expert Dr. Fombonne originated the term "clearly regressive autism." (P-1 at 53--"in Dr. Fombonne's words.") But they failed to offer a citation to the record for that assertion. My study of the record indicates that petitioners are mistaken on this point. Dr. Fombonne did, of course, point out that when children with regression are studied retrospectively, in most cases pre-regression abnormality can be identified. (Ex. M, para. 37.) But it was Dr. Greenland who suggested that we apply the label "clearly regressive autism" to that group of children in whom *no* pre-regression signs of abnormality are identified. (Ex. 24, pp. 6-7.) In fact, Dr. Greenland explicitly indicated that he himself was coining a term, stating that "*I will label* such cases as clearly regressive autism." (*Id*. at p. 7, emphasis added.)

127-28.) He acknowledges that he does not know of *any evidence* supporting the idea that thimerosal-containing vaccines are associated with the "clearly regressive" group, or any other subgroup of autism. (Tr. 128-31, 134-35.) His point is merely that the currently-available epidemiologic evidence does not mathematically *rule out the possibility* that thimerosal-containing vaccines are associated with the theorized "clearly regressive" group, or some other equally small subgroup of autism. (Tr. 94-96, 116, 130-31.)

b. Analysis of Dr. Greenland's point

Several observations are appropriate regarding Dr. Greenland's point.

i. In a narrow technical sense, Dr. Greenland's point has validity.

My first observation concerning Dr. Greenland's point is that it does have a certain technical validity. Respondent's epidemiologic experts generally do *not* dispute that the epidemiologic studies concerning the thimerosal-containing vaccines/autism issue do not *mathematically rule out the possibility* of an association between thimerosal-containing vaccines and some tiny subset of autism.[105] However, those epidemiologic experts explained that, concerning *any* epidemiologic issue, no matter how many studies address the issue of whether Factor A causes Disease B, and no matter how large and well-conducted those studies are, and no matter that no association is found in any study, such studies can *never* mathematically *completely rule out* the possibility that Factor A is associated with some *tiny subset* of Disease B, an association too small to be detectable. (Ex. M, para. 127; Ex. O, pp. 6-7; Tr. 3098-99, 3308, 3310-11, 3678-79.) Thus, in the view of respondent's experts, while Dr. Greenland is technically correct in his point, that point does not provide substantial support to the petitioners' "general causation" argument in this case, since the same point could be made concerning *any* allegation that *any* factor causes *any* disease.

[105]I note that Dr. Fombonne has argued that if there were a significant association between thimerosal-containing vaccines and even the narrow category of "clearly regressive autism," such association *would* have been detectable at least in some of the larger epidemiologic studies. (Ex. M, paras. 121(f), 128.) And petitioners did not offer rebuttal testimony on that specific point after Dr. Fombonne made that argument. If Dr. Fombonne is correct in that regard, that would be another reason to reject the petitioners' "general causation" argument. However, it is difficult to assess Dr. Fombonne's presentation on this particular point, since no one really knows what percentage of autistics with regression, if any, actually fall into the "clearly regressive" category. Thus, I do not reach a firm conclusion on the issue of whether Dr. Fombonne is right that such an association would have been detectable; for purposes of analyzing petitioners' argument concerning "clearly regressive autism," I assume that Dr. Greenland's point is mathematically correct.

ii. The petitioners' apparent narrowing of their "general" causation" argument, to focus only on a newly-theorized subgroup of "clearly regressive autism" rather than "regressive autism," is inconsistent with most of the petitioners' own expert testimony.

A second observation is that by adopting Dr. Greenland's approach, in the section of their main post-hearing brief concerning "epidemiology" (see P-1, pp. 52-54), petitioners appear to be in effect *narrowing* their general causation argument to focus *only* on the newly-theorized subset of "clearly regressive autism," rather than the broader group of "regressive autism." This narrowing of their argument is understandable in light of the epidemiologic evidence. As noted above, the epidemiologic studies, taken as a whole, are entirely *incompatible* with the proposition that thimerosal-containing vaccines have any association with *autism in general*. (Even Dr. Greenland does not take issue with that conclusion.) Further, respondent's epidemiologic experts Dr. Fombonne and Dr. Rutter have argued that even if thimerosal-containing vaccines were associated with only *regressive autism*, the epidemiologic studies *would* have uncovered that association. (*E.g.*, Ex. M, paras. 41, 128; Tr. 3310-11.) And Dr. Greenland did not take issue with *that* argument of Dr. Fombonne and Dr. Rutter, either.[106] Dr. Greenland did *not* argue that the epidemiologic studies left open the possibility of an association between thimerosal-containing vaccines and *regressive autism*. (See fn. 103 above.) Rather, he argued *only* that the studies left open the possibility of an association between thimerosal-containing vaccines and the much narrower theoretical subset of "*clearly regressive autism*," a hypothetical subset of autism newly theorized by Dr. Greenland himself. (*E.g.*, Tr. 90-91, 94-96, 116, 121, 125-26.)

Of course, Dr. Greenland's point does afford the petitioners a way to avoid having their "general causation" argument be completely refuted by the epidemiologic evidence. However, the fact that the petitioners must resort to this purely mathematical argument of Dr. Greenland, in order to get around the epidemiologic evidence, further emphasizes the enormous weakness of their overall "general causation" argument. That is because Dr. Greenland's "clearly regressive autism" suggestion is simply *inconsistent* with the presentations of petitioners' *other four* expert witnesses. All of those other four experts--Drs. Kinsbourne, Aposhian, Deth, and Mumper--provided *no testimony at all* about the possible relevance of a theorized "clearly regressive autism" group.[107]

---

[106]At one point in his oral testimony, Dr. Greenland stated that "[a]n association between thimerosal-containing vaccines and regressive autism, especially clearly regressive autism, would have been seriously diluted in all the available epidemiologic studies * * *." But that sentence is ambiguous, and in the rest of his oral testimony and in his expert report (Ex. 24), Dr. Greenland does *not* seem to opine that an association with the *broader* category of regressive autism could have been missed by the epidemiologic studies, but only that an association with the *narrower* category of "clearly regressive autism" could have been missed.

[107]Dr. Mumper in her hearing testimony did briefly mention "clearly regressive autism." (Tr. 1488-89, 1610-11.) However, she never explained what she understood that phrase to mean. Judging by her brief comments, she apparently meant only that certain patients "clearly" fell into the

To put the same point in another way, Dr. Greenland acknowledged that the petitioners' "general causation" theory is not negated by the epidemiologic evidence *only* if one assumes that thimerosal-containing vaccines contribute to the causation of "clearly regressive autism" *only*, and have no effect on other forms of autism. Yet all of petitioners' other experts not only fail to explain why "clearly regressive autism" might be a distinct entity that might have different causes than other forms of autism, they also fail even to mention the *existence* of "clearly regressive autism" as a distinct category of autism. This complete inconsistency, between the approach of Dr. Greenland and that of the petitioners' other experts on this crucial point, is yet another telling indication that the petitioners' general causation argument is logically incoherent and completely without merit.[108]

---

category of "regressive autism." (*Id*.) She did *not* seem to understand the term "clearly regressive autism" as Dr. Greenland used it, to constitute a *distinct subgroup* of "regressive autism" that was *much smaller* than the "regressive autism" group. Note, for example, that Dr. Mumper stated that about *50 percent* of her autism patients were "clearly regressive." (Tr. 1610; see also Tr. 1221 line 16.) That would be a very high percentage even for "regressive autism" (the usual estimates are that 20 to 40 percent of autistics suffer regression, see p. 43 above), and is *completely inconsistent* with Dr. Greenland's suggestion of a small subgroup consisting of 28% or less of those with "regressive autism."

Similarly, at one point in his testimony Dr. Kinsbourne used the adverb "clearly" to modify the adjective "regressive." (Tr. 784, line 22.) But in that reference Dr. Kinsbourne, too, seems merely to indicate that some children "clearly" fall into the category of "regressive autism," not to denote a *distinctive subcategory* of regressive autism.

In any event, neither Dr. Mumper nor Dr. Kinsbourne ever provided any explanatory testimony concerning the concept of "clearly regressive autism." Neither ever testified that "clearly regressive autism" was a distinct subgroup likely to have different causal factors than other forms of autism.

[108]It is telling to note the *progression* of the arguments of those who advocate the proposition that thimerosal can cause autism. Their causation theory originally did not distinguish between forms of autism. Then, once the epidemiologic studies made it clear that there was no association between thimerosal-containing vaccines and *autism in general*, they shifted their focus to the idea that thimerosal-containing vaccines might cause only the narrower category of "regressive autism," which had not been specifically addressed in the epidemiologic studies. Now, the petitioners in this case have engaged an epidemiologic expert, who, based upon his testimony, apparently does not disagree with the statements of respondent's experts that even an association between thimerosal-containing vaccines and "regressive autism" *would* have been detectable in the epidemiologic studies. Therefore, the petitioners now have shifted the focus of their thimerosal/autism causation theory *once again*, to the brand-new idea that thimerosal-containing vaccines might be associated with an *even narrower* subcategory of autism, the previously-unheard-of category of "clearly regressive autism."

This pattern, in which the proponents of a thimerosal/autism connection continue to change their theory as the evidence continues to disprove their previous theories, is yet another indication of the extremely dubious nature of the thimerosal/autism causation argument.

iii. There is absolutely no evidence for the proposition that there is an association between thimerosal-containing vaccines and "clearly regressive autism."

Finally, with respect to Dr. Greenland's point regarding "clearly regressive autism," it is important to stress again that there is not a *shred of evidence* to support the idea that there is an association between thimerosal-containing vaccines and "clearly regressive autism." Dr. Greenland was the only one of petitioners' experts who testified at all concerning the concept of "clearly regressive autism," and he acknowledged that his own new theory concerning "clearly regressive autism" concerns purely a *mathematical*, *statistical possibility*. (Tr. 130, 135.) He claims no expertise in autism (Tr. 126), and does not claim to know anything about whether the theorized "clearly regressive" group *actually* differs causally in any way from other autistic children (Tr. 127). He acknowledges that he does not know of *any evidence* supporting the idea that thimerosal-containing vaccines are associated with the "clearly regressive" group. (Tr. 128-131, 134-35.) And petitioners' other experts also offered no evidence that thimerosal-containing vaccines might be associated with "clearly regressive autism."

