In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 98-916V

(Filed: February 12, 2009)

To be published[1]

THERESA CEDILLO and MICHAEL CEDILLO, as parents and natural guardians of Michelle Cedillo,	*	
Petitioners,	*	Vaccine Act Entitlement; Causation-in-fact; MMR/Autism Causation Issue; MMR/ Gastrointestinal Dysfunction Causation Issue; Thimerosal/ Immune Damage Causation Issue.
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Ronald Homer and Sylvia Chin-Caplan, Boston, Massachusetts, for petitioners.

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

DECISION

HASTINGS, ***Special Master***.

This is an action in which the petitioners, Michael and Theresa Cedillo, seek an award under the National Vaccine Injury Compensation Program (*see* 42 U.S.C. § 300aa-10 *et seq*.[2]) on account of several conditions, including autism and chronic gastrointestinal symptoms, which afflict their

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[1]On October 30, 2008, petitioners filed a notice 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*. (2000). Hereinafter, for ease of citation, all "§" references will be to 42 U.S.C. (2000). I will also sometimes refer to the act of Congress that created the Program as the "Vaccine Act."

daughter, Michelle Cedillo. I conclude that the petitioners have *not* demonstrated that they are entitled to an award on Michelle'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 a causation theory that has several parts, including contentions (1) that thimerosal-containing vaccines can cause immune dysfunction, (2) that the MMR vaccine can cause autism, and (3) that the MMR vaccine can cause chronic gastrointestinal dysfunction. However, as to each of those issues, I concluded that the evidence was 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 most of the key points. The numerous medical studies concerning these issues, performed by medical scientists worldwide, have come down strongly against the petitioners' contentions. Considering all of the evidence, I found that the petitioners have *failed* to demonstrate that thimerosal-containing vaccines can contribute to causing immune dysfunction, or that the MMR vaccine can contribute to causing either autism or gastrointestinal dysfunction. I further conclude that while Michelle Cedillo has tragically suffered from autism and other severe conditions, the petitioners have also failed to demonstrate that her vaccinations played any role at all in causing those problems.

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 question 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).

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

[4]As will be detailed below, no Table Injury is alleged in this case.

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 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 the 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. Most recently, *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.

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

A. Undisputed facts

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

1. Michelle's early period

Michelle Cedillo was born on August 30, 1994. (Ex. 1, p. 1.[5]) The pregnancy leading to her birth, and her birth, appear to have been uncomplicated. (Ex. 23, pp. 47-52.) The records of her visits to the pediatrician during her first 16 months of life indicate that Michelle's health appeared relatively normal during that period. (Ex. 8, pp. 2-6;[6] Ex. 28, p. 265.) Those records show a few mild illnesses, but mostly normal examinations. (*Id*.) Michelle received the typical infant vaccinations during that period. Her initial hepatitis B vaccination was administered in the hospital shortly after her birth. (Ex. 23, pp. 45, 63.) On September 27, 1994, she received a second hepatitis B vaccination. (Ex. 18, p. 1.) On three occasions--October 31, 1994, December 27, 1994, and March 8, 1995--she received three different vaccinations, namely, diphtheria/tetanus/pertussis ("DTP"), hemophilus influenza ("Hib"), and polio ("OPV"). (Ex. 18, p. 1; Ex. 8, pp. 4, 5.) On the last of those three dates, March 8, 1995, she also received another hepatitis B vaccination. (Ex. 18, p. 1.) On September 6, 1995, Michelle received a varicella ("chicken-pox") vaccination. (*Id*.)

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[5]Both parties have filed numerous documents in this case. Petitioners have filed, on various occasions, exhibits numbered 1 through 133. I will refer to those exhibits as Ex. 1, Ex. 2, etc. Respondent has filed exhibits, on various occasions, 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 June of 2007, 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 June 11 through June 26, 2007. 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 June 12 through 27, 2007. 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 February 5, 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 April 23 through June 11, 2008. Accordingly, "Tr." citations are to the pages of the "Revised and Corrected" transcript. (Note that the parties' *briefs* contain references to the *original*, uncorrected transcript pages.)

I also 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 ordinarily refer to the pages of the expert reports and other exhibits as *originally numbered*, usually at the bottom of the pages.

[6]References to Ex. 8 will be to the hand-written page numbers at the *bottom* of the pages.

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

Michelle experienced relatively few illnesses as an infant. A pediatrician noted that she had an episode of vomiting and loose stools on March 3, 1995, when she was seven months old, with the diagnosis of "probable viral syndrome." (Ex. 28, p. 265.) On June 2, 1995, it was noted that Michelle was "extremely constipated on 2% milk." (Ex. 8, p. 3.) The pediatric records also indicate that from age six months through 16 months, Michelle's height, weight, and head circumference were substantially above normal. (Ex. 8, pp. 7-8; Tr. 1335-37, 1367-71, 1456A-59A.)

The pediatric records pertaining to Michelle's initial 16 months of life contain relatively little information concerning her development, other than the frequent notation of "normal" in various physical examination categories. The pediatrician notes indicate that at two months of age Michelle was able to fix her eyes on a movement and follow the movement ("fixes + follows"), and that she startled appropriately to loud noises. (Ex. 8, p. 5.) They also record that on September 6, 1995, at one year of age, Michelle had "several words," was able to "pull to stand," was "not cruising or walking," and that she "crawls on knees." (Ex. 8, p. 2.) Her "neurological" examination at that visit was described as "normal." (*Id*.)

2. The MMR vaccination and following pediatric visits

On December 20, 1995, Michelle visited her pediatrician, where she appeared well. (Ex. 8, p. 2.) At that visit, she received a measles, mumps, rubella ("MMR") vaccination. (Ex. 18, p. 1.)

Michelle's next visit to the pediatrician was on January 6, 1996. (Ex. 8, p. 1.) The record of that visit indicates that Michelle had suffered a number of symptoms since her previous visit on December 20, 1995. The record indicates that "1 week after" Michelle's MMR vaccination on December 20, she had "fever and rash;" the fever got "better," but later "spiked up" again. (*Id*.) The record further indicates that Michelle's second episode of fever "started [with] cough yesterday [January 5] gagging to point of vomiting." (*Id*.) By the following morning ("today" in the exam note), Michelle's temperature, taken at home, was 105.7 degrees. (*Id*.) At the pediatrician's office, Michelle's temperature was recorded as 100.3 degrees, she was crying, and she had a "purulent postnasal drip." (*Id*.) The pediatrician's diagnosis was "sinusitis vs. flu," and Michelle was treated with antibiotics. (*Id*.)

Michelle next visited her pediatrician on March 15, 1996, where she went for her scheduled "well check" at 18 months of age. (Ex. 8, p. 1.) No major problems with Michelle's health are noted in the record of that visit; among the notations are that Michelle "seems to hear well" and "stools well." (*Id*.) The physician did note, however, that Michelle was "talking less since ill in Jan." (*Id*.)

3. Diagnosis of autism in 1997

After the visit of March 15, 1996, Michelle was not taken to see any physician again for about one year. The next record of her contact with a physician is a record that indicates that on March 7, 1997, her mother filled out a "patient information sheet" for a pediatrician, Dr. Emilia Matos. (Ex. 17, p. 2.) There are no notes of a pediatrician exam on that date, but notes of a visit to Dr. Matos on April 24, 1997, indicate "developmental delay suspected," and that Michelle was being referred to a specialist for further evaluation. (Ex. 17, p. 5.) On May 2, 1997, Michelle saw Dr. Masland, a neurologist, who took a history. (Ex. 19, p. 1.) Dr. Masland recorded that at age 16 months Michelle had developed "a fever of 105+, that lasted for four days. This occurred two weeks after immunization." (*Id*.) He added that "[s]ince then she lost her ability to verbalize and has continued with repetitive movement." (*Id*.) He also stated that "[i]t would appear that there was some neurological harm done at the time of the fevers. Whether this was a post-immunization phenomenon or a separate occurrence, would be very difficult to say." (*Id*.)

Beginning with those medical visits in early 1997, it quickly became clear that Michelle's development was quite abnormal. On July 21, 1997, she was examined by a developmental psychologist, Dr. Karlsson Roth, who concluded that Michelle suffered from "severe Autism" as well as "profound Mental Retardation," and that her overall future potential "is going to be extremely limited." (Ex. 7, p. 7.) Michelle was diagnosed with the particular disorder, within the autism spectrum, known as "autistic disorder."[7] (Ex. 31, p. 12.) Michelle's evaluations over the subsequent years confirmed these diagnoses, and confirmed also the tragic severity of Michelle's condition. For example, Dr. Ira Lott, a pediatric neurologist, wrote on March 1, 1999, that Michelle had "autism of a severe degree," and that she "does not have much in the way of communicative speech." (Ex. 28, p. 218.)

4. Other medical difficulties

In addition to her autism and severe mental retardation, Michelle has also experienced a number of other medical problems over the years. One very significant problem has been her gastrointestinal symptoms. Michelle has experienced chronic problems, lasting for years, with both constipation and diarrhea. For example, a notation of Michelle's treating gastroenterologist, Dr. Ramon Montes, written on May 22, 2000, describes the early years of Michelle's constipation and diarrhea symptoms. (Ex. 44, p. 58.) The note indicates that Michelle's chronic *diarrhea* began about one year prior to that visit of May 2000--*i.e.*, about May of 1999. (*Id*.) That note of Dr. Montes does not say when the chronic *constipation* began, but indicates that the constipation was associated with milk consumption (*id*.), and another record made on June 2, 1995, states that Michelle was "[e]xtremely constipated on 2% milk" (Ex. 8, p. 3), possibly indicating that the chronic constipation began about that time.

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[7]Respondent does *not* contest that diagnosis.

Michelle has also experienced other gastrointestinal problems over the years, in addition to her constipation and diarrhea. For example, on May 22, 2000, Dr. Montes noted that Michelle had symptoms "suggestive of possible gastroesophageal reflux disease" (Ex. 28, p. 246), and on June 12, 2000, that physician diagnosed "erosive esophagitis" (Ex. 28, p. 185). Other medical records include further reports of gastroesophageal reflux disease (sometimes described as "GERD"), and notations concerning fecal impaction. (Ex. 36, pp. 9, 29.)

As a result of Michelle's gastrointestinal problems, a number of diagnostic procedures, such as "endoscopies," were performed. During one such procedure, on January 1, 2002, a biopsy (tissue sample) was taken from her intestine. A "Measles Virus Detection" test on that biopsy was performed by the Unigenetics Ltd. Laboratory in Dublin, Ireland. The report of that test, issued on March 15, 2002, stated that "measles virus was detected" in the tissue. (Ex. 28, p. 179.) (Note that the validity of that test result is in dispute, and that I have concluded that the test was *not* reliable--see pp. 41-78 below.)

In addition to her autism, mental retardation, and gastrointestinal symptoms, Michelle has also suffered from other medical conditions. Michelle has at times suffered from symptoms of arthritis (Ex. 34, p. 4), uveitis (Ex. 33, p. 20), and pancreatitis (Ex. 47, p. 61). She has suffered from severe feeding problems, requiring the use of a feeding tube. (Ex. 28, pp. 475-76.) In more recent years she has experienced a severe seizure disorder, and suffered a fractured leg due to a fall caused by a seizure. (Ex. 27, pp. 261-62.) In short, Michelle has continually suffered from a tragic series of medical misfortunes.

B. Other factual representations

Michelle's mother, Theresa Cedillo, has on several occasions provided written statements concerning Michelle's medical and developmental history, either for the purpose of providing details for Michelle's physicians, or for litigation purposes. (*See*, *e.g.*, Exs. 18, 22, and 54.) Mrs. Cedillo also testified during the evidentiary hearing in this case. (Tr. 222-406, 2874-84.) For the most part, Mrs. Cedillo's representations, in both her written statements and in her hearing testimony, have been consistent with the information contained in the medical records. In a few instances, however, Mrs. Cedillo's representations have varied from the medical records. Those representations are relevant to petitioners' causation contentions concerning two issues--(1) the onset of Michelle's initial symptoms of autism, and (2) the history of gastrointestinal symptoms. I will discuss those issues separately below.

III

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

This case concerning Michelle Cedillo 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 "autism 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. (Ex. JJ,[8] 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"). (*Id*. at 32; Ex. HH[9] at 23-25.) 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. (Ex. JJ. at 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. (Ex. JJ, p. 33.) Autism can widely vary in severity. For many, such as Michelle Cedillo, the condition can be extremely severe and devastating, rendering the autistic individual completely unable to care for himself or herself.

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[8]Institute of Medicine, IMMUNIZATION SAFETY REVIEW: VACCINES AND AUTISM (The National Academies Press 2004). (Ex. JJ.)

[9]Institute of Medicine, IMMUNIZATION SAFETY REVIEW: MEASLES-MUMPS-RUBELLA VACCINE AND AUTISM (National Academy Press 2001). (Ex. HH.)

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.[10] (Ex. HH, p. 22; Tr. 1054.) In recent years, the rate of *diagnosis* of autism has increased dramatically. (Ex. JJ, 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 factors. Other experts argue that the increase in diagnosis 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. (Ex. JJ, p. 35; Ex. P, pp. 24-31.)

In any event, there is no doubt that at this time autism is a *very common* condition, in this country and throughout the world. For example, one survey of recent studies in the United States found that the current prevalence rate of autism in this country--that is, the proportion of the population that suffers from autism at a particular time--is about 1 out of 152 children.[11] That figure is roughly consistent with the results of several other recent studies.

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.[12] (Ex. JJ, 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. (Ex. JJ, 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.

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

[11] Centers for Disease Control and Prevention, *Prevalence of Autism Spectrum Disorders -- Autism and Developmental Disabilities Monitoring Network, 14 Sites, United States, 2002*, 1 (Feb. 9, 2007). (Ex. P, Att. 24, p. 1.)

[12] Andrew Wakefield et al., *Ileal-Lymphoid-Nodular Hyperplasia, Non-specific Colitis, and Pervasive Developmental Disorder in Children*, 351 LANCET 637 (1998). (Ex. P, Att. 152.)

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 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*.[13] 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

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[13]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 a few documents 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.

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.[14] The plan has been that once the OAP concerning 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 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. The PSC proposed that the instant case, of Michelle Cedillo, be that first test case.

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[14]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 sought to present their own *substantive causation evidence*, aside from the petitioners in the six "test cases" described below at p. 15 fn.16.

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 this *Cedillo* case as a "test case" in June of 2007. (See Autism Update issued January 19, 2007.) 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 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. (Therefore, it was envisioned that a total of *nine* decisions in individual cases, three decisions as to each theory, would eventually be issued. But see fn. 16 below.)

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 over the following months. This *Cedillo* case has been a major part of that plan.

Pursuant to that general plan, the parties filed, into the record of this *Cedillo* case, a vast amount of evidence, concerning not only the specifics of Michelle Cedillo's case, but also the petitioners' first "general causation" theory, that the MMR vaccine and thimerosal-containing vaccines can *combine* to cause autism. The two parties filed, in this *Cedillo* case alone, a total of 23 expert reports concerning Michelle's case and/or the "general causation" issue. They have filed copies of 658 medical journal articles or medical text excerpts. During a three-week evidentiary hearing held in June of 2007, the parties presented testimony from 17 witnesses, 16 of them experts.

Much of the evidence filed into the record of this *Cedillo* case, of course, is relevant beyond this specific case. The PSC's intent was to present, in the context of this case, *all* of its evidence supporting the PSC's first *general causation* theory, *i.e.*, that the MMR vaccine and thimerosal-containing vaccines can combine to cause autism; the respondent's intent was to present all of the respondent's evidence in opposition to that theory. Accordingly, during the evidentiary hearing in this *Cedillo* case, Special Masters Vowell and Campbell-Smith sat on the bench with me. Their role was *not* to decide this particular *Cedillo* case, but to hear the *general causation* evidence provided

by the expert witnesses, so that each of those two special masters could apply that evidence to the *individual test cases* assigned to them.

After the evidentiary hearing in this *Cedillo* case, evidentiary hearings were then held in the other two test cases. Specifically, in one of those cases, *Hazlehurst v. Secretary of HHS*, No. 03-654V, a hearing was held before Special Master Campbell-Smith on October 15-18, 2007, in Charlotte, North Carolina. In the other case, *Snyder v. Secretary of HHS*, No. 01-162V, a hearing was held on November 5-9, 2007, in Orlando, Florida, before Special Master Vowell. Both Special Master Vowell and I attended the *Hazlehurst* hearing as observers, to hear any expert evidence relevant to the "general causation" issue. Similarly, both Special Master Campbell-Smith and I attended the *Snyder* hearing as observers, for the same purpose.[15]

Since the conclusions 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. For example, much of the documentary evidence and much of the hearing testimony in this *Cedillo* case, as discussed above, relates to "general causation." Thus, copies of that "general causation" evidence from this *Cedillo* case have been introduced into the case files of the *Hazlehurst* and *Snyder* cases (at the request of the petitioners in those cases). Further, it developed that in the course of the *Hazlehurst* and *Snyder* cases, an additional amount of "general causation" evidence was also

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[15]It is important to understand the roles of the three special masters who have jointly presided over the Omnibus Autism Proceeding over the past two years. 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 have 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 first 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* of each of the three rulings, however, were undertaken *separately* and independently.

introduced into the records of those cases. The Cedillos have requested that I consider that "general causation" evidence from *Hazlehurst* and *Snyder* in resolving this *Cedillo* case. Though respondent argued to the contrary (see "Respondent's Objection" filed on October 12, 2007), I have granted this request of the Cedillos, and, therefore, I have evaluated that "general causation" evidence from *Hazlehurst* and *Snyder* in resolving this case.[16]

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. Jones for his theory that Vaccine A causes Disease B, Dr. Jones might need to repeat the same "general causation"

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[16]Extensive steps have also been taken toward resolving the PSC's *second general theory* of causation in the OAP, *i.e.*, the theory that thimerosal-containing vaccines can, by themselves, *directly* cause autism by affecting the brain. Several weeks of evidentiary hearings were held during May and July of 2008, in which petitioners' counsel presented both their *general causation* evidence concerning that second general causation theory, and their *specific causation* evidence concerning three test cases, the cases of *King v. Secretary of HHS*, No. 03-584V, *Mead v. Secretary of HHS*, No. 03-215V, and *Dwyer v. Secretary of HHS*, No. 03-1202V. The parties to those three cases are currently engaged in an extensive post-hearing briefing process, which will conclude in the late spring of 2009. Thereafter, three separate decisions in those three cases will be issued by the three special masters.

Concerning the *third general theory* of causation originally proposed by the PSC, however, it appears that the PSC will *not* be presenting a third theory. It now appears 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 this *Cedillo* case as well as the *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.

To follow the course of the Omnibus Autism Proceeding, interested persons may regularly consult this court's website. See fn. 13 above.

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. Jones 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. Jones 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 necessity 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.[17]

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

[17]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.

general causation evidence developed in the test case may be "imported" into the records of the other cases, facilitating the decisions in those cases.[18]

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 Cedillo case

Petitioners filed their Program petition in this *Cedillo* case on December 9, 1998. The case was originally assigned to Special Master Elizabeth Wright, but, due to Special Master Wright's retirement from the Office of Special Masters, the case was reassigned to Special Master John Edwards on April 12, 1999. During the first two years after the filing of the petition, petitioners' counsel were primarily engaged in the tasks of (1) assembling and filing the voluminous medical records pertaining to Michelle's illness, and (2) searching for one or more expert witnesses who could opine that Michelle's illness was vaccine-caused. On October 31, 2000, the petitioners filed the expert report of Dr. Cindy Schneider, and on May 8, 2001, they filed the expert report of Dr. Marcel Kinsbourne, both reports contending that Michelle suffered a "Table Injury." Respondent then filed an opposing expert report, of Dr. Max Wiznitzer, on July 11, 2001. (None of those three expert reports were assigned exhibit numbers.)

On January 14, 2002, however, the petitioners filed a notice that they were changing their theory of the case from a "Table Injury" claim, as set forth in their two prior expert reports, to a "causation-in-fact" claim. Also, at that time discussions were being initiated that led to the creation of the Omnibus Autism Proceeding. Thus, after the OAP was created by the Chief Special Master's *Autism General Order #1* on July 3, 2002, this case, along with several hundred other cases, was transferred to my docket for processing under the OAP. (Order of August 30, 2002.) On September 16, 2002, the petitioners filed in this case a "Notice to Defer Proceedings in Autism Case," which requested that case-specific proceedings in this case be deferred indefinitely, pending the outcome of the OAP.

Accordingly, at the Cedillos' request, during the following four years I did not conduct case-specific proceedings in this case.

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[18]Note that the outcome of a "test case" is not formally "binding" on any other case. Petitioners 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 *Cedillo* case have, in general, done such a comprehensive job.)

Then, as explained above, at the end of 2006 the PSC, along with the petitioners' own counsel, proposed that Michelle's case become the first "test case" in the OAP. (See p. 12-13 above; see also the Order filed in this case on February 1, 2007.) Thereafter, petitioners filed a number of expert reports on February 20, 2007, and respondent filed a number of expert reports on April 24, 2007. (A few additional expert reports were filed by both parties thereafter.) A three-week evidentiary hearing, as previously noted, was held in June of 2007, and both parties thereafter filed a number of lengthy post-hearing briefs.[19] Further, as described above, the petitioners in this case requested that I consider certain "general causation" evidence from the *Hazlehurst* and *Snyder* cases in resolving this *Cedillo* case. Though respondent argued to the contrary (see "Respondent's Objection" filed on October 12, 2007), I granted that request of the Cedillos, and, thus, certain "general causation" evidence from *Hazlehurst* and *Snyder* has been formally introduced into the record of this case, via my Orders of February 4, 2009.[20]

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 June of 2007. However, two major factors should be recognized.

First, the completion of the three-week evidentiary hearing in this *Cedillo* case in June of 2007 did *not* mark the end of the presentations by the parties relevant to this case. Additional "general causation" expert testimony, much of it relevant to this *Cedillo* case, was presented during the evidentiary hearings in the *Hazlehurst* and *Snyder* cases in the fall of 2007, with the *Snyder* hearing not concluding until November 9, 2007. Then, the parties' process of *briefing* this *Cedillo* case extended into May of 2008. Finally, even at that point the petitioners in this case were still keeping alive their option to submit *additional* "general causation" evidence that they hoped to obtain from a British litigation file. It was not until July of 2008 that the Petitioners' Steering

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

Petitioners' Post-Hearing Brief, filed on November 12, 2007----------cited as P1.
Petitioners' Supplemental Post-Hearing Brief (*Hazlehurst / Snyder*
Evidence) filed Feb. 1, 2008----------cited as P2.
Petitioners' Reply to the Respondent's Post-Hearing Brief, filed Feb. 11, 2008---------cited as P3.
Petitioners' Supplemental Post-Hearing Reply Brief (*Hazlehurst*/
Snyder Evidence) filed May 9, 2008----------cited as P4.
Respondent's Post-Hearing Brief, filed January 11, 2008----------cited as R1.
Respondent's Supplemental Post-Hearing Brief Regarding *Hazlehurst / Snyder*
Evidence, filed April 4, 2008----------cited as R2.

[20]Compact discs containing the "general causation" evidence from the *Snyder* and *Hazlehurst* cases were originally filed into the record of this case on August 1 and August 7, 2008, respectively. However, there were errors on those discs. Accordingly, all of the "general causation" evidence from *Hazlehurst* and *Snyder* was *refiled*, into the record of this case, on February 4, 2009.

Committee in the OAP concluded that they would not attempt to obtain further evidence from that British litigation. (See discussion at p. 83 below.) Thus, it was only at that time that I could, as I did on July 30, 2008, file an Order declaring that the evidentiary record in this case was closed.

Second, it should be recognized that the evidentiary record, based upon which I have decided this case, is massive. This record dwarfs, by far, any evidentiary record in any prior Program case. A few statistics may give a flavor of the amount of material involved. The record contains about 7,700 pages of Michelle Cedillo's medical records alone. The parties filed a total of 23 expert reports in this *Cedillo* case alone, and a total of 50 expert reports including the *Hazlehurst* and *Snyder* cases. During the evidentiary hearings, 16 expert witnesses testified in *Cedillo*, four in *Hazlehurst*, and eight in *Snyder*. The hearing transcripts totaled 2,917 pages in *Cedillo*, 1,049 pages in *Snyder*, and 570 pages in *Hazlehurst*. The parties filed six post-hearing briefs in this *Cedillo* case alone, totaling 462 pages.

In addition, the amount of *medical literature* filed into the records of the three cases was staggering. In the *Cedillo* case alone, the parties filed a total of 658 medical journal articles, medical textbook excerpts, or other items of medical literature. Many more such documents were filed into the *Hazlehurst* and *Snyder* cases, so that a total of 939 different items of medical literature were filed into the three case files (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.*, Ex. JJ, 163 pages; Ex. L, Att. 1, 617 pages; Ex. BB, Att. 94, 306 pages.) I have not attempted to calculate the total number of pages of those 939 documents, but clearly the total runs well into the tens of thousands of pages. And most of those documents are densely packed with difficult, technical information, so that studying even a medical journal article that is only a few pages long can require a lengthy time period.

Further, the complexity of the material involved here is daunting as well. The medical records, expert testimony, and medical literature involve many different subspecialties of biology and medicine, including neurology, gastroenterology, virology, 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 Michelle suffered a "Table Injury."[21] Their contention, instead, is one of "causation-in-fact," also known as "actual causation."

[21] Petitioners originally alleged a Table Injury, but on January 14, 2002, they filed a notice that (continued...)

The petitioners and their expert witnesses contend that Michelle's chronic gastrointestinal symptoms and her autism were caused by a combination of the thimerosal-containing vaccines that she received during her early months of life and the MMR vaccination that she received on December 20, 1995. Petitioners' overall causation theory[22] in this case can be summarized as follows: (1) The thimerosal-containing vaccines that Michelle received during her first 16 months of life weakened her immune system. (2) That weakening of the immune system allowed the measles virus contained in the MMR vaccine to persist within Michelle's body. (3) The persisting vaccine-strain measles virus damaged Michelle's digestive system, causing her gastrointestinal difficulties. (4) The persisting vaccine-strain measles virus also damaged Michelle's brain, causing her autism, mental retardation, and seizures.

The respondent's expert witnesses, on the other hand, disagreed strenuously with most parts of petitioners' overall theory. Respondent's experts do not dispute that the *fever* and *rash* that Michelle experienced about one week after the MMR vaccination was a reaction to that vaccination.[23] But those experts do not believe that any of Michelle's *chronic* symptoms--including her autism, which they believe to have been evident even *prior* to the MMR vaccination in question--were vaccine-caused.

Accordingly, 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[24] either that

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[21](...continued)
they were changing their theory of the case from a Table Injury claim to a "causation-in-fact" claim.

[22]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. 1731A; *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. (*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 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.

[23]The fact that those acute symptoms were likely caused by her MMR vaccination does *not* mean that Michelle is entitled to a Vaccine Act award on account of those symptoms, because those particular symptoms did not last for more than six months. *See* § 300aa-11(c)(1)(D)(i).

[24]As to each of Michelle's conditions that petitioners allege to have been vaccine-caused, it
(continued...)

thimerosal-containing vaccines *can* harm infant immune systems in general, or that Michelle's own thimerosal-containing vaccinations *did* harm her own immune system. In section VI, I will explain why I have found that the testing for the presence of the measles virus in both Michelle and in other autistic children, on which the petitioners rely with respect to all of their causation claims, was *unreliable*. In section VII, I will explain that petitioners failed to demonstrate either that the MMR vaccine *can* contribute to the causation of autism in general, or that Michelle's own MMR vaccination *did* contribute to her own autism. In section VIII, I will explain that petitioners failed to demonstrate either that the MMR vaccine *can* contribute to the causation of gastrointestinal dysfunction in general, or that Michelle's own MMR vaccination *did* contribute to her own gastrointestinal problems. In section IX, I will explain that the evidence concerning the causation of regressive autism *combined* with gastrointestinal dysfunction in some individuals does not offer persuasive evidence that either or both conditions can be vaccine-caused. In section X, I will explain that petitioners have not demonstrated that Michelle's MMR vaccination contributed to the causation of either her mental retardation or her seizure disorder. In section XI, I will discuss an argument concerning Michelle's treating physicians. In section XII, I will discuss an argument of petitioners concerning whether Michelle's case is similar to certain Program cases. In section XIII, I will explain how my previously-stated analysis of petitioners' 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 XIV I will set forth some concluding comments.

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, I find the first part of the petitioners' theory of this case--*i.e.*, their contention that thimerosal-containing vaccines damaged Michelle's immune system, thereby making it possible for the vaccine-strain measles virus to persist within Michelle's body--to be essentially *unnecessary* to the rest of their causation argument. That is, if petitioners were able to persuade me that the vaccine-strain measles virus *did* likely persist in Michelle's body and cause damage to either (or both) her brain or gut, I *would* compensate such damage. It would not matter *why* the measles vaccine-strain virus was able to persist; whether that persistence was the result of thimerosal-containing vaccines or for some other reason would be irrelevant. Therefore, resolution of that part of petitioners' theory is not strictly necessary for resolution of this case. However, as explained above, this case was designated by the Petitioners' Steering Committee (PSC) in the Omnibus Autism Proceeding as a "test case." The PSC desires that the special masters test and evaluate its causation theories, in order to *provide guidance* for the other pending autism cases. Therefore, I will evaluate that contention of the petitioners.

As another example, I note that petitioners' expert witness who testified that Michelle's autism was caused by her MMR vaccination, Dr. Marcel Kinsbourne, explained that he was

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[24](...continued)
is the *petitioners' burden* to demonstrate that it is "more probable than not" that the vaccination was a substantial factor in causing that condition. *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).

assuming the accuracy of the hotly-disputed laboratory test that purported to find vaccine-strain measles virus in Michelle's intestinal tissue. Since I have found that test result to be unreliable (see pp. 77-78 below), the foundation for Dr. Kinsbourne's opinion has disappeared, and, therefore, there is no necessity that I evaluate the soundness of Dr. Kinsbourne's opinion in other respects. Nevertheless, I have chosen to include an 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 full analysis of *all* of the petitioners' major causation theories raised in this case, whether necessary for resolution of this case or not, in order to provide guidance for the remaining autism cases.

V

PETITIONERS HAVE NOT DEMONSTRATED EITHER THAT THIMEROSAL-CONTAINING VACCINES *CAN* HARM INFANT IMMUNE SYSTEMS IN GENERAL, OR THAT SUCH VACCINES *DID* HARM MICHELLE'S IMMUNE SYSTEM

The first part of petitioners' overall causation theory is their contention that thimerosal-containing vaccines damaged Michelle's immune system, thereby making it possible for the vaccine-strain measles virus[25] to persist within Michelle's body.

First, as noted above, I observe that I find this portion of petitioners' theory to be essentially *unnecessary* to the rest of their causation argument. That is, if petitioners were able to persuade me that the vaccine-strain measles virus *did* likely persist in Michelle's body and cause damage to either (or both) her brain or gut, I *would* compensate such damage. It would not matter *why* the vaccine-strain measles virus was able to persist. Therefore, resolution of this part of petitioners' theory is not strictly necessary for resolution of this case. However, as explained above, this case was designated as a "test case," to *provide guidance* for the other pending autism cases. Therefore, I will evaluate this contention of the petitioners, and explain why I find that the evidence in the record does *not* support either the proposition that thimerosal-containing vaccines *can* damage immune systems *in general*, or the proposition that such vaccines *did* damage *Michelle's own* immune system.

*A. The evidence does not support the general proposition that thimerosal-containing vaccines can damage infants' immune system*s.

Petitioners have relied upon the opinions of certain expert witnesses, along with references to a number of items of medical literature, for their general theory that the thimerosal contained in

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[25]The measles virus exists naturally in its ordinary, "wild," full-strength form. The MMR vaccination, on the other hand, utilizes an intentionally *weakened* ("attenuated") version of the measles virus. (Ex. JJ, p. 40; Ex. V, p. 3; Tr. 2774.) I will refer to that version of the measles virus, contained in the MMR vaccination, as the "vaccine-strain measles virus."

infant vaccines can damage an infant's immune system. Respondent offers the testimony of expert witnesses, and references to medical literature, in response. After a thorough review, I find that the evidence offered by respondent is substantially more persuasive concerning this issue. I find that the evidence falls far short of demonstrating that it is "more probable than not" that thimerosal-containing vaccines can damage infants' immune systems.

1. Thimerosal in vaccines

Thimerosal is a compound consisting of mercury and other components (49.6% mercury by weight) that has been used in vaccines, and in other biological and pharmaceutical products, since the 1930s. (Ex. JJ, p. 36; Ex. 55, Tab A, 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. (Ex. JJ, pp. 36-37.) Thimerosal has been used in more than 30 vaccines licensed in the United States. During the 1990s, it was used in a number of vaccines given to infants in the United States, including the diptheria/tetanus/pertussis ("DTP"), hemophilus influenza ("Hib"), and hepatitis B vaccinations.[26] (*Id*. at p. 37.)

Michelle Cedillo received thimerosal-containing vaccinations on a number of occasions. She received hepatitis B vaccinations on three occasions--in the hospital shortly after birth; on September 27, 1994; and on March 8, 1995. (Ex. 23, pp. 45, 63; Ex. 18, p. 1.) She received both DTP vaccinations and Hib vaccinations on four occasions: October 31, 1994; December 27, 1994; March 8, 1995; and March 15, 1996. (Ex. 18, p. 1; Ex. 8, pp. 1, 4, 5.)

2. General analysis of testimony of Dr. Aposhian and Dr. Brent

Concerning this issue, the petitioners rely primarily on the opinion of Dr. H. Vasken Aposhian, Ph.D., who is a professor of molecular biology, cellular biology, pharmacology, and toxicology at the University of Arizona. (Ex. 56, p. 1.) Dr. Aposhian submitted a lengthy expert report detailing many examples of how mercury, in its various forms, can be very toxic (poisonous) to humans. (Ex. 55.) At the hearing, he testified that he could see a "possible path" by which the mercury in thimerosal-containing vaccines could cause "immune disregulation and immune suppression in humans." (Tr. 109-110.) He also testified that the mercury that Michelle Cedillo received in her thimerosal-containing vaccines "could be a substantial contributing factor to the onset of [her] immune disfunction." (Tr. 114.)

Dr. Aposhian raised a number of points in support of his conclusion that thimerosal-containing vaccines can damage infants' immune systems. He relied on the evidence outlined in his expert report, demonstrating that mercury in various forms can be toxic to humans. (Ex. 55; Tr. 67-88.) He pointed out that the amount of mercury received by infants from thimerosal-containing

[26]Between 1999 and 2002, thimerosal was phased out of most of the vaccines commonly given to infants in the United States. (Ex. JJ, pp. 37-39.) However, thimerosal remains in influenza vaccines, which are commonly given to infants. (Ex. JJ, p. 38, Table 1.)

vaccines exceeds a "reference-dose" standard developed by the Environmental Protection Agency for a type of mercury known as methylmercury. (Tr. 112-113.) He described the theory that autism might be caused in some children because they suffer from a "mercury efflux disorder"--*i.e.*, an inability to excrete mercury as efficiently as most children do, so that a resulting build-up of mercury in the body might damage the function of the body's cells, including cells of the immune system. (Tr. 70, 97-106, 197-98.) Dr. Aposhian also suggested that autistic children may be autistic because they are genetically "hypersusceptible" to mercury, leaving them especially vulnerable to immune system damage when exposed to thimerosal. (Tr. 92, 115, 129-31.)

Respondent countered Dr. Aposhian chiefly with the expert report and hearing testimony of Dr. Jeffrey Brent, M.D., Ph.D., who is a physician and Clinical Professor of Pediatrics and Internal Medicine at the University of Colorado. (Ex. M, p. 1; Tr. 2296, 2302-03.) Although Dr. Aposhian has excellent credentials and experience in the area of "toxicology"--that is, the study of the adverse effects of chemical substances on living systems (Tr. 2310)--Dr. Brent has even more impressive qualifications to opine in this area.[27] 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. 2311.) He is one of about 250 board-certified medical toxicologists in the United States (Tr. 2311-12), and he has experience in treating children with actual mercury toxicity.[28] (Tr. 2306-2308.)

Dr. Brent testified persuasively that the available evidence does *not* justify a conclusion that the thimerosal contained in childhood vaccines can damage infants' immune systems. Dr. Brent did not dispute that mercury in some of its forms, at certain dosages, can be toxic, or even fatal, to humans. But he stressed that Dr. Aposhian was inappropriately relying on instances of mercury toxicity involving mercury in *forms* quite different from the ethylmercury found in thimerosal, and on instances involving exposure to vastly greater *amounts* of mercury than the small amounts used as preservatives in vaccines.

As to the forms of mercury, Dr. Brent explained that the many different types of mercury have toxological properties quite different from one another, so that it is inappropriate to generalize, as Dr. Aposhian does, from one form of mercury to another. (Ex. L, pp. 9-15; Tr. 2342A-43.) Dr. Brent quoted a medical toxicity text which noted that "no other metals better illustrate the diversity of effect caused by different chemical species than does mercury." (Tr. 2342-43.)

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[27]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).

[28]Those instances of mercury toxicity involved mercury in forms other than thimerosal, and did not involve autism. (Tr. 2306-08.)

In this regard, Dr. Brent pointed out one specific problem with Dr. Aposhian's theory, in which Dr. Aposhian relied on a "reference dose" standard that was developed with regard to a species of mercury known as "methylmercury." Dr. Brent explained that as soon as thimerosal in a vaccine enters the body, it breaks down into its component parts, and the mercury released from the thimerosal compound is the species of mercury known as "ethylmercury." (Tr. 2314.) Dr. Brent pointed out that ethylmercury has toxological properties that are very different from methylmercury, so that it was quite inappropriate for Dr. Aposhian, in devising his theory that thimerosal can damage the immune system, to rely on the "reference dose" standard for a *different* type of mercury, methylmercury. (Ex. L, pp. 10-14; Tr. 2346-51.)

Dr. Brent also testified that Dr. Aposhian's causation theory erroneously ignored the "dose-response" principle, a foundation of medical toxicology. Dr. Brent explained that almost any substance can be toxic if administered in high enough quantities, while substances that are toxic at high doses can be harmless or even beneficial at low doses. (Ex. L, p. 6; Tr. 2335-46.) He noted that even *water* can be fatally toxic to humans at extreme levels. (Tr. 2336.) Dr. Brent acknowledged that mercury in large amounts, far above the amounts involved in thimerosal in vaccines, can be toxic to humans. (Tr. 2421.) He testified, however, that the historical examples of mercury toxicity upon which Dr. Aposhian relies involved *vastly greater* amounts of mercury, compared to the amount of ethylmercury contained in the thimerosal in vaccines. For example, Dr. Brent pointed to three studies cited by Dr. Aposhian in which the subjects had their mercury blood levels measured at approximately 1,000 micrograms per liter, 150,000 micrograms per liter, and 500,000 micrograms per liter, respectively. This contrasted sharply to the mean mercury blood level of 1.6 micrograms per liter found in one group of two-month-olds after receiving thimerosal-containing vaccines. (Tr. 2341-42; R. Tr. Ex. 17, p. 24; Pet. Ex. 55, Tabs P, LL, MM.)

Dr. Brent also criticized the reliance of Dr. Aposhian, in forming his theory that thimerosal can cause human immune system dysfunction, on *in vitro* studies. Dr. Brent 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 "petri dish" or other laboratory setting. (Ex. L, pp. 6-7; Tr. 2320-21.) He explained 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 that cell was part of a living being. (Ex. L, pp. 7-9; Tr. 2320-23.) Dr. Brent 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. L, pp. 7-9; Tr. 2320-24.) In this regard, Dr. Brent noted that Dr. Aposhian, in forming his theory that thimerosal causes immunosuppression, had relied

particularly on certain studies by Goth[29] and Agrawal.[30] Dr. Brent opined that those two studies, both *in vitro* studies, did *not* offer significant support for the proposition that thimerosal-containing vaccines could cause human immunosuppression. (Ex. L, pp. 8-9; Tr. 2324-34.)

Dr. Brent noted many problems with the Goth study. Not only was the study an *in vitro* study, but it involved mouse cells, not human cells. Dr. Brent explained that the results of animal studies cannot be extrapolated to humans, but are useful mainly to *generate hypotheses* for human testing. (Tr. 2325, 2333-34.) Further, the mouse cells were exposed to thimerosal itself, whereas human cells in the body would be exposed not to *thimerosal*, but to *ethylmercury*, since thimerosal converts to ethylmercury soon after entering the body. (Ex. L, p. 8; Tr. 2325-26.) In addition, Dr. Brent testified, the amount of thimerosal to which the mouse cells were exposed was *greatly higher* than the amounts of ethylmercury to which human cells would be exposed in an infant vaccinated with thimerosal-containing vaccines. (Tr. 2326-30.) He also pointed out other problems with the Goth study. (Tr. 2330-31; Ex. L, p. 8.)

Dr. Brent pointed out similar problems with the Agrawal study. (Ex. L, pp. 8-9; Tr. 2331-33.) The Agrawal study, again, was an *in vitro* study. The Agrawal study did involve human, not animal cells, but the cells, as in the Goth study, were exposed to *thimerosal*, not *ethylmercury*. (Tr. 2331; Ex. L, p. 8.) In addition, as with the Goth study, in the Agrawal study the cells were exposed to thimerosal in amounts *far greater* than would be comparable to the exposure of human cells to ethylmercury after receipt of thimerosal-containing vaccines. (Tr. 2331-32.)

3. Assertion of "genetic hypersusceptibility"

Petitioners have suggested that there may exist a group of humans who, unlike most humans, are genetically "hypersusceptible" to mercury, leaving them vulnerable to immune system damage when exposed to ethylmercury. Dr. Aposhian's testimony seemed to assert this theory. (Tr. 92, 115, 129-131.) After review, however, I find that petitioners have failed to demonstrate that this theory has any validity.

First, neither Dr. Aposhian nor any other of petitioners' experts pointed to any *scientific research*[31] that even suggests that such "hypersusceptibility" exists. Rather, petitioners' experts

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[29]Samuel Goth et al., *Uncoupling of ATP-mediated Calcium Signaling and Dysregulated Interleukin-6 Secretion in Dendritic Cells by Nanomolar Thimerosal*, 114 ENVTL. HEALTH PERSP. 1083 (2006). (Ex. 55, Tab Q.)

[30]Anshu Agrawal et al., *Thimerosal Induces TH2 Responses via Influencing Cytokine Secretion by Human Dendritic Cells*, 81 J. LEUKOCYTE BIOLOGY 474 (2007). (Ex. 55, Tab A.)

[31]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.
(continued...)

seem to be merely *speculating* in suggesting that such a "hypersusceptibility" phenomenon *might* explain why only a small proportion of the children who are exposed to thimerosal end up suffering from autism. For example, Dr. Aposhian, instead of pointing to any evidence of human "hypersusceptibility" to *thimerosal* or *ethylmercury*, attempted to rely upon an analogy to a condition known as acrodynia or "Pink Disease." Acrodynia was caused, in the early part of the 20th century, by infants' exposure to a different form of mercury, mercuric chloride, in teething powders. Noting that the condition seemed to develop in only some of the children exposed to the mercuric chloride, Dr. Aposhian suggested that might be because the suffering children were "hypersusceptible" to mercury. (See Ex. 55, pp. 8-9; Tr. 92; P. Tr. Ex. 1 at 16-17.) Dr. Brent, however, testified that acrodynia was more likely to have been a *dose-related* condition than an example of genetic hypersusceptibility. That is, he explained that measurements of urine mercury levels in victims of acrodynia showed that those who suffered the disease had been exposed to *particularly high levels* of mercuric chloride; this indicates that acrodynia was suffered by children that were *exposed to more mercury,* rather than by children who happened to be *more susceptible* to mercury. (Ex. L, pp. 22-23; Tr. 2365-68, 2483.)

Dr. Brent also testified that there exists no support in the medical literature for the petitioners' "hypersusceptibility" theory, despite intensive study of the autistic population. (Tr. 2363-64, 2460-61.) Further, he explained that in instances in the past in which researchers have determined that some persons are more genetically susceptible than others to certain substances, the *specific gene* involved was "easily identified" by genetic researchers; in contrast, no such specific gene has been identified for the alleged hypersusceptibility to mercury. (Tr. 2363-64.)

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[31](...continued)
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 1329; *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 as a factor raising doubt about the validity of the theory. (See the cases cited at pp. 122-23, below.)

In this case, as to this "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 petitioners' causation theories to be discussed below. 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.

Respondent also offered another expert concerning the issue of a purported genetic hypersusceptibility to thimerosal. Dr. Edwin Cook, M.D., is a psychiatrist (autism is considered a psychiatric condition) who, in a medical career that began in 1981, has specialized in the treatment of autistic children and in genetic research related to autism. (Tr. 1466-80.) Dr. Cook, like Dr. Brent, testified that he was aware of no evidence to support the theory that some persons may be genetically hypersusceptible to thimerosal. (Tr. 1505-06.) He described the theory as "speculation." (Tr. 1505.)

In sum, the only support that Dr. Aposhian was able to provide for petitioners' "genetic hypersusceptibility" theory was his analogy to acrodynia, but Dr. Brent pointed to data indicating that acrodynia was *not* likely an example of hypersusceptibility. Thus, concerning this issue, I conclude that the testimony of Drs. Brent and Cook was persuasive, and that the testimony of Dr. Aposhian was not. I conclude that the petitioners' "genetic hypersusceptibility" theory [32] has not been shown to have any validity.

4. "Mercury efflux disorder" theory

Dr. Aposhian testified[33] that autism in some individuals, perhaps including Michelle Cedillo, may be caused by a "mercury efflux disorder," meaning that the child is unable to excrete mercury as efficiently as most children do, and a resulting build-up of mercury in the body damages the function of the body's cells, including cells in the immune system. Dr. Aposhian stated that the problem in the "mercury efflux disorder" is that the children "can't get rid of mercury in the cell. They can take mercury into the cell, but they can't get rid of it. That's true for the brain, it's true for about all the tissues in the body," including the immune system. (Tr. 102A.) Thus, under Dr. Aposhian's theory, the mercury remains in the cells, causing cell dysfunction. (Tr. 94A-106A, 197A-202.)

Dr. Brent, however, testified effectively that petitioners' "mercury efflux disorder" theory is highly dubious. (Tr. 2351-63.) He noted that such a disorder is not recognized by the medical

[32]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. (Ex. JJ, 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 p. 124 below.) The committee concluded that it could find "no corroborating data" to support such theory. (Ex. JJ, p. 139.)

[33]It is not clear whether Dr. Aposhian's theories about "genetic hypersusceptibility" and "mercury efflux disorder" were separate or overlapping theories. He may have been suggesting that those who are "genetically hypersusceptible" are the same as those who have a "mercury efflux disorder." However, whether those two theories are separate or not, I was not persuaded that *either* theory has any validity at all.

community.[34] (Tr. 2361-62.) He also pointed to severe problems with the studies on which Dr. Aposhian principally relied for his "mercury efflux disorder" theory, the Holmes[35] and Bradstreet 2003[36] studies.

In the Holmes study (Ex. 55, Tab X), 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 suggest 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. L, pp. 19-21; Tr. 2351-54.) Among those reasons was the fact that the mercury hair levels found in the autistic individuals tested by Holmes actually were squarely within the *normal range* of what other testing indicated would be the normal level of mercury in hair in U.S. children. (Ex. L, pp. 19-20; Tr. 2351-53.) Dr. Brent explained that the Holmes investigators' conclusion, that the autistics 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. (Ex. L, p. 20; Tr. 2350-51.) Dr. Brent found that this unexplained deviation from the prior accepted mercury hair level data made the Holmes study extremely suspect.

Dr. Brent explained further that when two other groups of researchers performed studies similar to the Holmes study, both found *no significant differences* in the mercury hair levels between the autistics and controls studied. (Ex. L, p. 20; Tr. 2462-66.) I find that at least one of those studies, the Kern study,[37] supports Dr. Brent's testimony in that regard. He also discounted another study which Dr. Aposhian had described as supporting the Holmes study. Dr. Brent stated that this

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[34]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 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).

[35]A.S. Holmes et al., *Reduced Levels of Mercury in First Baby Haircuts of Autistic Children*, 22 INT'L. J. TOXICOLOGY 277 (2003). (Ex. 55, Tab X.)

[36]J.J. Bradstreet et al., *A Case-Control Study of Mercury Burden in Children with Autistic Spectrum Disorders*, 8 J. AM. PHYSICIANS & SURGEONS 76 (2003). (Ex. 55, Tab E.)

[37]Janet Kern et al., *Sulfhydryl-Reactive Metals in Autism*, 70 J. TOXICOLOGY & ENVTL. HEALTH 715 (2007). (Ex. L, Att. 34.)

study, the Hu study,[38] involved only three autistic individuals, and suffered from the same grave problem as the Holmes study--*i.e.*, the mercury hair levels in the autistics were actually precisely that which would be *expected* in average, non-autistic American children. (Ex. L, p. 20, fn. 12; Tr. 2354-56.)

Dr. Brent also criticized the other study upon which Dr. Aposhian chiefly relied, the Bradstreet 2003 study. In that 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 autistics, concluding therefrom that autistic children have a decreased ability to excrete mercury. Dr. Brent, however, explained that the study suffered from so many methodological and conceptual errors that it essentially provided no useful information whatever. (Ex. L, pp. 21-22; Tr. 2356-61.) As one example, he noted that urinary excretion following chelation has been shown to be an *inaccurate* measure of mercury body burden. (Ex. L, p. 22.) He also noted that the way in which the controls were selected for the study was problematic. (Ex. L, p. 22; Tr. 2358.) 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 (Tr. 2359-60), and even Dr. Aposhian himself acknowledged that he would have done the study differently in that regard (Tr. 166). Dr. Brent described problems with the statistical methodology that the study authors used. (Ex. L, p. 22; Tr. 2358.) He also stated the Bradstreet 2003 study was published in a "fringe" medical journal.[39] (Tr. 2360.) Finally, Dr. Brent noted that another research group performed a study similar to Bradstreet's, but without the methodological flaws, and published it in a "legitimate" medical journal.[40] (*Id*.) That study, in contrast to Bradstreet's, found *no difference* between autistics and controls in urinary mercury levels after chelation. (Tr. 2360-61.)

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[38]Lin-Wen Hu et al., *Neutron Activation Analysis of Hair Samples for the Identification of Autism*, 89 TRANSACTIONS AM. NUCLEAR SOCIETY 681 (2003). (Ex. L, Att. 28.) Dr. Aposhian referred to this study as the "MIT study." (Tr. 98.)

[39]Dr. Brent referred to the journal that published the Bradstreet 2003 article as a "fringe" journal because that journal is not "indexed" by the National Library of Medicine. (Tr. 2360.) An "indexed" medical journal is one that is included in databases assembled for medical-scientific literature search engines. (Ex. BB, p. 6.) A journal may not be indexed because it is new, or because it is thought to be "insufficiently rigorous" to be reliable. (*Id*.) Respondent's expert Dr. Ward stated that non-indexed journals are "generally ignored by scientists as sources of reliable scientific information." (*Id*.) He also noted that the journal in which the Bradstreet 2003 article was published, although in operation for more than 50 years, is *not* an indexed journal. (*Id*.)

[40]Sarah 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). (Ex. OO.)

Dr. Aposhian also relied (Tr.101-03) on the Adams study.[41] 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. (Tr. 2467-69.)

I find that Dr. Brent's testimony on this point was persuasive, and that the testimony of Dr. Aposhian was not. I conclude that the Holmes, Bradstreet 2003, and Adams studies[42] are of doubtful reliability,[43] and that the contrary studies cited by Dr. Brent provide better evidence. I conclude that the petitioners have failed to show that their "mercury efflux disorder" theory has any validity.[44]

5. Petitioners' other general citations to medical literature

In their briefs, petitioners have stressed that they have pointed to much medical literature indicating in general that mercury, *in some forms and dosages*, can be toxic to humans. (P1, pp. 207-211.) I have examined all of the items of medical literature cited by petitioners, and those items do contain some evidence indicating that mercury in some forms and dosages can be toxic. However, a thorough examination of the record makes it clear that there is *no* evidence, beyond Dr. Aposhian's own assertion, that *ethylmercury, in the very small amounts contained in thimerosal-containing vaccines*, can damage infant immune systems, or otherwise contribute to autism in any way. For example, none of the medical articles, cited by petitioners at the pages of their brief set forth above, conclude or even suggest that thimerosal or ethylmercury, in the amounts contained in infant

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[41]James Adams & Jane Romdalvik, *Mercury, Lead and Zinc in Baby Teeth of Children with Autism Versus Controls*, 70 J. TOXICOLOGY & ENVTL. HEALTH 1046 (2007). (Ex. 82.)

[42]It is noteworthy that when the Holmes investigators found allegedly *low* levels of mercury in hair, 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, they also found that to be supportive of the same theory.

[43]I also note that a committee of the Institute of Medicine specifically reviewed the Holmes and Bradstreet 2003 studies, and pointed out problems with both studies. (Ex. JJ, pp. 132-34.)

[44]An expert presented by the petitioners in the *Hazlehurst* case, Dr. Jean-Ronel Corbier, also stated the opinion that autism in some individuals may be related to an impaired ability to excrete mercury. (*Hazlehurst* Tr. 379A-82A.) Dr. Corbier, however, did not offer any substantial *explanation* for this opinion. He merely pointed briefly to the same three studies cited by Dr. Aposhian--the Bradstreet 2003, Holmes, and Adams studies. I have considered this testimony of Dr. Corbier, but I do not find it persuasive, and I find that the contrary testimony of Dr. Brent was substantially more persuasive.

vaccines, can damage immune systems or cause other harm. Accordingly, I conclude that those general citations of petitioners to medical literature do *not* offer any substantial support to their theory that thimerosal-containing vaccines can damage the infant immune system.[45]

6. Testimony of Dr. Byers and Dr. Kinsbourne

Two additional experts also gave brief testimony on behalf of petitioners concerning this general issue. Dr. Vera Byers, M.D., Ph.D., an immunologist, offered testimony that seemed to generally support Dr. Aposhian's theory that the thimerosal in thimerosal-containing vaccines can cause immune system damage. (Ex. 57, pp. 4-5; Tr. 872, 893-913, 931-32, 935.) The testimony of Dr. Byers, however, was quite vague. She repeatedly emphasized that concerning this issue of the possible effects of mercury on the immune system, it was her intent to "defer" to Dr. Aposhian, or that she was "relying" on Dr. Aposhian (Tr. 894-896, 930, 935, 946, 983, 984-85), indicating that she was merely adopting *Dr. Aposhian's* conclusion on this issue, not developing her *own* opinion. Beyond relying on Dr. Aposhian, she did not offer any analysis concerning how she reached her opinion on this point, except to indicate that she was relying on the Goth and Agrawal studies, which I have found to be of dubious value for reasons discussed above. (Tr. 900-903.)

The main point of Dr. Byers' testimony seemed to be her conclusion that *Michelle Cedillo* had a malfunctioning immune system, thereby allowing the vaccine-strain measles virus to persist in her system. To be sure, Dr. Byers generally indicated the conclusion that this malfunction of Michelle's own immune system was at least in part the result of her thimerosal-containing vaccines. (Dr. Byers indicated that Michelle's immune dysfunction was also *in part* the result of the vaccine-strain measles virus itself.) But in this regard, Dr. Byers again was not relying entirely on her *own* analysis. Rather, her reasoning seemed[46] to be as follows: (1) Dr. Aposhian has demonstrated that thimerosal-containing vaccines *in general* can damage infant immune systems. (2) *Michelle Cedillo* suffers from a damaged immune system. (3) Given the preceding two points, it is reasonable to infer that Michelle's own immune system damage was, at least in part, the result of her thimerosal-containing vaccines. However, other than her brief discussion of the Goth and Agrawal articles (Tr. 900-903), Dr. Byers did not provide any *support* for her apparent conclusion that thimerosal-containing vaccines can damage immune systems, saying only that she was relying on Dr. Aposhian for that point.

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[45]Further, respondent's expert Dr. Christine McCusker, a pediatric immunologist, noted that recent large studies failed to identify any pattern of abnormal immune function in autistic children. (Ex. Z, p. 2; Tr. 2207.)

[46]At a number of places in their briefs and their presentations during the evidentiary hearing, petitioners' counsel and experts stated their arguments somewhat vaguely. Accordingly, when summarizing such arguments, I will sometimes state that the petitioners "seem to" or "appear to" present a certain argument.

I conclude that Dr. Byers' testimony, concerning this *general issue* of whether thimerosal-containing vaccines can damage the immune system, was not persuasive. Dr. Byers' testimony in this regard was far outweighed by the testimony of Dr. Brent and respondent's other witnesses, discussed above.

Additionally, petitioners pointed to the opinion of another of their experts, Dr. Marcel Kinsbourne, asserting that he listed "mercury" as a "possible cause of immune dysregulation." (P2, p. 16.) A close reading of the section of the transcript cited by petitioners, however, indicates that Dr. Kinsbourne was careful to offer no opinion of his own concerning this topic. He stated only that mercury was "one of the possibilities" as a cause for the alleged immune dysregulation of Colten Snyder (*Snyder* Tr. 486, line 25), and he also noted that even in going that far, he was not stating his *own* opinion, but was "relying on another expert's independent opinion on that" (*Snyder* Tr. 485, lines 14-15). Dr. Kinsbourne also made it quite clear, during his testimony in this *Cedillo* case, that he does *not* have an opinion *of his own* as to whether thimerosal-containing vaccines can cause immune dysfunction. (Tr. 1125, 1173-74.)

Accordingly, I find that the testimony of Dr. Kinsbourne, like that of Dr. Byers, offered no support to the petitioners' assertion that thimerosal-containing vaccines can damage human immune systems.[47]

7. Summary concerning general theory of thimerosal-caused immune dysfunction

For all the reasons set forth above, I conclude that the evidence offered by the respondent concerning this general issue is substantially more persuasive than the evidence offered by petitioners. I conclude that while Dr. Aposhian does have impressive credentials as a Ph.D. toxicologist, Dr. Brent, a medical doctor and a medical toxicologist, has *superior* credentials concerning this issue. I found the testimony of Drs. Brent and Cook to be substantially more persuasive, in general, than that of Dr. Aposhian.[48] While all the experts agree that mercury, in some

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[47]I also note that another of petitioners' experts, Dr. Ronald Kennedy, at one point stated generally that "mercury," in some unspecified form and dosage, can cause "immune dysfunction." (Tr. 709.) Dr. Kennedy explained that he had read in *textbooks* that heavy metals (such as mercury) can in general have a substantial immunosuppressive effect, although he did not consider himself to be an expert in that area. (Tr. 776-783.) However, Dr. Kennedy never opined that *thimerosal* or *ethylmercury*, in the amounts contained in thimerosal-containing vaccines, can damage infant immune systems. (Tr. 776-783.) (To be sure, one theme of Dr. Kennedy's testimony was that the *measles vaccine* can cause immune system suppression (*e.g.*, Tr. 720-21), but he did not testify that *thimerosal-containing vaccines* can cause such suppression.)

[48]Another of respondent's experts, Dr. Brian Ward, a medical doctor specializing in infectious diseases, also noted in his written report that he saw no substantial evidence to support the theory that thimerosal can damage the immune system. (Ex. BB, pp. 9-10.) Like Dr. Brent, Dr. Ward stated that no conclusions can be drawn from the *in vitro* studies. (Ex. BB, p. 9.) These (continued...)

forms and dosages, can be toxic, I find that Dr. Brent was quite persuasive in explaining why, for the reasons set forth above, there is no good reason to conclude that mercury in its *ethylmercury* form, in the small amounts contained in infant vaccines, can damage infant immune systems. I find Dr. Brent to be convincing in his testimony that Dr. Aposhian erred in his reliance upon *in vitro* studies, especially the Goth and Agrawal studies. I find that the petitioners' theories concerning "genetic hypersusceptibility" and "mercury efflux disorder" have *not* been shown to have validity. And I find that the medical literature cited by petitioners lends no substantial support to their theory concerning this issue. In short, I find that the evidence falls far short of demonstrating that it is "more probable than not" that thimerosal-containing vaccines can damage infants' immune system.

B. Petitioners have not demonstrated that thimerosal-containing vaccines harmed Michelle's own immune system.

In the prior several pages of this Decision, I have explained why I conclude that the petitioners have failed to demonstrate that thimerosal-containing vaccines *in general* can damage infants' immune systems. In this section, I conclude that the petitioners have also failed to demonstrate that it is "more probable than not" that thimerosal-containing vaccines damaged *Michelle's own* immune system.

Petitioners' argument with regard to Michelle can be summarized as follows: (1) Thimerosal-containing vaccines *in general* can damage infant immune systems. (2) Michelle suffers from a damaged immune system. (3) Given the preceding two points, it is reasonable to infer that Michelle's own immune system damage was the result of her thimerosal-containing vaccines. I must reject petitioners' overall argument, however, because I reject *both* of the first two parts of petitioners' three-part argument.

1. I have found above that petitioners' general causation theory concerning immune damage is without merit.

As to part (1) of petitioners' three-step theory (see previous paragraph), I have already explained in detail, at pp. 22-34 of this Decision, why I have found no merit in the petitioners' theory that thimerosal-containing vaccines *in general* can damage infant immune systems. Therefore, since I have rejected that *general causation* theory, it follows inescapably that petitioners have failed to demonstrate that thimerosal-containing vaccines damaged *Michelle's own* immune system.

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[48](...continued)
opinions of Dr. Ward offer additional support for my conclusion here.

2. Petitioners have failed to demonstrate that Michelle has a substantially abnormal immune system.

I also reject part (2) of petitioners' three-step argument, since I find that petitioners have *failed* to demonstrate that it is "more probable than not" that Michelle has a damaged immune system.

a. Petitioners' evidence--Dr. Byers

Concerning this issue of Michelle's own immune system, the petitioners rely primarily on the testimony of Dr. Byers, a medical doctor specializing in immunology. She testified that Michelle has a malfunctioning ("dysregulated" was the term she used most often) immune system. (Tr. 872, 929A.) Dr. Byers seemed to base this conclusion primarily upon a set of tests of Michelle's immune system performed by an immunologist, Dr. Gupta, in 1997 when Michelle was three years old. (Tr. 879A.) Dr. Byers stated that this testing showed that Michelle's immune function was abnormal, pointing out several specific tests on which Michelle's results deviated from normal test results. One abnormality, she testified, was that Michelle has "Th1/Th2 skewing," meaning an imbalance of too few "Th1" cells and too many "Th2" cells. (Ex. 57, pp. 3-4; Tr. 879A.) Another problem, according to Dr. Byers, was that Michelle had an unusually low "CD8 count," which meant that she had an abnormal ratio between two types of immune system cells known as CD4 and CD8. (Ex. 57, p. 4; Tr. 880A, 884A.) Third, Dr. Byers said, Michelle had an elevated "CD20" test, which meant that she had abnormally elevated amounts of the immunoglobulin subclasses IgG2 and IgG4. (Ex. 57, p. 3; Tr. 880A-81A.)

Dr. Byers also mentioned several other factors that contributed to her view that Michelle has an abnormal immune system. She stated that one such factor was Michelle's "aberrant reaction to the MMR vaccine," meaning Michelle's high fever that began about one week post-vaccination. (Tr. 874A, 929A, 936.) Another factor, according to Dr. Byers, was that Michelle has suffered from "chronic inflammatory conditions," including "chronic inflammatory bowel disease." (Tr. 874A, 879A, 888A, 929A.) A third factor that she listed was Michelle's alleged "inability to clear the measles virus vaccine strain from her body." (Tr. 879A.)

b. Respondent's evidence--Dr. McCusker

Respondent's primary witness[49] concerning this issue was Dr. Christine McCusker, a medical doctor who specializes in pediatric immunology. (Tr. 2202-03.) She opined that Michelle has a normal immune system. (Ex. Z, pp. 4, 6; Tr. 2244A-45.) Dr. McCusker evaluated in detail the immunological testing of Michelle done by Dr. Gupta in 1997. (Ex. Z, pp. 2-5; Tr. 2217A-25A, 2240, 2257A-58.) She concluded that that testing demonstrated that Michelle has an "entirely normal immune response." (Tr. 2225A.[50])

Dr. McCusker explained what she found to be the primary error in Dr. Byers' evaluation of the 1997 testing by Dr. Gupta. Dr. McCusker noted that Dr. Byers had compared the results from several of the tests on Michelle to a set of "normal" values for such tests. The normal values utilized by Dr. Byers, however, were for *adults*, not children. According to Dr. McCusker, this inappropriate usage of normal values for adults, rather than age-adjusted values, explain the supposedly "abnormal" results for Michelle cited by Dr. Byers. Dr. McCusker stated that when she herself instead compared Michelle's results to an *age-adjusted* set of normal values, Michelle's results fell within the normal ranges. (Ex. Z, pp. 2-4; Tr. 2217A-2225A.)

Dr. McCusker testified further that if Michelle had had a damaged immune system, she would have suffered from an abnormal number of infections, yet, in fact, that did *not* happen to Michelle. (Tr. 2240-41A.)

c. Analysis concerning Michelle's own immune system

After full consideration, I have found the testimony of Dr. McCusker concerning this issue to be substantially more persuasive than that of Dr. Byers. There are a number of reasons for this conclusion.

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[49]Two other experts for respondent also briefly addressed the issue of whether Michelle has a defective immune system. Dr. Ward, the infectious disease expert, examined Michelle's records and found "no evidence of clinically relevant immune suppression in Michelle's case." (Ex. BB, p. 8.) Similarly, Dr. Diane Griffin, a medical doctor with extensive experience studying the measles virus and related issues, also stated that she found no evidence of immune suppression in Michelle's records. (Tr. 2792A-93.) However, neither of those experts testified extensively concerning this issue, nor is either an immunologist. Accordingly, while their opinions do provide additional support for the conclusion that I have reached, those opinions were secondary in importance to Dr. McCusker's opinion.

[50]According to the transcript, Dr. McCusker stated that Michelle has an "entirely immune response." (Tr. 2225A, line 10.) However, the audio recording of the hearing, which is available on this court's website, demonstrates that Dr. McCusker said the word "normal" between the words "entirely" and "immune." That is consistent with the rest of her expert report and testimony.

Initially, Dr. Byers' opinion that Michelle had a defective immune system was based in part on two assumptions of fact which I have rejected as incorrect.[51] First, Dr. Byers assumed Michelle's "inability to clear the measles virus vaccine strain from her body." (Tr. 879A.) In other words, Dr. Byers assumed the validity of the much-disputed laboratory testing that concluded that Michelle had the presence of measles vaccine in her intestinal tissue years after her MMR vaccination. However, I have concluded that such testing was *not* reliable. (See pp. 41-78 below.) Second, Dr. Byers based her opinion on the assumption that Michelle has suffered from "chronic *inflammatory* conditions," including "chronic *inflammatory* bowel disease." (Tr. 874A, 879A, 888A, 929A, emphasis added.) However, I have concluded that petitioners have *failed* to demonstrate that Michelle suffers from a chronic *inflammatory* bowel condition (though she certainly has had non-inflammatory chronic gastrointestinal problems).[52] (See pp. 148-161 below.)

Next, Dr. Byers relied upon Michelle's high fever after the MMR vaccination as evidence that her immune system was defective. (Tr. 874A, 929A, 936.) However, Dr. McCusker responded that high fever does occur occasionally after MMR vaccination, without any long-term ramifications. (Tr. 2206.) More importantly, respondent's expert concerning the measles virus, Dr. Diane Griffin, testified that about five to fifteen percent of MMR recipients get a fever of 103° or more. (Tr. 2779A.) Thus, it appears that Michelle's fever was not so uncommon as to constitute substantial evidence of damage to her immune system.

Dr. McCusker also testified that, according to the 1997 testing, Michelle's immune system did appropriately make antibodies to the components of the vaccines that she received, including diphtheria, tetanus, rubella, polio, and pneumococcus. (Tr. 2217A-18A.) In Dr. McCusker's view, that indicates a properly functioning immune system. Petitioners did not attempt to refute this point.

In addition, Dr. McCusker testified, as noted above, that if Michelle had a damaged immune system, she would have suffered from a greater-than-normal amount of infections, while in fact her number of infections does not appear to have been abnormal. (Tr. 2240-41A.) Even Dr. Byers admitted that Michelle did not have a history of especially frequent or unusual infections. (Tr. 874A.)