Again, the fact that when confronted by the epidemiologic evidence the petitioners need to alter their causation theory in a fashion inconsistent with the rest of their expert testimony, and to rely on the mathematical possibility of a hypothetical association between thimerosal-containing vaccines and "clearly regressive autism" for which there is *zero evidence* in the record, is further evidence of the lack of merit to the petitioners' "general causation" theory.

In addition, there is no good reason to even *suspect* that there might be an association between thimerosal-containing vaccines and "clearly regressive autism." As respondent's epidemiologic expert Dr. Goodman explained, to even seriously consider Dr. Greenland's hypothetical "clearly regressive autism" theory, there must be some plausible biologic reason to suspect that "clearly regressive autism" might be causally different than other forms of autism. (Tr. 3104, 3141.) But petitioners' experts have never even proposed such a biologic reason. As explained in detail above (pp. 44-47), there is no reason to think that *regressive autism* might have different causal factors than autism in general. For similar reasons, the record of this case contains no reason to suspect that the theorized category of "*clearly regressive autism*" might have different causal factors than autism in general. (Ex. M, para. 124.)

In sum, the petitioners' "clearly regressive autism" argument is completely devoid of any supporting evidence.

c. Summary concerning "irrelevancy" argument

In sum, it is true, as a statistical matter, that the epidemiologic studies detailed at pp. 79-84 above, while showing clearly that thimerosal-containing vaccines could not be causing any substantial portion of the cases of *autism in general*, do not completely rule out the possibility that thimerosal-containing vaccines might be associated with some theoretical very small *subgroup* of autism. Nonetheless, the balance of evidence from those studies weighs substantially against the

petitioners' causation theory. First, it is an *exceedingly slight* point in the petitioners' favor for them to claim that these many studies by different researchers in different countries have *not completely ruled out the possibility* of any merit to their "general causation" claim. The larger point is that *none* of those many competent studies *has yielded the slightest bit of evidence in the petitioners' favor*--and, of course, it is the *petitioners' burden* to show that thimerosal-containing vaccines *do* likely contribute to the causation of some form of autism, *not* the respondent's burden to show that there is absolutely no possibility of a causal link.

Second, in my view the failure of so many studies to find any association between thimerosal-containing vaccines and autism, while not *completely ruling out* a possible causal role with respect to a *subset* of autism, at least *casts doubt* upon the proposition that thimerosal-containing vaccines *ever* play a role in causing any kind of autism, including "regressive autism" or "clearly regressive autism." This is especially true given the absence of any credible evidence that "regressive autism" or "clearly regressive autism" might constitute a *distinctive* subtype of autism that might be likely to have different causative factors than other forms of autism (see discussion at pp. 44-47 above).

4. Case law concerning epidemiologic evidence

The case law is clear that there is no *requirement* that a petitioner supply supportive epidemiologic evidence. Causation-in-fact *can* be demonstrated, in an appropriate case, in the absence of epidemiologic evidence supporting an association between the type of vaccine in question and the type of injury in question. *Capizzano v. Secretary of HHS*, 440 F.3d 1317, 1325-26 (Fed. Cir. 2006). Indeed, causation-in-fact can be demonstrated without any support from *medical literature* at all. *Id.*; *Althen v. Secretary of HHS*, 418 F.3d 1274, 1281 (Fed. Cir. 2005). That case law, of course, is appropriately premised upon the fact that with respect to many causation-in-fact claims raised in Program cases, the question of whether the *type* of vaccine in question can cause the *type* of injury in question simply has never been the subject of an epidemiologic study. For example, the *Althen* court noted that concerning the particular causation allegation in that case--that a tetanus inoculation caused neurologic damage--the field was simply "bereft of * * * proof" as to whether such a vaccine could cause such an injury. 418 F.3d at 1280. In such a situation, where there simply have been no epidemiologic studies concerning the *general causation* issue, it makes sense that evidence such as medical opinions and circumstantial evidence may be enough to demonstrate causation, in a particular case, to the required level of "more probable than not."

However, the case law also teaches that when deciding issues of general causation that *have* been studied, a special master *may* properly consider whatever epidemiologic evidence, or other relevant medical literature, that does exist. In *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), the Supreme Court listed certain factors that federal trial courts should utilize in evaluating proposed expert testimony concerning scientific issues. In *Terran v. Secretary of HHS*, 195 F.3d 1302, 1316 (Fed. Cir. 1999), the Federal Circuit ruled that it is appropriate for special masters to utilize *Daubert's* factors as a framework for evaluating the *reliability* of causation-in-fact theories presented in Program cases. One of the factors listed in *Daubert* is whether the scientific theory "has been subjected to peer review and publication." 509 U.S. at 593. The Court noted that

while publication does not "necessarily" correlate with reliability, since in some instances new theories will not yet have been published, nevertheless "submission to the scrutiny of the scientific community is a component of 'good science,'" so that the "fact of publication (or lack thereof) in a peer reviewed journal thus will be a relevant, though not dispositive, consideration in assessing the scientific validity" of a theory, technique, or methodology. *Id*. at 593-94.

Thus, *Daubert* supports the use of published medical literature as a tool in evaluating causation theories. And, in fact, in the *Terran* case, the special master relied upon a published *epidemiologic* study, known as the National Childhood Encephalopathy Study (NCES), in denying the petitioner's causation claim (*Terran v. Secretary of HHS*, No. 95-451V, 1998 WL 55290, at *10-11 (Fed. Cl. Spec. Mstr. Jan. 23, 1998)), and the Federal Circuit affirmed (195 F.3d at 1315-17). Further, in *Grant v. Secretary of HHS*, 956 F.2d 1144, 1149 (Fed. Cir. 1992), the Federal Circuit *specified* that in Vaccine Act cases "epidemiological studies are probative medical evidence relevant to causation," though such studies are not necessarily dispositive.

Consistent with the teachings of *Daubert*, *Terran*, and *Grant*, special masters have routinely found that epidemiologic evidence, and/or other medical journal articles, while not *dispositive*, should be *considered* in evaluating scientific theories. For example, in *Scott v. Secretary of HHS*, No. 03-2211V, 2006 WL 2559776, at *21 (Fed. Cl. Spec. Mstr. Aug. 21, 2006), a special master found medical literature submitted in that case to be helpful, though not necessarily "dispositive," in resolving a dispute between medical experts. In *Garcia v. Secretary of HHS*, No. 05-720V, 2008 WL 5068934, at *3, *10 (Fed. Cl. Spec. Mstr. Nov. 12, 2008), a special master found the argument of the petitioners' expert to be more persuasive than that of the respondent's expert, in part because the theory of the petitioner's expert was supported by a published report of a committee of the Institute of Medicine. And in *Williams v. Secretary of HHS*, 04-1725V, 2007 WL 2775190, at *26 (Fed. Cl. Spec. Mstr. Sep. 11, 2007), a special master noted that "medical or scientific literature" can help to carry a petitioner's causation burden.

Further, in the Program case law there have been many rulings in which *judges* explicitly stated approval of a special master's reliance upon *epidemiologic studies* to evaluate causation theories. *See*, *e.g. Moberly v. Secretary of HHS*, 85 Fed. Cl. 571, 596 (2009), *aff'd*. 592 F. 3d 1315 (Fed. Cir. 2010); *Estep v. Secretary of HHS*, 28 Fed. Cl. 664, 668 (1993); *Sharpnack v. Secretary of HHS*, 27 Fed. Cl. 457, 459 (1993); *Sumrall v. Secretary of HHS*, 23 Cl. Ct. 1, 8 (1991); *Hennessey v. Secretary of HHS*, No. 01-190V, 2010 WL 94560, at *6-7, *11-13 (Fed. Cl. Jan. 7, 2010).

Finally, I note that in the first three "test cases" in the Omnibus Autism Proceeding, the three special masters relied, in part, on epidemiologic studies and other medical literature, and three judges of this court affirmed. *Cedillo v. Secretary of HHS*, 89 Fed. Cl. 158 (2009); *Snyder v. Secretary of HHS*, 88 Fed. Cl. 706 (2009); *Hazlehurst v. Secretary of HHS*, 88 Fed. Cl. 473 (2009).

Accordingly, the case law concerning the use of epidemiologic evidence in Program cases is clear. There is *no requirement* that epidemiologic evidence support a causation-in-fact claim. Nor would it be proper for a special master to base a causation ruling *entirely* on epidemiologic evidence;

the special master must consider *all* the evidence in the record, including opinion evidence, circumstantial evidence, etc. However, in those relatively infrequent instances in which a general causation issue *has* been the subject of epidemiologic studies, and therefore published studies are available in peer-reviewed medical journals, it is quite appropriate for the special master to consider such epidemiologic evidence, and to give that evidence appropriate weight under the circumstances, along with all of the other evidence of record.

5. Summary concerning epidemiology

The numerous epidemiologic studies done over the past ten years, when taken together, make it *extremely unlikely* that thimerosal-containing vaccines have played any significant role in the *overall causation* of autism. It is true, as the petitioners argue, that the available epidemiologic studies do not *completely rule out the possibility* that thimerosal-containing vaccines might be associated with some small subgroup of autism, such as the newly-theorized subgroup of "clearly regressive autism." However, the epidemiologic evidence *still* must be said to provide significant evidence *against* the petitioners' general causation theory set forth in this case. First, none of the numerous competent studies *has yielded the slightest bit of evidence in the petitioners' favor*. Second, the failure of so many studies to find any association between thimerosal-containing vaccines and autism, while not ruling out a possible causal role with respect to a very small subgroup of autism, at least *casts doubt* upon the proposition that thimerosal-containing vaccines have *ever* played a role in causing any kind of autism, including "regressive autism" or "clearly regressive autism." This is especially true given the absence of any evidence that "regressive autism" or "clearly regressive autism" might constitute a *distinctive* subtype of autism that might be likely to have different causative factors than other forms of autism.