The next point is the most important one with respect to this issue of whether Michelle's immune system was damaged. Dr. Byers and McCusker, as noted above, differed on the issue of which set of "normal" values to utilize when evaluating the 1997 testing of Michelle's immune system by Dr. Gupta. Dr. Byers utilized a set of normal values developed by the same laboratory that

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[51]An expert opinion may be rejected if based on an incorrect assumption. *E.g.*, *Perreira v. Secretary of HHS*, 27 Fed. Cl. 29, 33-34 (1992).

[52]The distinction between inflammatory and non-inflammatory gastrointestinal disorders is very important in this regard, since an inflammatory disorder would likely indicate involvement of the immune system, while non-inflammatory conditions such as diarrhea and constipation, from which Michelle chronically suffered, would not necessarily involve the immune system.

did the actual testing on Michelle, but that set was developed via testing of *adults*. Dr. McCusker, in contrast, found it more appropriate to utilize a published set of *age-adjusted* normal values developed in testing of children. (Tr. 884A-87; Ex. Z, pp. 2-4; Tr. 2210A-13.)

Concerning this issue, Dr. Byers did make a noteworthy point when she explained that there are variations in laboratory techniques, so that the best range of normal values to use may be the one developed by the *same laboratory* doing the testing. (Tr. 885A.) But Dr. McCusker responded that while there are variations between laboratories, it is even more important to use *age-appropriate* values when evaluating immune testing results of *children*, because children do differ significantly from adults in immune testing results. (Tr. 2210A-13, 2250A, 2266-67.) She noted, for example, that if you evaluated newborn children's immune systems using adult ranges, *all* such children would appear to have abnormal immune systems. (Tr. 2267.) She explained that U.S. and Canadian pediatric immunologists routinely use a published set of normal values for children, which have not changed appreciably since 1992. (Tr. 2212A-13.) I found that Dr. McCusker was far more persuasive on this point. She demonstrated that, in evaluating the immune systems of children, it is much more appropriate to utilize *age-appropriate* normal values, even if developed by other laboratories, than to use *adult* values developed in the same laboratory where the testing was done.[53]

Dr. McCusker also made another important point. She stated that even using the adult values utilized by Dr. Byers, Michelle's results on the several specific tests cited by Dr. Byers deviated from the normal range only by *slight amounts*. (Tr. 2268.) Therefore, she said, as an immunologist evaluating Michelle's test results, even comparing Michelle's results to the *adult values*, she would still deem Michelle's immune system to be *normal*. Further, it is important that Michelle's own treating immunologist, Dr. Gupta himself, after doing the 1997 testing in question, described Michelle as having "almost normal immune functions." (Ex. 3, p. 16.) Dr. McCusker testified that Dr. Gupta would not have made that general statement had he believed that Michelle's immune system substantially deviated from normal.[54] (Tr. 2250A.)

Thus, for all the reasons set forth above, I find that the petitioners have *failed* to demonstrate that it is likely that Michelle's immune system was substantially abnormal. I acknowledge that Dr. Gupta's comment that Michelle's immune functions were "*almost* normal" indicates that he perceived the possibility of some *slight* abnormality in Michelle's system. But the word "almost" *also* indicates that Dr. Gupta considered her immune system to at least be *close* to normal. His

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[53]Respondent's expert Dr. Ward, a medical doctor with experience in vaccine immunology (Tr. 1799), also testified that normal values for immunology testing change appreciably as children age. (Tr. 1799-1800A.)

[54]In addition, Dr. McCusker presented additional testimony related to the issue of the "Th2 skewing" that Dr. Byers purportedly found in Dr. Gupta's testing of Michelle's immune system. Dr. McCusker stated that if Michelle actually had "Th2 skewing," she would have had abnormal levels of the immunoglobulin subclass IgE, which she did not. (Tr. 2240.)

overall report certainly does not indicate that he found anything *substantially* abnormal in Michelle's immune system.

Further, Dr. McCusker was simply far more persuasive than Dr. Byers concerning this issue, for the reasons that I have outlined above. In addition, I note that Dr. McCusker's experience and background are also superior concerning this issue. Both Dr. McCusker and Dr. Byers have solid credentials in immunology. However, Dr. McCusker has the distinct advantage of specializing in *pediatric* immunology, which is not true of Dr. Byers. In addition, Dr. McCusker has extensive experience in recent years in the clinical practice of treating pediatric immunology patients (Tr. 2204-06), whereas Dr. Byers does not seem to have had any clinical experience, with children or adults, since around the year 2000 (Tr. 869A).

d. Dr. Kennedy

Petitioners in their briefs also relied on certain statements by Dr. Ronald Kennedy concerning Michelle's immune system. (P1, pp. 89, 95.) Dr. Kennedy is not a medical doctor, but has a Ph.D. in microbiology, and has a great deal of experience in studying viruses and in the development of vaccines. (Tr. 684-85; Ex. 110, pp. 1-2.) His expert report for the most part did *not* deal specifically with Michelle's own case, or with immunology in general. However, Dr. Kennedy did include three unexplained sentences which mentioned Michelle's immune system. In the first sentence, he stated that the "most plausible scientific reason" for the persistence of measles virus in Michelle's body is that "there is a selective immune dysfunction with her immune system." (Ex. 110,[55] p. 8.) He added a similar sentence as his penultimate sentence at the end of his report. (Ex. 110, p. 9.) Then, in his final sentence, he stated that the "skewing of the T cell responses," an apparent reference to Dr. Gupta's testing, "indicated that Michelle Cedillo exhibited immune dysfunction." (Ex. 110, p. 9.)

During his hearing testimony, Dr. Kennedy again briefly mentioned Michelle's immune system. (Tr. 741-43A.) He pointed to a result of one of Dr. Gupta's tests that he believed indicated an "elevated" response by her immune system (Tr. 741-42), which he interpreted as evidence of "some sort of immune dysfunction" (Tr. 742).

I have considered these statements by Dr. Kennedy, but they certainly do *not* alter my analysis stated above. In the quoted sentence from page 8 of his expert report, and in the penultimate sentence on page 9, Dr. Kennedy seems to be indicating, as Dr. Byers did, that *the fact that the measles virus has persisted in Michelle's body* is an indication of immune dysfunction in Michelle. However, I have found, for reasons to be detailed below, that the testing that purported to find persisting measles virus in Michelle's body was *unreliable*. (See pp. 41-78 below.) Therefore, this pont of Dr. Kennedy is of no value, since it is based on an incorrect assumption.

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[55]Dr. Kennedy's initial expert report was filed as Ex. 110; later, the same document was filed again, with a signature, as Ex. 112. I will cite to that report as Ex. 110.

Finally, I note that Dr. Kennedy's observations in his final sentence of his expert report, and in his hearing testimony, apparently were based on his interpretation of Dr. Gupta's testing as showing certain of Michelle's results as outside the normal range. But this analysis seems to have resulted from the *same error* made by Dr. Byers as discussed above--*i.e.*, comparing Michelle's testing results to *adult* values rather than age-adjusted values. Therefore, I must reject Dr. Kennedy's analysis in this regard for the same reason that I have rejected Dr. Byers' similar testimony.

Accordingly, having considered Dr. Kennedy's brief statements concerning Michelle's immune system, I conclude that they add nothing of persuasive value to petitioners' argument that Michelle has a defective immune system.

C. Summary concerning immune system allegations

For all the reasons set forth above, I conclude that the petitioners have failed to demonstrate either that thimerosal-containing vaccines *can* harm infant immune systems *in general*, or that thimerosal-containing vaccines *did* harm Michelle's own immune system.[56]

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[56]Petitioners also mentioned, in one of their briefs, the fact that Dr. Kennedy argued that the *measles vaccine* (rather than the thimerosal-containing vaccines) can cause immune suppression. (P1, pp. 93-94.) It is true that Dr. Kennedy, and Dr. Byers as well, did testify that the measles vaccine can have a suppressive effect on the human immune system for a period of time after vaccination. (Tr. 710, 720-21A, 764-69, 1012A.) However, the petitioners never attempted to tie this point into the rest of their causation arguments. How this point might fit within their overall causation theory is a mystery. And, in any event, I have considered the question of whether the petitioners have demonstrated that Michelle's *MMR vaccination* of December 20, 1995, had any significant immunosuppressive effect on her, and I find that they did not.

In this regard, one of respondent's experts, Dr. Griffin, did acknowledge that infection by the measles virus in its *wild*, *full-strength*, *non-vaccine* form, can have a temporary immunosuppressive effect. (Tr. 2767-69, 2799-2800A.) However, Dr. Griffin also testified that with the *vaccine-strain* form of the measles virus, there is no immunosuppression that is "clinically important." (Tr. 2779A-81, 2799.) According to Dr. Griffin, the vaccine-strain virus does cause minor temporary changes in the immune system response that could be measured via testing, such as changes in the lymphocytes that are circulating. (Tr. 2780-81.) But those changes do not suppress the immune system enough to cause increased susceptibility to disease. (Tr. 2779A-81, 2807, 2809.) Dr. Griffin noted that a number of studies have looked for evidence of increased susceptibility to infection after MMR vaccination, but have found none. (Tr. 2780-81A.) She repeated that point later, stating that there is no evidence that vaccines "make people more susceptible to opportunistic organisms" (Tr. 2807, lines 11-17), and that scientists have not recognized any evidence that the measles vaccine affects the vaccinee's "ability to fight off infection" (Tr. 2809, lines 7-16).

Further, another of respondent's experts, Dr. Burton Zweiman, who has outstanding credentials concerning immunology, testified in the *Snyder* case in agreement with Dr. Griffin that there is no *clinically relevant* immunosuppression caused by the measles *vaccine*. (*Snyder* Tr. 590A-

(continued...)

VI

THE UNIGENETICS TESTING THAT PURPORTED TO FIND EVIDENCE OF PERSISTING MEASLES VIRUS IN THE INTESTINAL TISSUE OF MICHELLE AND OTHERS WAS NOT RELIABLE

As noted above, the petitioners contend in this case that the MMR vaccine *can*, in general, contribute to the causation of both autism and chronic gastrointestinal dysfunction, and *did* contribute to the causation of Michelle Cedillo's own autism and chronic gastrointestinal symptoms. There is one key factual allegation that underlies *all* of those causation contentions. That is, all of the petitioners' causation theories depend upon the validity of certain testing that purported to find evidence of persisting measles virus in the biological materials of Michelle and a number of other autistic children. Specifically, the petitioners' primary expert concerning the causation of *autism*, Dr. Marcel Kinsbourne, made it clear that his opinion in any individual case would depend upon the existence of a reliable laboratory finding of persisting vaccine-strain measles virus in the body of the individual in question. (Tr. 1180A, 1183A, 1196A.) Similarly, the petitioners' primary expert concerning the causation of chronic *gastrointestinal dysfunction*, Dr. Arthur Krigsman, also specified that his opinion in any individual case would depend upon the existence of such a reliable laboratory finding of persisting vaccine-strain measles virus in the individual. (Tr. 531-33A, 538A.)

Therefore, a key issue in this case concerns the *reliability and validity* of the laboratory testing that purported to find evidence of persisting measles virus in the intestinal tissue of Michelle and other autistic children.[57] Both parties to this case have offered extensive evidence concerning this critical issue. After careful consideration, I conclude that the evidence indicates strongly that the testing in question was *not reliable*.

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[56](...continued)
91A.) Dr. Ward also testified to the same effect (Tr. 1881-82A, 1890-91), as did one of respondent's experts in the *Snyder* case, Dr. Bertus Rima (*Snyder* Tr. 831A).

As will be explained below, Dr. Griffin has extraordinary credentials as an expert concerning the measles virus. (See pp. 108-09 below.) I found her testimony, as supported by the testimony of Dr. Zweiman, Dr. Ward, and Dr. Rima, to be persuasive on this point. Accordingly, concerning this issue of whether the *vaccine-strain* measles virus has a clinically significant immunosuppressive effect, I credit their opinions over those of Dr. Kennedy and Dr. Byers.

Moreover, as explained above, I have concluded that there has been *no* showing that Michelle has a substantially abnormal immune system, so that even if the MMR vaccination had some *temporary* effect on Michelle's immune system, there has been no demonstration that the vaccination had any substantial long-lasting effect.

[57]Indeed, the petitioners acknowledged in their briefs that the validity of the Unigenetics testing of Michelle's own biopsy is a "*sine qua non* in her quest for entitlement." (P3 at 14.)

A. The measles virus testing conducted by the Unigenetics laboratory

On January 31, 2002, a biopsy (*i.e.*, a small piece of living tissue) was taken from Michelle's ileum, a part of her small intestine, for diagnostic purposes. (Ex. 44, pp. 13-14.) A "Measles Virus Detection" test on that biopsy was performed by the Unigenetics Ltd. laboratory operated by Dr. John J. O'Leary and colleagues, in Dublin, Ireland. (Ex. 28, p. 179.) The report of that test, issued on March 15, 2002, stated that "measles virus was detected" in the tissue. (*Id*.)

Michelle was not the only person whose tissue was tested for the possible detection of measles virus by a laboratory operated by Dr. O'Leary in Dublin. Dr. O'Leary's laboratory also performed testing that was reported in an article published by Uhlmann and colleagues in 2002.[58] (I will refer to that article hereinafter as the "Uhlmann article," and the study that the article described as the "Uhlmann study.") That article was co-authored by 11 individuals, including Dr. Andrew Wakefield, the British physician who was the primary author of the above-mentioned 1998 article that initiated the controversy concerning whether the MMR vaccine can cause autism. (Ex. 63, Tab U, pp. 84, 89.) Many of the other authors, including Uhlmann, were listed as affiliated with Trinity College in Dublin, Ireland, or the Coombe Women's Hospital in Dublin. (*Id*.) Two of the Dublin authors, in addition to Uhlmann, were Dr. O'Leary and Dr. Orla Sheils. (*Id*.)

The record of this case indicates that Dr. O'Leary and Dr. Shiels, in addition to being two of the authors of the Uhlmann article, have worked together at Dr. O'Leary's laboratory in Dublin, affiliated with Trinity College and the Coombe Women's Hospital. They were two of the principal members of the research team that carried out the Uhlmann study in Dublin. (Ex. 110, p. 7; Tr. 810-12, 817, 845, 851A, 1938A; *Snyder* Tr. 331A-32A, 853A-54A.) Uhlmann was a post-doctoral student who worked for them at the Dublin laboratory. (Tr. 1938A.) Unigenetics Ltd. was established by Dr. O'Leary and colleagues as a for-profit company to do testing for measles virus, apparently for the purpose of providing testing of claimants in certain British litigation in which it was alleged the MMR vaccine can cause autism. (That litigation will be described below, at p. 49 fn. 69.) (Tr. 811A-13;[59] *Snyder* Tr. 928A-29.) Later, Unigenetics did testing for measles virus on samples from other individuals, such as Michelle Cedillo. (Ex. 28, p. 179.)

It is not clear from the record whether the testing described in the Uhlmann study was performed under the Unigenetics Ltd. name. However, it is clear, and undisputed, that it was the Dublin laboratory group headed by Drs. O'Leary and Shiels that performed *both* the above-mentioned test on Michelle's tissue *and* the testing described in the Uhlmann article. The

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[58]V. Uhlmann et al., *Potential Viral Pathogenic Mechanism for New Variant Inflammatory Bowel Disease*, 55 MOLECULAR PATHOLOGY 84 (2002). (Ex. 63, Tab U.)

[59]Petitioners' expert Dr. Kennedy explained that it is common for scientific investigators at universities to be permitted to set up their own for-profit biotech companies in addition to their university duties. (Tr. 812-13.)

methodology was the same. (*See*, *e.g.*, Ex. 110, p. 7; Tr. 810-12, 817, 845, 851A, 1938A; *Snyder* Tr. 331A-32A.)

In the record of this case, the parties and witnesses have referred to the laboratory group that performed both the Uhlmann study, as well as the testing on Michelle Cedillo and similar commercial clients, interchangeably as the "O'Leary laboratory," the "O'Leary and Shiels laboratory," the "Unigenetics laboratory," or simply "Unigenetics." In this Decision, for ease of reference, I will usually refer to the "Unigenetics laboratory," or simply "Unigenetics;" it should be clear, however, that in such instances I am referring to *all* of the measles virus detection testing done by this Dublin laboratory group, whether it was performed under the "Unigenetics Ltd." name or not.[60]

The Uhlmann article described testing of intestinal tissue (specifically, ileal lymphoid tissue) from two groups of children. (Ex. 63, Tab U, p. 84.) The testing was done by a methodology known as PCR (polymerase chain reaction), the same form of testing done on Michelle Cedillo's tissue. The first group of 91 children each had both a "developmental disorder" and also intestinal dysfunction; the second group consisted of 70 developmentally normal children who had suffered various types of intestinal problems. (*Id*.) The tissue samples were tested for the presence of measles virus RNA,[61] by several different PCR techniques. The authors reported that they found measles RNA in the samples of the large majority of the developmentally disabled children, but in only a few of the developmentally normal children. (*Id*.)

The Uhlmann authors concluded that their results raised an important question, namely, "does MV [measles virus] play an aetiological role in intestinal inflammation in developmental disorder?" (*Id*. at 89.)

The Unigenetics laboratory, as noted above, has performed testing for measles virus on other tissue specimens besides those tested in the Uhlmann study. That laboratory performed the above-described test on Michelle Cedillo. In addition, it appears that biopsy tissue from other autistic children, whose families had concerns about a possible causal link between the MMR vaccine and

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[60]Dr. Kennedy indicated that Dr. O'Leary's academic, not-for-profit, Trinity College laboratory, and the Unigenetics laboratory, were "two different labs," even though operated by overlapping individuals. (*Snyder* Tr. 412A-13A.) It certainly appears that there were "two laboratories" at least in the sense that Unigenetics operated separately, for business purposes, from the other lab work done by Dr. O'Leary and colleagues at the Dublin hospital. The record does not make it clear whether the Unigenetics work was done in a *different physical space* than the other Dublin lab work. But that is not important, since it is clear that when experts described visiting the Unigenetics laboratory, they were certainly describing the physical space where the O'Leary group performed the *measles virus testing* done in the Uhlmann study and on samples from individuals such as Michelle Cedillo.

[61]RNA is short for "ribonucleic acid," which is part of the genetic material of a cell. *Dorland's* at 1638.

autism, has been sent to Unigenetics for testing to detect measles virus. For example, in one of the other Vaccine Act "test cases" described above, the *Snyder* case, biologic material from Colten Snyder was sent to Unigenetics, which found such material to be positive for the presence of measles virus. (*Snyder* Ex. 22, pp. 1-3.)

The "Unigenetics Ltd." laboratory company is no longer in business, apparently dissolved in 2005. (Tr. 856; *Snyder* Ex. X, p. 4; *Snyder* Tr. 400A.) However, the Dublin laboratory of Drs. O'Leary and Sheils does continue to operate and publish work. (Ex. 110, p. 7.)

B. Additional studies

The publication of the Uhlmann article raised concerns. Obviously, the reported finding that the large majority of the developmentally disabled children in the study had measles virus RNA in their intestinal tissue, while the vast majority of the developmentally normal children did not, gave rise to concern that the measles virus might be causing developmental disorders, including autism. And because the MMR *vaccine* contains a weakened but live version of the measles virus, the Uhlmann article contributed to the controversy concerning whether the *MMR vaccine* might be causing autism, the theory first raised in the above-mentioned 1998 Wakefield article.[62] Criticisms of the *Wakefield article* and its general causation theory will be discussed below (pp. 143-44), but at this point I note that the publication of the *Uhlmann article* caused some experts to question the conclusion of the Uhlmann authors that measles virus RNA had actually been found in the tested children. Accordingly, other researchers undertook studies to see if they could replicate the results of the Uhlmann study. Those researchers performed testing procedures similar to these described in the Uhlmann article, looking for the presence of the measles virus in the children.

An article describing one such study was published by Afzal and colleagues in 2006.[63] The Afzal authors tested certain blood cells, known as "PMBCs," of 15 children suffering from autism spectrum disorders (ASD), all of whom had received the MMR vaccine, for measles virus. The researchers utilized a number of testing methodologies, but found none of the samples positive for measles virus by any test. (Ex. T, Att. 2.)

An article describing another important study was also published in 2006, by D'Souza and colleagues.[64] The D'Souza researchers tested the blood cells (PMBCs) of 88 children, 54 diagnosed

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[62]Four of the authors of the 1998 Wakefield article, including Dr. Wakefield, were also authors of the Uhlmann article.

[63]M. Afzal et al., *Absence of Detectable Measles Virus Genome Sequence In Blood of Autistic Children Who Have Had Their MMR Vaccination During the Routine Childhood Immunization Schedule of UK,* 78 J. MED. VIROLOGY 623 (2006). (Ex. T, Att. 2.)

[64]Yasmin D' Souza, Eric Fombonne, Brian J. Ward, *No Evidence of Persisting Measles Virus*
(continued...)

with ASD and 34 developmentally normal, for measles virus. (Ex. T, Att. 6, p. 1664.) At least 51 of the 54 ASD children, and at least 31 of the 34 developmentally normal children, had received MMR vaccine. (*Id*. at 1669.) The authors' ultimate conclusion was that *none* of the studied children, in either the ASD group or the developmentally normal group, in fact had persisting measles virus infection. That result was reached after a *series* of procedures, the history of which sheds important light on the results of the Uhlmann study.

In PCR testing, the scientist's goal is to look at a sample of biologic material and see if it contains a certain "target," such as measles virus RNA. To do so, the scientist uses "primers" that are designed to "amplify" the target. The PCR scientist attempts to develop a set of primers that will pinpoint *the target material, and only the target material*, for "amplification" in the PCR test. The D'Souza team, therefore, utilized the same set of primers that the Uhlmann team had developed and used in the Uhlmann study, in order to test the performance of those primers. When the D'Souza team performed its testing utilizing the Uhlmann primers, the testing initially yielded "positive" findings of measles virus for almost all of the tested samples, including samples from *both* the ASD children and the developmentally normal children. (*Id*. at 1670.) However, the D'Souza group thereafter subjected those apparently positive samples to *additional* testing techniques in order to determine whether the PCR testing using the Uhlmann primers was truly identifying measles virus and *only* measles virus. The first technique involved analysis of "melting curves," and the second involved analysis of the size of "amplicons," a technique also known as "gel electrophoresis." The application of those two techniques revealed that all but nine of the samples that had initially tested positive by the PCR test using the Uhlmann primers were, in fact, *not* measles virus. (*Id*. at 1670-71; Ex. BB, p. 12; Tr. 1850-51.)

Finally, on the nine remaining apparently positive samples, the D'Souza team performed a procedure known as "sequencing," which, it is undisputed, is the "gold standard" for determining whether the material being examined actually is measles virus RNA, rather than some other substance. The D'Souza group was able to successfully complete the sequencing procedure in seven of the nine samples, and all seven turned out *not* to contain measles virus RNA. The sequencing, rather, demonstrated that the material, which in the PCR testing had appeared to be measles virus material, was in fact not measles virus material, but human genetic material. (Ex. T, Att. 6, p. 1671; Tr. 1853A, 1856A.)

The D'Souza authors, thus, concluded that their results demonstrated that the data published in the Uhlmann article "is unlikely to be true." (*Id*. at 1671.) The D'Souza group detailed what they found to be "several plausible explanations" for the Uhlmann authors' erroneous conclusion that they had found measles virus in the tissue samples. (*Id*. at 1672; Tr. at 1853A-55.) Their primary explanation was that the "primers" used in the Uhlmann study were not as "specific" as they needed to be to positively identify measles virus material and *only* measles virus material. Instead, the

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[64](...continued)
in Peripheral Blood Mononuclear Cells From Children With Autism Spectrum Disorder, 118 PEDIATRICS 1664 (2006). (Ex. T, Att. 6.)

D'Souza authors demonstrated that the Uhlmann primers were *nonspecific* enough that they mistakenly identified human genetic material as measles virus material. (*Id*. at 1672; Tr. 1853A-1858A.)

C. Petitioners' evidence

As noted above, the petitioners' two primary experts concerning their causation claims, Drs. Kinsbourne and Krigsman, both relied on the validity of the above-described Unigenetics testing of Michelle Cedillo and other children. However, while those two experts *relied upon* the validity of the Unigenetics testing, neither purported to be an *expert* concerning the specific, highly contested issue of whether, in fact, the Unigenetics testing results should be considered *reliable*. Concerning that issue of the *reliability* of the Unigenetics testing, rather, the petitioners have relied chiefly upon two expert witnesses, Dr. Karen Hepner and Dr. Ronald Kennedy.[65]

1. Dr. Hepner

Petitioners' first witness, Dr. Karen Hepner, has a Ph.D. in molecular biology, and more than ten years' experience in utilizing PCR technology. (Ex. 64; Tr. 583A-84A, 636-37.) In her expert report and hearing testimony, Dr. Hepner indicated the opinion that the Unigenetics test results were reliable. (Tr. 639.) Discussing the Uhlmann article, she opined that the positive and negative controls used by the Uhlmann authors were appropriate, that the operating procedure employed in the testing was appropriate to minimize the possibility of "contamination," and that the "assays" utilized were appropriately selected and implemented. (Ex. 63, pp. 1-3; Tr. 610A-28.)

Dr. Hepner also discussed two of the studies often cited by critics of the Unigenetics testing, the Afzal 2006 and D'Souza 2006 studies, which are described above at pp. 44-46. Dr. Hepner stated that the failure of those studies to find evidence of persisting measles virus in the bodies of autistic children is *not* a good reason to doubt the reliability of the Unigenetics testing. She stated that the failure of the Afzal and D'Souza studies to replicate the findings of the Uhlmann study was probably due to two factors. First, in those Afzal and D'Souza studies, the authors tested certain *blood* cells of the children, not *intestinal tissue* as did the authors of the Uhlmann article. Second, the Afzal and D'Souza studies tested autistic children, but not autistic children *with gastrointestinal dysfunction* as was the case with the Uhlmann testing. (Ex. 63, pp. 4-5; Tr. 629A-31A.)

Finally, Dr. Hepner pointed to a study that is currently in progress, conducted by herself and several others, to which I will refer as the "Walker study." She stated that the "preliminary data"

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[65] An expert witness for the petitioners in the *Hazlehurst* case, Dr. Corbier, did briefly state the opinion that the Unigenetics test results were reliable. (*Hazlehurst* Tr. 279A.) But he provided little explanation as to *why* he reached that conclusion, and he did not claim to have any expertise in PCR testing. I do not find that Dr. Corbier's brief statements concerning this matter offer any substantial support for the validity of the Unigenetics testing.

from that study "present another step in support" of the proposition that the measles virus persists in the intestinal tissue of autistic children. (Ex. 63, p. 5; Tr. 634A-35A.)

2. Dr. Kennedy

Concerning this issue of the validity of the Unigenetics findings, petitioners also rely on the opinion of Dr. Ronald Kennedy, who also testified, as noted above, concerning the issue of whether thimerosal-containing vaccines can cause immune system damage. As noted, Dr. Kennedy has a Ph.D. in microbiology, and much experience in studying viruses and in the development of vaccines. (Tr. 684-85; Ex. 110, pp. 1-3.) Dr. Kennedy opined that the laboratory group that performed the testing in question was competent. He stated that the laboratory of Dr. John O'Leary, Dr. Orla Sheils, and their colleagues has a good reputation, and has had its work published frequently in peer-reviewed medical journals in recent years. (Ex. 110, p. 7; Ex. 121,[66] pp. 1-2; Tr. 738A-39, 818; *Snyder* Tr. 344A, 351A-52A; *Snyder* Ex. 30, p. 9.) He explained that in order to perform the particular testing that resulted in the Uhlmann article, Drs. O'Leary and Sheils and colleagues opened a separate, for-profit laboratory business under the Unigenetics Ltd. name. (Tr. 812-13.) The implication of Dr. Kennedy's testimony was that the general good reputation of the O'Leary laboratory in Dublin indicates that the work of the Unigenetics laboratory is also likely to have been competent.

Dr. Kennedy also stated that in the Unigenetics testing in question, the laboratory used proper procedures, and took appropriate measures to avoid contamination. (Ex. 110, pp. 7-8; *Snyder* Ex. 30, p. 9.)

In addition, Dr. Kennedy described a meeting that he attended with several other medical scientists, involving a discussion of the work of the Unigenetics laboratory that resulted in the Uhlmann paper. He stated that he and the other scientists asked a Unigenetics representative who attended the meeting, Dr. Sheils, many questions about the testing procedures, and that Dr. Kennedy and the other scientists came away with the impression that the testing was valid. (Tr. 808-17, 824A-25, 844-48, 851A-52; *Snyder* Tr. 333A-39A.)

[66]The petitioners first filed a version of Ex. 121, Dr. Kennedy's supplemental expert report, on October 22, 2007. However, that version contained an error, so that on November 6, 2007, they filed a corrected version. My citations to Ex. 121 in this Decision are to the corrected version filed on November 6, 2007.

D. Respondent's evidence

Respondent relied upon several witnesses concerning this issue, principally Dr. Brian Ward, Dr. Stephen Bustin, Dr. Bertus Rima, and Dr. Thomas MacDonald.[67]

1. Dr. Ward

Respondent first presented the testimony and expert report of Dr. Brian Ward, a medical doctor specializing in infectious diseases and immunology, who has experience in the field of the PCR testing technique used in the Uhlmann, Afzal, D'Souza, and similar studies. (Ex. CC; Tr. 1795-98A, 1839, 1848-64A.) Dr. Ward explained that PCR is a sensitive technique, not easy to do properly, and subject to frequent false positives. He explained that the possibility of contamination, thereby yielding false positives, is a frequent and serious problem in any laboratory carrying out PCR testing. (Tr. 1839-43.)

Dr. Ward, one of the authors of the D'Souza article, described in detail how that study was conducted. (Tr. 1848-56.) He explained that, as noted above, when his group performed PCR testing utilizing the primers used by the Uhlmann team in their PCR work, the testing did yield "positive" findings of measles virus from almost all of the tested children, including both the ASD children and the developmentally normal children. However, when the D'Souza researchers performed the additional testing techniques described in their article, it became clear that the samples which the PCR testing had found to be positive, did *not*, in fact, contain measles virus. (Tr. 1850-51, 1853A, 1856A.) This result was confirmed by the final technique known as "sequencing," which he described as the "gold standard" test, the test that will "guarantee" that one is in fact identifying

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[67]I also note that respondent also submitted reports, relating to the issue of the validity of the Unigenetics testing, from two additional experts who did *not* ultimately testify at the evidentiary hearings in *Cedillo*, *Hazlehurst*, or *Snyder*. One such report was authored by Dr. Peter Simmonds, a Ph.D. expert in virology and PCR techniques, who studied the Unigenetics testing and found it to be unreliable, with its positive results due to either nonspecific primers or contamination. (*Snyder* Ex. P, entire report, especially pp. 8-9, 43, 84, 87, 119.) In addition, respondent submitted the report of Dr. Michael Gershon, a medical doctor specializing in neurogastroenterology, who also opined that the Unigenetics measles virus testing should not be considered reliable. (Ex. T, pp. 8-12.)

Because Dr. Simmonds and Dr. Gershon did not testify at any evidentiary hearing, their opinions have played only a secondary role in my analysis, but they do add additional support to the conclusion that I have reached.

In addition, the report and hearing testimony of another of the respondent's experts, Dr. Dianne Griffin, while dealing mostly with other matters, did offer some commentary on the issue of the validity of the Unigenetics testing. (Ex. V, pp. 5-9; Tr. 2831-36, 2854, 2861A-63.) Dr. Griffin indicated the view that the Unigenetics efforts at testing for measles virus were not reliable. (*Id.*; see especially Tr. 2833, 2854.) However, while Dr. Griffin is very knowledgeable concerning the measles virus in general, she stated that she does not claim to be a "PCR expert" in particular. (Tr. 2835B.) Accordingly, I have *not* relied upon her opinion concerning this issue.

the genetic material in question. (Tr. 1853A.) The process of sequencing demonstrated that the samples that had initially appeared to be measles virus material by the PCR testing using the Uhlmann primers in fact turned out to be human genetic material, not measles virus. (Tr. 1853A, 1856.)

Dr. Ward explained, in sum, that the D'Souza study demonstrated that a major error of the Uhlmann group had been to use primers that produced "non-specific amplification." Those primers erroneously caused the testing to identify measles virus material, when in fact no such measles virus material was present. (Tr. 1850-51, 1853A-58A; Ex. BB, p. 12; *Snyder* Tr. 964A-65A.)

Dr. Ward further testified that his laboratory later tested the Uhlmann primers on samples of *intestinal* (*gut*) *tissue*, and the results were similar to the analysis of blood cells in the above-described D'Souza 2006 study. (Tr. 1859A-61; Ex. BB, p. 12; Ex. BB, Att. 29.) The PCR testing using the Uhlmann primers on the intestinal tissue did generate a number of positive results, but when Dr. Ward and his colleagues completed the "sequencing" procedure, once again the results showed human genetic material, not measles virus material. (Tr. 1860A.) These results were published as the D'Souza 2007 article.[68] (Ex. BB, Att. 29.)

Accordingly, Dr. Ward expressed the ultimate opinion that he could place *no reliance* on the work of the Unigenetics laboratory in purportedly finding evidence of measles virus in the tissue of autistic children, including in the tissue of Michelle Cedillo. (Tr. 1865.)

2. Dr. Bustin

Respondent also presented the testimony of Dr. Stephen Bustin, a Ph.D. molecular biologist who has extensive experience in PCR testing. (Tr. 1933-36A.) Dr. Bustin was involved in certain litigation in Great Britain, which concerned the same general causation issue involved in this case, *i.e.*, whether the MMR vaccine can cause autism.[69] Engaged as an expert witness by the vaccine

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[68]Y. D'Souza, S. Dionne, E. Seidman, A. Bitton & B.J. Ward, *No Evidence of Persisting Measles Virus in the Intestinal Tissues of Patients with Inflammatory Bowel Disease*, 56 GUT 886 (2007). (Ex. BB, Att. 29.)

[69]During the early part of this decade, litigation proceeded in Great Britain in which a number of claimants contended that MMR vaccinations contributed to the causation of their autism spectrum disorders. *Sayers v. SmithKline Beecham Plc.*, 2004 WL 1640222 (Queen's Bench 2004). Under the British legal system, a British governmental body known as the Legal Services Commission (LSC) provided funding to the claimants to help them assemble and present evidence supporting their claims. In September of 2003, however, the LSC withdrew funding for the claimants concerning their autism claims, concluding that the claimants were not likely to be able to demonstrate that the MMR vaccinations caused their autism. *Id*. at paras. 1, 7. (*See also* Tr. 1116A-1120.) Subsequently, in the absence of LSC funding, most of the autism claimants decided not to pursue their claims any further. *Sayers*, 2004 WL 1640222 at paras. 2, 24, 31. (*See also Hazlehurst*

(continued...)

manufacturers, he was asked to assess the validity of the Unigenetics laboratory's findings as reported in the Uhlmann article. Dr. Bustin was given physical access to the Unigenetics laboratory, was able to inspect and utilize the lab's equipment, and had access to all of the data compiled by the Uhlmann researchers in their study. (Tr. 1962A, 1964A-66A; Ex. WW, pp. 3-6.) Dr. Bustin spent more than 1500 hours in his analysis of the Uhlmann work. (Tr. 1967A.) He prepared two extensive reports that were filed with the court presiding over the British litigation. (Exs. WW, XX.)

Dr. Bustin concluded that the work of the Unigenetics lab with respect to the detection of measles virus was severely flawed, and should not be considered reliable. (*E.g.*, Ex. WW, pp. 7, 58, 61; Ex. XX, pp. 7, 53; Tr. 2035-37.) In addition to the lengthy expert reports that he prepared for the British litigation, he prepared an expert report (Ex. UU) for this case, and he also testified at length during the evidentiary hearing in this case (Tr. 1933-2069). In his reports and his testimony, Dr. Bustin identified many different problems with the Unigenetics laboratory and its work.

Dr. Bustin explained that proper use of "controls" is crucial to determining whether a PCR technique is working properly. "Positive controls" are samples that definitely *do* have the targeted gene, while "negative controls" are samples that definitely *do not* include the targeted gene. Only if the positive controls routinely test positive in a lab's PCR testing, and negative controls routinely test negative, can one be confident that the lab's test is working accurately. (Tr. 1938A-40.) But when Dr. Bustin closely examined the results of the Uhlmann study, he found that in approximately one-third of Unigenetics' testing procedures ("runs"), the lab obtained *positive* results for their *negative* controls. Dr. Bustin testified that this result meant that contamination was rampant in the Unigenetics lab. (Tr. 1995-96; Ex. WW, pp. 50-52.)

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[69](...continued)
Tr. 661A.) (As far as I am aware, the British court has not issued any formal ruling concerning any of the autism claims.)

A number of the experts presented in this case, by both the petitioners and the respondent, previously prepared expert reports for use in that British litigation. Those experts included petitioners' experts Dr. Kinsbourne, Dr. Kennedy, Dr. Byers, and Dr. Krigsman, along with respondent's experts Dr. Bustin, Dr. Rima, and Dr. MacDonald. Apparently, by order of the British court, experts who submitted such reports to the British court are not at liberty to divulge copies of those reports, and have restrictions as to the extent to which they may publicly discuss the contents of those reports. Those expert reports, and other documents that were submitted to the British court, remain in a sealed file under the control of that court.

As will be discussed below (p. 79), there is a procedure by which access to documents from the sealed file may be sought from the court. In the spring of 2007, respondent's counsel petitioned the British court and obtained copies of four expert reports that were filed with the British court by experts for the vaccine manufacturers. Copies of two of those reports, by Dr. Bustin, were filed into the record of this case (Exs. WW and XX), while copies of the other two reports, by Dr. Peter Simmonds and Dr. Rima, were filed into the record of the *Snyder* case (*Snyder* Exs. P and S).

Dr. Bustin explained a particular problem with the physical layout of the laboratory, which might well have resulted in the contamination that he believes to have plagued the Unigenetics laboratory. (Tr. 2021-23.) In addition, he discussed problems with the laboratory's notebooks, which describe in detail their testing procedures. Those notebooks, he discovered, had been altered after the fact, which was certainly improper and perhaps fraudulent. (Tr. 2026-2032; *see also* Ex. WW, pp. 35, 37-38.)

Dr. Bustin also testified that the Unigenetics Ltd. laboratory was not accredited, and that the laboratory declined to participate in a quality-control program,[70] so that "there was never any independent quality assessment made of any of the work that was carried out by Unigenetics." (Tr. 2034, 2057A.)

In addition, Dr. Bustin pointed out serious problems with the physical equipment that he observed in the Unigenetics lab, problems that would have affected the PCR testing results. (Tr. 1998-2000; Ex. WW, pp. 15-16.) He noted inconsistencies in the Unigenetics laboratory procedures. For example, sometimes the guidelines of the testing equipment manufacturers were not followed, which could erroneously make negative results appear to be positive results.[71] (Tr. 2002, 2005, 2009-10A.) As another example, the technicians on some occasions used twice as much of a certain "probe" substance as on other occasions. (Tr. 2025A.) Dr. Bustin also pointed out problems with the quality of the RNA being used for the testing, concluding that about one-third of the samples used by Unigenetics should have been considered unacceptable for PCR because of the poor quality of the RNA. (Tr. 1996-98; Ex. WW, pp. 17-19.)

Dr. Bustin explained that some types of tissue samples are better suited for PCR testing than others, and that Unigenetics received two types of tissue samples, "fresh-frozen" and "formalin-fixed." (Tr. 1970A; Ex. WW at 18.) He testified that on a number of occasions the Unigenetics testing yielded equivalent outcomes from fresh-frozen and formalin-fixed samples, a result that could only occur if the test was detecting a contaminant, rather than measles virus. (Tr. 1970A-73, 2035; Ex. UU, p. 6; Ex. WW, p. 18.)

Dr. Bustin noted that on two occasions, the Unigenetics technicians failed to perform the necessary "reverse-transcription" procedure, and yet still reported positive results for detection of measles virus on each occasion. (Tr. 1980-83A.) Dr. Bustin stated that such a result is impossible,

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[70]A published article confirmed that Unigenetics had declined to participate in the quality-control program. M. Afzal et al., *Comparative Evaluation of Measles Virus-Specific RT-PCR Methods Through an International Collaborative Study*, 70 J. MED. VIROLOGY 171 (2003). (Ex. V, Att. 1, p. 175.)

[71]Dr. Bustin's testimony suggested the possibility that the Unigenetics personnel might have been *deliberately* using incorrect settings on their testing machine, in order to generate "positive" results that might support the MMR/autism causation theory. (Tr. 2009-11A.)

so that the supposedly positive results can only be explained by contamination in the laboratory. (Tr. 1975A-76A; 1982-83A.)

Another problem described by Dr. Bustin involved "discordant replicates"--*i.e.*, instances in which the Unigenetics laboratory tested two samples from the same source, which should have either been both positive for measles virus or both negative, but instead one tested positive and one negative. (Ex. WW, pp. 43-48; Tr. 2013-14.) Dr. Bustin stated that it is inappropriate for a lab in such a situation to report the biopsy as either positive or negative; instead, the samples should be tested again. (Ex. WW, p. 43.) Yet Unigenetics repeatedly reported positive results in such situations, which Dr. Bustin described as an "unacceptable scientific practice." (Ex. WW, p. 9, fourth para.)

Dr. Bustin's overall conclusion, after his complete assessment of the Unigenetics work,[72] was that it is "clear" that, in its testing for measles virus RNA, that laboratory was erroneously detecting a DNA *contaminant*, and *not* detecting measles virus RNA. (Tr. 2035-37.) He stated that "I do not believe there is any measles virus in *any* of the cases they have looked at." (Tr. 2036, emphasis added.) He added that this opinion extended specifically to the Unigenetics test result reported for Michelle Cedillo. (Tr. 2037.)

3. Dr. Rima

Respondent also relied upon the testimony of Dr. Bertus Rima, whose expert reports and hearing testimony were presented in the *Snyder* case.[73] (*Snyder* Exs. S and V; *Snyder* Tr. 824A-938A.) Dr. Rima is a Ph.D. virologist with extensive experience in studying the measles vaccine and in PCR testing. (*Snyder* Tr. 826A-829A, 851A-52A.) Like Dr. Bustin, Dr. Rima was retained by the vaccine manufacturers involved in the above-described British litigation, and in that capacity obtained access to the Unigenetics laboratory and its records. (*Snyder* Tr. 849A-50A, 853A-54A.) Dr. Rima prepared a lengthy expert report for the British court. (*Snyder* Ex. S.) Like Dr. Bustin, Dr. Rima stated the opinion that the measles virus detection results reported by the Unigenetics laboratory, both in the Uhlmann study and in the testing of individuals such as Michelle Cedillo and Colten Snyder, were invalid and unreliable. (*See*, *e.g.*, *Snyder* Tr. 846A, 902, 928A-29A; *Snyder* Ex. S, part B, pp. 75-76.)

A number of Dr. Rima's observations, concerning severe problems he saw with the work of the Unigenetics laboratory, were similar to those of Dr. Bustin. For example, Dr. Rima confirmed Dr. Bustin's description of an alteration made in one of the Unigenetics laboratory notebooks.

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[72]In his lengthy expert report filed in the British litigation, Dr. Bustin also pointed to many other problems that he found with the Unigenetics work, too numerous to list here. (Ex. WW.)

[73]An affidavit of Dr. Rima was filed into the record of this *Cedillo* case on May 22, 2007, attached to respondent's "Motion *In Limine*." However, his opinion was presented in a much more complete fashion in the *Snyder* case, so I quote here from those materials.

(*Snyder* Tr. 855A-56A.) He noted the fact that in certain instances the Unigenetics technicians had failed to do the necessary step of "reverse transcription," yet still obtained a positive finding for measles virus RNA, an impossibility that indicated that the positive results could only have been a result of contamination. (*Snyder* Tr. 897A-98A.) Dr. Rima also agreed with Dr. Bustin's observation that when Unigenetics obtained similar results from "fresh-frozen" samples and "formalin-fixed" samples, it was a nonsensical result that could be explained only by contamination. (*Snyder* Tr. 898A.) In addition, Dr. Rima agreed with Dr. Bustin that Unigenetics seriously erred in the way in which it treated "discordant replicates"--instances in which testing of two samples from the same source yielded one positive and one negative result. Dr. Rima stated that the Unigenetics practice of simply ignoring the negative result in such situations "is a wholly unscientific practice and indicates bias in the interpretation of these results." (*Snyder* Ex. S, part B, p. 45, para. 4.31; *see also Snyder* Ex. S, part B, p. 19, para. 3.35; *Snyder* Tr. 865A.)

Dr. Rima also pointed to additional reasons for concluding that contamination was the reason for Unigenetics' positive findings of measles virus. He pointed out that perhaps the most risky situation with regard to contamination in a laboratory is when the lab uses large numbers of "plasmids" of a particular virus, and noted that the Unigenetics laboratory in fact did utilize measles virus plasmids in its work, making it seem quite possible that contamination from plasmids was the reason for the Unigenetics positive findings of measles virus. (*Snyder* Tr. 853A.) Further, he pointed out that in many instances in the Unigenetics testing, samples that were located closer to a positive control on the testing plate were more likely to be found positive, a probable result of contamination. (*Snyder* Tr. 879A-80A; *Snyder* Ex. S, part B, p. 19, para. 3.34.)

In short, Dr. Rima testified that a number of measles experts, like himself, had studied the efforts of the Unigenetics laboratory to detect measles virus in human tissue, and concluded that the Unigenetics testing "simply does not work"--*i.e.*, such testing is *not* able to *reliably* detect whether measles virus is present. (*Snyder* Tr. 928A-29A.) Dr. Rima found the Unigenetics measles testing results to be completely unreliable and invalid. (*Snyder* Tr. 846A, 902, 928A-29A; *Snyder* Ex. S, part B, pp. 75-76.)

Dr. Rima added that this opinion applies to all of the Unigenetics testing for measles virus, including the test performed on Michelle Cedillo. (*Snyder* Tr. 903.)

4. Dr. MacDonald

Another of respondent's experts was Dr. Thomas MacDonald, who filed an expert report and testified in the *Hazlehurst* case. (*Hazlehurst* Ex. A; *Hazlehurst* Tr. at 603-76A.) Dr. MacDonald is a Ph.D. immunologist who specializes in the immunology of the human gut (intestines). (*Hazlehurst* Ex. A, p. 1; *Hazlehurst* Tr. at 603-11A.) Like Drs. Bustin and Rima, Dr. MacDonald was an expert in the British MMR/autism litigation described above. (*Hazlehurst* Tr. at 611A.) Unlike the situation with respect to Drs. Bustin and Rima, however, Dr. MacDonald's expert report filed in the British litigation has *not* been unsealed by the British court, and, therefore, has not been filed into the record of this case or the *Snyder* or *Hazlehurst* cases. Therefore, Dr. MacDonald, as

an expert who was apparently given access to medical records of the claimants in the British litigation, was not free to testify concerning the Unigenetics testing records of those claimants. (*Id*. at 650A.)

Dr. MacDonald did, however, provide an opinion concerning the validity of the Unigenetics testing. He stated that the Uhlmann article was "one of the worst" medical journal articles that he has ever seen (*Hazlehurst* Tr. at 650A), which was published in the "worst journal that has ever been seen, a journal which is subsequently no longer in existence" (*id*. at 649A). He opined that the Unigenetics testing was *not* credible or reliable. (*Id*. at 650A.)

Dr. MacDonald's assignment in the British litigation was to look at one particular type of PCR testing among the techniques used by Unigenetics. Concerning his analysis of that technique as used in the Uhlmann study, he wrote as follows:

> I have had the opportunity to examine the majority of those so-called positive in cell-PCR slides and discovered worrying discrepancies between the methodologies reported in the Uhlmann et al paper and what was actually done in the lab. The technique is completely unreliable with an unacceptably high experimental failure rate, many of the control sections were destroyed during the processing, the wrong technical controls were being used, and the claims of positivity or negativity were subjective and spurious. In cell-PCR does not detect measles virus in the lymphoid tissue of children with autism.

(*Hazlehurst* Ex. A, p. 14.)

E. Analysis

As noted above, after considering all of the evidence, I conclude that the Unigenetics testing for the detection of measles virus was *not* reliable. I conclude that it is *not* likely that Unigenetics ever reliably detected the presence of measles virus, in the case of Michelle Cedillo, in the Uhlmann study, or in the other children whose specimens were tested by that laboratory. I found the testimony of the respondent's experts concerning this point to be far more persuasive than that of the petitioners' experts. I will detail the main reasons for my conclusion below.

1. Failure of other researchers to replicate the Unigenetics findings

In science, when one research team makes a finding concerning an important issue, the scientific community usually does not immediately endorse that finding as accurate. Instead, the first research team publishes its results, explaining its experimental procedures. Then, other research teams will attempt to "replicate" the first group's findings, by utilizing either the same experimental techniques as the first team, or other experimental procedures. Only if different research teams are able to reach the same results, after their own experiments, does the scientific community become likely to accept the finding as probably true. (*E.g.*, *Snyder* Ex. S, part B, p. 23, para. 3.49.) This is especially true in PCR testing, in which there is a great possibility that contamination in a laboratory can create "false positives." (*Id*.)

In the case of the Unigenetics testing for detection of measles virus in humans, the Unigenetics findings were, in fact, published in the Uhlmann article. Then, two other research teams did perform similar experiments in an attempt to replicate the results of the Uhlmann study, and those teams published their own results. But those other research groups have *not* confirmed the Uhlmann findings; instead, those groups reached results that, to the contrary, *strongly cast doubt* on the validity of the Unigenetics study.

One of the attempts to replicate the Uhlmann study, as noted above, was the Afzal 2006 study. Afzal and colleagues tested certain blood cells, known as "PMBCs," of 15 children suffering from autism spectrum disorders, all of whom had received the MMR vaccine, for measles virus. The researchers utilized a number of testing methodologies, but found none of the samples positive for measles virus by any test. (Ex. T, Att. 2; Tr. 1848.)

The second study was also published in 2006, by D'Souza and colleagues. As also detailed above, the D'Souza researchers tested the blood cells (PMBCs) of 88 children, 54 diagnosed with ASD and 34 developmentally normal, for measles virus. (Ex. T, Att. 6, p. 1664.) At least 51 of the 54 ASD children, and at least 31 of the 34 developmentally normal children, had received the MMR vaccine. (*Id*. at 1669.) The authors' ultimate conclusion was that *none* of the studied children, in either the ASD group or the developmentally normal group, in fact had persisting measles virus infection. (*Id*. at 1670-71.)

Thus, two independent research teams have made efforts to replicate the Unigenetics results, but have failed to do so. This fact alone gives substantial reason to doubt the validity of the Unigenetics testing. (Moreover, the work of the D'Souza team has not only failed to replicate the Unigenetics findings, but has also added an *additional* strong reason to doubt the validity of the Unigenetics testing, as I will detail in the following subsection.)

With respect to this issue of replication, witnesses for both parties have reported that one British research scientist, Dr. Cotter, did attempt, in the context of the above-described British litigation, to replicate the Uhlmann team's work, but those witnesses differ concerning the *results* of Dr. Cotter's testing. Petitioners' expert Dr. Kennedy, during hearing testimony, stated that he

attended a meeting during which Dr. Cotter orally reported that his testing reached results similar to those reported by Uhlmann. (*Snyder* Tr. 347A-49A.) Petitioners argue, thus, that Dr. Cotter's alleged results *support* the validity of the Unigenetics testing. (P2, p. 13; P4, p. 9.)

However, two of respondent's experts directly contradicted Dr. Kennedy's statements in this regard. Dr. Rima testified that Dr. Cotter was asked by the claimants' attorneys to attempt to replicate the Uhlmann work, but that when he did attempt to do so, he *failed* to obtain any positive results. (*Snyder* Tr. 894A-95A, 897A.) Similarly, Dr. Bustin stated that Dr. Cotter's replication efforts failed to yield any positive results. (Tr. 2015A-16.) Accordingly, respondent argues that Dr. Cotter's work is yet more evidence of the *unreliability* of the Unigenetics testing.

Given this very limited record concerning Dr. Cotter's work, I conclude that it is simply impossible to draw any conclusions *either way*. No records of Dr. Cotter's work, and no testimony or statement from him, have been presented. No conclusions can reasonably be drawn.

What is undisputed, however, is that Dr. Cotter's work, whatever its result, has never been published. On the other hand, the Afzal and D'Souza groups did, in fact, *publish* their work, subjecting it to scientific scrutiny. This publication factor affords good reason to place reliance upon their results. *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 593-94 (1993). I do find it appropriate to place reliance on the published results of the Afzal and D'Souza studies, while I can draw no conclusions, in either direction, from the testimony concerning Dr. Cotter.[74]

2. Sequencing

Another important reason for my conclusion concerns a procedure known as "sequencing." As noted above, when testing for the presence of genetic material of a certain target, sequencing is the ultimate test that can give assurance that the testing has actually identified the genetic material in question, and not some other sort of genetic material. (Tr. 1853A.) Petitioners' own expert

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[74]One other scientist involved in the British litigation, Dr. Peter Simmonds, also tried to replicate the findings of the Uhlmann study. He performed PCR testing on samples from claimants from the British litigation discussed above, but the results of his testing were different from those of Unigenetics. While Unigenetics reported positive results for measles virus in some of those samples, Dr. Simmonds found all of the samples to be *negative* for the presence of measles virus. (*Snyder* Tr. 896A-97A; *Snyder* Ex. P, see especially p. 43.) Dr. Simmonds' own lengthy report, filed into the *Snyder* record, describes those efforts. (*Snyder* Ex. P.) However, the results of Dr. Simmonds' effort have *not* been published, to my knowledge. (It seems likely that Dr. Simmonds was not at liberty to publish this work, because it was performed for the British court.) Further, Dr. Simmonds did not testify in *Cedillo*, *Snyder*, or *Hazlehurst*. Accordingly, in my resolution of this issue, I have *not* accorded heavy weight to Dr. Simmonds' results. On the other hand, we do have Dr. Simmonds' *lengthy written report*, which provides even more detail concerning his replication efforts than would likely be contained in a published paper. Therefore, Dr. Simmonds' failure to replicate the Uhlmann findings does add at least some additional reason to doubt the reliability of the Unigenetics testing efforts.

Dr. Hepner acknowledged that sequencing is the "gold standard" for assuredly identifying the presence of the targeted material, and petitioners' other expert, Dr. Kennedy, agreed that sequencing is important. (Tr. 673A, 824A.) Both Dr. Ward and Dr. Bustin testified that in developing a new PCR test for a particular target, as Unigenetics was attempting to do, a laboratory needs to perform the sequencing step on some of the samples that its new test has identified as containing the target, to ensure that the test is identifying the target and *only* the target. (Tr. 1856A, 1945A.) Dr. Rima, too, testified that sequencing is a "required" step in such a testing process, in order to confirm the identification of the target and ensure that the test is not a "false positive." (*Snyder* Ex. S, part B, p. 21, para. 3.41; *see also* p. 46, para. 4.34.) He added that because of the high risk in PCR testing of contamination causing false positives, it is especially important to carry out sequencing. (*Id*. at p 22, para. 3.47.) And Dr. Kennedy acknowledged that "anyone that was doing PCR at the time, * * * you knew that you needed to sequence to verify it." (Tr. 825.)

In the case of the measles virus detection testing performed by the Unigenetics laboratory, however, there is no persuasive evidence that Unigenetics ever performed the sequencing step to confirm their theory that they were identifying measles virus. The Uhlmann article does *not* state that sequencing was undertaken. (Ex. 63, Tab U.) Both Dr. Bustin and Dr. Rima had access to the Unigenetics records, and neither mentioned any records of sequencing. Dr. Ward confirmed that there is no evidence that Unigenetics ever performed sequencing to confirm its allegedly positive measles detection results. (Ex. BB, p. 12; Tr. 1857A.) One of petitioners' two experts concerning this issue, Dr. Hepner, acknowledged flatly that the Uhlmann researchers "did not" do sequencing. (Tr. 673.) And petitioners' other expert, Dr. Kennedy, acknowledged that, to his knowledge, no sequencing data has never been *published* by Unigenetics. (Tr. 826.)

Moreover, when other researchers did perform the sequencing procedure, in conjunction with attempts to identify measles virus using PCR techniques similar to those used by the Unigenetics laboratory, their results cast grave doubt upon the reliability of the Unigenetics techniques. First, as noted above, the D'Souza 2006 research team used the Uhlmann primers in PCR testing on human blood cells, and did obtain positive results for measles virus on most of the samples tested. But when the sequencing procedure was then performed, it turned out that the material identified by the PCR test as measles virus material was, in fact, *not* measles virus, but human genetic material. (Ex. T, Att. 6, p. 1671; Tr. 1853A, 1856A.)

A similar result occurred when the D'Souza team later tested the Uhlmann PCR primers on samples of intestinal (gut) tissue. That is, they obtained some "positive" results purporting to detect measles virus, but when they completed the sequencing procedure, once again the results showed human genetic material, not measles virus material. (Tr. 1859-61; Ex. BB, p. 12; Ex. BB, Tab 29.)

PCR testing for measles virus was also performed by Nicholas Chadwick, who in 1996 was a Ph.D. student working in a London laboratory for Dr. Andrew Wakefield. (Tr. 2283-84; Ex. QQ, pp. 1-2.) Chadwick performed PCR testing on human gut biopsy material for measles virus detection, and, although the samples usually tested negative, occasionally he did obtain positive

results. (Tr. 2284; Ex. QQ, paras. 8, 12.) But when he then performed sequencing on those positive samples, the sequencing revealed that all had been *false* positives. (Tr. 2284; Ex. QQ, para. 12.)

In this regard, it is true that petitioners' expert Dr. Kennedy did testify that he was told orally by Dr. Sheils of Unigenetics that the Uhlmann authors *had* done sequencing that confirmed their positive findings of measles virus in the Uhlmann study children. (Tr. 824A.) However, I simply find it to be quite unlikely that such sequencing was in fact done. The Uhlmann article itself does *not* mention sequencing. As Dr. Kennedy himself admitted, no sequencing data was ever published. (Tr. 826.) The petitioners have not offered any statements from any of the 11 Uhlmann article authors to verify Dr. Kennedy's assertion that sequencing was done. Moreover, the petitioners have failed even to *suggest* any reason *why* the Uhlmann authors might have actually successfully done sequencing, yet never published the data. And, given how much public attention has been given to the MMR/autism controversy, it simply seems extremely unlikely that the Uhlmann authors would have failed to publish their sequencing work had they actually done it as Dr. Kennedy describes. Accordingly, I *cannot* credit the assertion that Unigenetics conducted sequencing, confirming a finding of measles virus in the tested samples, but never published such work.

In short, the evidence concerning sequencing provides very important evidence that the Unigenetics testing should *not* be considered reliable, in two respects. First, the failure of Unigenetics to ever publish any sequencing data, to confirm that laboratory's alleged findings of measles virus in their testing of human tissue, is very damaging by itself. As Drs. Ward, Rima, and Bustin persuasively argued, when PCR researchers devise a new test, sequencing is a necessary step in order to have any degree of confidence in the result. Unigenetics' failure to publish sequencing data in this instance means that there is simply no reason to have confidence in their results. As Dr. Ward added, the lack of sequencing by Unigenetics was a "fatal flaw" in their work. (Tr. 1912A.)

Second, as explained above, when *other* researchers (*i.e.*, the D'Souza group and Dr. Chadwick) obtained purportedly positive findings of measles virus using PCR techniques, the follow-up sequencing procedures proved, in fact, that any apparently positive results for detection of measles virus by those techniques were in fact *false positives*.

In short, the evidence concerning sequencing shows very strongly that the Unigenetics results must be considered unreliable and invalid.

3. Problems with Unigenetics procedures, facilities, and equipment

As explained above, Drs. Bustin and Rima had full access to the Unigenetics laboratory, equipment, and records, and both of those highly-qualified experts pointed out a host of severe problems with Unigenetics' facilities, equipment, and procedures. I have already detailed above some of the problems pointed out by those experts (see pp. 49-53 above), and will not repeat them here. I simply note that I found both witnesses to be sincere and persuasive, so that all of those

problems identified by the two experts give me another strong reason to doubt the validity of the Unigenetics testing.

Concerning this matter, the testimony of Drs. Bustin and Rima was also supported by the testimony of Dr. MacDonald. Dr. MacDonald, as noted above, also was an expert witness in the British litigation, and also had access to the Unigenetics records and facilities. (*Hazlehurst* Tr. 650A; *Hazlehurst* Ex. A, p. 14.) Dr. MacDonald commented only very briefly concerning this issue. But he reported that in the particular type of PCR testing that he examined, the Unigenetics technique was "completely unreliable with an unacceptably high experimental failure rate, * * * the wrong technical controls were being used, and the claims of positivity or negativity were subjective or spurious." (*Hazlehurst* Ex. A, p. 14.) Dr. MacDonald's comments, thus, while extremely brief and undetailed, do provide at least some support for the conclusions of Drs. Bustin and Rima about the Unigenetics procedures.

Another important problem with the Unigenetics' work was the failure to use the procedure of "blinding" in performing the Uhlmann study. "Blinding" means that the laboratory technicians do not know whether the particular samples that they are analyzing are from the patient group of interest (in the Uhlmann study, autistic children), or the "control" group (in the Uhlmann study, the non-autistic children). In scientific experiments, blinding is "critical," to prevent conscious or subconscious biases, or the desire to reach a certain result, from affecting the results. (*E.g.*, 669-70, Tr. 2863.) The Uhlmann article did not state whether the technicians were blinded, but respondent's expert Dr. Griffin stated that if blinding were used, that would have been noted in the article. (Tr. 2866.) Respondent's expert Dr. Ward, who has performed PCR experiments himself, confirmed that his interpretation of the Uhlmann study was that it was not blinded. (Tr. 1846.)

I conclude that the Uhlmann study likely was *not* blinded, and that such failure to use the blinding procedure provides another strong reason to doubt the reliability of the Unigenetics testing reported in that study.

To be sure, I note that the petitioners' two witnesses concerning this general issue, Drs. Hepner and Kennedy, did try to defend the Unigenetics laboratory against the criticisms of Dr. Bustin and Dr. Rima. Both Dr. Hepner and Dr. Kennedy made general statements to the effect that, in its measles virus detection work, the Uhlmann team used appropriate controls, appropriate operating procedures, and appropriate steps to minimize the possibility of contamination. (Ex. 63, pp. 1-3; Ex. 110, pp. 7-8; Tr. 610A-28.) In addition, Dr. Kennedy also described a meeting that he attended with several other medical scientists, involving a discussion of the work of the Unigenetics laboratory that resulted in the Uhlmann paper. He stated that during that meeting he and the other scientists asked the Unigenetics representative, Dr. Sheils, many questions about the testing procedures, and that he and the other scientists came away with the impression that the testing was valid. (Tr. 808-17, 824A-25, 844-48, 851-55; *Snyder* Tr. 333A, 344A-45A, 386A-89A.)

However, after full consideration, I found the efforts of Drs. Hepner and Kennedy to defend the Unigenetics work to be largely ineffective. Their testimony was simply too summary and

nonspecific to answer the criticisms leveled by Drs. Bustin and Rima, which were specific and detailed.

In this regard, I note that I have considered Dr. Kennedy's testimony concerning the meeting described above. I do not doubt that such a meeting took place, that Dr. Sheils participated, and that Dr. Kennedy and the others questioned her about the Unigenetics work in question. But I do not find that this testimony from Kennedy gives me a strong reason to conclude that the Unigenetics testing can be considered reliable. The meeting described by Dr. Kennedy was not a meeting of disinterested scientists. Rather, that meeting was called by the attorneys representing those claimants in the British litigation described above (see fn. 69) who contended that their autism was caused by the MMR vaccine. The attending scientists apparently were individuals who either had already agreed to serve as paid experts for those claimants, or who were being recruited to serve as paid experts. (Tr. 809-810.) Thus, even to the extent that one accepts Dr. Kennedy's assertion that the group was favorably impressed by Unigenetics work, the fact that such a group reached such a conclusion is not a particularly strong item of evidence that the Unigenetics testing was reliable.

Further, Dr. Kennedy has told us very little about *exactly what* Dr. Shiels said that so impressed the group. No transcript or notes of the meeting have been produced. None of the other participants in the meeting have provided confirmation of Dr. Kennedy's account.

Given all of those circumstances, and in light of all of the other evidence of record in this case *casting doubt* on the validity of the Unigenetics work in question, I simply cannot accept Dr. Kennedy's summary assurance about this meeting--*i.e.*, his testimony to the effect that "we asked lots of questions, we were satisfied with Dr. Sheils' answers"--as strong evidence that the Unigenetics testing was valid. In the context of all of the evidence concerning that issue in the record before me, I cannot find that Dr. Kennedy's testimony about the meeting is sufficient to persuade me to simply ignore all of the specific criticisms of Drs. Bustin and Rima and to conclude that the Unigenetics testing was reliable.[75]

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[75]Another item of evidence is a letter from Dr. Michael Oldstone, a medical doctor specializing in viral immunobiology. (*Snyder* Ex. AA.) Petitioners' expert Dr. Kennedy acknowledged that Dr. Oldstone is a "very eminent virologist" with many publications in that field. (*Snyder* Tr. 393A.) Dr. Oldstone had been asked to consider engaging in a collaborative research project with Drs. Wakefield and O'Leary relating to the Wakefield MMR/causation theory. (*Id*.; *Snyder* Tr. 954A.) To help him decide whether to participate, Dr. Oldstone decided to test the performance of the O'Leary laboratory in detecting measles virus. He prepared samples, some of which were infected with measles virus, some not, and sent them to Dr. O'Leary for testing. Dr. O'Leary's assessments were wrong about 20 percent of the time during each of two rounds of testing. (*Snyder* Ex. AA; *Snyder* Tr. 954A-958A.) Dr. Oldstone then decided not to engage in the collaborative project with Dr. O'Leary. (*Snyder* Ex. AA; *Snyder* Tr. 958A.) Dr. Oldstone attempted to have the results of his test of the O'Leary lab published, but the group that gave Oldstone the funding to prepare the samples prohibited him from doing so. (*Snyder* Tr. 954A, 958A.) Dr. Ward explained that the 20 percent error rate would be considered completely unacceptable ("wildly

(continued...)

4. Petitioners' arguments

With respect to this issue of the validity of the Unigenetics testing for measles virus, petitioners in their briefs have raised several arguments. Some of those arguments I have already addressed above; others I will address here.

a. Dr. Hepner's criticisms of the Afzal and D'Souza studies

One of the petitioners' primary arguments concerning this issue (see P1 at 140-41, 151-53) has been that the Afzal 2006 and D'Souza 2006 studies were flawed as attempts to replicate the Uhlmann work. Petitioners' expert Dr. Hepner pointed to two differences between the Uhlmann study and both the Afzal 2006 and D'Souza 2006 studies, which she found to be significant. First, while Uhlmann tested *intestinal* (gut) tissue, Afzal and D'Souza tested *blood cells* ("PMBCs"). Second, while Uhlmann tested children who had a "developmental disorder" *plus* some type of gastrointestinal symptoms, both Afzal and D'Souza tested children who were autistic but did not have gastrointestinal problems. (Ex. 63, p. 4; Tr. 629A-31A.)

Respondent's experts, however, responded effectively to this argument. As to the Afzal and D'Souza groups' decision to test blood cells instead of intestinal tissue, respondent's experts stated that those researchers were unable to readily obtain a sufficient number of intestinal biopsy samples from autistic children. They explained that it would have been unethical to take intestinal biopsies from autistic children merely for such a research purpose, in the absence of a demonstrated need for gut biopsy because of actual intestinal problems. (*See*, *e.g.*, Tr. 1858A-59A, 1900A-01A; *Snyder* Tr. 895A-96A, 938A.) But, more importantly, respondent's experts argued that testing blood cells instead of gut tissue was a *fair* and *appropriate* way to test the validity of the Uhlmann findings, for two reasons. First, Dr. Ward explained that if, in fact, as the Uhlmann group theorized, measles virus was replicating in the intestinal tissue of autistic children, then measles virus would necessarily have to be in those children's blood cells as well. (Tr. 1849-50.) Dr. Bustin and Dr. Rima agreed.

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[75](...continued)
inappropriate") for diagnostic testing of this type. (*Snyder* Tr. 956A.)