Accordingly, my conclusion is that the epidemiologic evidence *does* provide yet another strong reason to *reject* the petitioners' general causation theory presented in this case.[109]

H. Conclusions of the Institute of Medicine committee, and other medical groups

Another part of the record in this case adds at least some additional weight to my conclusion concerning this thimerosal/autism "general causation" issue. That is, a number of very well-qualified groups of medical experts have studied the issue of whether thimerosal-containing vaccines cause autism, and have reached conclusions *against* the proposition that thimerosal-containing vaccines cause autism.

I refer first to a 2004 report published by the Institute of Medicine, which is the medical arm of the National Academy of Sciences. The National Academy of Sciences ("NAS") was created by

---

[109]In any event, even if there existed no epidemiologics studies at all regarding thimerosal-containing vaccines and autism, my ultimate conclusion in this case would remain the *same*, since the non-epidemiologic evidence concerning the petitioners' "general causation" theory also weighs strongly against petitioners, for the reasons discussed at pp. 31-78 above and pp. 96-99 below.

Congress in 1863 to be an advisor to the federal government on scientific and technical matters (*see* An Act to Incorporate the National Academy of Sciences, ch. 111, 12 Stat. 806 (1863)), and the Institute of Medicine ("IOM") is an offshoot of the NAS established in 1970 to provide advice concerning medical issues. (RML 255, p. iv.) When it enacted the Vaccine Act in 1986, Congress specifically directed that the IOM conduct studies concerning potential causal relationships between vaccines and illnesses. (§ 300aa-1 note.) In the intervening years, the IOM has formed committees which have prepared numerous reports concerning issues of possible relationships between vaccinations and injuries. (For a list of such reports, see RML 255, p. 25.) Two of those reports are of direct relevance to the general causation issue involved in this case. (RML 254, 255.)

In the first of those reports, issued in 2001, an expert committee selected by the IOM examined the information then available concerning the same general causation controversy at issue here, *i.e.*, the question of whether thimerosal-containing vaccines can contribute to the causation of autism or other neurodevelopmental disorders. At that time, only about two years after concerns about the possibility of such a causal relationship had first been raised, the evidence concerning the topic was quite sparse. After reviewing the evidence, the 2001 IOM committee[110] reached the conclusion that "the evidence is inadequate to accept or reject a causal relationship between thimerosal-containing vaccines and * * * autism." (RML 254, p. 66.)

By 2004, however, considerable additional evidence was available concerning the thimerosal/autism general causation issue, so the IOM assembled another committee to study the issue again. This time, the committee found that the evidence was sufficient to support a firm conclusion. The 2004 IOM committee, after studying the additional evidence that had become available since 2001, along with the earlier evidence, concluded that "the evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism." (RML 255, pp. 65, 151.)

---

[110]The petitioners pointed out in one of their briefs (P-1, p. 5) that in the 2001 report, the IOM committee stated that the hypothesis that the thimerosal-containing vaccines might have a role in causing neurodevelopmental disorders, including autism, is "biologically plausible" (RML 254, p. 13). However, respondent's expert Dr. Goodman, who was a member of both the 2001 and 2004 IOM committees (RML 254, p. v; RML 255, p. v), explained that the term "biologically plausible" was used in the 2001 report to mean only that a causal connection was "not impossible." (Tr. 3080, line 22.) He testified that the term was "used in the sense of just that this is possible. It doesn't violate physical principles" (Tr. 3080, lines 17-18), and "it didn't violate any known biologic or physical principles" (Tr. 3080, line 25, to Tr. 3081, line 2). Dr. Goodman explained further that after the 2001 report was issued, when some people erroneously interpreted the use of the "biologically plausible" phrase to be supportive of a possible causal relationship, the IOM determined that it would not use that phrase in future IOM reports. (Tr. 3081; see also RML 255 at 3.)

Thus, the use of the phase "biologically plausible" does *not* indicate that the 2001 IOM committee found any *merit* in the thimerosal/autism causation theory. To the contrary, when the 2004 IOM committee re-examined the issue after a substantial amount of evidence became available, the 2004 committee reached the strongest possible conclusion *against* the possibility of a causal connection.

The committee's conclusion, that the evidence "favors rejection" of a causal relationship, was the strongest possible negative conclusion that the committee could have reached, and was adopted unanimously by the committee. (Tr. 3085-86.)

It is appropriate that I assign at least some evidentiary weight to the conclusion of the 2004 IOM committee. As noted above, when it enacted the Vaccine Act in 1986, *Congress specifically directed* that the IOM conduct studies concerning potential causal relationships between vaccines and illnesses. That direction obviously implies that when such studies are performed by IOM committees, a special master should carefully consider those studies in deciding Vaccine Act cases.

Moreover, I note that during the 20-year history of the Vaccine Act, special masters have consistently relied upon the reports of the Institute of Medicine, and reviewing judges have consistently indicated approval of such reliance. *E.g.*, *Terran v. Secretary of HHS*, 41 Fed. Cl. 330, 337 (1998) (affirming special master's reliance on conclusions of IOM), *aff'd,* 195 F.3d 1302 (Fed. Cir. 1999); *Ultimo v. Secretary of HHS*, 28 Fed. Cl. 148, 152 (1993) (proper for a special master to rely on IOM report); *Cucuras v. Secretary of HHS*, 26 Cl. Ct. 537, 540 (1992) (same); *Manville v. Secretary of* HHS, 63 Fed. Cl. 482, 491 (2004) (same); *Ryman v. Secretary of HHS*, 65 Fed. Cl. 35, 39 (2005) (same); *Capizzano v. Secretary of HHS*, No. 00-759V, 2004 WL 1399178, at *2 n.6 (Fed. Cl. Spec. Mstr. Golkiewicz June 8, 2004) ("Considering the IOM's statutory charge, the scope of its review, and the cross-section of experts making up the committee, the special masters have consistently accorded great weight to the IOM's findings."), *rev'd on other grounds*, 440 F.3d 1317 (Fed. Cir. 2006); *Larive v. Secretary of HHS*, No. 99-429V, 2004 WL 1212142, at *11 (Fed. Cl. Spec. Mstr. Millman May 12, 2004); *Falksen v. Secretary of HHS*, No. 01-317V, 2004 WL 785056, at *13 (Fed. Cl. Spec. Mstr. Abell Mar. 30, 2004) ("[T]he Court gives great deference to the findings of the Institute of Medicine on the issue of cause and effect between vaccines and discrete injuries."); *Malloy v. Secretary of HHS*, No. 99-193V, 2003 WL 22424968, *15 (Fed. Cl. Spec. Mstr. Edwards Aug. 6, 2003); *Hill v. Secretary of HHS*, No. 96-783V, 2001 WL 166639, at *3-4 n.2 (Fed. Cl. Spec. Mstr. French Jan. 29, 2001); *Castillo v. Secretary of HHS*, No. 95-652V, 1999 WL 605690, at *11 (Fed. Cl. Spec. Mstr. Wright Jul. 19, 1999); *Schell v. Secretary of HHS,* No. 90-3243V, 1994 WL 71254, at *5 (Fed. Cl. Spec. Mstr. Baird Feb. 22, 1994).

Of course, the 2004 IOM committee's conclusion obviously was based upon the evidence available in 2004, and much additional evidence has become available since then. However, the evidence that has been published since 2004, with the exception of the discredited Geier articles discussed above, has simply offered *further support* to the IOM committee's conclusion that there is *no causal relationship*.

Moreover, respondent has also filed reports by a number of other prestigious medical groups, in addition to the report of the IOM committee. Each of those groups, like the IOM, stated a conclusion that the evidence does *not* support a causal relationship between thimerosal-containing vaccines and autism or any other health risks. *See* reports by the Global Advisory Committee on Vaccine Safety of the World Health Organization (2006) (Ex. TT, p. 1); the American Academy of Pediatrics (2003) (Ex. TT, pp. 2-3); the European Agency for the Evaluation of Medical Products (2004) (Ex. TT, pp. 4-5); the Centers for Disease Control and Prevention of the United States (2007)

(Ex. TT, pp. 6-7); the Infectious Diseases and Immunization Committee of the Canadian Paediatrics Society (2007) (Ex. TT, pp. 26-29); and the National Advisory Committee on Immunization of the Public Health Agency of Canada (2007) (Ex. TT, pp. 30-39).

To be sure, I stress that I am certainly *not* allowing the judgment of the IOM committee, or the judgments of the other medical groups cited above, to substitute for my own. The conclusions of those committees and organizations constitute only one small item of evidence, among many, concerning the thimerosal/autism "general causation" issue in this case. My own conclusion concerning this general causation issue would, indeed, be *exactly the same* if the 2004 IOM report, and the other reports cited above, had never been issued. I simply find it appropriate to acknowledge the conclusions of those reports, and to point out that those conclusions do harmonize with my own ruling here.