Petitioners' expert Dr. Kennedy attempted to answer Dr. Oldstone's letter, suggesting that it might have been the Oldstone laboratory that erred. (*Snyder* Tr. 335A-37A.) However, I found Dr. Ward to be persuasive in arguing that such a possibility is not likely, in light of Dr. Oldstone's 50-year history as a meticulous reknowned scientist. (*Snyder* Tr. 958A-60A.)

Because Dr. Oldstone himself did not testify, and because his data were not published (for whatever reason), I have not placed any reliance on this item of evidence. I merely note that this would simply amount to *another* reason to doubt the accuracy of the Unigenetics laboratory's measles virus testing.

(Tr. 1961; Ex. UU, p. 11; *Snyder* Tr. 881A-82A.) None of the petitioners' experts persuasively refuted this point.[76]

Second, Dr. Ward also pointed out another reason why testing the blood cells was an appropriate way to test the validity of the Uhlmann study. He noted that the D'Souza 2006 study demonstrated, through its sequencing data, that the Uhlmann primers were *not* effective at identifying measles virus *only*. The Uhlmann primers were, instead, "nonspecific"--*i.e.*, they erroneously identified, as measles virus, material that was in fact human genetic material. (Tr. 1850-57; Ex. BB, p. 12; *Snyder* Tr. 964A-65A.) He pointed out that if those primers give "nonspecific results" in *any* human biologic material (*i.e.*, blood cells), then they are suspect to give nonspecific results in *all* biologic materials (*e.g.*, gut tissue). (Tr. 1858A.) Petitioners did not attempt to refute this specific point.

Next, the testimony from respondent's experts, discussed above, also makes it clear that Dr. Hepner is mistaken in the *second* part of her argument, when she argues that the Afzal 2006 and D'Souza 2006 studies should be disregarded because they studied autistic children without regard to gastrointestinal dysfunction, while Uhlmann studied children with both a developmental disorder *and* gastrointestinal dysfunction. That is, the work of the D'Souza group in its 2006 and 2007 articles demonstrates that it *doesn't matter* whether the Uhlmann group studied children with or without gastrointestinal dysfunction, because the D'Souza group showed, with its sequencing data, that the Uhlmann primers *simply are not specific to measles virus only*. The Uhlmann testing, rather, was erroneously identifying human genetic material as measles virus. As Dr. Ward pointed out without refutation, if primers give nonspecific results in *one* type of biologic material, such primers are suspect in *all* types of material. (Tr. 1857A-58A.)

I find that respondent's expert evidence in this regard was persuasive, and that such evidence convincingly refutes this argument of Dr. Hepner.

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[76]Petitioners' expert Dr. Kinsbourne stated that, under his causation theory, the measles virus would travel through the body via the bloodstream. (*E.g.*, Tr. 1085, 1135A, 1139.) Therefore, said Dr. Ward, if Dr. Kinsbourne's theory is right, then the virus should be found in the blood as well as the intestines and brain. (Tr. 1849-50.) To be sure, Dr. Kinsbourne did state that it was a "possibility" that at times the virus would be present only in gut and brain, but not in the blood. (Tr. 1141-43.) But Dr. Kinsbourne did not explain *why* that possibility could occur. I found Dr. Ward to be persuasive concerning this point, in testifying that, if Dr. Kinsbourne's causation theory is correct that a persistent measles virus infection is causing autism, then the presence of measles virus ought to be detectable in the blood.

Further, another of petitioners' experts, Dr. Hepner, acknowledged that if measles virus was present in the body, it could be in the blood. (Tr. 646-47.)

b. The O'Leary laboratory's general reputation

Another argument raised by petitioners involved Dr. Kennedy's testimony that the O'Leary laboratory *in general* has had a good reputation, frequently having its work published in peer-reviewed medical journals in recent years, and even winning an award.[77] (P1, pp. 155, 159, 253; Ex. 110, p. 7; Ex. 121, pp. 1-2; Tr. 738A-39, 818; *Snyder* Tr. 320A-21A, 344A; *Snyder* Ex. 30, p. 9.) This argument does have some appeal. Respondent has not demonstrated the existence of any problems with the O'Leary laboratory outside of the measles virus detection efforts that are relevant here.[78] It is, indeed, somewhat difficult to reconcile Dr. Kennedy's testimony, concerning the general work of the O'Leary laboratory, with the evidence in this case of severe problems in its measles virus detection efforts.

However, I conclude that the *overall* evidence weighs strongly in favor of a conclusion that, whatever the *general* caliber of the work of the O'Leary laboratory group, the group's *measles virus* detection work, done largely under the Unigenetics Ltd. name, simply is not reliable. The overall evidence specific to that measles virus detection issue is simply too strong to be outweighed by mere evidence of a good general reputation concerning other work.

In this regard, two further observations are relevant. First, as noted above, the measles virus detection work was done, at least for the most part, under the Unigenetics Ltd. name. Dr. Bustin testified that *Unigenetics Ltd.* was not accredited, and that Unigenetics Ltd. declined to participate in a quality control program, so that "there was never any independent quality assessment made of any of the work that was carried out by Unigenetics." (Tr. 2034, 2057A.) Significantly, petitioners never attempted to rebut that aspect of Dr. Bustin's testimony.

Second, the record also indicates that Unigenetics Ltd. is no longer in business, and there is no evidence that the O'Leary laboratory has ever published any work defending the reliability of the Uhlmann study, despite the criticism of that study. Thus, it seems that the O'Leary laboratory has *not* publicly defended the reliability of its efforts at measles virus detection during the early 2000s.

Accordingly, considering all of the evidence of record, I conclude that, *regardless* of whether the O'Leary laboratory might have a solid reputation with respect to its *other* work, nevertheless that laboratory's efforts to detect *measles virus* in the early 2000s were flawed and unreliable.

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[77]Dr. Kinsbourne made a comment to the same effect. (*Snyder* Ex. 29, p. 14.)

[78]I note that respondent's expert Dr. Griffin, when asked by petitioners' counsel about the general reputation of the O'Leary laboratory in the scientific community, replied that it was "not very good." (Tr. 2866-67.) But she was not asked whether she was aware of work by that laboratory in areas other than measles virus testing, so it is not clear if she was referring to any other work besides the measles detection efforts. Therefore, I do *not* place any reliance on this particular statement by Dr. Griffin.

c. The Walker study

Petitioners have also relied on a study that is currently in progress, conducted by Dr. Hepner and several others, often described as the "Walker study." (*See* Ex. 59, Tab K; P. Trial Ex. 3.) Dr. Hepner stated that the "preliminary data" from that study "present another step in support" of the proposition that the measles virus persists in the intestinal tissue of some autistic children. (Ex. 63, p. 5; *see also* Tr. 634A-35A.) After consideration of the Walker study and the testimony about it in the record of this case, however, I conclude that the study does *not* provide any substantial support to the proposition that the measles virus persists in the bodies of Michelle Cedillo or any other autistic individuals.

Dr. Hepner reported that she and three other researchers--Steve Walker, Jeff Segal, and Dr. Arthur Krigsman, the latter being another of petitioners' experts in this case--are engaged in a study similar to the Uhlmann study, in that their objective is to perform PCR testing for the detection of measles virus on intestinal biopsies of children with both developmental delay and gastrointestinal symptoms. (Ex. 63, p. 5; Tr. 634A-35A.) Dr. Hepner stated that the researchers generated "multiple primer sets" and "tested them for their specificity and sensitivity" in identifying the presence of measles virus. (Tr. 635A; Ex. 63, p. 5.) Dr. Hepner and Dr. Krigsman testified that the study, which began in 2003, is not yet complete, but that the group conducted some initial testing and presented "preliminary data" from the study at an autism-related conference in 2006, in the form of a "poster presentation" (literally, a poster board describing the study was set on an easel at the conference).[79] (Ex. 63, p. 5; Tr. 474A-75, 634A.) Dr. Hepner reported that of 82 biopsy samples tested in the study's initial testing, which all came from children with both "developmental delay" and "GI [gastrointestinal] symptoms," 70 tested positive for measles virus. (Ex. 63, p. 5.) She further stated, without explanation, that her group was able "to confirm[80] vaccine strain specificity" in some of the positive samples. (Tr. 635A.)

Petitioners, in their post-hearing briefs, have relied on the Walker study as supportive of their view that the Unigenetics measles virus testing should be considered reliable. (P1, pp. 141, 154-55, 242; P3, pp. 33-34.) After full consideration, however, I cannot agree.

First, two of respondent's experts, Dr. Ward and Dr. Bustin, each pointed to a number of flaws in the Walker study, based on the description in the poster presentation. (Tr. 1861-65; 1952A-59A.)

Moreover, a second important reason to discount the Walker study is the testimony of Dr. Hepner herself. Dr. Hepner stated that the initial data from her study were only "very preliminary

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[79] A copy of the material on the poster, describing the study, was filed as Petitioners' Trial Ex. 3, and an abstract (summary) of the poster presentation is filed as Ex. 59, Tab K.

[80] The transcript says "confer." I conclude, from the context, that Dr. Hepner likely said "confirm."

data." (Tr. 659.) She acknowledged that it would be inappropriate to "draw any conclusions" from those preliminary results. (Tr. 682.) She acknowledged that her group at this time is still attempting "to test this assay, to optimize the assay" (Tr. 660A)--*i.e.*, to *develop* the test to a point where they can *then* be confident that their test is yielding reliable results. Part of developing any such test is to use "negative controls"--*i.e.*, to test samples that are known to be free of the target, to make sure that the test is not erroneously identifying the target in samples that do not contain it. However, Dr. Hepner explained that her group is still at the point of developing their negative controls. (Tr. 658, 681.)

In short, Dr. Hepner was forthright in acknowledging that, in terms of drawing any conclusions with regard to the issue of the validity of measles virus testing, the preliminary data available from her study simply are "not useful at this time." (Tr. 659.)

In sum, it is clear that the Walker study must be disregarded. First, both Dr. Ward and Dr. Bustin pointed out a number of reasons why one cannot draw any conclusions from, or place any reliance on, the preliminary data from the Walker study. And even petitioners' expert Dr. Hepner, one of the study's own authors, has acknowledged that the preliminary data from the study are "not useful at this time." (Tr. 659.) Accordingly, I must agree with Dr. Hepner on this point. I conclude that the Walker study is *not* useful in deciding the issue of whether the Unigenetics measles virus detection testing was reliable.

d. Additional argument of Dr. Hepner concerning D'Souza study

Petitioners have also relied on another argument advanced by Dr. Hepner. (P1, p. 249.) Dr. Hepner pointed out that the D'Souza 2006 research group, when doing PCR testing using the Uhlmann primers, was *successful* in finding measles virus in the "positive controls"--*i.e.*, samples known to contain measles virus used in that study. She argues that this proves that the "Uhlmann primer sets are capable of amplifying the predicted MV [measles virus] target." (Ex. 120, p. 2.) This argument, however, misses the key point of the D'Souza 2006 article and Dr. Ward's testimony. The crucial point of the D'Souza 2006 article is *not* that the Uhlmann primers fail to identify actual measles virus when it *is* present, but that the Uhlmann primers *are nonspecific*, and thereby purport to identify measles virus when it is, in fact, *not* there. (*See*, *e.g.*, Ex. T, Att. 6, p. 1672; Tr. 1850, 1853A-58A; Ex. BB, p. 12; *Snyder* Tr. 964A-65A.)

e. Argument concerning viral protein and immunohistochemistry

Petitioners also assert that the Unigenetics laboratory found measles virus *protein* in the intestinal tissue of autistic children in the Uhlmann study, via a technique known as "immunohistochemistry." (P1, pp. 155-56, 159 fn. 156; P3, pp. 29-30; P4, pp. 7, 31-32.) In this regard, the petitioners rely, once again, on the testimony of Dr. Kennedy about information that he allegedly received orally from Unigenetics personnel. Dr. Kennedy testified that during his above-described meeting with Dr. Sheils of Unigenetics and other scientists in the course of the British MMR/autism litigation, Dr. Sheils stated that Unigenetics had detected the measles virus nuclear

protein, by immunohistochemistry, in samples "from autistic enterocolitis children."[81] (Tr. 744-45, 828A; Ex. 110, p. 8.)

The record concerning this point is confusing, because the issue was mentioned only briefly in the expert reports and expert testimony–-primarily, by Dr. Kennedy for petitioners (Ex. 110, p. 8; Tr. 744-45, 828A; *Snyder* Tr. 329A-30A), and by Dr. Rima for respondent (*Snyder* Tr. 849A, 914A-16A, 935A-36; *Snyder* Ex. S, part B, p. 44, paras. 4.25, 4.26). Dr. Rima stated at one point that the technique of immunohistochemistry "was not used in the Uhlmann paper." (*Snyder* Tr. 849A, line 16.) However, the balance of Dr. Rima's testimony indicates quite clearly that Dr. Rima understood that, according to the Uhlmann article, immunohistochemistry[82] *had* been used in the Uhlmann study. Dr. Rima's criticism, rather, was that the usage of immunohistochemistry was just *mentioned* in the article, with no *data* or *details* concerning the use of the technique being set forth in the paper. (*Snyder* Tr. 914A-16A, 935A-936.)

The record supports Dr. Rima's criticism. Dr. Kennedy in his testimony did not point to any specific part of the Uhlmann article, but my own examination of the article indicates that the use of immunohistochemistry was simply *mentioned*, without explanation, at four places. (Ex. 63, Tab U, pp. 84, 87, 88, 89.) However, I found nothing in the Uhlmann article stating that any immunohistochemistry work had actually *identified measles virus protein*. And Dr. Rima was certainly correct that there seems to be no substantial presentation of any *details* or *data* in the article regarding any immunohistochemistry work. Indeed, Dr. Kennedy himself acknowledged that the alleged immunohistochemistry *data* were *not* published anywhere. (Tr. 744.)

Petitioners did allege in one of their briefs that Figure 4E of the Uhlmann article (Ex. 63, Tab U, p. 88) "showed that protein was detected by the use of antibody CNA 42 by the O'Leary group." (P3, p. 29.) It is true that the words "immunohistochemistry with monoclonal antibody CNA42" appear in the caption to Figure 4E. However, as far as I can tell, that caption does *not* indicate that *measles protein was detected*--the word "protein" does not appear. Moreover, neither Dr. Kennedy nor any other expert witness for petitioners has ever provided an interpretation of what that caption means, or in any way attempted to demonstrate that the text of the Uhlmann article itself indicates that measles protein was detected. Again, Dr. Kennedy himself clearly conceded that the *only* evidence that measles protein was detected is *not* contained in the Uhlmann article, but instead that information came to Dr. Kennedy *only* in the form of the alleged statements by Dr. Sheils at the above-described meeting during the British litigation. That is, during the hearing, Dr. Kennedy was explicitly asked whether the information about the "detection of MV protein" was "contained in the [Uhlmann] paper?" He replied: "No. I'm talking about additional information that I have from

[81]Dr. Kennedy did not specify *which* children he was talking about. Presumably, he was referring to the children who were the subjects of the Uhlmann study.

[82]Dr. Rima used the term "immunocytochemistry," which is another name for immunohistochemistry. (*Snyder* Tr. 935A.)

attending a meeting where Dr. Sheils presented work * * *." (Tr. 744; *see also* Ex. 110, p. 8, line 11--information came from "personal communications;" Tr. 853A.)

Further, Dr. Rima was the *only* expert to comment in the record specifically about Figure 4E of the Uhlmann article, and he commented that this Figure did *not* present a "convincing picture" supporting the presence of measles virus protein. (*Snyder* Ex. S, part B, p. 44, para. 4.25.)

Therefore, based on the available evidence, I conclude that the *Uhlmann article itself* does *not* demonstrate that immunohistochemistry performed by Unigenetics demonstrated the presence of measles protein in the tissue of autistic children. Therefore, we have another situation in which the petitioners, as they did with respect to the issues concerning sequencing and Dr. Cotter's replication efforts, rely simply upon Dr. Kennedy's unsubstantiated representations about experiments that were allegedly done, and positive results that were allegedly achieved, by other researchers. Once again, no written record of the alleged testing was produced, no testimony from the researchers who allegedly performed the work was produced, nor did petitioners even produce statements from the other scientists who were allegedly in the room with Dr. Kennedy when Dr. Sheils allegedly described the immunohistochemistry results.

On this issue, as with the sequencing issue, I again find it to be crucial that the data in question has *never been published* or otherwise made available to other scientists. The gist of Dr. Rima's testimony was that, in science, a mere statement in an article that certain testing has been done and certain results were achieved, *without showing the data*, is *not* sufficient to demonstrate to other scientists that, in fact, such results were accurately achieved. To have scientific credibility, rather, the data must be shown. (*Snyder* Tr. 914A-16A, 935A-36.) In this instance, therefore, he believes that it is unwarranted to accept the conclusion that immunohistochemistry finding measles viral protein was done, and done properly, since the data were *not* published. (*Id*.)

Accordingly, after full consideration of this issue, I *cannot* find it to be likely that Unigenetics ever found measles virus protein via immunohistochemistry[83] in any autistic children in conjunction with its measles virus PCR testing.[84]

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[83]Petitioners' other PCR expert, Dr. Hepner, also commented briefly upon the issue of immunohistochemistry in the Uhlmann study. (Tr. 650-52A.) This testimony was somewhat confusing, but Dr. Hepner seemed to concede either that immunohistochemistry was *not used* in the Uhlmann study, or at least that the Uhlmann article does not *demonstrate* that immunohistochemistry was used to detect measles protein.

[84]As to the issue of *Michelle's own case*, petitioners argue, without citation to the record, that because Unigenetics "routinely used immunohistochemistry to detect protein before labeling a sample 'positive,'" then it can be reasonably inferred that Unigenetics did immunohistochemistry and found measles virus protein in the particular sample of Michelle Cedillo. (P3, p. 30.) But, as explained above, there is no persuasive evidence that Unigenetics "routinely" did immunohistochemistry, or that Unigenetics *ever* reliably found measles virus protein by (continued...)

f. Argument concerning "high copy numbers"

Petitioners have argued that even if I conclude that there were some problems with the Unigenetics testing in *general*, I should nevertheless conclude that the Unigenetics testing was able *in certain instances* to accurately identify the presence of measles virus. Petitioners argue that in instances in which the Unigenetics testing found a "high copy number"--which they argue happened in Michelle Cedillo's case--such results should be accepted as accurately indicating the persistence of measles virus. (*See*, *e.g.*, P1, pp. 140, 142, 155, 161, 246-48; P3, pp. 34-37; P4, pp. 34-38.)

I cannot agree, for several reasons. First, the apparent premise of petitioners' argument is wrong. Petitioners seem to imply that it is always true that the higher the "copy number" reported on a test of a particular biologic sample, the greater the *amount* of measles virus RNA that is necessarily contained in that sample. (*E.g.*, P4, p. 35, lines 13-16.) According to the testimony of Dr. Rima, however, this assumption of the petitioners is *not* correct. Dr. Rima explained that the "copy number" in a PCR test is derived from a *ratio* between the number of actual copies found of the target, such as the F-gene of the measles virus, and the number of copies found of a "housekeeping gene" (which is found in all cells of the body) known as "GAPDH." Therefore, if the test detects low numbers of the GAPDH gene, then even if the actual number of measles virus F-genes detected is *low*, the reported "copy number" for the measles virus F-gene will nevertheless be "high." (*Snyder* Tr. 868A-78A; *Snyder* Ex. S, part B, pp. 11-12.) Therefore, Dr. Rima explained, when Unigenetics reported a "high copy number," or "high headline number," for a particular sample, it did *not* necessarily mean that a particularly large amount of measles virus material had been (allegedly) detected.[85] (*Id*.) To the contrary, Dr. Rima testified that when he studied the data from the Unigenetics measles detection efforts, he found that the reported high copy numbers ("headline figures") largely were coming from situations involving *low GAPDH counts*, so that the tests were *not* necessarily indicating high levels of measles virus material. (*Snyder* Tr. 877A-78A.)

Dr. Ward fully agreed with that explanation by Dr. Rima. (*Snyder* Tr. 950A, 965A.) And Dr. Bustin, too, testified that the fact that Unigenetics reported a "high copy number" in a particular test does *not* mean that he would find that test to be reliable. (Tr. 2061A-64A, 2068A.)

In addition, Dr. Rima further testified that even high copy numbers can be the result of contamination. (*Snyder* Tr. 878A.) Dr. Ward, as well, testified that a high copy number does not mean that the result is not a product of contamination. (*Snyder* Tr. 965A-66A.)

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[84](...continued)
immunohistochemistry. Thus, there is no valid basis to conclude that measles virus protein was found in Michelle's tissue.

[85]Dr. Kennedy agreed that copy numbers are derived from a relationship between the number of actual copies found of the target gene and the number of copies found of the "housekeeping gene." (*Snyder* Tr. 385A.)

Moreover, Dr. Rima added that the extremely high copy numbers for measles virus reported for some samples, including those of Colten Snyder and Michelle Cedillo, were so high as to be "completely and utterly biologically implausible" on their face. (*Snyder* Tr. 930.) He explained that if the cells in those samples really had within them the presence of as many copies of the measles virus F-gene as reported in the Unigenetics results, they would be so "stuffed" with the measles virus F-gene alone that there would be no room in the cells for the other cell components that must be there, such as the housekeeping gene. (*Id*. at 930–31A; *see also Snyder* Tr. 883A.) Dr. Ward made the same point. (Ex. BB, p. 12.)[86] Petitioners' experts did not reply to this argument.

Finally, I note that I have concluded that the Unigenetics testing for measles virus was *clearly flawed*. The overall evidence demonstrates that it is unlikely that Unigenetics ever developed a test that *reliably* detected the presence of measles virus. Therefore, even if a particular test, in the case of Michelle's Cedillo's tissue sample or any other biologic sample, was found to have a "high copy number," there is still simply no reason to find that test to be valid. That is, if the test itself is clearly flawed as a general matter, there is no reason to think that a "strongly positive" result on that test is any more reliable than a "weakly positive" result. Accordingly, I find the petitioners' argument concerning "high copy numbers" to be without merit as well.

5. No persuasive evidence of <u>vaccine-strain</u> measles virus

The petitioners in this case, of course, need to demonstrate not only that Michelle Cedillo and other autistic children have persisting *measles virus* in their bodies, but that such persisting measles virus is *vaccine-strain* measles virus, *i.e.*, derived from an MMR vaccination rather than from the natural, "wild" form of measles virus. The Uhlmann article, however, does not even *purport* to show that the measles virus, which was claimed to have been found in the children's biopsies, was *vaccine-strain* measles virus. Similarly, the specific Unigenetics test of Michelle Cedillo's tissue purported to identify only measles virus, not *vaccine-strain* measles virus.

As explained elsewhere in this Part VI of this Decision, I have found that the Unigenetics testing is *not* reliable, and that the petitioners have *failed* to demonstrate that measles virus *of any type* persists in the body of Michelle Cedillo, or in the bodies of any other autistic children. Accordingly, there is no need to discuss the evidence offered by the petitioners for the proposition that any measles virus that allegedly persists in these children's bodies is *vaccine-strain* measles

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[86]This particular aspect of Dr. Rima's testimony was also supported by testimony from respondent's expert Dr. Griffin. Dr. Griffin does not purport to be an expert in PCR (Tr. 2835B), but she has excellent credentials as an expert concerning the *measles virus* (see pp. 108-09, below). Dr. Griffin testified that the extremely high copy number reported for Michelle Cedillo was not "biologically plausible." (Tr. 2783.) According to Dr. Griffin, that copy number, on its face, indicated the presence in the biopsied bowel tissue of more measles virus than would be present even at the *peak* of an infection by the *wild measles virus*. (Tr. 2783-84.) If that was true, Michelle would have had, on January 31, 2002, the date of the biopsy, all the symptoms of the measles disease. (Tr. 2784.) Yet there is no evidence that Michelle was suffering from the symptoms of measles when the biopsy was taken.

virus. Nevertheless, in the interest of completeness, I will briefly address the items of evidence offered by petitioners in this regard.

a. Exhibit 130

Remarkably, in all of the petitioners' expert reports filed in this *Cedillo* case, and in the lengthy hearing testimony by the petitioners' experts, the petitioners offered *virtually no evidence* concerning this necessary element in their proposed chain of proof-- *i.e.*, their claim that the measles virus, which they claim to persist in these children, is *vaccine-strain* measles virus. Nor did they address this issue in their initial post-hearing brief. (P1.) Rather, on January 31, 2008, many months after the evidentiary hearing in this case, the petitioners filed a one-page document as their Ex. 130. The document contains four brief "synopses of papers." One of the four synopses, five paragraphs in length, seems to summarize an article by Dr. Sheils, Dr. O'Leary, and two other co-authors. The synopsis begins with the following language:

> In a recent study [apparently a reference to the Uhlmann study], our group described the presence of measles virus RNA genes in a new form of inflammatory bowel disease with concomitant developmental disorder. One of the many questions raised by the study asked if the measles virus detected was wild or vaccine type in origin. The objective of this pilot study was to address this point.

(Ex. 130.) The next three paragraphs describe the "pilot study," in highly technical language. They indicate that the authors used a technique known as "allelic discrimination" in their attempt to distinguish between wild measles and vaccine-strain. The last paragraph then reads as follows:

> The assay identified wild type measles in three brain blocks from an SSPE patient while 12 gut biopsies from affected children were deemed to have *vaccine strain* present. This pilot study further corroborates our previous findings of an association between the presence of measles virus and gut abnormalities in children with developmental disorder and *indicates the origins of the virus to be vaccine strain*.

(Ex. 130, emphasis added.) The petitioners, in their later briefs filed in this case, then quoted the same language set forth above from Ex. 130, and argued that Ex. 130 proves that the measles virus detected in Michelle Cedillo's intestinal tissue was *vaccine-strain* measles virus. (P3, p. 31; P4 p. 33.)

However, there are severe problems with Ex. 130 as an item of proof. First, if indeed Ex. 130 is a "synopsis" of a larger article, then petitioners have failed to submit the entire article. This synopsis provides only a very brief summary of the pilot study, with no details. In addition, there is no evidence that either the synopsis or the larger article (if such exists) was submitted for scientific peer review and publication, a circumstance which, by itself, causes one to be cautious about giving any credence to the article.

Second, none of the petitioners' expert witnesses in either this case or the *Snyder* or *Hazlehurst* cases, so far as I am aware, has discussed this synopsis or endorsed its accuracy.

Third, the *only* expert witness to address Ex. 130 seems to have been Dr. Rima, an expert for respondent in the *Snyder* case. Dr. Rima did discuss what *appears* to be the "pilot study" described in Ex. 130,[87] though it was never specified exactly what study he was discussing. (*Snyder* Tr. 856A-863.) Dr. Rima explained in detail why he believes that the study did *not* accurately discriminate between wild measles virus and vaccine-strain measles virus. Petitioners have offered no evidence to contradict this testimony.

Accordingly, I find that Ex. 130 does *not* offer significant evidence that *vaccine-strain* measles virus has been found in the biologic material of any autistic person.

b. The Walker study

Petitioners also, in their final post-hearing brief in this case, pointed to another item of evidence in the record. (P4, pp. 33-34.) They pointed to the ongoing Walker study, discussed above, and note that one of their experts who has worked on that study, Dr. Krigsman, stated that in the study's initial testing, six specimens were determined to be positive "for vaccine-strain-specific RNA." (Tr. 487A.) However, as I have already discussed above, the preliminary data from the Walker study, in the words of the petitioners' own expert and co-author of that study, Dr. Hepner, is simply "not useful at this time." (Tr. 659.) Thus, again in Dr. Hepner's own words, it would not be appropriate for me to "draw any conclusions" from that data. (Tr. 682.)

c. Dr. Krigsman's opinion

Finally, with respect to this issue, petitioners assert in their brief that "Dr. Krigsman stated that Michelle's biopsy revealed *vaccine-strain* measles virus in the terminal ileal portion of the small bowel." (P3, p. 32, emphasis added.) Petitioners cite Dr. Krigsman's expert report, where Dr. Krigsman did seem to assert, in a single unexplained sentence, that the Walker study demonstrated "with 100 percent certainty the vaccine origin" of the measles RNA allegedly detected in Michelle. (Ex. 59, p. 8, lines 27-29.) But, Dr. Krigsman's sentence points only to the *Walker study* as the evidence for his apparent "100 percent certainty" that Michelle had *vaccine-strain* measles virus RNA. And, as explained above, I do *not* find the Walker study to be significant evidence concerning this point. Thus, I cannot assign any weight at all to Dr. Krigsman's expressed opinion concerning this point.

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[87]It is not *absolutely* clear that Dr. Rima's discussion at *Snyder* Tr. 856A-63 describes the "pilot study" abstracted at Ex. 130, but that appears likely. Certainly, Dr. Rima was describing the *same general work* described in Ex. 130, *i.e.*, the attempts by the O'Leary/Sheils laboratory group, using "allelic discrimination," to distinguish between the *wild* measles virus and the *vaccine-strain* measles virus. Further, even without that testimony of Dr. Rima, I would nevertheless find Ex. 130 to be without evidentiary value, for the *first two* reasons set forth above.

d. Summary concerning vaccine-strain issue

In sum, I have found all of the items of evidence, upon which the petitioners rely concerning this issue, to be insubstantial.[88] Accordingly, even if I somehow could conclude (which I *do not*) that the Unigenetics testing demonstrates the presence of measles virus in the children in question, then petitioners would *still* have failed to demonstrate that such measles virus was *vaccine-strain* measles virus.

6. Analysis of other articles that purportedly found measles virus in children with developmental disorders

The petitioners in their briefs have, as noted above, relied heavily on the Uhlmann article. However, there have also been three other published articles in which researchers have reported that they have utilized PCR testing to find measles virus in the biologic material of children with developmental disorders. Petitioners in their briefs in this case have *not* specifically relied upon those other three articles. Nevertheless, because those other articles have been cited or mentioned in the expert reports or hearing testimony in this case, I note that I have studied those articles, and that I conclude that those articles, like the Uhlmann article, do *not* offer any persuasive evidence that measles virus in fact has been found in the biologic material of autistic persons.

a. Martin article

The first of those articles, the Martin article,[89] was authored by five of the authors of the Uhlmann article. (Tr. 1847; compare Ex. BB, Att. 67, p. 2, to Ex. 63, Tab U, p. 1.) The Martin article, like the Uhlmann article, describes measles virus detection attempts in the ileal lymphoid tissue of children with developmental disorders, and of "control" children without developmental disorders. The detection techniques were the same as those listed in the Uhlmann article. As in the Uhlmann article, the authors reported finding measles virus in most of the children with developmental disorders, but in only a few of the control children.

None of petitioners' experts discussed the Martin paper, or cited it as support for the proposition that measles virus has been reliably detected in the tissue of autistic children. For that reason alone, I can not find that the Martin article supports a conclusion that measles virus has been reliably detected in autistics. Moreover, the only expert to discuss the article was respondent's expert Dr. Ward, who explained that there is little detail in the Martin article, so that it may be that

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[88]I note also that an expert committee of the Institute of Medicine explored this issue, and indicated skepticism that the Unigenetics testing had reliably identified *vaccine-strain* measles virus. (Ex. JJ, p. 128.) (For a discussion of that Institute of Medicine Report, see p. 124 below.)

[89]C. Martin, V. Uhlmann, A. Killalea, O. Sheils & J. O'Leary, *Detection of Measles Virus in Children with Ileo-Colonic Lymphoid Nodular Hyperplasia*, *Enterocolitis and Developmental Disorder*, 7 MOLECULAR PSYCHIATRY S47-8 (2002). (Ex. BB, Att. 67.)

the article is describing the testing of the *very same* samples as described in the Uhlmann article. (Tr. 1847; Ex. BB, p. 11.) In any event, given the authors and the testing techniques described, it is fair to infer that the testing described in the Martin articles, even if not the *same exact samples* described in the Uhlmann article, was done by the *Unigenetics laboratory*, utilizing the same techniques utilized in the Uhlmann study. Therefore, the Martin study certainly provides no independent support for the proposition that the Unigenetics measles virus testing was reliable.

b. Bradstreet 2004 article

Another of the three articles is the Bradstreet 2004 article.[90] Among the authors of this article are both Dr. J.J. Bradstreet, who testified for the petitioners in the *Snyder* case, and Dr. Andrew Wakefield. The article describes testing for measles virus on samples from six children, three autistic and three developmentally normal. The testing found the presence of measles virus in the three autistics, but not in the developmentally normal children.

Though the Bradstreet study was very small, the results might be considered supportive of the validity of the Unigenetics testing, except for one circumstance. At the end of the article, the authors reveal that the testing was in fact, done by *Unigenetics itself*. (Ex. 61, Tab M, p. 44, in the "Acknowledgments.") Thus, this study again provides no independent support for the petitioners' argument concerning the issue of the reliability of the Unigenetics measles virus testing.[91]

c. The Kawashima 2000 article

The last of the three articles, the Kawashima 2000 article,[92] also included Dr. Wakefield as a co-author. (Ex. BB, Att. 55, p. 723.) In the study, the authors utilized PCR to test blood cells ("PMBCs") for measles virus. Of nine autistic children examined, three samples tested positive for measles virus, while samples from eight developmentally normal children all were negative.

The Kawashima articles does not make clear in what laboratory the PCR testing was done. However, there is no evidence that it was the Unigenetics laboratory, and another article in the record

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[90]J.J.Bradstreet et al., *Detection of Measles Virus Genomic RNA in Cerebrospinal Fluid of Children with Regressive Autism*, 9 J. AM. PHYSICIANS & SURGEONS 38 (2004). (Ex. 61, Tab M.)

[91]Dr. Rima also pointed out additional reasons for distrusting the data contained in the Bradstreet 2004 article. (*Snyder* Tr. 884A-894A.) Further, Dr. Ward argued that the Bradstreet article was published in a journal of dubious merit. (Ex. BB, p. 6; Tr. 1837.)

[92]H. Kawashima, T. Mori, Y. Kashiwagi, K. Takekuma, A. Hoshika & A. Wakefield, *Detection and Sequencing of Measles Virus from Peripheral Mononuclear Cells from Patients with Inflammatory Bowel Disease and Autism*, 45 DIGESTIVE DISEASES & SCIENCES 723 (2000). (Ex. BB, Att. 55.)

indicates that Dr. Kawashima runs a laboratory in Tokyo, Japan. (Ex. V, Att. 1, p. 172.[93]) Therefore, the fact that at least a few samples tested positive for measles virus in testing by a non-Unigenetics laboratory might be viewed as supportive of the validity of the Unigenetics measles detection efforts. However, I cannot find that the Kawashima study offers any significant support, for several reasons.

First, even the petitioners' own expert witnesses in the PCR area did *not* discuss the Kawashima study, or opine that it supports their view that the Unigenetics testing was valid. If none of the *petitioners' experts* believe that the Kawashima study supports their theory, I certainly cannot rely on it.

Second, the record contains several items of evidence that *cast doubt* on the validity of the Kawashima measles virus testing. In the D'Souza 2006 study, the researchers in fact attempted to replicate the Kawashima 2000 study. The D'Souza researchers used the same primer set utilized by Kawashima, and tested the same type of blood cells tested by Kawashima. However, the D'Souza team did *not* find any positive results on the samples tested, casting doubt on the reliability of the Kawashima results. (Ex. T, Att. 6, pp. 1665, 1667-68, 1671.) The D'Souza group concluded that the Kawashima PCR data is "unlikely to be true" (*id*. at 1674), and stated that "unintentional contamination" was a plausible explanation for this apparent error by the Kawashima testing (*id*. at 1672).

Next, Dr. Rima pointed out that the Kawashima laboratory (unlike the Unigenetics laboratory) participated in an international comparison of laboratories that did measles testing. The result, however, was that the Kawashima lab "turned out to be extremely incapable of detecting measles virus." (*Snyder* Tr. 901A; *see also* Ex. V, Att. 1, pp. 172, 175.) Another article also points out problems with the Kawashima 2000 study. (Ex. T, Att. 1.[94])

Finally, as noted above, Nicholas Chadwick in 1996 was a Ph.D. student working in a London laboratory for Dr. Wakefield. (Tr. 2283-84; Ex. QQ, pp. 1-2.) At that time both Dr. Wakefield and Dr. Kawashima were seeking to determine if the measles virus was connected with a certain type of *bowel disease*, rather than autism. Chadwick's interactions with the Kawashima laboratory make it appear very likely that Dr. Kawashima's positive results in measles virus testing were "false positives," the result of contamination. (Tr. 2286-87; Ex. QQ, paras. 10-11.)

For all those reasons, I conclude that the Kawashima 2000 article does not offer any support to the petitioners' claim that the Unigenetics measles testing was reliable.

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[93]M. Afzal et al., *Comparative Evaluation of Measles Virus-Specific RT-PCR Methods Through an International Collaborative Study*, 70 J. MED. VIROLOGY 171 (2003). (Ex. V, Att. 1.)

[94]M. Afzal & P. Minor, *Vaccines, Crohn's Disease and Autism*, 7 MOLECULAR PSYCHIATRY S49-50 (2002). (Ex. T, Att. 1.)

d. Summary concerning the three articles

For the reasons set forth above, I conclude that *none* of the three cited articles offer any support to the petitioners' claim that the Unigenetics measles testing was reliable.

7. Experience of the experts

Comparison of the experience and credentials of the parties' experts further supports a finding that petitioners have failed to demonstrate the reliability of the Unigenetics measles virus testing. As noted above, respondent's expert Dr. Ward is a medical doctor who has practiced medicine and held medical academic positions since 1981, specializing in internal medicine, infectious diseases, and microbiology. (Tr. 1796A-97; Ex. CC, pp. 1-2.) He has been a member of the medical faculty at McGill University in Montreal since 1992, serving as Chief of the Infectious Diseases Section of that medical school from 2002 to 2006. (Ex. CC, p. 2; Tr. 1797.) He has published extensively, including over 80 peer-reviewed articles and a number of medical textbook chapters. (Ex. CC, pp. 13-23, 25-26; Tr. 1797-98A.) His testimony in this case and his list of publications indicate extensive experience in PCR testing and extensive experience with the measles virus. (Ex CC; Tr. 1796A-98A, 1839; *Snyder* Tr. 940.)

Respondent also relied upon the testimony of Dr. Bustin, an expert who is extraordinarily well-qualified to testify concerning the validity of PCR testing results. Dr. Bustin is a molecular biologist who obtained his Ph.D. in that field in 1982. (Tr. 1933; Ex. VV, p. 1.) He is the chief of the Molecular Science section of the medical school of the University of London. (Tr. 1934A.) Dr. Bustin has very extensive experience in PCR testing in its various forms, which he uses every day in his scientific research and practice. (Tr. 1934A-36A.) During the past five years his laboratory has published fourteen peer-reviewed articles concerning PCR. (Tr. 1935.) In 2000 he wrote a medical review article concerning PCR that has since been cited over 1,000 times in other articles in the peer-reviewed medical literature, and another of his PCR articles has been cited more than 500 times. (Tr. 1935-36A.) He is the co-author of a book entitled *A to Z of PCR*, and has contributed chapters to other books on PCR. (Tr. 1936A.)

Respondent's expert Dr. Rima is also very well-qualified in the area of PCR testing for measles virus. A Ph.D. virologist, he has more than 33 years of research experience since receiving his Ph.D. (*Snyder* Tr. 825; *Snyder* Ex. W, pp. 1-2.) The primary focus of his research has been the measles virus and related viruses. (*Snyder* Ex. W, pp. 6-25; *Snyder* Tr. 826A.) Dr. Rima is head of the school of Biomedical Sciences at the Queens University of Belfast, Northern Ireland. (*Snyder* Tr. at 824A-25.) He has published extensively, including well over 100 articles concerning measles virus alone, and approximately 20 book chapters. (*Snyder* Tr. 826A-27A.)

Respondent's expert Dr. MacDonald is well-qualified to opine concerning the validity of the Unigenetics testing as well. A Ph.D. immunologist, he is a Professor of Immunology and Dean for Research at the medical school of the University of London. (*Hazlehurst* Ex. A, p. 1; *Hazlehurst* Tr. at 603-04A.) During a medical research career of more than 30 years, Dr. MacDonald has

specialized in the immunology of the human gut (intestines). (*Hazlehurst* Ex. A, p. 1; *Hazlehurst* Tr. at 604A-11A.) He stated that he has had "a particular interest in the lymphoid tissue of the human gut" (*Hazlehurst* Ex. A, p. 1), which is the type of tissue which Unigenetics tested in Michelle Cedillo and in the Uhlmann study. He has published at least 158 articles concerning gut immunology, written a book on that topic and edited several other such books, written many book chapters, and served in editorial positions on a number of medical journals. (*Hazlehurst* Tr. 607A-09A.)

Moreover, in addition to extensive general experience in the field, each of those four experts for respondent has *particular* experience that is especially relevant to the Unigenetics testing in question. That is, as described above, Drs. Bustin, Rima, and MacDonald, as experts in the above-described British MMR/autism litigation, each had extensive access to the Unigenetics laboratory's records, facilities, and/or equipment. Dr. Ward, on the other hand, was a lead researcher on a team that actually used the Uhlmann primers and performed PCR testing in order to test the accuracy of the Unigenetics testing, then published the results of its efforts in peer-reviewed medical journals, in the form of the D'Souza 2006 and D'Souza 2007 articles discussed above.

The petitioners, on the other hand, relied on two experts concerning the issue of the reliability of the Unigenetics measles virus testing. Dr. Hepner received her Ph.D in molecular biology about four years before the trial in this case; she has about ten years of experience in working with PCR technology, including the years prior to obtaining her Ph.D. (Tr. 583A-84A, 636-37.) Dr. Kennedy received a Ph.D. in microbiology in 1981, and is expert in microbiology and virology. (Tr. 684; Ex. 110, p. 1; Ex. 111, p. 1.) He is chairman of the Department of Microbiology and Immunology at Texas Tech University, and has a great deal of experience in studying viruses, including the measles virus, and in the development of vaccines. (Tr. 685; Ex. 110, pp. 1-2; *Snyder* Tr. 357.) He has published more than 200 peer-reviewed scientific articles. (Ex. 110, p. 2.)

In addition, Dr. Kennedy, as an expert in the British MMR/autism litigation, also had the opportunity to review many of the Unigenetics laboratory records (Tr. 853A-54A), and to question one of the Unigenetics' principals, Dr. Sheils. (Tr. 808-17, 824A-25, 844-48, 851-55; *Snyder* Tr. 333A-39A.)

Weighing the credentials and experience of the primary experts for both sides concerning the issue of the validity of the Unigenetics testing, I note as follows. Dr. Bustin clearly has the most impressive credentials and experience of all, in the particular field of *PCR testing*. Dr. Rima clearly has the most experience in studying the *measles virus* in particular. Drs. Ward and MacDonald also, like Drs. Bustin and Rima, have very impressive academic backgrounds, publications, and length of experience, while Dr. Kennedy, too, has very impressive credentials in terms of academic background, publications, and length of experience. Dr. Hepner, on the other hand, while certainly qualified to opine as an expert concerning PCR, has far less experience, and far lesser academic and publication credentials, than all of the other experts.

Thus, on the whole, there is certainly a strong contrast, in the experience and background relevant to this issue of the validity of the Unigenetics testing, between the respondent's four primary experts and the petitioners' two experts. Each of the respondent's four experts has vastly more experience and academic credentials than Dr. Hepner. Dr. Kennedy does have impressive credentials in terms of academic background, publications, and length of experience. However, Dr. Bustin's PCR experience and Dr. Rima's experience with the measles virus far exceed Dr. Kennedy's. Overall, the scale tips considerably in the favor of respondent's experts. Therefore, this factor adds yet another reason for me to conclude that the Unigenetics measles virus testing should not be considered reliable.[95]

8. Summary concerning reliability of the Unigenetics testing

As explained in detail above, a number of factors have contributed to my conclusion that the Unigenetics testing for measles virus *cannot* be considered reliable. As explained, the most important factors in my rejection of the Unigenetics testing are that the laboratory failed to publish any sequencing data to confirm the validity of its testing, the failure of the efforts by other laboratories to replicate the Unigenetics testing, and the demonstration by the D'Souza group that the Uhlmann primers were "nonspecific."

In addition, the testimony of Drs. Bustin, Rima, and MacDonald convinced me that severe problems existed with the procedures, facilities, and equipment of the Unigenetics laboratory, adding a secondary, additional reason to doubt the reliability of the Unigenetics testing. Other important factors are the failure of the petitioners to supply any persuasive evidence that any purportedly detected measles virus material was *vaccine-strain* measles virus material, the dramatic contrast between the credentials of the expert witnesses for the two sides, and the lack of persuasiveness of the petitioners' main arguments.[96]

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[95]Of course, this is not to say that a factfinder need *always* adopt the view of the expert with more experience or more striking academic credentials. Sometimes an expert with lesser experience or credentials may offer superior analysis. 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 topic of the reliability of PCR testing for measles virus.

[96]As I will discuss in detail below, two committees selected by the prestigious Institute of Medicine (IOM) have examined the evidence concerning the issue of whether the MMR vaccine can cause autism, and both answered that question in the *negative*. (See p. 124 below.) The 2004 IOM committee also commented specifically concerning the reported finding by the *Unigenetics laboratory* of evidence of measles virus in the intestinal tissue of autistic children, as reported in the Uhlmann article. (Ex. JJ, pp. 127-28.) The committee reached no firm conclusion concerning the validity of the Unigenetics testing. The committee's discussion, however, indicated that the committee had doubts concerning the reliability of the testing, describing the test results as "questionable." (*Id*. at 128.)

For all of those reasons, I conclude that the Unigenetics testing for measles virus was *not* reliable. I conclude that the Unigenetics laboratory *never* reliably detected the presence of measles virus, in the Uhlmann study or in the testing of individual samples of persons such as Michelle Cedillo and Colten Snyder. And, in particular, I conclude that the purported detection by Unigenetics of measles virus in the tissue of *Michelle Cedillo* was *not* reliable and cannot be considered valid.

F. Motion concerning Dr. Bustin

Petitioners have requested that I exclude from consideration in this case the hearing testimony of Dr. Bustin, as well as two of his expert reports, Exs. WW and XX, because those two reports were filed shortly before the hearing in this case, and because Dr. Bustin had access to the Unigenetics laboratory and records that may not have been available to petitioners' experts. There are two answers to this argument. First, while some of petitioners' concerns in this regard may have some appeal at first glance, upon complete analysis of the issue I see no good reason to disregard the reports and testimony of this competent and relevant witness. The second answer is that the issue is really a moot one. That is, while I have elected to include an analysis of Dr. Bustin's testimony and those reports in this opinion, even if I were to *completely exclude* Dr. Bustin's testimony and all of his expert reports, nevertheless my rulings concerning (1) the issue of the reliability of the Unigenetics testing, and (2) the outcome of this case, would be the *same*. I will explain my reasoning concerning this matter below.

1. Background

As explained above, on December 20, 2006, the Petitioners' Steering Committee (PSC) in the Omnibus Autism Proceeding (OAP) proposed that this *Cedillo* case become a "test case" in the OAP. They proposed that an evidentiary hearing be held in June of 2007, concerning both the evidence concerning the PSC's first theory of *general causation*, and the evidence *specific* to this *Cedillo* case. (See pp. 12-13 above.) According to that proposal, which the three special masters adopted, the petitioners' expert reports in this case were to be filed in February of 2007, and the respondent's expert reports were to be filed in April. (Order filed February 1, 2007.) Eventually, a number of expert reports were, in fact, filed by the petitioners on February 20, 2007, and by the respondent on April 24, 2007.

A number of additional expert reports, however, were filed after those agreed-upon February and April deadlines. Petitioners filed expert reports of Dr. Hepner on May 22, 2007, and Dr. Kennedy on May 28, 2007. (Exs. 63, 110.) Respondent on May 31, 2007, filed an expert report from Dr. Bustin, as a response to the report of Dr. Hepner. (Ex. UU.) All three of those experts were added to the list of witnesses scheduled to testify at the hearing. No party objected to the filing of any of those three expert reports, or to the addition of any of those three experts to the hearing schedule.

On June 7, 2007, four days before the scheduled start of the evidentiary hearing on June 11, respondent filed Exhibits WW and XX.[97] Those exhibits were copies of expert reports that Dr. Bustin had prepared and filed in 2003 and 2004 in the course of the above-described British MMR/autism litigation. (See p. 50 and fn. 69 above.) A recorded status conference to discuss those reports was conducted on June 8, 2007. (Tr. 6-8-07.) At that conference, respondent's counsel explained in detail the circumstances under which respondent had obtained those two documents from the British court file, which is sealed and unavailable to the public absent special permission from the presiding judge. (Tr. 6-8-07 at 13-23.) Petitioners' counsel then requested that I disregard those two exhibits in deciding this case, and that Dr. Bustin and other witnesses be prohibited, during the upcoming hearing, from discussing the contents of those two reports. (Tr. 6-8-07 at 23-30, 39-41.)

I filed a written Evidentiary Ruling on that same day, June 8, 2007, after the conference. In that Ruling I stated that, during the upcoming hearing, I would allow questions concerning the two reports to be asked of Dr. Bustin or other witnesses. I also stated, however, that I would *defer*, until after the hearing, the decision whether to *rely upon* those two reports in deciding this case.

After the hearing, on August 8, 2007, petitioners addressed this matter again, filing a motion asking that I disregard both the two reports *and* all of the hearing testimony of Dr. Bustin. Respondent filed a detailed response to that motion on September 7, 2007. On October 2, 2007, I filed an Order concerning the petitioners' motion filed on August 8. I stated that petitioners--

> have, as of this time, *not* demonstrated good reason for me to exclude these evidentiary items from consideration in this case. The arguments made in petitioners' motion were extremely vague, failing to explain exactly what portions of Dr. Bustin's reports and testimony are prejudicial, and why. Accordingly, I will not, at this time, exclude any of those items from consideration. I will defer, rather, until the post-hearing briefing in this case, the decision whether to *rely upon* those items in deciding the *Cedillo* case. Petitioners may make additional arguments concerning this issue, if desired, in their post-hearing briefs.

Subsequent to my Order of October 2, 2007, petitioners have filed four lengthy post-hearing briefs. In those briefs, however, they did *not* explain how they had been disadvantaged at the hearing, nor did they further address the issue of whether I should disregard Exs. WW and XX and Dr. Bustin's hearing testimony in deciding this case.

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[97]Under the court's electronic filing system, respondent actually filed with the court on June 7, 2007, only the electronic "notice of filing" the documents (items 124 and 126 of the docket entries); the compact discs containing the reports were not physically filed with the court until later. But *petitioners' counsel* actually received the *full text* of the documents, electronically, on June 7, 2007.

2. Discussion

The petitioners have raised two issues which, at first glance, might seem to have at least some appeal. One concern is the fact that two of Dr. Bustin's expert reports were filed just four days before the hearing, limiting the time for petitioners' counsel to study the documents and prepare to deal with them at the hearing. The second concern is that there might be a possible perception of "unfairness" to petitioners, arising from the circumstance (1) that Dr. Bustin had access to records of the Unigenetics testing that may no longer be available, and (2) that respondent obtained only a few documents from the British MMR/autism litigation, while many other documents remain under seal in that file. I will discuss those two concerns separately below.

a. Filing shortly before trial

It is very unfortunate that the two reports were filed just four days before the hearing. Obviously, that circumstance limited the opportunity for the petitioners' counsel and experts to study the documents before the hearing, to prepare a response thereto at the hearing, and to prepare to question Dr. Bustin about the reports. However, there are other considerations that affected my original decision to allow the two reports to be discussed at the evidentiary hearing, and that now militate *against* the option of simply disregarding the two reports and Dr. Bustin's testimony in this opinion.

First, in this case, a *number* of evidentiary items were filed by *both* parties at a very late stage of the proceedings. For example, as noted above, the petitioners' expert reports were due to be filed in February of 2007, and petitioners did file four expert reports on February 20, 2007. (Exs. 55, 57, 59, 61.) Yet, while it was quite clear from those four filed expert reports that the validity of the Unigenetics testing was crucial to the case, none of petitioners' initial four expert reports were authored by experts in PCR. Rather, the petitioners did not file the expert reports of their two PCR experts, Drs. Hepner and Kennedy, until May 22 and 28, respectively, very close to the hearing date and more than three months after the due date for petitioners' expert reports. Further, a number of other documents were filed in this case by *both* parties after May 25, 2007, which was the prescribed deadline for filing evidentiary items.[98]

Second, one expert report (Ex. UU) and an affidavit[99] of Dr. Bustin were already filed in this case *prior* to the filing of Exs. WW and XX, and Dr. Bustin was *already* scheduled to testify. Dr. Bustin's earlier-filed report and affidavit had already addressed the *same general issue* addressed

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[98]During the conference held on June 8, 2007, I asked petitioners' counsel if she was proposing that I should disregard *all evidence* filed after May 25, 2007. She declined to suggest such a course. (Tr. 6-8-07, p. 46.)

[99]On May 22, 2007, respondent filed a "Motion *In Limine*," seeking to exclude the testimony of petitioners' expert Dr. Krigsman. Attached to that motion, as Attachment 4, was an affidavit of Dr. Bustin. (I note that I denied that "Motion *In Limine*" on May 29, 2007.)

in Exs. WW and XX--*i.e.*, the reliability of the Unigenetics lab results. Further, much *additional* evidence was already in the record, filed by *both* parties, addressing that same general issue, so the petitioners' counsel certainly were already generally prepared to address that issue at the hearing.

In addition, respondent filed the two reports on June 7 within about an hour of receiving them, so that there is no indication that the respondent unreasonably delayed in filing those reports after receiving them. (Tr. 6-8-07, pp. 44.) Petitioners' arguments have suggested that respondent's counsel were negligent or dilatory in not obtaining those reports from the British court at an earlier time. But, as respondent's counsel explained, it was not clear that petitioners' theory of causation depended on the validity of the Unigenetics testing until after the filing of the petitioners' expert reports on February 20, 2007. (Tr. 6-8-07 at 13.) Further, respondent's counsel described the process by which the respondent thereafter sought documents relevant to Unigenetics from the British court, eventually receiving certain documents on June 7. (*Id*. at 13-23.) Considering all of the circumstances, I can find no failure of diligence by respondent in that regard.

Further, throughout the history of the Vaccine Act, the special masters, including myself, have often been lenient in allowing new items of evidence to be filed just prior to, or even during the course of, evidentiary hearings. Most often, the party seeking to introduce the late evidence has been the petitioner in the case. The special masters' reasoning in these situations has been that it is generally better to hear all of the relevant evidence than to decide a case based on incomplete evidence. The remedy for the late filing in such situations has been to give the opposing party additional time, after the hearing, to obtain and file any new evidence to rebut the late-filed item. On some occasions this practice has resulted in the need for a second evidentiary hearing in the case, but the special master on those occasions generally has been willing to conduct such a second hearing when necessary, in the interest of reaching a decision based upon *all* of the relevant evidence.[100] As I stated in my Evidentiary Ruling on June 8, 2007, I considered it appropriate to apply that general rationale to this case. Moreover, because this case had been designated as a "test case" in the Omnibus Autism Proceeding, the outcome of which would give direction to other autism petitioners, it seemed all the more important to explore all potentially relevant evidence.

I also note that, in this case, I have given the petitioners a *very fair chance* to rebut the late-filed evidence contained in Dr. Bustin's two reports. In my Evidentiary Ruling on June 8, 2007, I promised petitioners a reasonable period of time after the hearing in which to seek evidence to rebut

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[100]The case law concerning this point is scant, since most such discretionary determinations, regarding whether to permit the filing of evidence, are made without written rulings. However, two decisions illustrate the general concept that the Vaccine Act special masters should avoid the exclusion of relevant evidence. In *Kaminski v. Secretary of HHS*, 39 Fed. Cl. 253, 255, 258 (1997), a judge found that the special master's refusal to hear the testimony of an important witness was error, even though the witness was offered by respondent only after the evidentiary hearing. Similarly in *Horner v. Secretary of HHS*, 35 Fed. Cl. 23, 27-28 (1996), a judge concluded that when relevant evidence was discovered one month after the dismissal of the case, the special master erred in failing to re-open the case and consider the evidence. *See also Plavin v. Secretary of HHS*, 40 Fed. Cl. 609, 612 (1998); *Erve v. Secretary of HHS*, 39 Fed. Cl. 607, 612 (1997).

the material contained in the two reports. Indeed, they have actually had a post-hearing period of *well over a year* in which to submit such evidence. And, in fact, they *have* submitted such rebuttal evidence, in the form of supplemental expert reports from their two PCR experts. (See Exs. 120 and 121, supplemental expert reports of Dr. Hepner and Dr. Kennedy, filed on October 22 and November 6, 2007.)

Further, in my Evidentiary Ruling on June 8, 2007, I explicitly offered petitioners a *second evidentiary hearing*, if desired, in which to present any such evidence that they might be able to obtain. They never requested such a hearing. Also, they never requested that Dr. Bustin be made available for additional cross-examination, a request that I would have granted.

Finally, in my Order issued on October 2, 2007, I explicitly invited petitioners, in their post-hearing briefs, to explain exactly what portions of Dr. Bustin's reports and/or testimony were prejudicial, and why--*i.e.*, to further explain their vague arguments that the late filing of those two reports hampered them at the hearing. Petitioners' four lengthy post-hearing briefs, however, contained no such specific argument.

Accordingly, for all the reasons stated above, I conclude that the fact that Exs. WW and XX were filed shortly before the hearing does *not* require that I disregard those reports, or any portion of Dr. Bustin's testimony.

b. Access to British litigation file

Petitioners' arguments concerning this matter have also suggested that the filing of Dr. Bustin's two reports obtained from the British litigation file is "unfair" to the petitioners, in two closely related but analytically distinct ways. First, they perceive unfairness in the fact that respondent obtained only a few documents[101] from the British file, while many other documents remain in the sealed file, inaccessible without special permission of the British court. Second, they see unfairness in the fact that, in preparing the two reports in question, Dr. Bustin had access to records of the Unigenetics testing that may not have been available to petitioners' experts.

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[101] Along with Dr. Bustin's two reports, respondent also obtained, from the British court, copies of two other expert reports that had been filed into the British litigation. Those reports were authored by Dr. Rima and by Dr. Peter Simmonds. Respondent shared those other two reports with petitioners' counsel at the time, but did not file them into the record of this *Cedillo* case. (See my Evidentiary Ruling filed on June 8, 2007, footnote 2.) Respondent did later, however, file those two Rima and Simmonds reports into the evidentiary record of the *Snyder* case. (*Snyder* Exs. P and S.) Then, it was at the *Cedillos' own request*, and over respondent's objection, that the "general causation" evidence from the *Snyder* and *Hazlehurst* cases, including the Rima and Simmonds reports from the British litigation, came to be "imported" into the evidentiary record of this *Cedillo* case. (See pp. 14-15 above.)

While these suggestions of unfairness might have some appeal at first glance, I conclude that they do *not* offer a good reason to disregard, in this case, the evidentiary value of the two reports and Dr. Bustin's hearing testimony.

Concerning the issue of access to the British litigation file, I note that in my Evidentiary Ruling issued on June 8, 2007, I encouraged (p. 3) petitioners' counsel to seek additional documents from that file after the hearing, even pledging to join petitioners' counsel in such a request.[102] And efforts in that direction were, in fact, made on behalf of the Cedillos and the other autism petitioners, by the Petitioners' Steering Committee (PSC) in the Omnibus Autism Proceeding (OAP), led by attorney Thomas Powers of the PSC. During the regular OAP status conferences between July of 2007 and July of 2008, Mr. Powers reported that the PSC was exploring the possibility of petitioning the British court for release of additional documents. (*See*, *e.g.*, Autism Updates filed into the Autism Master File on March 27, 2008, pp. 2-3; April 23, 2008, pp. 2-3.) The PSC requested that the OAP special masters provide a letter supporting the PSC's possible request, which the special masters did provide. (See Autism Update filed March 27, 2008, p. 2 and Ex. A.) Mr. Powers finally reported, however, in July of 2008, that the PSC would *not* file an application with the British court. (See Autism Update filed July 8, 2008, p. 2; Order filed in this *Cedillo* case on July 30, 2008.) Mr. Powers explained that the PSC had sought to obtain six reports filed by experts for the British claimants, but was unable to obtain the agreement of all such experts to have their reports disclosed publicly; British attorneys consulted by the PSC advised that without agreement of the experts, the British court was unlikely to grant disclosure of the reports, so the PSC never filed an application. (See Autism Updates filed March 27, 2008, p. 3; April 23, 2008, p. 3; July 8, 2008, p. 2.[103])

While it is unfortunate for the petitioners that they have been unable to obtain cooperation from the claimants' experts in the British litigation, and therefore have been unable to obtain any additional expert reports from the British litigation file, I cannot see why that means that I should disregard the reports and testimony of Dr. Bustin. Dr. Bustin was willing to publicly affirm and defend, in 2007, the opinions that he stated in his British litigation reports. He was willing to answer, under oath, petitioners' questions about those reports. Apparently the experts who supplied reports for the British claimants were *not* willing to do the same, but that is not the fault of Dr. Bustin or respondent. I have been willing to study *any* item of evidence put before me by the

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[102]Petitioners were given a list of the materials contained in the British litigation file, the same publicly-available document that respondent used when deciding which materials to seek from that file. (See Item 129 on the electronic docket of this case, respondent's filing of June 8, 2007, Attachment 1.)

[103]In the "PSC Notice Re: UK Litigation Materials," filed into the Autism Master File on July 31, 2008, the PSC implied that it secured the agreement of *some*, though not all of the British claimants' experts, to have their reports disclosed. Also, Dr. Kennedy, one of those claimants' experts, testified that he had no objection to the release of his report. (*Snyder* Tr. 424A-25A). In these circumstances, assuming that the PSC actually does find it important to see those expert reports, it is unclear why the PSC did not petition the British court for access to those expert reports for which it *could* obtain the authors' permission.

parties, and I would have been happy to analyze any further documents obtained from the British file, but I simply do not find it logical that I should disregard the reports of Dr. Bustin in these circumstances. Nor have petitioners cited any legal authority suggesting why I should do so.

The other suggested point of alleged unfairness seems to be that Dr. Bustin in 2003 and 2004 had access to Unigenetics records that may not now be available to petitioners' experts. In this regard, it *may* be that some or all of the Unigenetics records are unavailable, either because they are sealed in the British court file, or because they no longer exist due to the demise of Unigenetics, or for some other reason. Petitioners' counsel, however, have *not* demonstrated that they have made *any* efforts to determine exactly where such records are located, whether such records have been destroyed, etc., so they are in a poor position to complain about a lack of access to such records.[104]

Further, it appears that the British litigation file includes, in addition to expert reports, certain Unigenetics records. Neither the Cedillos' counsel nor the PSC attorneys have explained why, if they believe that they are disadvantaged by a lack of access to Unigenetics records, they have never petitioned the British court for access to those *Unigenetics records*, even if they believed that the court would not likely grant access to the *expert reports*.

Moreover, petitioners' current expert Dr. Kennedy *was*, like Dr. Bustin, an expert in the British litigation, and has expertise in PCR testing. Dr. Kennedy explained that he *did* have his own non-publicly-available information about the operation of the Unigenetics laboratory. (Tr. 813-15.) Dr. Kennedy described not only receiving information orally from Unigenetics principal Dr. Sheils during the above-described meeting of experts, but stated also that he and other experts had "asked for a lot of things" that were not presented initially by Dr. Sheils, and those items of information were provided to him by Unigenetics at an unspecified later time. (Tr. 815, lines 10-23.) Further, Dr. Kennedy explained that he had access to many of the Unigenetics laboratory notebooks. (Tr. 854A.) Therefore, it appears that Dr. Kennedy did, in fact, have access to at least some of the information to which Dr. Bustin also had access.[105]

To be sure, although the petitioners have not *demonstrated* as much, it does seem quite *possible* that access to the Unigenetics records is unavailable to petitioners at this time, because such

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[104]That is, it seems to me that if the petitioners wish me to disregard relevant evidence based upon the petitioners' alleged lack of access to certain documents, it is incumbent on the petitioners' counsel to *demonstrate* that they in fact have no access to those documents despite efforts to obtain them.

[105]In fact, Dr. Kennedy had *already* introduced into the record of this case his own "inside information" about the Unigenetics laboratory--*i.e.*, his "personal communications" from Dr. Sheils, Ex. 110, p. 8, line 11--*before* respondent filed the two reports of Dr. Bustin which drew upon Dr. Bustin's access to the Unigenetics laboratory. Thus, having *themselves* relied on Dr. Kennedy's "inside information" about the Unigenetics laboratory that was not available to respondent's experts, petitioners are not well-placed to complain that it is unfair that Dr. Bustin had his own non-publicly-available source of information about Unigenetics.

records either are in sealed British court files or were destroyed. If that is the case, it would mean, as petitioners have pointed out, that petitioners are unable to have their own expert now scrutinize the Unigenetics records to determine whether Dr. Bustin's analysis is accurate. However, even if I *assume* that petitioners *do not* in fact have any way to access such records at this time, I do not see why that logically means that I should therefore ignore the reports and testimony of Dr. Bustin, just because he did have such access at the time that he prepared Exs. WW and XX. Petitioners have not explained *why*, or pointed to any legal authority explaining why, I should therefore ignore a witness who did provide relevant evidence.

c. Even if I were to disregard Dr. Bustin's expert reports and hearing testimony, all my conclusions in this case would remain the same.

Finally, even if I were to completely exclude and disregard all of Dr. Bustin's reports and all of his hearing testimony, nevertheless *all* of my conclusions in this case would remain *exactly the same*.

First, the testimony and reports of Dr. Bustin were relevant chiefly in establishing my conclusion discussed at pp. 58-60 above, *i.e.*, that there were severe problems with the facilities and procedures of the Unigenetics laboratory. But even concerning this narrow point, Dr. Bustin's testimony was *not* the only evidence. Dr. Rima provided extensive, convincing evidence to the same effect, and Dr. MacDonald provided some corroboration as well. (See discussion at pp. 52-54, 58-59 above.) I would have reached the same conclusion, that there were severe problems with the Unigenetics facilities and procedures, based just on the evidence supplied by Dr. Rima and Dr. MacDonald, even without any information from Dr. Bustin.

Second, even if there had been no testimony from Dr. Bustin, Dr. Rima, Dr. MacDonald, or any other expert who participated in the British litigation, concerning the problems with the Unigenetics procedures and facilities, nevertheless I still would have concluded that the Unigenetics testing was *not reliable*. That is, as explained above (p. 77), the *most important* points in my rejection of the Unigenetics testing were (1) the fact that the laboratory failed to publish any sequencing data to confirm the validity of its testing, (2) the failure of other laboratories to replicate the Unigenetics testing, and (3) the demonstration by the D'Souza group that the Uhlmann primers were "nonspecific." The testimony by Drs. Bustin, Rima, and MacDonald, about the many problems with the Unigenetics laboratory and procedures, was merely a *secondary*, *additional* reason to doubt the reliability of the Unigenetics testing. Accordingly, I would still have found the Unigenetics testing to be unreliable even if there had been no reports or testimony at all from Drs. Bustin, Rima, or MacDonald.

Accordingly, for all the reasons set forth above, I conclude (1) that there is no valid reason for me to disregard the evidence supplied by Dr. Bustin, and (2) that even if I did disregard that evidence, my conclusions concerning all of the issues in this case would remain the same.

VII

PETITIONERS HAVE NOT DEMONSTRATED THAT THE MMR VACCINE *CAN* CAUSE AUTISM IN GENERAL, OR THAT AN MMR VACCINATION *DID* CAUSE MICHELLE'S AUTISM

A. Summary of petitioners' theory

The next step in petitioners' theory is that the vaccine-strain measles virus, persisting in Michelle's body, damaged her brain, thereby causing her autism. In this regard, they rely primarily on the testimony of Dr. Marcel Kinsbourne, who has substantial credentials as a pediatric neurologist. Dr. Kinsbourne accepts the accuracy of the testing of the gut biopsy of Michelle discussed above, as a demonstration that the vaccine-strain measles virus persisted and replicated in her body. (Tr. 1180A, 1183A, 1196A.) He opined that the persisting virus invaded Michelle's brain, prompting a response of her immune system, and that the inflammation produced by that response disorganized certain critical circuits in her brain, thereby causing the autism. (*E.g.*, Tr. 1098A-1100.)