I. Summary concerning "general causation" issue

For all the reasons stated above, I conclude that the petitioners have *failed completely* to demonstrate that it is "more probable than not" that thimerosal-containing vaccines can be a substantial factor in contributing to the causation of autism, in individuals suffering from regressive autism, "clearly regressive autism," or any type of autism. To the contrary, the evidence in the record of this case makes it appear *extremely unlikely* that thimerosal-containing vaccines contribute to the causation of any form of autism.[111]

[111]I also note that in two lawsuits litigated outside the Vaccine Act, in actions alleging that thimerosal-containing vaccines contributed to the causation of autism, judges have prevented the cases from proceeding to trial, finding basic deficiencies in the causation theories presented by the plaintiffs' expert witnesses, and/or excluding the testimony of the plaintiffs' experts as scientifically unfounded. See, *e.g.*, *Blackwell v. Wyeth*, 971 A. 2d 235, 268 (Md. 2009) (excluding testimony of Dr. Deth, Dr. Mumper, and Dr. Mark Geier, among others); *Blackmon v. American Home Products*, 346 F. Supp. 2d 907, 918-19 (S.D. Tex. 2004). Two other suits alleging that thimerosal caused autism were similarly dismissed, although those actions involved thimerosal delivered in forms other than thimerosal-containing vaccines for infants. *Doe v. Ortho-Clinical Diagnostics, Inc.*, 440 F. Supp. 2d 465 (M.D.N.C. 2006) (granting summary judgment against the plaintiffs' allegation that the thimerosal received by the autistic child's *mother* during the pregnancy caused the child's autism); *Redfoot v. B.F. Ascher & Co.*, 2007 WL 1593239 (N.D. Cal. June 1, 2007) (granting summary judgment against plaintiffs alleging that the thimerosal contained in a *nasal mist* administered to a young child caused the child's autism). See also *Easter v. Aventis Pasteur, Inc.*, 358 F. Supp. 2d 574 (E.D. Texas 2005) (excluding testimony of plaintiff's expert that an autistic child's "co-morbid conditions" were caused by thimerosal-containing vaccines).

VI

PETITIONERS HAVE NOT DEMONSTRATED THAT THIMEROSAL-CONTAINING VACCINES SUBSTANTIALLY CONTRIBUTED TO THE CAUSATION OF *JORDAN KING'S* AUTISM

Petitioners' sole expert witness concerning "specific causation"--*i.e.*, their allegation, that Jordan King's autism was vaccine caused--was Dr. Mumper.[112] Dr. Mumper's testimony may be summarized as follows. As noted above, Dr. Mumper did not explain in detail why she believes that, *in general*, thimerosal-containing vaccines can contribute to causing autism; she indicated that she relied on the general reasoning and evidence cited by Drs. Deth, Aposhian, and Kinsbourne. (Ex. 13, pp. 3, 8-9; Tr. 1224-29.) As to Jordan King's case, she indicated that she was relying on the fact that Jordan suffered from "regressive autism," meaning that he appeared developmentally normal during his first year of life, then experienced his first symptoms of autism in the form of a "regression"--*i.e.*, a loss of skills--during his second year. Dr. Mumper noted that Jordan received the course of thimerosal-containing vaccines that was typical for American children in the 1990s, through which he received 187.5 micrograms of ethylmercury during his first six months of life, and another 50 micrograms of ethylmercury at about age two.[113] (Ex. 13, p. 3; Tr. 1249-52, 1317-18; P. Trial Ex. 5; see also p. 6 above.) Dr. Mumper pointed to the results of a number of laboratory tests performed on Jordan, arguing that such tests supported a conclusion that thimerosal contributed to his autism. She also pointed to what she believed to be Jordan's positive response to certain treatments, as supportive of her causation conclusion. Putting these factors together, Dr. Mumper concluded that Jordan's thimerosal-containing vaccines likely contributed to the causation of his autism.

I must reject the claim that thimerosal-containing vaccines substantially contributed to the causation of *Jordan King's* own autism, for several reasons set forth below.

---

[112]Dr. Kinsbourne, Dr. Deth, and Dr. Aposhian offered "general causation" testimony, supporting the conclusion that thimerosal-containing vaccines *in general* may be capable of contributing to the causation of autism, but did not offer an opinion as to whether thimerosal-containing vaccines contributed to the *specific* autism of Jordan King.

[113]As explained above and below, petitioners never came close to making a showing that the amount of ethylmercury that Jordan received from his vaccinations was sufficient to cause *any* type of harm, to him or to any child. To the contrary, respondent's experts testified persuasively that the amounts of ethylmercury that Jordan and other American children received from vaccines during the 1990s actually delivered *less* mercury to his brain than most infants *naturally* receive from breastfeeding, ordinary infant diet, breathing, and the other sources of small amounts of mercury that are routinely received by humans. (See, *e.g.*, p. 51 above.)

A. I have rejected petitioners' "general causation" theory.

In the pages above, I have explained at length why I have rejected the petitioners' *general causation* theory, concerning how thimerosal-containing vaccines allegedly *can* contribute to the causation of autism. Further, as explained above (p. 78), the petitioners' sole "specific causation" expert in this case, Dr. Mumper, relied on that *general causation* theory in reaching her opinion that thimerosal-containing vaccines contributed to the causation of *Jordan King's* autism. Thus, since the petitioners have failed to demonstrate any validity to their *general causation* theory, it follows inescapably that they have also failed to demonstrate that thimerosal-containing vaccines played any role in the causation of the autism of Jordan King.

The discussion concerning Jordan King's case, therefore, could reasonably end here. However, in the interest of completeness, I note that there are *additional* reasons to reject the petitioners' "specific causation" contention that thimerosal-containing vaccines played a role in the causation of Jordan King's own autism. I will discuss those additional reasons below.

B. Relative expertise of the competing experts

Respondent has argued (R-1, pp. 80-82) that Dr. Mumper, the petitioners' sole expert concerning "specific causation," is not qualified to offer a competent opinion on the "specific causation" issue of whether thimerosal-containing vaccines contributed to the causation of Jordan King's autism. Respondent points to a recent ruling of a Maryland appellate court excluding Dr. Mumper's testimony in a civil suit alleging that thimerosal-containing vaccines caused autism, in which the court acknowledged that Dr. Mumper was qualified to testify concerning the *treatment* of autism, but concluded that "her experience was not relevant to the ability to assess the underlying cause" of the child's autism. *Blackwell v. Wyeth*, 971 A. 2d 235, 266 (Md. 2009).

I cannot agree with respondent's argument that Dr. Mumper's causation opinion should be excluded from consideration, or given no weight whatsoever, in this Vaccine Act proceeding. The issue before the Maryland court was whether to exclude Dr. Mumper's testimony from a *jury trial*. In Vaccine Act cases, which are tried before a special master without a jury, the practice of special masters has generally been to hear and consider causation opinions from medical doctors offered by petitioners, even when such medical doctors may be testifying beyond the boundaries of their individual medical specialties. I believe that such practice of the Vaccine Act special masters has been reasonable and appropriate, given the remedial purpose of the Vaccine Act combined with the fact that the special masters, as specialist jurists dealing continuously with medical issues, are better situated than the average juror to carefully evaluate medical testimony and assign weight as appropriate.

In this case, I conclude that Dr. Mumper has sufficient qualifications for me to accept her as at least basically qualified to offer an opinion concerning "specific causation" in this Vaccine Act case. As noted above (p. 22), Dr. Mumper is a medical doctor who has practiced pediatric medicine for more than 25 years. She has a creditable academic background in pediatrics, and very substantial experience in treating autistic children.

Respondent's arguments concerning Dr. Mumper's qualifications, however, are properly applicable concerning the issue of the *weight* to be given to Dr. Mumper's testimony concerning the causation issue. As respondent argued, Dr. Mumper is not the ideal medical specialist concerning the *causation* of autism. Dr. Mumper is not a pediatric neurologist or a psychiatrist (autism is considered both a neurologic and a psychiatric disorder), nor is she a psychologist (psychologists are also often the specialists who diagnose autism). Dr. Mumper acknowledged that although she regularly *treats* autism, she does not *diagnose* autism, but instead requires her autistic patients to have an independent diagnosis by another professional. (Tr. 1480-81.)

In contrast, the respondent's experts who reviewed Jordan's medical records and offered an opinion concerning "specific causation" were Dr. Rust, a *pediatric neurologist* who has a long history of diagnosing and treating autistic children, and Dr. Fombonne, a *psychiatrist* who also has extensive experience in diagnosing and treating autistic children. (See pp. 23-24 above.) It is also noteworthy that Dr. Fombonne has spent much of his career studying the issue of the *causation* of autism, working on epidemiologic studies of autism. (See p. 24 above.) I conclude that, as to the issue of the *specific causation* of Jordan King's autism, respondent's experts have expertise *far superior* to that of Dr. Mumper.

This contrasting expertise of the experts, then, is another factor, among many, supporting my conclusion that there has been no showing that thimerosal-containing vaccines contributed to the causation of Jordan King's autism.

C. Dr. Mumper's reliance on the testing of Jordan was misplaced.

Dr. Mumper seems to have placed strong reliance on the results of certain laboratory tests that were performed on Jordan. (Ex. 13, pp. 2, 5; Tr. 1318-36.) But the testimony of respondent's experts demonstrated that this reliance of Dr. Mumper was misplaced.

1. Deficiencies in the laboratories

One factor is that the evidence casts serious doubt upon the reliability of the *laboratories* that performed the tests upon which Dr. Mumper relies.

First, Dr. Mumper herself acknowledged there has been a "lot of criticism" of the laboratories that provide the type of testing that she relies upon in this case, involving allegations that such laboratories "aren't reliable." (Tr. 1352.) Those criticisms have raised enough concern on Dr. Mumper's part that she is involved in a project evaluating the reliability of those laboratories. (Tr. 1352-54.) Those reliability concerns of Dr. Mumper herself obviously cast at least some doubt on the results of the tests upon which Dr. Mumper relies in this case.

Second, one laboratory that conducted several of the tests upon which Dr. Mumper initially relied, in her expert report, is the Great Smokies Diagnostic Laboratory.[114] At the evidentiary hearing, however, Dr. Mumper acknowledged that, based upon her subsequent knowledge of severe problems with that laboratory's work, she now would *not* be comfortable relying upon any testing results from that laboratory. (Tr. 1532-33.)