In support of this theory, Dr. Kinsbourne opined that autism is a neurological disorder, the product of defective brain circuitry. (Ex. 61, p. 7.) He explained that the measles virus, in its "wild" non-vaccine form, has been found in the past to cause a number of neurologic disorders. Those disorders include "measles encephalitis," which used to be a relatively common disorder after measles infection, and also two rare fatal neurologic disorders known as SSPE (subacute sclerosing panencephalitis) and MIBE (measles inclusion body encephalitis). (Ex. 61, pp. 15-16; Tr. 1067A-69A.) He stated that the measles virus, once inside a human body, is known to be both "enterotropic," meaning prone to invade the intestines, and "neurotropic," meaning prone to invade the central nervous system and brain. (Ex. 61, p. 14; Tr. 1073.) He opined that since Michelle has experienced both chronic gastrointestinal problems and the chronic neurologic disorder known as autism, the most reasonable conclusion is that a *single* causative agent--*i.e.*, the vaccine-strain measles virus--is the cause of *both* chronic conditions. (Ex. 61, pp. 12-14.)

In Michelle's case, Dr. Kinsbourne also found the *timing* of the onset of Michelle's chronic intestinal symptoms and her symptoms of autism to be quite important. He opined that Michelle was a normally developing infant up until the time of her MMR vaccination on December 20, 1995, when she was about 16 months old. (Ex. 61, p. 19; Tr. 1040.) He testified that the episode of fever and rash that Michelle experienced about one week after that vaccination was caused by the vaccination. (Tr. 1070-71.) He stated that Michelle began to suffer diarrhea "within two weeks" of the vaccination, which he viewed as the onset of her chronic gastrointestinal problems. (Tr. 1042.) He also stated that Michelle's first symptoms of neurologic dysfunction, which later were recognized to be symptoms of *autism*, began *abruptly* during the period of fever that began one week after that vaccination. (Ex. 61, p. 3; Tr. 1041, 1175A ("unusually abrupt"), 1176 ("came on really fast"), 1184A.) Thus, Dr. Kinsbourne's understanding concerning the *timing* of Michelle's symptoms--*i.e.*, his understanding that the onset of both Michelle's chronic gastrointestinal symptoms and her autism

occurred *abruptly* within about two weeks after her MMR vaccination--also contributed to his conclusion that the MMR vaccination was a substantial factor in causing Michelle's autism.

Finally, Dr. Kinsbourne also seemed to find it important that Michelle's autism falls, in his opinion, into the category of "regressive autism." Regressive autism is a form of autism in which the child does not merely fail to develop normally, but actually *loses* skills in language and related areas, usually sometime during the second year of life. (Ex. 61, pp. 9-10; Tr. 1054-55, 1059A-60, 1176.) This aspect of Dr. Kinsbourne's testimony seemed to indicate his view that the MMR vaccine is likely to play a causative role *specifically* in cases of *regressive autism*, as opposed to autistic cases in which the child does not experience regression. And the petitioners' briefs also indicate that the petitioners' causation theory in this case is specifically targeted to cases of *regressive* autism, as opposed to other cases of autism.[106] (*E.g.*, P1 at 122.)

B. Reasons for rejecting petitioners' general theory

After a complete analysis of the record, I conclude that I must reject both petitioners' *general theory* concerning the causation of autism, and their contention that the measles virus substantially contributed to *Michelle's own* autism. Petitioners have failed to demonstrate that it is "more probable than not" either that the MMR vaccine *can* cause or contribute to autism in general, or that a MMR vaccination *did* cause or contribute to Michelle's autism. In this Part B of Section VII of this Decision, I will discuss petitioners' and Dr. Kinsbourne's *general* theory that the measles virus can cause or contribute to autism. Thereafter, in Part C, I will discuss the issue of the *specific* causation of Michelle's own autism.

I will divide my discussion, concerning petitioners' *general theory* that the measles virus can contribute to the causation of autism, into nine parts below. Those points may be summarized as follows:

First, Dr. Kinsbourne's general causation theory depends, in *any* individual case, upon the existence of a reliable laboratory test that finds persisting measles virus in the autistic child's body. Such a *reliable* test, however, likely does not exist.

Second, even if in some case a reliable test *could* demonstrate the existence of persisting vaccine-strain measles virus in an autistic person's body, the available evidence still does not demonstrate that measles virus persistence in the brain would result in *autism*.

Third, the fact that the *wild measles virus* has never been shown to cause autism makes it quite unlikely that the *vaccine-strain* form of the measles virus can cause autism.

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[106]Dr. Kinsbourne elaborated further concerning his general causation theory in his expert reports and hearing testimony in the *Snyder* case. (*Snyder* Exs. 29, 215; *Snyder* Tr. 438-563A.) I have fully considered those reports and that testimony of Dr. Kinsbourne in reaching my conclusions stated in this opinion.

Fourth, Dr. Kinsbourne's causation theory seems unlikely in light of several accepted understandings concerning the causation of autism. The theory seems doubtful in light of the accepted points that there is a strong genetic component to autism, and that the only non-genetic factors that have ever been conclusively found to contribute to autism are factors that influence development during the *early prenatal* period. The petitioners' theory is also *directly contradicted* by autopsy studies demonstrating that the brains of autistic individuals show abnormal features that, of necessity, would have occurred during specific parts of the *prenatal* period.

Fifth, there are other difficulties with Dr. Kinsbourne's theory, especially the contradictions and inconsistencies in Dr. Kinsbourne's testimony concerning the appropriate *time period* between MMR vaccination and onset of autism symptoms, under his causation theory.

Sixth, the testimony of Dr. Corbier, Dr. Hepner, and Dr. Kennedy fails to provide any substantial support to Dr. Kinsbourne's causation theory.

Seventh, the qualifications of the respondent's experts concerning this issue substantially exceed the qualifications of the petitioners' expert witnesses.

Eighth, the epidemiologic evidence, consisting of numerous studies by qualified medical researchers around the world, adds another reason to reject the petitioners' theory that the MMR vaccine can contribute to the causation of autism.

Ninth, two well-qualified committees of medical experts, selected by the Institute of Medicine, have extensively studied the general MMR/autism causation issue, and have concluded that the evidence favors *rejection* of the proposition that the MMR vaccine can cause autism.

I will explain each of these nine points in detail below.

1. Petitioners' theory depends upon the existence of reliable laboratory test findings of persisting measles virus, but no such reliable findings exist.

Dr. Kinsbourne made it clear that his causation theory depended upon *assuming* the existence of a reliable laboratory test that finds persisting measles virus in the autistic child's body. (*E.g.*, Tr. 1180A, 1196.) Dr. Kinsbourne indicated that in *no case* could he opine that a person's autism was caused by the MMR vaccine in the absence of a reliable finding of persisting measles virus in the vaccinee's body. (Tr. 1180A, 1183A, 1196A; *Snyder* Tr. 453A, 491A-93A, 535A, 538A.) However, for the reasons already explained above in section VI of this Decision, I have concluded that the Unigenetics laboratory results purporting to find persisting measles virus in *Michelle*'s case, and purporting to find persisting measles virus in *other* autistic children, are *not* reliable. Petitioners clearly have failed to demonstrate that *any* laboratory has reliably found persisting measles virus in *any* autistic individual. Therefore, petitioners' and Dr. Kinsbourne's *general causation* theory, that the MMR vaccine can contribute to the causation of autism, is left without expert support, and must be rejected for that reason alone.

2. The available evidence does not demonstrate any substantial likelihood that measles virus persistence in the brain would cause autism.

Dr. Kinsbourne hypothesizes that Michelle's autism resulted, in substantial part, from the persistence of measles virus in Michelle's brain. However, respondent's experts argued convincingly that there is no good reason for concluding that the persistence of measles virus in a human brain would cause *autism*. Rather, those experts argued, the available evidence indicates that the persistence of measles virus in a brain would much more likely result in *death*.

First, I note the testimony of Dr. Diane Griffin, who has very impressive credentials as an expert on the measles virus. (Tr. 2743A-48A.) Dr. Griffin testified that Dr. Kinsbourne's hypothesis that the measles virus enters the brain and causes autism is not biologically plausible. (Tr. 2795A-97.) She stated that "[w]e know a lot about what measles virus does when it gets in the brain, and none of it is autism." (Tr. 2796; *see also* Tr. 2865.) She explained that persisting measles virus infections of the brain are known to result in one of two conditions: SSPE and MIBE.[107] (Ex. V, pp. 9-10; Tr. 2785.) Dr. Griffin stated that SSPE is the "only disease caused by persistent MV [measles virus] infection in immunologically competent individuals." (Ex. V, p. 9.) In individuals who are severely immunologically *deficient*, on the other hand, persistent measles virus infection of the brain results in MIBE. (Ex. V, p. 10.) Both conditions almost always result in death, with MIBE taking a swifter course to that end. (Ex. V, pp. 9-10.)

A second expert of respondent, Dr. Brian Ward, a medical doctor specializing in infectious disease and virology who has also studied the measles virus, similarly testified that Dr. Kinsbourne's hypothesis was speculative and unlikely. Dr. Ward explained that when measles virus persists in a human brain, death results from SSPE or MIBE, and any other outcome would be "new biology," currently unknown to medical science. (Tr. 1828A-29A, 1834A, 1914-15; Ex. BB, pp. 6-7; *Snyder* Tr. 980A-81A.)

Two additional experts of respondent, pediatric neurologists Dr. Max Wiznitzer and Dr. Robert Rust, made essentially the same point. Dr. Wiznitzer testified that the only known result of a persisting measles virus brain infection would be death by SSPE or MIBE. (Tr. 1626-29.) He explained that the symptoms known to be caused by measles virus in the brain are "totally different" from the symptoms of autism. (Tr. 1627-28.) Dr. Wiznitzer opined that Dr. Kinsbourne's theory "does not follow any [known] biologic model of a measles infection of the brain" (Tr. 1774A), so that Dr. Kinsbourne's theory would require a "novel biologic model," for which no evidence exists (Tr. 1776A). Similarly, Dr. Rust testified that "we understand especially what measles virus may or may not do within the nervous system," and that knowledge is incompatible with the theory that the persisting measles virus would cause *autism*. (*Hazlehurst* Tr. 507A.) Dr. Rust explained that

[107]Respondent's experts explained that the measles virus can have a third type of effect on the central nervous system--namely, post-infectious encephalomyelitis. That condition, however, is not directly caused by the measles virus, but is the result of an immune-mediated process *prompted* by a measles virus infection. (Tr. 1626-29.)

persisting measles virus would result in SSPE or MIBE. (*Id*. at 508A-09A.) He added that medical scientists were "try[ing] to keep an open mind" concerning the issue of whether measles virus might cause autism as well, but noted that researchers had looked for that possibility ("gone at that with a will"), but simply had not found any evidence to support that theory. (*Id*. at 508A.)

Of course, it is not impossible that persisting measles virus in a human brain might in some individuals have a result different from SSPE or MIBE. But Dr. Kinsbourne has supplied no *evidence* for such a possibility, beyond his own unsubstantiated speculation.[108] And as to the issue of whether I should adopt Dr. Kinsbourne's unsubstantiated speculation on this point, concerning what effect a persisting measles virus *might* cause in a human brain, I find the evidence to weigh heavily in respondent's favor. On this point, I have on one side the testimony of Drs. Griffin and

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[108]At the end of the evidentiary hearing in this case, the petitioners produced an "editorial" published in a medical journal by Dr. Paul Dyken, in which Dr. Dyken presented a theory concerning the existence of a syndrome that he calls "Measles Induced Neuroautistic Encephalopathy" or "MINE." Paul Dyken, *Some Aspects about the Clinical and Pathogenetic Characteristics of the Presumed Persistent Measles Infections: SSPE and MINE*, 2 J. PEDIATRIC NEUROLOGY 121 (2004). (P. Trial Ex. 17.) Dr. Dyken wrote that his postulated syndrome was "first recognized in the late 1990s by Wakefield." (*Id*. at 122.) According to this theory, the vaccine-strain measles virus causes autism. (*Id*. at 122-23.)

This document of Dr. Dyken, and his MINE theory, were never mentioned by any of the petitioners' experts in this *Cedillo* case, nor did petitioners mention the document or theory in their post-hearing briefs. The record contains no significant description of Dr. Dyken's training, experience, or credentials. Strangely, the only use of the document by petitioners in this *Cedillo* case was to ask a question about it to one of respondent's witnesses, during the final minutes of the last day of hearing testimony in this case. (Tr. at 2847-53.) However, Dr. Kinsbourne did mention the document briefly during his hearing testimony in the *Snyder* case. (*Snyder* Tr. 455A-56A.) He noted that Dr. Dyken was one of the physicians involved in the above-described British litigation, and seemed to suggest that Dr. Dyken's advocacy of the MINE theory supported Dr. Kinsbourne's MMR/autism causation theory.

However, respondent's expert Dr. Ward opined that Dr. Dyken's MINE theory, which was published in an "obscure" medical journal, is not scientifically sound. (*Snyder* Tr. 942A-43A.) I reach the same conclusion. Dr. Dyken's editorial does not explain his theory in any detail. Dr. Dyken does not describe any research of his own supporting his conclusion. Rather, as Dr. Ward suggested (*Snyder* Tr. at 943A), Dr. Dyken seems to have merely looked at Dr. Wakefield's 1998 article, accepted it as true, and proposed a new name for the type of measles-caused autism that Wakefield had postulated. But I have found that Wakefield's 1998 article provides no support for the general MMR/autism causation theory. (See pp. 117-18 below.) I conclude that Dr. Dyken's editorial, too, offers no support to the petitioners' MMR/autism causation theory.

(I also note that when the petitioners electronically filed their Trial Ex. 17, the Dyken editorial, they filed only two of the article's four pages. I have read the entire document, and obtained my page references set forth above, from a "paper copy" of the exhibit supplied by petitioners' counsel during the hearing.)

Ward, with vast experience studying the measles virus, plus the similar testimony of Drs. Wiznitzer and Rust; on the other side is the testimony of Dr. Kinsbourne, who has no special expertise concerning the measles virus. I find the respondent's experts to be much more credible and persuasive on this point. I find it to be quite unlikely that a persisting measles virus in the brain would result in *autism*.[109]

3. The evidence indicates that the wild measles virus has not been a cause of autism.

The petitioners' contention is that the *vaccine-strain* form of the measles virus can persist in a child's body and contribute to the causation of autism. Yet petitioners have virtually ignored the very important point that the available evidence makes it appear *very unlikely* that the measles virus in its *natural*, "*wild*" *form* has ever been a cause of autism. It is noteworthy that in many causation controversies in the history of the Vaccine Act, petitioners have urged that if the *wild* form of a virus can cause an injury, then it is plausible that the *vaccine form* of that virus can cause the *same* injury, since the vaccine-strain version is an intentionally attenuated--*i.e.*, weakened--form of the virus. In this case, in contrast, the petitioners seem to be advancing a *novel* approach to vaccine causation, by arguing that the weakened, *vaccine-strain* form of the measles virus can cause autism, even though the *wild* measles virus has never been shown to cause autism. However, none of the petitioners' experts have ever *explained* why the *vaccine-strain* form of the measles virus might be capable of causing autism, even though the wild form of the measles virus has never been shown to cause autism.

In this regard, I note that respondent's expert Dr. Ward supplied testimony demonstrating that it is *extremely unlikely* that the wild measles virus has ever caused autism. Dr. Ward noted that billions of infants worldwide were infected by the wild measles virus just during the period from 1948 until the early 1970's, when measles vaccines began to be widely implemented. (Ex. BB, p.

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[109]Dr. Kinsbourne pointed to research articles indicating that brain inflammation is present in autism. *E.g.*, D. Vargas et al., *Neuroglial Activation and Neuroinflammation in the Brain of Patients with Autism*, 57 ANNALS OF NEUROLOGY 67 (2005). (EX. 61, TAB MMM); C. Pardo et al., *Immunity, Neuroglia and Neuroinflammation in Autism*, 17 INT'L REV. PSYCHIATRY 485 (2005). (Ex. 61, Tab ZZZ.) Respondent's experts, however, did *not* contest the proposition that *inflammation* may be present in the brains of autistic persons, and may possibly play a causal role in autism. They argue, rather, that Dr. Kinsbourne has failed to offer any persuasive evidence that the *vaccine-strain measles virus* can play any role in *causing* brain inflammation in autistic persons. For example, Dr. Wiznitzer noted that the authors of the Vargas article did *not* suggest that the inflammation described in the articles could result from a measles infection, MMR vaccine, or any type of viral infection. (Tr. 1783A-84A.)

Moreover, as set forth above, respondent's experts argued persuasively that a chronic infection of the brain by the measles virus would likely result in *death*, not autism or chronic inflammation. Thus, I conclude that, although *inflammation* may play a role in causing autism, petitioners have wholly failed to demonstrate that it is probable that the *MMR vaccine* can play a role in causing chronic brain inflammation or autism.

5; Tr. 1826A-27.) Even today, perhaps 500,000 children each year are infected with wild measles worldwide. (Tr. 1827.) Yet there have been no reported cases of autism being caused by wild measles since 1948. (Ex. BB, p. 5; Tr. 1827.)

Further, Dr. Ward explained that if the wild measles virus was in fact causing autism, epidemiologists would not have missed that association. That is because measles outbreaks typically come in waves, so that epidemiologists could easily notice if increases in autism occurred soon after measles epidemics. (Tr. 949A.) Dr. Ward noted that after widespread outbreaks of measles in certain areas of the U.S. and Canada during the 1990s, no coincidental increases in *autism* in those areas were noted. (*Id*.)

Dr. Ward's testimony in that regard was supported by an epidemiologic study discussed by Dr. Fombonne during the hearing.[110] The study analyzed whether the incidence of autism was affected by the waves of measles outbreak during the period between 1966 and 1986, and found no association. (Tr. 2549-50A; Ex. P, Att. 28, p. 548.)

Petitioners' expert Dr. Kinsbourne did offer one item of evidence intended to suggest that the wild measles virus might be capable of causing autism. He wrote that a medical article, published in German by Bosch in 1948[111] reported that "Heller's disease," a disease that "often reaches an autistic endpoint," was "triggered by a wild measles infection." (Ex. 61, p. 11.) Petitioners filed only a copy of the Bosch article in its original German (Ex. 61, Tab QQQ), not an English translation. However, respondent's expert Dr. Ward obtained an English translation of a summary of the article,[112] and testified that the article described just *two* cases of "infantile dementia," with onset shortly after wild measles infection. (Tr. 1825A-26A.)

The Bosch article cannot be said to offer significant support for the proposition that the wild measles virus can contribute to the causation of autism. First, it is unclear to what extent the condition reported in the article, described as "Heller's Disease" or "infantile dementia," actually resembles autism. Moreover, Dr. Ward testified that there have been no cases of autism after measles infection reported in the medical literature *since* 1948 (Ex. BB, p. 5; Tr. 1826A-27), and that the authors of the Bosch article itself stated that they found no reported cases *prior* to 1948 (Tr. 1827). Accordingly, even assuming that Heller's Disease resembles autism, the existence of only two case reports of autistic-like disorders, among the *billions* who have suffered measles infection over many decades, hardly constitutes evidence of a causal relationship. Further, as noted above, the testimony of Dr. Ward and Dr. Fombonne indicates that an association of measles infection and

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[110]W. Chen et al., *No Evidence for Links Between Autism, MMR and Measles Virus*, 34 PSYCHOLOGICAL MED. 543 (2004). (Ex. P, Att. 28.)

[111]Gerhard Bosch, *Demenz als Folge von Masernencephalitis im Kleinkindesalter*, 19 DER NERVENARZT 254 (1948). (Ex. 61, Tab QQQ.)

[112]Apparently that English translation was never filed into the record of this case.

autism likely *would* have been noticed if it existed. Thus, the Bosch case reports *cannot* be considered as evidence that the wild measles virus can cause autism.

To the contrary, the evidence provided by Dr. Ward and Dr. Fombonne makes it *extremely unlikely* that the wild measles virus has ever caused autism. And the petitioners have not even attempted to explain why the *vaccine-strain* measles virus might cause autism when the *wild* measles virus apparently does not.[113] To the contrary, the respondent's well-credentialed measles expert, Dr. Griffin, testified that she could not understand how the *vaccine-strain* measles virus might cause something that the *wild* measles virus does not. (Tr. 2779A.) This analysis concerning the wild measles virus, thus, provides another strong reason to conclude that the petitioners' MMR/autism causation theory has no validity.[114]

4. Petitioners' theory seems unlikely 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 have argued that petitioners' general causation theory advanced in this case seems unlikely in light of certain accepted scientific understandings concerning the causation of autism. 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 appear to be well-accepted and not disputed by the petitioners in this case, are relevant here. The first basic point is that there is a

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[113]The petitioners did file a medical article that offers a suggestion why the *vaccine-strain* measles virus might cause autism while the *wild* measles virus does not. Paul Dyken, *Some Aspects about the Clinical and Pathogenetic Characteristics of the Presumed Persistent Measles Infections: SSPE and MINE*, 2 J. PEDIATRIC NEUROLOGY 121 (2004). (P. Tr. Ex. 17.) Dr. Dyken theorizes, without explanation, that while chronic brain infection with the full-strength *wild* measles virus causes death, the *vaccine-strain* form of the virus might instead cause autism, because it is attenuated. P. Trial Ex. 17 at 122. However, as discussed above (p. 90, fn. 108), none of the petitioners' experts have vouched for the validity of Dyken's theory, and respondent's expert Dr. Ward persuasively explained why that article should *not* be given any credence. As explained above (p. 90, fn. 108), I find the Dyken article to be of extremely dubious merit, and I do not find it to be competent evidence for *any* proposition.

[114]It is also noteworthy that while the petitioners contend that the strain of the measles virus contained in the *MMR* inoculation can cause autism, they have also never explained why that *MMR-strain* measles virus would be more likely to cause autism than the strains contained in the old *monovalent measles vaccines* (measles only, without rubella or mumps), which were used for many years prior to the introduction of the combined MMR vaccine.

very strong genetic component to the causation of autism. (Ex. HH, p. 22; Ex. JJ, pp. 33-34; Ex. P, paras. 43-53; Ex. N, p. 1; Ex. FF, p. 3; Tr. 1303A-08A, 1489A-1507, 1510.) 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). (Ex. JJ, p. 34; Ex. P, para. 49.) 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 about 25 times higher than an unrelated person; but among *identical* twins, who share 100% of their genes, the chance of the second twin having autism would be even greater, about 300 times the risk of an unrelated person. (Ex. JJ, p. 34; Ex. P, para. 50; Ex. N, pp. 1-2; Tr. 1306A-09A; 1489A-95; 1499-1501, 1514; *Hazlehurst* Tr. 473A-75A.) 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 one hundred percent of their genes, there is a small percentage of instances in which one twin experiences autism and the other does not, indicating that non-genetic factors must 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. For example, approximately three to four percent of children with autism have been identified as having a specific genetic defect known as "Fragile X," while another disorder involving a specific genetic defect, known as "tuberous sclerosis," is identified in perhaps another one percent. (Tr. 1304.) 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 *non-genetic* factors have been identified and accepted as factors in causing autism, but those consist of exposures during the *early prenatal* period. (Ex. JJ, p. 33; Ex. P, para. 54; Tr. 1494-95.) Specifically, *in utero* exposure to thalidomide, valproic acid, misoprostol, and rubella virus infection have been found to increase the risk of autism. (Ex. JJ, p. 33; Ex. P, para. 54.) 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, it appears that 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. P, para. 54; Ex. JJ, p. 33.)

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 particular abnormal features that of necessity would have occurred during specific parts of the *prenatal* period, as the unborn child developed. (Ex. JJ, pp. 33-34; Ex. P, paras. 56-57; Tr. 1310-13A, 1318A.)

b. The petitioners' argument

The petitioners in this case do not dispute that genetics play a large role in the causation of autism. They argue, rather, that it is likely that genetics and the MMR vaccine 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 vaccine-strain measles virus from the MMR-vaccination becomes the "second hit" that causes the individual to become autistic. (P1, p. 119 fn. 117, pp. 121-22; Tr. 1049A; Ex. 61, pp. 10-11.)

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 (p. 94), 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 *MMR vaccine* is another environmental factor that can contribute to the causation of autism. At that point, the petitioners' argument goes far beyond the existing evidence. Moreover, it seems to me that the three accepted points concerning the causation of autism, set forth above, make the petitioners general causation theory seem unlikely, in two ways. First, we know for certain that *genetic* factors and *prenatal* exposures can cause 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 the measles virus, but it does make one *cautious* about attributing causation to any postnatal factor. Secondly, as noted above (p. 94), autopsy studies 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 a vaccine that is received during the second year of life.

ii. Evidence concerning possibility of causation by postnatal factors

The petitioners' briefs have pointed to a number of medical articles or other places in the record where it is mentioned or speculated that the causation of autism might be influenced by "environmental factors." (P2, pp. 7-8, 20-21; P3, pp. 4-8.) But in many of the articles cited by petitioners, there is merely a general mention of "environmental factors" as being linked or possibly linked to the causation of autism, without any specification of *postnatal* environmental factors. (*See*,

e.g., the following items cited by petitioners at P2, pp. 7-8, 20-21 and P3, pp. 6-8: statements by Dr. Corbier in *Hazlehurst* Tr. at 270A, 418A-421A;[115] Libbey article,[116] *Hazlehurst* Ex. G, Tab 13, p. 252; Trottier article,[117] *Hazlehurst* Ex. G, Tab 51 (at p. 112, the article mentions "early environmental insult," but at p. 105 it is clarified that the author meant "insults early *in gestation*" (emphasis added)); Vojdani article,[118] *Hazlehurst* Ex. G, Att. 55, p. 189; Lainhart article,[119] *Snyder* Ex. 71, pp. 231, 234.) Thus, these mentions of "environmental factors" provide no support to the proposition that *postnatal* factors can cause autism, since, as explained above, it is well-accepted that certain *prenatal* environmental factors--specifically thalidomide, misoprostol, valproic acid, and rubella virus infection--are associated with autism.

Some of petitioners' other citations to the record require a bit more comment, but again fail to offer any substantial support to the proposition that *postnatal* factors can cause autism. First, the petitioners point (P3, p. 7) to an article (Hertz-Picciotto article[120]), that mentions in its abstract the possibility that the "early post-natal environmental milieu" (Ex. 61, Tab HH, p. 1119) might affect the development of autism. That article, however, cites, as examples of environmental factors associated with autism, *only* the same *prenatal* factors discussed above--*i.e.*, exposure to thalidomide, valproic acid, or rubella virus. (*Id*. at 1119.) They cite to (P3, p. 7) a few pages of the

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[115]Dr. Corbier listed a number of different "environmental factors" that he suspects might contribute to causing autism, but he did not specifically say whether such factors could work only prenatally, through the mother, or could work postnatally. (*Hazlehurst* Tr. 417A-22A.) Even assuming that he meant that some of the factors could cause autism by affecting a child postnatally, Dr. Corbier offered *absolutely no evidence or explanation as to why* he believes that such postnatal environmental factors might contribute to causing autism.

[116]Jane Libbey et al., *Are There Altered Antibody Responses to Measles, Mumps or Rubella Viruses in Autism?*, 13 J. NEUROVIROLOGY 252 (2007). (*Hazlehurst* Ex. G, Att. 13.)

[117]G. Trottier et al., *Etiology of Infantile Autism: A Review of Recent Advances in Genetic and Neurobiological Research*, 24 J. PSYCHIATRY & NEUROSCIENCE 103 (1999). (*Hazlehurst* Ex. G. Att. 51.)

[118]A. Vojdani et al., *Infections, Toxic Chemicals and Dietary Peptides Binding to Lymphocyte Receptors and Tissue Enzymes are Major Instigators of Autoimmunity in Autism*, 16 INT'L J. IMMUNOPATHOLOGY & PHARMACOLOGY 189 (2003). (*Hazlehurst* Ex. G, Att. 55.)

[119]Janet Lainhart et al., *Autism*, *Regression*, *and the Broader Autism Phenotype*, 113 AM. J. MED. GENETICS 231 (2002). (*Snyder* Ex. 71).

[120]Irva Hertz-Picciotto et al, *The CHARGE Study: An Epidemiologic Investigation of Genetic and Environmental Factors Contributing to Autism*, 114 ENVTL. HEALTH PERSPECTIVES 1119 (2006). (Ex. 61, Tab HH.)

transcript of an Institute of Medicine "workshop" on the topic of *Autism and the Environment*,[121] but at the cited pages the speakers suggest only that environmental triggers of autism should be *looked for*, and *might* be found, in the future. (*Hazlehurst* Ex. 58, pp. 17, 19, 20, 115.) Petitioners also rely (P3, pp. 7-8) on an article in which the authors suggest that *unspecified* environmental factors might be causing or affecting autism by causing neuronal cell death "some time after birth as a result of insult." (Kern and Jones article,[122] *Hazlehurst* Ex. G, Att. 4, p. 494.) But I found that article to be of doubtful validity, especially since it found to be "pivotal" (*id*. at 490) the two studies by Holmes and Bradstreet 2003 that I have found to be of dubious merit. (See pp. 29-30 above.)

Petitioners also point (P3, p. 6) to a statement by another of respondent's experts, Dr. Rust, indicating that autism can be "influenced" by "environmental influences." (*Hazlehurst* Tr. 463A.) It is unclear what Dr. Rust meant by that statement. He did *not* say that post-natal environmental factors can contribute to *causing* autism. The only example that Dr. Rust provided of such "environmental influences" was "deprivation, * * * where children don't get sensory input, sensory deprivation." (*Id*.) It seems doubtful that he thereby meant that sensory deprivation could *cause* autism; from the context, it seems likely that he meant that such deprivation could *influence the course* of autism. In any event, Dr. Rust's basic point, in this part of his testimony, was that regressive autism is actually a result *not* of environmental factors but of *genes*, which begin to be "expressed" around the second year of life ("it seems that that's a point at which additional genetic signals come on board that are meant to take the place of preceding signals"--*id*. at 460A). Note that Dr. Rust stated that *prenatal* exposures can cause autism (*id*. at 464A-65A), but added that he was not aware of any postnatal "toxic insults" that could cause autism (*id*. at 465A.) Thus, this unexplained remark by Dr. Rust hardly constitutes significant evidence that postnatal environmental factors can contribute to causing autism.

In addition, Dr. Kinsbourne himself testified that the question of whether infections can cause autism "is being looked at," and that there had been "rare" cases in which "encephalitis" had been said to cause autism. However, he cited no evidence for those statements. (Tr. 1052A-53A.)

On the other hand, several items in the record do seem to suggest the possibility that *postnatal* factors *might* play some role in the causation of autism. Petitioners cite (P3, p. 7) a case report of a boy who developed autistic behavior after experiencing herpes encephalitis at age 11.[123] Petitioners cite (P3, p.6) a statement made by Dr. Andrew Zimmerman, one of respondent's experts, who said that environmental factors "may" be involved in the causation of autism, in a context that

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[121] Institute of Medicine, AUTISM AND THE ENVIRONMENT: CHALLENGES AND OPPORTUNITIES FOR RESEARCH (The National Academies Press 2008.) (*Hazlehurst* Ex. 58.)

[122] Janet K. Kern & Anne M. Jones, *Evidence of Toxicity, Oxidative Stress, and Neuronal Insult in Autism,* 9 J. TOXICOLOGY & ENVTL. HEALTH 485 (2006). (*Hazlehurst* Ex. G, Att. 4.)

[123] M. Ghaziuddin et al., *Autistic Symptoms Following Herpes Encephalitis*, 11 EUR. CHILD & ADOLESCENT PSYCHIATRY 142 (2002). (*Hazlehurst* Ex. 37, Att. A.)

implied *postnatal* factors. (Ex. 131, p.1.) They also rely on another article, which states that research in recent years has suggested that autism may not, as previously thought by some experts, be exclusively prenatal in origin.[124] They point also to a French study which seems to suggest that "heavy metals" might possibly play a role in causing or influencing autism.[125]

Petitioners also cite an article by Pardo[126] suggesting the possibility of a role for *postnatal* environmental factors in causing autism. (Ex. 129.) At one point, that article states that "environmental factors, including both maternal/ uterine and *postnatal events*, may well modify the underlying genetic substrate and lead to greater abnormalities in neuronal [brain cell] organization." (*Id.* at p. 436, emphasis added.) At another point, the article states that "environmental factors" can influence "early postnatal brain development." (*Id.* at 435, figure 1.) (Neither reference, however, indicates *what type* of "environmental factors" the authors had in mind, or what was meant by the "early" postnatal period.)

Finally, petitioners cite an article by Cohly and Panja,[127] which also suggests that various postnatal factors *might* contribute to the causation of autism. And I also note a remark made by one of respondent's experts, Dr. Cook, that he was aware of a "series of cases in Tanzania where it appeared that malaria contributed" to the causation of autism. (Tr. 1541A.)

Thus, the articles and other cited items listed in the previous three paragraphs illustrate the important point 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. Clearly, some scientists are currently exploring the possibility of a causal role of postnatal factors, and possibly 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. Moreover, it is significant that none of the petitioners' *experts* have *discussed* those articles and the other cited items at all, failing to explain why such reports might offer any significant support to the proposition that *postnatal* environmental factors can contribute to the

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[124]Martha R. Herbert, *Autism: A Brain Disorder, or a Disorder That Affects the Brain*?, 2 CLINICAL NEUROPSYCHIATRY 354 (2005).

[125]Robert Nataf et al., *Porphyrinuria in Childhood Autistic Disorder: Implications for Environmental Toxicity,* 214 TOXICOLOGY & APPLIED PHARMACOLOGY 99, 106 (2006). (*Hazlehurst* Ex. G, Att. 25, pp. 99, 106.)

[126]Carlos A. Pardo & Charles G. Eberhart, *The Neurobiology of Autism*, 17 BRAIN PATHOLOGY 434 (2007). (Ex. 129.)

[127]H.H. Cohly & A. Panja, *Immunological Findings in Autism*, 71 INT'L REV. NEUROBIOLOGY 317 (2005). (*Hazlehurst* Ex. E, Att. 12.)

causation of autism.[128] Rather, as noted above (pp. 93-94), *most* of the existing data, 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 unconfirmed 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.[129]

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.