Third, another laboratory upon whose tests Dr. Mumper relied was the "[redacted]" laboratory. (See, *e.g.*, Tr. 1560.) Dr. Mumper testified that she had "relatively more faith" in that laboratory's expertise, apparently using the term "relatively" to compare [this laboratory] to laboratories such as Great Smokies. (Tr. 1550.) However, respondent's expert Dr. Brent was highly critical of the [name redacted] laboratory, stating that it engaged in dubious testing that was impossible to interpret. (Tr. 1853-55.) Respondent's expert Dr. Rust also criticized the work of the . . . laboratory, as well as that of the Great Smokies lab. (Ex. II, p. 7.) And Dr. Mumper herself, when shown documents indicating that the [name redacted] laboratory has been the subject of an investigation by the New York State Department of Health, and has been found to have deficient procedures (see R. Trial Exs. 2 and 3), acknowledged that such documents (which she had not previously seen) do cause her to have some concern about that laboratory's work. (Tr. 1560-68.)

Finally, Dr. Mumper has also relied, not in this case but in the companion test case of Colin Dwyer, upon testing performed by the Immunosciences Lab, Inc. (*Dwyer* Tr. 159-62.) During the evidentiary hearing in the *Dwyer* case, Dr. Mumper was shown documents indicating that Immunosciences has been found by the Centers for Medicare and Medicaid Services to have a number of deficiencies in its testing procedures. (*Dwyer* Tr. 166-176.) Dr. ~~Mumper stated that she~~

[114]In her expert report, Dr. Mumper included a section concerning "Laboratory evidence of impairments," in which she described a number of tests on which she relied. (Ex. 13, p. 5.) Her report did not give the page number of the medical records for each specific test, but a comparison of her description of each test with Jordan's medical records makes it apparent which tests she was describing. Three of those references clearly refer to test results from the *Great Smokies* laboratory.

First, in Dr. Mumper's second reference in that section, she noted that "[Jordan's] physician noted several markers for low glutathione." A review of the record of Jordan's pediatrican, Dr. John Green, indicates that this reference by Dr. Mumper is to Dr. Green's note of March 28, 2000 (Ex. 1, p. 13), in which Dr. Green discussed a Great Smokies laboratory report completed on March 8, 2000 (Ex. 1, pp. 48-50).

Next, Dr. Mumper's third reference in that section of her report was to an "amino acid analysis interpreted as demonstrating 'impaired xenobiotic detoxification.'" (Ex. 13, p. 5.) This reference is again to the same Great Smokies laboratory report completed on March 8, 2000 (Ex. 1, pp. 48-50), which included a finding of "impaired xenobiotic detoxification" (Ex. 1, p. 50).

Finally, Dr. Mumper's fifth reference in that section of her report described "laboratory assessments of intestinal dysbiosis." (Ex. 13, p. 5.) This reference seems to be to two Great Smokies laboratory reports completed February 7, 2000, and March 30, 2000, each of which found "severe bacterial dysbiosis" in Jordan's intestinal system. (Ex. 1, p. 47; Ex. 4, p. 5.)

had previously been unaware of the extent of the problem at Immunosciences (*Dwyer* Tr. 166-67, 173-74, 176), but acknowledged that in light of those documents, she would "give relatively less credence" to Immunosciences results, "or perhaps even be forced to discount the reliability" of that laboratory's challenged tests (*Dwyer* Tr. 176).

In addition, respondent has pointed out that a number of courts have found testing by Immunosciences to be unreliable. (R-1, p. 88.) *See*, *e.g., Cabrera v. Cordis Corp.*, 134 F.3d 1418, 1422 (9th Cir. 1998); *Pick v. Am. Med. Sys., Inc.*, 958 F.Supp. 1151, 1164-66 (E.D. La. 1997); *Gaudette v. Conn Appliances, Inc.*, 2007 WL 2493437, at *4-6 (Tex. Sept. 6, 2007); *Geffcken v. D'Andrea*, 137 Cal. App. 4th 1298, 1309-10 (Cal. Ct. App. 2006); *Whisnant v. United States*, 2006 WL 2861112, at *3-4 (W.D. Wash. Oct. 5, 2006).

In sum, as shown above, there are specific, identified problems with some of the laboratories upon whose results Dr. Mumper has relied in this case and the companion cases.[115] Further, Dr. Brent has testified that the type of testing upon which Dr. Mumper relied does not produce valid, interpretable results. (Tr. 1853-55.) And Dr. Rust testified that "the tendency has been for these laboratories to be sought out by a particular cadre of physicians whose views of autism fall outside of that of the general medical community." (Ex. II, p. 7.)

Accordingly, the general unreliability of these laboratories is sufficient reason to reject Dr. Mumper's argument that the testing of Jordan King supports a conclusion that thimerosal-containing vaccines played a role in causing his autism.

2. Even if the laboratories were reliable, the tests in question would still not offer evidence that thimerosal-containing vaccines played any role in Jordan's autism.

As demonstrated on the previous pages, the laboratory deficiencies by themselves give strong reason to doubt the reliability of any of the testing upon which Dr. Mumper relied. However, even if one were to assume that those laboratories generally performed accurate testing, the specific tests on which Dr. Mumper relies would *still* not constitute significant evidence supporting the idea that thimerosal-containing vaccines played any role in Jordan's autism, for the reasons set forth below.

a. Mercury testing

Some of the tests on which Dr. Mumper relied purported to measure amounts of mercury excreted by Jordan. This testing seems to have been the type of testing most important to

[115] Although Dr. Mumper did not rely on the Immunosciences laboratory in this case, her reliance on that laboratory in the *Dwyer* case offers support to the assertions of respondent's experts that, *in general*, the laboratories upon which Dr. Mumper relies for this type of testing have dubious records of reliability.

Dr. Mumper's causation opinion in the individual cases. For example, Dr. Mumper seemed to acknowledge that the other tests upon which she relied, which don't measure mercury, are only "consistent with" a conclusion of vaccine causation, "but not specifically suggestive" of vaccine-causation. (*E.g., Dwyer* Tr. 186.) Indeed, Dr. Mumper even seemed to admit, though her answer is not completely clear, that without a reliable laboratory test *specific to mercury*, she could not offer a causation opinion in a specific case. (*Dwyer* Tr. 186.)

The medical records in the three test cases for the petitioners' second theory of causation--*i.e.*, this *King* case and the *Mead* and *Dwyer* cases--include documentation of various types of testing involving mercury, including tests of hair, blood, urine, and fecal matter. For some of this testing, specifically urine or fecal testing, the subject is administered a "chelating" agent--*i.e.*, a substance designed to specifically "provoke" the excretion of mercury. Other urine or fecal tests are described as "unprovoked" or "pre-provocation" tests, since no chelating agent is administered prior to the test. Dr. Mumper explained, however, that in her view, the blood,[116] hair, and unprovoked urine tests are *not* reliable tests for measuring the exposure of infants to mercury. (Tr. 1513.) She also stated that there are problems with and limitations to fecal testing for mercury. (Tr. 1514-15.) Thus, Dr. Mumper in effect acknowledged that the only test that she believes to be a reliable test of mercury in an autistic child is a post-provocation urine test.

The problem with Dr. Mumper's reliance on such post-provocation urine tests, however, is that the evidence shows that there is *no established* "*reference range*" for such post-provoked urine testing. That is, there is no data from testing of the general population to tell us what is the *expected* outcome of post-provocation urine testing for *normal* children who do *not* suffer from mercury poisoning. Dr. Brent, the medical toxicologist, explained that because there is no established reference range, the results of such post-provocation urine tests on a particular individual are "uninterpretable"--that is, *meaningless* without the ability to compare the result of a particular test to an established "normal" result range. (Tr. 1850, 4343-45.) Dr. Mumper herself admitted that there is no established reference range for such tests. (*Dwyer* Tr. 201.) She further admitted that, as a result of the absence of such an established reference range, she did not know what kind of post-provocation urine testing result would be expected in a person *without* any type of mercury poisoning. (Tr. 1554-55.)

Nevertheless, that absence of an established reference range did not dissuade Dr. Mumper from relying upon post-provocation urine test results as evidence that Jordan had an unusually high "body burden" of mercury, which she regarded as evidence supporting a conclusion that thimerosal-containing vaccines played a causal role in his autism. For example, she testified that the result of a post-provocation urine test performed on Jordan on May 5, 2000, was a "very elevated reading on mercury, about twice the upper range of normal." (Tr. 1321.) She also stated that the result of another provoked urine test, in February of 2003, was "way off the chart" for mercury. (Tr. 1330.)

---

[116]Dr. Mumper stated that blood testing is useful for measuring a person's *acute* exposure to mercury, but is not useful for measuring the *cumulative* mercury exposure that she believes to be a factor in causing autism. (Tr. 1512-14, 1517.)

But how did Dr. Mumper conclude that Jordan's results on those two tests were "very elevated" or "off the chart" for mercury, when there was no established reference range for post-provoked mercury urine testing? She looked at the standard reference range for *unprovoked* urine testing. Both of those tests cited by Dr. Mumper were performed by the [name redacted] laboratory, and both state that the tests were "post provocative." (Ex. 1, pp. 45, 55.) Yet, the second [lab name redacted] test document specifies that the "reference range" provided by [lab name redacted] supplied for purposes of comparing the individual's result to "normal" results, is a reference range for "*non-provoked*" testing. (Ex. 1, p. 55, bottom of page.) Thus, as Dr. Brent explained, the comparison made in both the [laboratory] document and by Dr. Mumper[117] is erroneous and meaningless. It makes no sense to compare Jordan's *post-provocation* urine test result to a reference range that is based upon *non-provoked* urine testing.

Moreover, Dr. Brent explained that when the results of mercury testing of Jordan, both provoked and non-provoked, are viewed in their entirety, they are exactly what one would *expect* from an individual *without* any mercury-related problem. That is, Jordan's *non-provoked* test results were within the *normal* range for non-provoked testing. (Tr. 1852-53, 4340.) At the same time, while his *provoked* results were outside the normal range for *non-provoked* testing, that is not surprising since the provocation/chelation process is *designed* to specifically provoke an increased excretion of metals. (Tr. 1852-53, 4340-41, 4347.) As Drs. Brent and Fombonne explained, administration of a chelating agent to *anyone*, autistic or not, mercury-poisoned or not, will always be followed by increased excretion of mercury.[118] (Ex. M, p. 74; Tr. 1852, 4340-41, 4343.)

In short, a careful analysis of the record demonstrates that there is no valid basis for Dr. Mumper's view that the results of mercury excretion testing on Jordan King offer support for a conclusion that thimerosal-containing vaccines played a role in causing Jordan's autism. To the contrary, the evidence supports a conclusion that Dr. Mumper's reliance on such mercury tests has no basis in science or logic. Indeed, upon cross-examination even Dr. Mumper acknowledged that there is no particular profile or pattern of post-provocation test results that points to a finding that a child has mercury-induced autism. (Tr. 1555-60, 1568-69.) When pressed, Dr. Mumper could not even suggest an example of *any* type of result on a post-provocation mercury urine test that *would*

---

[117]It is evident that as to the first (May 5, 2000) test as well as the second, Dr. Mumper utilized the reference range for *non-provoked* testing, in order to conclude that the test result was "very elevated." It is the only reference range that she *could* have used, since no standard reference range exists for *post-provoked* testing.

[118]Dr. Rust also opined that the results of the mercury testing of Jordan King were dubious, and non-supportive of Dr. Mumper's causation opinion. (Ex. II, pp. 9-10.) Further, respondent has filed two medical journal articles that strongly support the proposition that chelation will be followed by substantial increases in urinary mercury excretion in *anyone*. *See* G. P. Archbold, et al., *Dimercaptosuccinic Acid Loading for Assessing Mercury Burden in Healthy Individuals*, 41 ANNALS CLINICAL BIOCHEMISTRY 233, 235 (2004) (RML 14); Howard Frumkin, et al., *Diagnostic Chelation Challenge with DMSA: A Biomarker of Long-Term Mercury Exposure*? 109 ENVTL. HEALTH PERSP. 167, 170 (2001) (RML 183).

not, in her analysis, support a claim of mercury-induced autism. (Tr. 1558-60.) Dr. Mumper's analysis in this regard was illogical, and completely unpersuasive.[119]

b. Other testing

Dr. Mumper also made brief references, in both her expert report and hearing testimony, to a number of additional allegedly abnormal test results derived from tests which did *not* measure mercury; she suggested that such results offer support to her conclusion that thimerosal-containing vaccines had a role in causing Jordan's autism. (Ex. 13, p. 5, "Laboratory evidence of impairments;" Tr. 1323-30.) Petitioners in their briefs also rely on such testing. (P-1 at 71-73.)

Dr. Mumper acknowledged that these additional tests upon which she relied, which do not measure mercury, are "not specifically suggestive" of vaccine-causation, but argued that such results are "consistent with" a conclusion of vaccine causation. (*Dwyer* Tr. 186.)

However, Dr. Mumper's references in this regard were quite fleeting and vague, and she failed to provide any substantial explanation as to *why* such test results might be relevant either to her general belief that thimerosal-containing vaccines *can* contribute to the causation of autism, or her allegation that thimerosal-containing vaccines *did* contribute to causing Jordan's autism. Based merely upon this failure to explain the relevance of these tests, I found that Dr. Mumper *completely failed* to make a case that the cited non-mercury test results have any relevance to the question of whether thimerosal-containing vaccines contributed to Jordan's autism.

Nevertheless, in the interest of completeness, I add that the non-mercury tests upon which Dr. Mumper chiefly relied during her hearing testimony were tests that, in her view, indicated that Jordan was under "oxidative stress." (Tr. 1327-30.) And there is particular reason to doubt the relevance of those "oxidative stress" tests. That is, Dr. Mumper failed to explain why one should conclude either (1) that thimerosal-containing vaccines can cause oxidative stress, or (2) that oxidative stress causes autism; and, as discussed above with respect to Dr. Deth, respondent's experts have testified persuasively that there is *no* scientific reason to conclude *either* that thimerosal-containing vaccines could cause any significant oxidative stress or that oxidative stress causes autism. (See pp. 70-75 above.) Also, respondent's expert with special expertise concerning oxidative stress, Dr. Roberts, testified that a number of different factors other than thimerosal-containing vaccines can cause oxidative stress (Tr. 2185), and Dr. Mumper herself so acknowledged (Tr. 4255; *Dwyer* Tr. 178).

---

[119]There are so many defects in Dr. Mumper's testimony that it is impossible to list them all. But another major point of illogic in her testimony is that even if Dr. Mumper's testimony showed that *mercury* did have some role in causing Jordan King's autism, she made no case that the inorganic mercury resulting from *thimerosal-containing vaccines* would be the culprit, rather than the *greater* amounts of mercury that Jordan likely received from other sources. (See, *e.g.*, discussion at p. 50, above.)

Further, Dr. Roberts explained that the typical tests used to measure oxidative stress do not demonstrate whether oxidative stress is occurring in the *brain* (Tr. 2182-83), the type of oxidative stress that would be relevant to Dr. Mumper's theory. Dr. Roberts additionally explained that there simply are no known biomarkers for "mercury-induced" oxidative stress. (Tr. 2186.)

3. Summary concerning laboratory testing results

In short, for the reasons set forth above, I conclude that the laboratory testing upon which Dr. Mumper relies offers no persuasive support for her causation opinion.

D. Jordan's purported positive responses to treatment

In her expert report, Dr. Mumper included a section entitled "Clinical evidence of improvement with medical treatment directed at removing mercury and improving the body's natural detoxification and immune mechanisms." (Ex. 13, p. 6.) Although not explained, this section implies that because Jordan allegedly improved after treatments designed to remove mercury from his system, and after other treatments, such improvement supports Dr. Mumper's conclusion that mercury from thimerosal-containing vaccines contributed to his autism. In her oral testimony, Dr. Mumper again at times implied the same argument (*e.g.*, Tr. 4195-4203), and at one point she explicitly confirmed that this reasoning was a part of her causation opinion (Tr. 1598).

Notably, the petitioners in their post-hearing briefs did *not* mention this argument at all, indicating that they have chosen not to rely upon it. Nevertheless, because Dr. Mumper herself did appear to raise the argument, I note that I do not find the argument to be persuasive.

Respondent's experts Dr. Rust and Dr. Fombonne argued persuasively that it would be inappropriate to draw any inferences concerning causation, in Jordan's case or any case, from Dr. Mumper's testimony concerning treatments, for several reasons. First, they pointed out that the treatments to which Dr. Mumper referred have *not* been demonstrated by scientific testing to have any beneficial effects on autism *in general*. (Ex. M, para. 177(f); Tr. 2451-54, 2458-59, 3702-03, 4274.) Dr. Brent provided similar testimony. (Tr. 1845, 4347-48.)

Second, respondent's experts explained that autistic children quite often have periods of substantial improvement in their symptoms in the *absence* of any treatment, so that it is not reasonable to conclude that a particular period of improvement was caused by any recent treatment. (Ex. M, paras. 46, 177(d); Tr. 2450-51, 2512-13, 2601, 2607, 3568-69, 3698, 4316-17.) Third, respondent's experts noted that because Jordan was often subjected to more than one treatment at a time, it is even more dubious to ascribe any improvements to *particular* treatments. (Ex. M, paras. 46, 142-43; Tr. 2459-60, 3697-99.)

Moreover, it is clear that chelation treatments do not remove mercury from the *brain*, so it is not logical to conclude that such treatment could affect autism. (Ex. G, p. 40; Ex. II, p. 16; Tr. 1599.) In this regard, on cross-examination Dr. Mumper herself acknowledged that she could *not*

explain how the other treatments upon which she relied could, even in theory, affect the persistent inorganic mercury in the brain that she believes to be a contributing cause of autism. (Tr. 4249-51.)

In sum, concerning this issue I find the arguments of respondent's experts to be persuasive. I find that Dr. Mumper's testimony concerning treatment offered no support to her causation opinion in this case.

E. References to other exposures besides thimerosal-containing vaccines

In her expert report, Dr. Mumper included a section which she entitled "Clinical Evidence," which seems to be a list of other potentially harmful environmental agents to which Jordan was exposed, in addition to thimerosal-containing vaccines. (Ex. 13, pp. 3-4.) Dr. Mumper's report contains no explanation of the relevance of this list of factors to her opinion that thimerosal-containing vaccines contributed to causing Jordan's autism. However, in her hearing testimony, Dr. Mumper briefly mentioned that she was concerned that these other factors might have *combined with* thimerosal-containing vaccines to cause Jordan's autism. (*E.g.*, Tr. 1657-59.)

After reviewing Dr. Mumper's statements in this regard, however, I see no reason to give any credence to Dr. Mumper's suggestion that Jordan's autism might have been caused by a combination of those cited factors and thimerosal-containing vaccines. This suggestion seems to constitute sheer speculation by Dr. Mumper. She did not explain the reasoning behind her suggestion, or point to any evidence supporting it. As Dr. Rust commented, Dr. Mumper's statements in this regard "are speculative and not supported by the literature." (Ex. II, p. 9.) I simply see no persuasive evidence in the record that thimerosal-containing vaccines play *any* role in causing autism, by themselves or in combination with any other factors.[120]

F. Question of whether Jordan was developmentally normal prior to his regression

Respondent, through respondent's expert Dr. Fombonne, acknowledged that Jordan King clearly has autism, and that he did suffer a "regression"--*i.e.*, a *loss* of skills that he had previously demonstrated--sometime around his 18th month of life. (Tr. 3693-94.) Thus, there is no dispute that Jordan has suffered from "regressive autism" as the petitioners in this case have defined that category--*i.e.*, autism which includes a *loss* of previously-demonstrated skills. However, Dr. Mumper seemed to premise her opinion that Jordan's autism was vaccine-caused on the *additional* assumption that Jordan was developmentally *completely normal* prior to his regression. For example, in both her expert report and her hearing testimony, Dr. Mumper stressed that Jordan's

---

[120]Dr. Mumper also included a section in her expert report noting that Jordan has experienced intestinal problems, diarrhea, lethargy, and sleep disruption. (Ex. 13, pp. 5-6.) However, Dr. Mumper never provided any coherent explanation as to why these problems might offer support to her vaccine-causation opinion in Jordan's case. I conclude that the existence of such problems, and the fact that such problems may have improved at times after various treatments, offers no support to Dr. Mumper's causation opinion in this case.

medical records do not indicate any developmental abnormalities during Jordan's first year of life. (*E.g.*, Ex. 13, p. 2; Tr. 1303-04.)

Whether Jordan was actually developmentally normal prior to his regression is not completely clear from the record in this case. Respondent argues that the evidence supports a conclusion that Jordan was *not* developmentally normal prior to his regression. (R-1, pp. 84-85.) As explained in detail above (pp. 45-46), the evidence strongly demonstrates that the fact that children suffer regression during the second year of life, and thereafter are diagnosed with autism, does *not* mean that such children were completely normal prior to the regression. To the contrary, when the pre-regression histories of such children are retrospectively studied, by examining records or videos or other means, it is often found that a child had unrecognized symptoms of autism even prior to the observed regression. In this case, respondent relied upon testimony of respondent's expert Dr. Fombonne, who has experience in using videos to evaluate potential autistic symptoms for research and clinical purposes. (Tr. 4306, 4310-11.) Dr. Fombonne testified that, based upon his review of videos and medical records of Jordan, Jordan likely was exhibiting subtle signs of autism, unrecognized by his family or pediatrician, even prior to the onset of his regression. (Ex. M, para. 138; Tr. 3695, 3794-96, 4283-85.)[121]

One example cited by Dr. Fombonne was a video made when Jordan was about 13 to 16 months of age, in which Jordan failed to interact with people and failed to babble or vocalize, which Dr. Fombonne found to be pre-regression evidence of autism. (Tr. 4284-85.) Neither Dr. Mumper, nor any other expert for petitioners, ever expressed specific disagreement with Dr. Fombonne's interpretation of that particular video.

I have considered this argument of respondent, that Jordan King was demonstrably developmentally abnormal even prior to his regression. I conclude that this is *possible*, but is not clearly demonstrated from the available evidence. The evidence in the record of this case makes it clear that Jordan did experience a regression during his second year of life, but *exactly when* that happened during that second year is not clear. Moreover, the videos upon which Dr. Fombonne relied are not precisely dated. It is not clear to me, therefore, whether the videos relied upon by Dr. Fombonne were of behavior that occurred *prior* to Jordan's regression.

Thus, *if*, as respondent argues, Jordan was displaying evidence of autism prior to his regression, that would be yet another reason to doubt Dr. Mumper's view of Jordan's case. However, that possible factor has *not* played a role in my analysis of this case, because, while there

[121]Dr. Rust also presented brief testimony to the effect that the number of words used by Jordan prior to his regression may have been abnormally low. (Tr. 2445-46.) However, Dr. Rust's testimony in this regard was not well-developed. I reach no conclusion concerning that contention of Dr. Rust, and attach no importance to it.

is some evidence of pre-regression abnormality in Jordan's case, that evidence is not completely clear.[122]

G. Absence of a specific, identified cause for Jordan's autism

Petitioners point out that the record of this case does not contain evidence of a specific, identified cause for Jordan's autism. (P-1, pp. 70-71.) They note that Dr. Mumper looked for evidence of a specific cause, other than thimerosal-containing vaccines, but found none. (P-1, p. 70.) Petitioners seem to suggest that this lack of another known cause for Jordan's autism supports the theory that thimerosal-containing vaccines were the cause.

To draw such an inference of vaccine-causation from the lack of another specifically identified cause, however, would be erroneous. Rather, the evidence indicates that in about 80 to 95 percent of autism cases, no specific cause is ever identified. (Tr. 2376, 3266; Ex. M, para. 47.) Thus, the lack of a specific, identified cause for Jordan's autism is not a substantial item of support for a "vaccine-causation" inference.

H. Dr. Mumper's failure to relate her causation views to "regressive autism"

As described above, Dr. Mumper explained that she was relying, in general, on the "general causation" opinions of Drs. Kinsbourne, Deth, and Aposhian. Further, as also noted above, the argument of Dr. Kinsbourne, and of the petitioners in their briefs, is that thimerosal-containing vaccines can contribute to the causation *specifically* of "regressive autism." Yet Dr. Mumper never explained why her causation views might be specifically applicable to autism with regression, rather than to autism in general. To the contrary, on cross-examination she admitted that she *did not know* whether her causation theory would apply only to regressive autism. (Tr. 1501.)

As discussed above (pp. 79-84), the epidemiologic studies show clearly that thimerosal-containing vaccines *are not* a significant cause of autism *in general*. Therefore, Dr. Mumper's inability to explain why thimerosal-containing vaccines would be any more likely to cause "regressive autism," in comparison to autism without regression, is yet another reason to doubt the validity of her testimony.[123]

---

[122]In other words, even assuming that Jordan was *completely normal* prior to his regression, I find the rest of Dr. Mumper's causation theory to be totally unpersuasive.

[123]As explained above, in most parts of their briefs the petitioners seem to argue that thimerosal-containing vaccines can contribute to causing "regressive autism." Confusingly, in one section of one brief, they appear to shift their focus to a theoretical narrower *subset* of "regressive autism" that they label "clearly regressive autism." (See pp. 88-94 above.) But, in any event, Dr. Mumper, like Drs. Kinsbourne, Aposhian, and Deth as well, did *not* explain why her causation theory might be particularly applicable to cases of "clearly regressive autism" but not to other forms of autism.

I. Summary concerning "specific causation"

For all the reasons set forth above, I conclude that the petitioners have failed completely to demonstrate that it is "more probable than not" that thimerosal-containing vaccines contributed to the causation of Jordan King's own autism.[124]

VII

PETITIONERS' CASE FAILS THE *ALTHEN* TEST

A. The Althen *test*

In its ruling in *Althen*, the U.S. Court of Appeals for the Federal Circuit discussed the "causation-in-fact" issue in Vaccine Act cases. The court stated as follows:

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury. If Althen satisfies this burden, she is "entitled to recover unless the [government] shows, also by a preponderance of evidence, that the injury was in fact caused by factors unrelated to the vaccine."

Althen v. Secretary of HHS, 418 F.3d 1274, 1278 (Fed. Cir. 2005) (citations omitted). In the pages above, I have already set forth in detail my analysis in rejecting petitioners' "causation-in-fact" theories in this case. In this section of my Decision, then, I will briefly explain how that analysis fits *specifically* within the three prongs of the *Althen* test, enumerated in the first sentence of the *Althen* excerpt set forth above. The short answer is that the petitioners' causation evidence in this case falls *far short* of satisfying the *Althen* test.

---

[124] As explained above, while in most of their post-hearing briefs the petitioners seem to argue that thimerosal-containing vaccines can contribute to the causation of "regressive autism," at one point in one brief they seem to narrow their focus to a theoretical narrower *subset* of regressive autism that they label "clearly regressive autism." (See p. 88 above.) As fully described above, the petitioners have failed to make a persuasive causation case concerning *either* "regressive autism" or "clearly regressive autism." But it is noteworthy that even had they somehow demonstrated a causal connection to "clearly regressive autism," that demonstration still might have done them no good in this case. That is, while it is clear that Jordan King fits within the "regressive autism" category, it is *unclear* whether he would actually fit within the category of "clearly regressive autism" as the petitioners have defined it. In this regard, see the discussion whether Jordan actually showed evidence of developmental abnormality *prior to* his regression, at pp. 109-110 above.

B. Application of **Althen** *Prongs 1 and 2 to this case*

The first two prongs of the *Althen* test, as noted above, are that the petitioners must provide "(1) a medical theory causally connecting the vaccination and the injury," and "(2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury." Initially, it is not absolutely clear how the two prongs differ from each other. That is, at first glance, each of the two prongs seems to require a demonstration of a causal connection between "the vaccination" and "the injury." However, a number of Program opinions have concluded that these first two elements reflect the analytical distinction that has been described as the "can cause" vs. "did cause" distinction. That is, in many Program opinions issued prior to *Althen* involving "causation-in-fact" issues, special masters or judges stated that a petitioner must demonstrate (1) that the *type* of vaccine in question *can* cause the *type* of injury in question, and also (2) that the *particular* vaccination received by the specific vaccinee actually *did* cause the vaccinee's *own* injury. *E.g.*, *Kuperus v. Secretary of HHS*, No. 01-60V, 2003 WL 22912885, at *8 (Fed. Cl. Spec. Mstr. Oct. 23, 2003); *Helms v. Secretary of HHS*, No. 96-518V, 2002 WL 31441212, at *18 n.42 (Fed. Cl. Spec. Mstr. Aug. 8, 2002). (As an example of the "can cause/did cause" distinction, in this very case the petitioners have attempted to demonstrate (1) that thimerosal-containing vaccines *can* contribute to the causation of autism, in general, and (2) that thimerosal-containing vaccines *did* cause Jordan's own autism.) The Federal Circuit subsequently confirmed that distinction between the two prongs in *Pafford*, stating explicitly that the "can it?/did it?" test, used by the special master in that case, was equivalent to the first two prongs of the *Althen* test. *Pafford v. Secretary of HHS*, 451 F.3d 1352, 1355-56 (Fed. Cir. 2006). Thus, interpreting the first two prongs of *Althen* as specified in *Pafford*, under Prong 1 of *Althen* a petitioner must demonstrate that the *type* of vaccination in question *can* cause the *type* of condition in question, and under Prong 2 of *Althen* the petitioner must then demonstrate that the *particular* vaccination actually *did* cause the condition of the *particular* vaccinee in question.

A few decisions of judges and special masters have discussed issues with respect to the *precise* interpretation of Prongs 1 and 2 of *Althen*. However, it is *not* necessary, in this case, to delve into any such potential interpretative issues, since under virtually any interpretation of *Althen*, the causation evidence offered by the petitioners in this case could *not* satisfy the *Althen* test. That is, as described in detail above, I have concluded that petitioners have fallen *far short* of demonstrating either that thimerosal-containing vaccines *can* contribute, in *general*, to the causation of *autism*, or that thimerosal-containing vaccines *did* contribute to the causation of *Jordan King's* own autism. Thus, the petitioners' arguments concerning both of those causation issues would fail under virtually any interpretation of *Althen*'s Prongs 1 and 2.

Moreover, there can be no doubt whatsoever that the *Althen* test ultimately requires that, as an *overall matter*, a petitioner must demonstrate that it is *more probable than not* that the *particular* vaccine was a substantial contributing factor in causing the *particular* injury in question. That is clear from the statute itself, which states that the elements of a petitioner's case must be established by a "preponderance of the evidence." § 300aa-13(a)(1)(A). And, regardless of the precise meaning of Prongs 1 and 2 of *Althen*, in this case the overall evidence falls far, far short of demonstrating that

it is "more probable than not" that thimerosal-containing vaccines contributed to the causation of *Jordan King's* autism.

C. Discussion of Althen *Prong 3*

Because the petitioners have failed to satisfy the first two prongs of *Althen*, there is really no need to analyze the third prong, but a few comments concerning that third prong may still be appropriate. The third element of the *Althen* test, set forth above, requires "a showing of a proximate temporal relationship between vaccination and injury." 418 F.3d at 1278. That is, under this third element of the *Althen* test, the petitioners would need to demonstrate that the first symptoms of Jordan's autism occurred within a *time frame* that would be consistent with causation by the thimerosal-containing vaccines in question.[125] The petitioners, however, have also failed to satisfy this third element of *Althen*.

Initially, it seems to me that, as a matter of logic, it would be impossible to satisfy the third prong of *Althen* without making a persuasive case concerning the *first* prong. That is, without first supplying a reliable theory by which a certain type of vaccine *can* cause a certain type of injury, one logically cannot establish an "expected" time frame for the onset of symptoms. In other words, without understanding *how* Vaccine A can cause Condition B, one cannot logically predict during what *time period* after vaccination one would expect to see the first symptoms of an occurrence of Condition B that was purportedly caused by Vaccine A.

Moreover, it would be especially difficult for the petitioners to prove Prong 3 in this case, where the petitioners are not pointing to a *particular* vaccination as the alleged cause of injury. The petitioners' theory in this case, of course, is that an *accumulation* of inorganic mercury in the brain resulting from a *series* of thimerosal-containing vaccines can cause autistic behavior in some individuals. The petitioners' experts, however, made no serious attempt to explain *when* one would expect to see the first symptoms of a case of autism in which thimerosal-containing vaccines were a causative factor. Dr. Kinsbourne, as explained above (p. 33), did not even purport to know *how much* thimerosal it might take to trigger his suggested causation process, so he could not, and he did not, say *when* in a child's life one might expect to see the *first symptoms* of such a causation process.[126] And none of the petitioners' other experts ever provided a discussion concerning this "timing" issue under *Althen's* third prong. Dr. Mumper, for example, acknowledged that she could

---

[125]In other words, the petitioners must demonstrate the existence of a "scientific temporal relationship" as discussed in *Pafford v. Secretary of HHS*, 64 Fed. Cl. 19, 29-30 (2005), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2005).

[126]At one point Dr. Kinsbourne stated that *neuroinflammation* would probably begin in a child's brain "within days or weeks" after the deposition of mercury into the brain. (Tr. 896-97.) But such neuroinflammation in the brain obviously would not be a symptom of autism noticeable by anyone, in the absence of a brain biopsy. Thus, Dr. Kinsbourne did *not* say when in a child's life he would expect to see the first observable *symptoms* of autism.

not say when she would expect to see the first symptoms of a case of autism to which vaccines contributed. (Tr. 1502-03.)

Nor did even the petitioners' *counsel* attempt to provide an argument concerning this third prong of *Althen*. Notably, in their short discussion in their post-hearing brief concerning the *Althen* standard and why they have supposedly satisfied that standard in this case (P-1, pp. 74-79), the petitioners simply *fail to mention* Prong 3 of the *Althen* test.

In short, I conclude that the petitioners have failed to make the showing required under Prong 3 of *Althen*, either in general or in Jordan's specific case.

D. Summary concerning application of* Althen *elements to this case

Accordingly, for the reasons explained above, I conclude that petitioners clearly have failed to satisfy the *Althen* test[127] in this case.

E. Legal arguments raised by petitioners

In their initial post-hearing brief filed in this case, the petitioners set forth a brief discussion of the legal considerations in a causation-in-fact case, under the Program statute and the *Althen* test. (P-1, pp. 74-75.) Most of their points are correct statements of the applicable law. As the petitioners stress, their burden is to demonstrate causation by a "preponderance of the evidence"--*i.e.*, "more probable than not"--*not* "scientific certainty." *Althen*, 418 F.3d at 1279. They need not demonstrate that Jordan's thimerosal-containing vaccines were the *sole* cause or even a *predominant* cause of Jordan's autism, but only that thimerosal-containing vaccines were a "substantial factor" in causing his autism, and a "but for" cause. *Shyface v. Secretary of HHS*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). Petitioners' causation showing need not necessarily be supported by epidemiologic evidence or other medical literature, but could, in appropriate circumstances, be accomplished by medical opinion and/or circumstantial evidence. *Althen*, 418 F.3d at 1279-80; *Capizzano v. Secretary of HHS*, 440 F.3d 1317, 1325 (Fed. Cir. 2006). Petitioners need not demonstrate the exact biological *mechanism* of causation. *Knudsen v. Secretary of HHS*, 35 F.3d 543, 549 (Fed. Cir. 1994). And the Federal Circuit has also stated that "close calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F.3d at 1280.

I have kept *all* of these points in mind in deciding this case. I have not required a level of proof greater than "more probable than not," which has also been described as "50 percent plus a feather." I understand fully that petitioners are not claiming that Jordan's thimerosal-containing vaccines were the *sole* cause of his autism, but are alleging only that such vaccines *contributed* to

---

[127]Because the petitioners have not met their burden, pursuant to § 300aa-13(a)(1)(A), of demonstrating that any of Jordan's vaccinations played any role in causing his autism, the burden *never shifted* to respondent to establish an "alternative cause" for Jordan's autism. *DeBazan v. Secretary of HHS*, 539 F.3d 1347, 1353-54 (Fed. Cir. 2008).

the causation of his autism, allegedly in concert with an underlying genetic vulnerability. I have looked beyond the epidemiologic evidence to determine whether the *overall evidence--i.e.*, medical opinion, circumstantial evidence, and other evidence considered *as a whole*--tips the balance even slightly in favor of a causation showing as to Jordan's autism.

This case, however, is *not a close case*. The overall weight of the evidence is *overwhelmingly contrary* to the petitioners' causation theories. The result of this case would be the same even if I totally ignored the epidemiologic evidence. The result would be the same if I restricted my consideration to the evidence originally filed into the record of this *King* case, disregarding the additional "general causation" evidence imported from the *Dwyer* case. The petitioners' evidence has been unpersuasive on many different points, concerning virtually all aspects of their causation theories, with each such deficiency having been discussed in detail above. The petitioners have failed to persuade me that there is validity to any of their *general causation* arguments, and have also failed to persuade me that there is any likelihood that Jordan's thimerosal-containing vaccines contributed in any way to the causation of *Jordan's own autism*. To the contrary, based upon all the evidence that I have reviewed, I find that it is *extremely unlikely* that Jordan's autism was in any way causally connected to his thimerosal-containing vaccines.

In short, this is a case in which the evidence is so one-sided that any nuances in the interpretation of the causation case law would make no difference to the outcome of the case.

VIII

CONCLUSION

The record of this case demonstrates plainly that Jordan King and his family have been though a tragic ordeal. I had the opportunity, in the courtroom during the evidentiary hearing, to meet and observe Jordan's mother. I have also studied the records describing Jordan's medical history, and the efforts of his family in caring for him. Based upon those experiences, the great dedication of Jordan's family to his welfare is readily apparent to me.

Nor do I doubt that Jordan's parents are sincere in their belief that vaccines played a role in causing Jordan's autism. Jordan's parents have heard the opinions of physicians who profess to believe in a causal connection between thimerosal-containing vaccines and autism. After studying the extensive evidence in this case for many months, I am convinced that the opinions provided by the petitioners' experts in this case, advising the King family that there is a causal connection between thimerosal-containing vaccines and Jordan's autism, have been *quite wrong*. Nevertheless, I can understand why Jordan's parents found such opinions to be believable under the circumstances. I conclude that the Kings filed this Program claim in good faith.

Thus, I feel deep sympathy for the King family. Further, I find it unfortunate that my ruling in this case means that the Program will not be able to provide funds to assist this family, in caring for their child who suffers from a serious disorder. It is certainly my hope that our society will find ways to ensure that generous assistance is available to the families of *all* autistic children, regardless

of the cause of their disorders. Such families must cope every day with tremendous challenges in caring for their autistic children, and all are deserving of sympathy and admiration. However, I must decide this case not on sentiment, but by analyzing the evidence. Congress designed the Program to compensate only the families of those individuals whose injuries or deaths can be linked causally, either by a Table Injury presumption or by a preponderance of "causation-in-fact" evidence, to a listed vaccine. In this case, the evidence advanced by the petitioners has fallen far short of demonstrating such a link. Accordingly, I conclude that the petitioners in this case are *not* entitled to a Program award on Jordan's behalf.[128]

/s/ George L. Hastings, Jr.

George L. Hastings, Jr.
Special Master

[128] In the absence of a timely-filed motion for review of this Decision, the Clerk of the Court shall enter judgment accordingly.

APPENDIX: TABLE OF CONTENTS