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[128]The petitioners should not have waited until their *post-hearing briefs* to raise the factual contention that postnatal factors *in general*, other than the MMR vaccination, have been shown to contribute to the causation of autism. Clearly, it would have been far better if petitioners had raised that contention in their prehearing expert reports, and then had one or more experts *discuss* that contention during the evidentiary hearing. It is true that special masters of this court are *legally entitled* to evaluate medical issues based on medical articles alone, if circumstances so necessitate. *Moberly v. Secretary of HHS*, No. 98-910V, slip op. at 31 (Fed. Cl. Jan. 30, 2009). However, it is far better when special masters are given the opportunity to hear *expert witnesses analyze* such issues and articles. Thus, special masters should be informed of the existence of a factual contention *prior* to an evidentiary hearing and should be supplied with any relevant articles prior to the hearing. The party raising the factual contention should then have an expert *address* those articles at the hearing.

To be sure, it seems likely that the petitioners filed these particular articles as a *response* to the respondent's argument that only genetic factors and prenatal exposures have been reliably demonstrated to cause autism. But that argument was clearly set forth in respondent's *expert reports*, filed well before the evidentiary hearing in this case. The petitioners certainly could have filed their articles concerning various potential postnatal causes prior to the hearing, and then had an expert *discuss and explain* those articles at the hearing.

[129]For example, respondent's expert Dr. Eric Fombonne, an expert with extensive experience studying the causation of autism, testified that, in contrast to the evidence with respect to *prenatal* factors, to date no *postnatal* environmental factors have been reliably demonstrated to play a causative role in autism. (Ex. P, para. 48.) Dr. Fombonne explained that scientists have specifically studied the question of whether *infectious diseases* suffered by children postnatally, *specifically including measles infection*, are associated with an increased risk of autism, but have found no such association. (Tr. 1305A.) Similarly, the report of the Institute of Medicine concerning the causation of autism (see p. 124 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 * * *. (Ex. JJ, p. 33.)

Second, the petitioners' theory is *strongly contradicted* by the above-discussed autopsy studies, which indicate that autism is caused by brain malformation 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 (pp. 97-98) raising the *possibility* that postnatal factors might play a causal role. Therefore, my point set forth in this section VII.B.4 of this decision is certainly *not* the strongest argument against the petitioners' theory. But this point does add at least 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 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.

Third, I also wish to be clear that I have *not* concluded that Michelle Cedillo'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 Michelle's vaccination contributed to the causation of her autism, so that the burden *never shifted* to respondent to demonstrate, under part (B) of §300aa-13(a)(1), that some *other* factor caused her autism. *See*, *e.g.*, *DeBazan v. Secretary of HHS*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). My point in this part VII.B.4 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 *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 the MMR vaccine, 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, the MMR vaccine, can contribute to the causation of autism. And that they have failed to do.

5. Other problems with Dr. Kinsbourne's theory

a. Dr. Kinsbourne's testimony concerning timing

Dr. Kinsbourne's testimony was vague and unpersuasive concerning the issue of what might be an appropriate *time period*, between MMR vaccination and the onset of symptoms of autism, under his causation theory. Dr. Kinsbourne stated that, in Michelle's case, he believed that the vaccine-strain measles virus entered Michelle's brain about seven days after her MMR vaccination (Tr. 1146), and he indicated that her autistic symptoms began during the period of fever about one week after the vaccination, or shortly thereafter. (Ex. 61, p. 3; Tr. 1041, 1175A-76, 1184A.) But Dr. Kinsbourne admitted that he really had no idea how long it would likely take, as a matter of pathologic process or physiologic process, for a measles virus entering the body via MMR vaccination to reach the brain. (Tr. 1146-47.) Under *Althen*, a petitioner must show a "proximate temporal relationship between vaccination and injury"--*i.e.*, it must be shown that the particular vaccinee's injury occurred within a time period after vaccination that would be medically *expected* for a vaccine-caused injury of that type. 418 F.3d 1274, 1278 (Fed. Cir. 2005). However, Dr. Kinsbourne, by acknowledging that he does not know how long it would take the measles virus to reach the brain after an MMR vaccination, has, in effect, acknowledged that he *doesn't know* what would be the appropriate time period for onset of an autism condition caused by an MMR vaccination. He acknowledged, in effect, that he is merely *guessing* or *speculating* when he indicates that the alleged onset of Michelle's autism symptoms, which he apparently assumes to have occurred about seven days after her MMR vaccination or shortly thereafter, was an appropriate time period for a vaccine-caused autism condition.

Moreover, Dr. Kinsbourne's assertion, that the vaccine-strain measles virus likely reached Michelle's brain in about seven days, seems to be inconsistent with the rest of his general theory, and petitioners' general theory, of causation. Petitioners' and Dr. Kinsbourne's general causation theory, as I understand it, is that it is the *persistence* of the measles virus that causes or contributes to autism. That is, according to Dr. Kinsbourne, in most infants who get the MMR vaccine, the measles virus is appropriately cleared from the body by the infant's immune system "in a few weeks." (Ex. 61, p. 20.) But, according to the petitioners' theory, in some children a defect in the immune system results in a failure to clear the measles virus from the body, and the *persisting* measles virus then adversely affects the brain. (*E.g.*, Ex. 61, p. 11-12; Tr. 1087.)

However, Dr. Kinsbourne seemed to indicate that in *Michelle's* case, her first autism symptoms occurred within about seven days of her MMR vaccination, or very shortly thereafter. (Ex. 61, p. 3; Tr. 1041, 1175A-76, 1184A.) That would be is *prior* to the period of a "few weeks" in which a *normal* immune system would clear the measles virus, according to Dr. Kinsbourne. Thus, if the vaccine-strain measles virus was in fact already damaging Michelle's brain within about seven days after her vaccination, then this would not seem to be an example of damage because of "persistence" of the virus, because, at seven days (or even two or three weeks) after vaccination, the period of abnormally long "persistence" had *not yet begun*.

There is another significant problem with Dr. Kinsbourne's comments concerning the timing of symptoms. Dr. Kinsbourne emphasized his view that Michelle was a normally developing child who experienced the onset of autism symptoms very soon after her MMR vaccination (*e.g.*, Ex. 61, p. 3; Tr. 1040-42, 1175A-76, 1184A). He seemed to imply that this apparent onset soon after the vaccination supported his theory that the vaccination *caused* the autism. For example, Dr. Kinsbourne asserted that this apparent timing of onset indicated that Michelle's autism was more likely the result of a "disease" process, "rather than the aftermath of congenital maldevelopment." (Ex. 61, p. 18.) He made similar comments during the *Snyder* hearing, stating that in regressive autism, "something must have most likely happened to change the trajectory of development in such a radical way." (*Snyder* Tr. 479A-80A.)

The testimony of respondent's experts, however, refuted this aspect of Dr. Kinsbourne's reasoning. First, they demonstrated, as will be discussed below (pp. 127-30), that in *Michelle's particular case,* her first signs of autism actually *preceded* her MMR vaccination.

Moreover, 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 significant evidence that some environmental factor played any type of causal role in the autism. In this regard, those experts noted that, as explained above (pp. 93-94), there is a strong genetic component to autism, and that a number of disorders that are undisputedly genetic in origin, such as Huntington's disease and Rett's syndrome, do not manifest themselves until long after birth. (*E.g.*, Tr. 1495-1500; Ex. FF, pp. 3-4; Ex. P, paras. 38-39.) 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. 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 what is known of many genetic disorders.

b. Dr. Kinsbourne's reliance on Dr. Wakefield's theory

It is also noteworthy that when Dr. Kinsbourne, in his expert report, described his view that the measles vaccine can cause both autism *and* chronic gastrointestinal dysfunction, he *began* his discussion by citing the above-mentioned 1998 article by Dr. Andrew Wakefield and colleagues, the article that initiated the controversy over whether the MMR vaccine can cause autism. (Ex. 61, p. 12.) In his very next sentence, Dr. Kinsbourne relied upon a follow-up article published by Wakefield and colleagues in 2000. (*Id*.) These references indicate that Dr. Kinsbourne's causation theory was influenced by Dr. Wakefield's causation theory. To be sure, Dr. Kinsbourne's theory concerning the *exact mechanism* by which the persisting measles theory harms the brain, thereby causing the autism, differs somewhat from Dr. Wakefield's original hypothesis. But Dr. Kinsbourne's references to Dr. Wakefield's original article do indicate that Dr. Kinsbourne's

theory was *influenced* by Wakefield's theory, and that Dr. Kinsbourne seems to rely on Wakefield's published articles as *corroboration* for his theory.

Accordingly, it is relevant to note that Dr. Wakefield's causation theory has not only failed to gain acceptance in the medical community, but instead has been *strongly criticized*. I will discuss those criticisms below, in my discussion of the petitioners' gastrointestinal claims, since petitioners' gastrointestinal expert, Dr. Krigsman seemed even more strongly influenced by Dr. Wakefield's theory. (See pp. 143-44 below.)

To be sure, this is a minor point, since Dr. Kinsbourne's causation theory does differ, in the proposed mechanism, from Dr. Wakefield's original theory. I have evaluated Dr. Kinsbourne's theory on its *own merits*, and simply found that theory to be unpersuasive. However, the fact that Dr. Kinsbourne's theory was influenced by Dr. Wakefield's theory is at least worthy of note.

c. Dr. Kinsbourne's table of potential causes

Another argument raised by respondent concerning Dr. Kinsbourne's presentation concerns his table of "Medical Concomitants of Autism," provided in his expert report, which lists "measles" among the viral causes of autism. (Ex. 61, pp. 7-8.) Respondent has pointed out that this table is very similar to the table provided by Dr. Kinsbourne in Chapter 18 of the 2006 edition of the medical textbook, *Child Neurology*, with the conspicuous exception that the table in the textbook did *not* include *measles* as a cause of autism. (Ex. 61, Tab PP, p. 1117.) Based upon this discrepancy, respondent has argued that when writing for the general scientific community, Dr. Kinsbourne does not state the conclusion that the measles virus can cause autism, yet when testifying in litigation in support of an MMR-autism link, he now concludes that the measles virus can cause autism. (R1 at 52-53.)

In raising this point, respondent obviously is suggesting a lack of sincerity in Dr. Kinsbourne's opinion offered in this case. However, I find it unnecessary to determine whether such a harsh inference is warranted. That is, even assuming the sincerity of Dr. Kinsbourne's opinion, I have simply found his theory to be very *unpersuasive*, for all the reasons set forth in this Section VII of this Decision.[130]

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[130]Respondent also criticizes Dr. Kinsbourne because his theory of causation in this case relies exclusively on the theory that the *vaccine-strain measles virus* caused Michelle's *autism*, without presenting his own opinion as to whether *thimerosal-containing vaccines* played a role in weakening Michelle's *immune system*. (R1 at 48-49.) This particular criticism is without merit. I do not see Dr. Kinsbourne's opinion as in any way "incompatible," as respondent asserts (R1 at 49), with the testimony of petitioners' other experts. As I have noted above, if Dr. Kinsbourne were able to persuade me that it is "more probable than not" that a persisting vaccine-strain measles virus was a substantial factor in causing Michelle's autism, then I would compensate her for that condition, regardless of *why* that virus was able to persist. Dr. Kinsbourne simply chooses, reasonably enough, to leave to other experts the issue of *why* the virus was allegedly able to persist.

(continued...)

6. Opinions of Dr. Corbier, Dr. Hepner, and Dr. Kennedy

a. Dr. Corbier

The Cedillos have stated in their briefs that, concerning this MMR/autism general causation issue, they also rely upon the testimony of an expert offered by the petitioners in the *Hazlehurst* case, Dr. Jean-Ronel Corbier. (P2, pp. 1-5; P4, pp. 1-5.) Dr. Corbier, a board-certified pediatric neurologist, does have considerable experience in treating autistic children. (*Hazlehurst* Tr. 328A.) And Dr. Corbier's testimony does indicate his view that the MMR vaccine can play a role in causing autism, either by itself or in conjunction with thimerosal-containing vaccines,[131] in persons with a "genetic susceptibility" to autism. (*Hazlehurst* Ex. 26; *Hazlehurst* Tr. 265A-440A.)

I was present for the oral testimony of Dr. Corbier, and have carefully studied both his expert report and his oral testimony. I conclude that his testimony does *not* provide any substantial support

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[130](...continued)

Similarly, some of respondent's other criticisms of Dr. Kinsbourne, for failing to be able to answer certain questions in the area of virology, also seems to be misplaced. (See R1 at 49-50, fn. 34.) I do not find it unreasonable for Dr. Kinsbourne to defer to other experts on certain specific questions outside the areas of his special expertise.

However, I do find that Dr. Kinsbourne's presentation was *very unpersuasive* in many *other* very important respects, which I have detailed above.

[131]Although his testimony was quite vague, Dr. Corbier seemed to take an approach to this "general causation" issue that is as least slightly different from the theory offered by the petitioners and Dr. Kinsbourne in this *Cedillo* case. That is, in this case Dr. Kinsbourne contends that the role of the thimerosal-containing vaccines is to *weaken the child's immune system*, thereby allowing the vaccine-strain measles virus to persist in the child's system, and that it is the *persisting measles virus* that affects the child's brain, causing the autism. Dr. Corbier, on the other hand, seemed to suggest that the thimerosal in the thimerosal-containing vaccines might also, in some cases, *directly affect* the child's brain, along with the measles virus. (*Hazlehurst* Tr. 284A, 370A-73A.)

Although the petitioners in this case purport to rely upon Dr. Corbier's testimony in *general*, they do *not* seem to adopt this "direct effect" aspect of Dr. Corbier's theory, so there is no need for me to discuss that theory here. (I note that this "direct effect" theory is the theory relied upon by the Petitioners' Steering Committee under the PSC's *second* theory of general causation. Three test cases involving that second theory were tried in May and July of 2008, and are currently in a post-hearing briefing process.) But even if the petitioners in this case were to rely on this "direct effect" approach, I would respond that I found *Dr. Corbier's testimony* in this regard to be unpersuasive. Dr. Corbier failed to offer a coherent explanation of *why* he thinks that the thimerosal in thimerosal-containing vaccines can affect infant brains by causing autism. To the extent that he did suggest some reasons for his views concerning thimerosal, he seemed to adopt faulty reasoning similar to that of Dr. Aposhian discussed above, relying on the same flawed Bradstreet and Holmes studies that I have also discussed above. (*See*, *e.g.*, *Hazlehurst* Tr. at 373A-414A.) I found Dr. Corbier's testimony in this regard to be quite unpersuasive.

for the theory that the MMR vaccine can play a role in causing autism. I conclude that Dr. Corbier has provided no persuasive explanation as to *why* he believes that the MMR vaccine can play a role in causing autism. Dr. Corbier, like Dr. Kinsbourne and many of the respondent's witnesses, did explain that the measles virus can in some instances cause injury or death in humans, in the form of disorders such as measles encephalitis, SSPE, etc. (*Hazlehurst* Tr. 274A-77A.) He seemed to then jump from that evidence to the conclusion that the MMR vaccine-strain form of the measles virus is capable of causing *autism* in a person with genetic susceptibility. But Dr. Corbier never persuasively explained *how* he can reasonably make that startling jump, in light of the fact that autism is a disorder quite different from measles encephalitis, SSPE, and the other disorders that are known to be caused by the measles virus.

Dr. Corbier indicated that his views in this regard are heavily influenced by the fact that in Yates Hazlehurst and many children who are diagnosed with regressive autism, the symptoms of the autism were first recognized relatively soon after an MMR vaccination. (*Hazlehurst* Ex. 26, p. 16; *Hazlehurst* Tr. 303-07.) But this reasoning ignores the fact that in the United States the first dose of MMR is usually administered between 12 and 18 months of age (Ex. P, Tab 38, p. 264; Ex. P, para. 35), while the first symptoms of regressive autism typically are observed during the second year of life. (Tr.1055, 1288A; Ex. 61, Tab YYY, pp. 937, 946.) Thus, the time when the first symptoms of regressive autism are typically recognized simply happens to *coincide* with the period of time when most children receive the MMR vaccination. Therefore, Dr. Corbier's inference of a causal relationship, whenever the initial symptoms of autism are observed within eight or nine months after an MMR inoculation (*Hazlehurst* Tr. 306), is not persuasive.

Dr. Corbier also stated that he has developed a "profile" of children, and he seemed to indicate that if a child fits within that profile, it is reasonable to conclude that an MMR vaccination contributed to that child's autism. (*Hazlehurst* Ex. 26, p.16; *Hazlehurst* Tr. at 313A-14A.) To fit the profile, a child must (1) experience normal development prior to receiving the MMR vaccine, (2) have significant chronic gastrointestinal (GI) problems, (3) have "immunological disturbances," and (4) experience the regressive phase of autism within nine months after an MMR vaccination. (*Hazlehurst* Ex. 26, p. 16; *Hazlehurst* Tr. at 306-07, 313A-14A.) But Dr. Corbier never explained persuasively *why* he believes that, simply because a child falls within his "profile," it can be reasonably inferred that the MMR vaccination contributed to the autism. Dr. Corbier seems to have been strongly influenced by the fact that Dr. Wakefield and colleagues hypothesized in their 1998 article that in children with *both* regressive autism and chronic gastrointestinal symptoms, a persisting vaccine-strain measles virus acquired from MMR vaccination might be the cause of both. (*Hazlehurst* Ex. 26, p. 13; *Hazlehurst* Tr. 314A.) But Dr. Corbier failed to point to any evidence indicating that the Wakefield hypothesis has any *validity*. (As I will set forth below (pp. 143-44), the Wakefield hypothesis has been strongly criticized, and has been abandoned even by most of the very authors of that 1998 article.[132])

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[132]S.H. Murch et al., *Retraction of an Interpretation*, (Letter) 363 LANCET 750 (2004). (Ex. T, Att. 25.)

I also note that after attending Dr. Corbier's hearing testimony, and carefully studying his opinion, I simply found no reason to conclude that he is a reliable expert. He failed to put forward a logical explanation as to *why* he holds his views concerning the causation of autism. His reasoning often seemed jumbled at best. He seemed to be unfamiliar with the medical literature upon which he purported to rely. Dr. Corbier has not published, in any peer-reviewed journal, any articles relevant to autism or to the causation issues concerning which he opined. (*Hazlehurst* Tr. 435A-36A.) Dr. Corbier seems to be willing to give opinions concerning causation, purportedly to the level of "more probable than not," based on *very* scant evidence. He is willing to opine, for example, that a *large number* of different factors can contribute to the causation of autism. (*Id*. at 418A-21A.) While I do not doubt that Dr. Corbier was *sincere* in his beliefs concerning the causation of autism, I simply did not find him to be a *reliable* expert.

In response to Dr. Corbier's expert report and oral testimony, respondent offered the expert report and oral testimony of Dr. Robert Rust, a pediatric neurologist with much more extensive experience than Dr. Corbier. (*Hazlehurst* Ex. E; *Hazlehurst* Tr. 442-552A.) The testimony of Dr. Rust was similar to the testimony of respondent's experts presented in this *Cedillo* case concerning this general causation issue, as discussed above. I found Dr. Rust's testimony to be far more logical and persuasive than the testimony of Dr. Corbier.

I conclude, therefore, that Dr. Corbier's testimony, concerning this general causation issue, again gives me no reason to conclude that the MMR vaccine can contribute to the causation of autism.[133]

b. Opinions of Dr. Hepner and Dr. Kennedy

As noted above, in discussing this MMR/causation issue in their briefs, the petitioners have relied primarily on Dr. Kinsbourne, and also secondarily on Dr. Corbier. They have not indicated reliance, concerning this issue, on any of their other experts. However, I note that two of the petitioners' other experts, Drs. Hepner and Kennedy, offered comments that might appear to offer at least some support to the petitioners' MMR/autism causation theory. Therefore, I will discuss those comments here.

i. Dr. Hepner

Petitioners' expert Dr. Hepner, as noted above, is a Ph.D. molecular biologist. She testified chiefly concerning the issue of the validity of Unigenetics testing. Dr. Hepner did note briefly, however, that she found the petitioners' general causation theory, that the MMR vaccine can

[133]The petitioners in their briefs in this case did *not* indicate any reliance upon the testimony of a medical doctor presented as a witness by the petitioners in the *Snyder* case, Dr. J.J. Bradstreet. In any event, I have studied the testimony of Dr. Bradstreet, and I find that it does *not* provide any persuasive support to the proposition that the MMR vaccine can contribute to the causation of autism.

contribute to the causation of autism, to be "plausible" and "logical." (Ex. 63, pp. 1, 6; Tr. 638-39.) However, other than testifying concerning the issue of the Unigenetics testing, Dr. Hepner did *not* explain *why* she finds that general causation theory to be "plausible." Moreover, Dr. Hepner, on cross-examination, was asked *specifically* whether she could opine that such theory has been proven to the level of "more likely than not." (Tr. 638.) She did *not* answer in the affirmative, preferring to stick to her wording that the theory is "plausible." (Tr. 638-39.)

Accordingly, since Dr. Hepner did not offer an opinion concerning the petitioners' MMR/causation issue to the level of "more probable than not," and offered no explanation of *why* she believes that the petitioners' theory is "plausible," I conclude that Dr. Hepner's opinion offers no support to this causation theory of the petitioners.

ii. Dr. Kennedy

Another of petitioners' experts in this *Cedillo* case, Dr. Ronald Kennedy, at certain points in his testimony seemed to opine that the MMR vaccine can cause autism. As previously noted, Dr. Kennedy is a Ph.D. microbiologist with experience in studying viruses and developing vaccines. In his written report, Dr. Kennedy indicated the general opinion that if an infant is in a state of immune dysregulation, receives an MMR vaccination, and experiences the onset of a "neurologic event" soon after, and there is evidence that the vaccine-strain measles virus persists in that child's system, then it is probable that the vaccine caused the neurologic event. (Ex. 110, p. 7.) Later, during cross-examination at trial, he seemed to indicate that if there existed evidence of persistent measles vaccine-strain virus in an autistic child's gut (intestines), then he could opine that the child's *autism was* "more likely than not" vaccine-caused. (Tr. 761, 788-89.)

The first major problem with Dr. Kennedy's opinion on this point, concerning whether the MMR vaccine can be said to cause autism, is that it clearly depends on the assumption that there is a *reliable* laboratory result in an individual, demonstrating that the vaccine-strain measles virus persisted in that person's body. (Tr. 784, 794-95.) But I have concluded above (pp. 41-78) that the Unigenetics laboratory results, purporting to find evidence of persisting measles virus in Michelle and others, *have not* been shown to be accurate or reliable. Thus, Dr. Kennedy's opinion on this point, based on an assumption that has been shown to be incorrect, simply offers no support to the petitioners' case.

Further, another problem with Dr. Kennedy's apparent opinion on this point is that he seemed to waver on this issue. It is significant that in neither his expert report, nor his oral testimony on *direct* examination in this case, did Dr. Kennedy ever state that the persisting vaccine-strain measles virus could cause autism *in general*, or that it *did* cause Michelle Cedillo's autism. The closest he came was in his written report, when he stated that a persisting measles virus could cause a "neurologic event." (Ex. 110, p. 7.) Only when asked by respondent's counsel as to *why* he believed that the MMR vaccine could cause autism, did Dr. Kennedy offer the testimony which seemed at times to indicate that a persistent vaccine-strain measles virus can cause *autism*. (Tr. 761, 788-89.)

Moreover, Dr. Kennedy seemed to go back and forth on the issue of whether the MMR vaccine can cause autism. For example, at one point he said that it is "plausible" that MMR vaccine "is causing autism" generally, but he cannot say so "absolutely." (Tr. 799, lines 19-24.) Then, asked whether it is "more likely than not" that the MMR vaccine causes autism, he did not answer "yes" or "no," but instead replied that the question "would have to be examined on an individual-to-individual basis." (Tr. 799, line 25 to Tr. 800, line 3.) Dr. Kennedy stated that the MMR vaccine "might and can" cause autism, "under the appropriate conditions" (Tr. 800, lines 5-6), and that the MMR vaccine "more likely than not" is causing autism "in an individual-to-individual situation" (Tr. 800, lines 12-15). But he immediately added, confusingly, "Do I say that MMR causes autism? Absolutely not. Can it, in an individual * * *? Yes, it could." (Tr. 800, lines 15-18.) Later, again in apparent contradiction to other portions of his testimony, Dr. Kennedy stated that he "absolutely" agreed with his own statement in a 2004 document that "investigators have failed to demonstrate causality between MMR vaccination and autism." (Tr. 806, lines 4-9.) Similarly, he stated that he agreed with the conclusion of a medical committee (to be discussed below) that the evidence favors *rejection* of a causal link between the MMR vaccine and autism. (Tr. 833-34.)

In addition, in his testimony in the *Snyder* case, Dr. Kennedy acknowledged that he does not know the *mechanism* by which the measles virus supposedly could cause autism. (*Snyder* Tr. 432A.)[134]

Accordingly, after reviewing all of Dr. Kennedy's testimony, I conclude that Dr. Kennedy likely does believe that it is probable than the vaccine-strain measles virus can persist in the system of an infant with immune dysregulation, and thereby cause autism in some individuals. But Dr. Kennedy's hesitation, wavering, and apparent self-contradiction on this point causes me to give his opinion little weight concerning this issue. Further, Dr. Kennedy offered little explanation concerning *why* he holds this opinion. And while Dr. Kennedy, as a Ph.D. in microbiology and immunology, is well-qualified to opine concerning *some* points of this case, the fact that he is not a medical doctor means that his testimony concerning this *medical causation* issue is substantially outweighed by the testimony to the contrary of the medical doctors who testified for respondent concerning this issue.

Therefore, I conclude that Dr. Kennedy's testimony gives me no reason to conclude that the MMR vaccine can substantially contribute to the causation of autism.

7. Experience of the experts

Another point concerns the experience and credentials of the experts upon whom the parties rely, concerning this issue of the alleged causation of autism by the vaccine-strain measles virus. Respondent's expert Dr. Griffin has studied the measles virus intensively for more than 30 years (Tr.

[134]I also note that, as far as I can find in the record, Dr. Kennedy was never asked to specifically opine, nor did he opine, concerning whether it is probable that *Michelle Cedillo's* own condition of autism was vaccine-caused.

2443A), and has extraordinary credentials as an expert concerning the measles virus (Tr. 2743A-48A), as even petitioners' own expert virologist, Dr. Kennedy, acknowledged (Tr. 851A). Dr. Griffin is a medical doctor specializing in molecular biology, immunology, and virology. (Tr. 2739A-41.) She is the chair of the Department of Molecular Microbiology and Immunology at the Johns Hopkins School of Public Health. (Tr. 2740-41.) She has been an editor or editorial board member on a number of scientific journals relating to virology. (Tr. 2742A-43A; Ex. F, p. 5.) She has published more than 240 research articles in scientific journals, about 100 of which relate specifically to the measles virus, the measles vaccine, or the MMR vaccine. (Ex. F, pp. 18-37; Tr. 2746.) She has written many book chapters and edited several textbooks concerning virology. (Tr. Ex. F, pp. 948, 37.) One of the textbooks that she has edited, and for which she also wrote the specific chapter on the measles virus, is *Field's Virology*, considered the "bible" of virology. (Tr. 2746-47.)

Respondent's expert Dr. Ward, as previously noted, also has outstanding academic and publication credentials, in a medical career since 1981. (See p. 75 above.) His testimony in this case and his publication list indicate that he, too, has extensively studied the measles virus. (Ex. CC; Tr. 1796A-98A, 1839; *Snyder* Tr. 940.)

Two other experts of respondent, Drs. Wiznitzer and Rust, are, like Dr. Kinsbourne, pediatric neurologists of impressive credentials, but Drs. Wiznitzer and Rust also have very extensive experience in *treating autistic children* in recent years, far more than does Dr. Kinsbourne. (Tr. 1565-1580, 1163A; *Hazlehurst* Tr. 452A-53A.) And another of respondent's experts, Dr. Eric Fombonne, also filed a lengthy expert report (Ex. P) and testified at length, opining that it is not reasonable to conclude that the MMR vaccine can cause or contribute to autism. Dr. Fombonne is a medical doctor who has a very extensive and impressive background in studying autism, publishing many medical articles concerning the disorder, and has treated autistic children on a regular basis for many years. (Tr. 1239-1262A.)[135]

Concerning this general causation issue, the petitioners rely, in contrast, on only two medical doctors, Drs. Kinsbourne and Corbier, who have expressed the opinion that the MMR vaccine can cause autism. Dr. Kinsbourne does have impressive credentials in the field of pediatric neurology, and Dr. Corbier also is a qualified pediatric neurologist. However, Drs. Kinsbourne and Corbier clearly have far less expertise concerning the *measles virus* than Drs. Griffin or Ward. And, while Dr. Kinsbourne has authored a medical textbook chapter on autism (Tr. 1168A-69), he also clearly has far less experience in treating autistic patients, especially in recent years, than either Dr. Wiznitzer, Dr. Rust, or Dr. Fombonne. (*Compare* Tr. 1163A with Tr. 1253A-54A, 1576A-77A,

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[135]Another pediatric neurologist with extensive experience with autism, Dr. Andrew Zimmerman, also filed an expert report for respondent. (Ex. FF.) Dr. Zimmerman stated the opinion that the evidence does *not* support the proposition that the MMR vaccine can cause autism. (Ex. FF, p. 4.) Thus, Dr. Zimmerman's report certainly supports the result that I have reached in this case. However, because he did not testify at the evidentiary hearing, his opinion has been far less important than that of the respondent's experts who did testify, in leading to my conclusion.

and *Hazlehurst* Tr. 452A-53A.) Indeed, Dr. Kinsbourne acknowledged that he has not had an active clinical pediatric practice, treating autistic children or any other children, for the past 17 years. (Tr. 1163A.) On the other hand, Dr. Corbier has certainly treated many autistic children, but his *length* of experience in that regard, and his *academic* and *research* credentials with respect to autism, are far less impressive than those of Drs. Rust, Wiznitzer, and Fombonne. (*Compare Hazlehurst* Tr. 266A, 328A, with Tr. 1239-62A, 1565-80, and *Hazlehurst* Tr. 446A, 452A-53A.)

This striking difference in the experience relevant to this MMR/autism causation issue, between the petitioners' two expert medical doctors concerning this issue and the respondent's primary experts, adds yet another reason for me to conclude that the petitioners's causation theory must be rejected.

8. Epidemiology

Numerous medical researchers have studied the issue of whether the MMR vaccine causes autism. The results of those epidemiologic studies, taken as a whole, add another significant reason to reject the petitioners' causation theory in this case.

a. All competent epidemiologic studies have found no association between MMR vaccine and autism.

Epidemiology is "the study of the distribution of disease in human populations and the study of factors which influence that distribution." (Tr. 2501.) After the above-described article by Wakefield in 1998 raised the issue of whether the MMR vaccine might cause autism, a number of research groups in several countries conducted epidemiologic studies concerning that issue. With the exception of two studies done by one suspect research pair (to be discussed below), all of the studies *found no evidence of any association*[136] between exposure to MMR vaccine and autism.

i. Controlled observational studies

Some of the studies fall within the category of "controlled observational studies," usually studies known as "cohort studies" or "case-control studies." (Ex. JJ, p. 84.) Several studies of this type have looked at the issue of whether the MMR vaccine is "associated" with autism--*i.e.*, whether children who received MMR vaccination are more likely to be autistic than those children who didn't receive MMR vaccination, or whether the likelihood of experiencing autism varies with the *age at*

[136]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. (Tr. 1058-59A; *Dorland's* at 167.) If an "association" is found, then medical experts will evaluate other factors to determine if that association is "causal." (Ex. P, Att. 176, 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 significant cause of Condition B.

receipt of MMR vaccination. *All* of those studies have *failed* to find any association. (Ex. JJ, pp. 84-85, 110-118; Ex. P, pp. 38-39; Tr. 2532-48.)

For example, the first major study of this type was conducted by Taylor and colleagues,[137] who surveyed records of British children and published their results in 1999. (Ex. P, Att. 145; Ex. P, para. 80; Ex. JJ, pp. 88-89, 110-112; Tr. 2533-37A.) That study took advantage of the fact that the MMR vaccine was first introduced in Britain in 1988, so that one could compare children born in earlier years who did not receive MMR vaccine with later-born children who did receive that vaccine. The study found that while there was a steady increase in autistic diagnoses throughout the studied period, which was consistent with the world-wide pattern, the introduction of the MMR vaccine did *not* result in any significant "step-up" in that steady trend; one would have expected a clear "step-up" if the MMR vaccine were in fact contributing to autism in any significant way. (Tr. 2533-35.)

A number of other controlled observational studies were done by researchers in several different countries, utilizing a variety of study designs, all designed to determine whether autism was associated with receipt of MMR vaccination, or whether autism was associated with the *timing* of MMR vaccination. Those studies included a study by DeStefano and colleagues[138] published in 2004, a case-control study involving American children (Ex. P, Att. 38; Ex. JJ, pp. 84-87, 110; Ex. P, pp. 38-39; Tr. 2537A-39A); a study by Smeeth and colleagues[139] published in 2004, involving British children (Ex. P, Att. 137; Ex. P, p. 38; Tr. 2541A-45A); a second study by Taylor[140] and colleagues, published in 2002, which included additional data concerning British children (Ex. P, Att. 146; Ex. JJ, pp. 92-93, 112-13; Ex. P, para. 109); a study by Farrington[141] and colleagues published in 2001, which applied a different form of analysis to the British data previously reviewed by Taylor in 1999 (Ex. P, Att. 43; Ex. JJ, pp. 90-91, 112; Ex. P, para. 108); a study by Fombonne and

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[137]Brent Taylor et al., *Autism and Measles, Mumps, and Rubella Vaccine: No Epidemiological Evidence for a Causal Association*, 353 LANCET 2026 (1999). (Ex. P, Att. 145.)

[138]Frank DeStefano et al., *Age at First Measles-Mumps-Rubella Vaccination in Children with Autism and School-Matched Control Subjects: A Population-Based Study in Metropolitan Atlanta*, 113 PEDIATRICS 259 (2004). (Ex. P, Att. 38.)

[139]Liam Smeeth et al., *MMR Vaccination and Pervasive Developmental Disorders: A Case-Control Study*, 364 LANCET 963 (2004). (Ex. P, Att. 137.)

[140]Brent Taylor et al., *Measles, Mumps, and Rubella Vaccination and Bowel Problems or Developmental Regression in Children with Autism: Population Study*, 324 BRIT. MED. J. 393 (2002). (Ex. P, Att. 146.)

[141]C.P. Farrington et al., *MMR and Autism: Further Evidence Against a Causal Association*, 19 VACCINE 3632 (2001) (Ex. P, Att. 43.)

Chakrabarti[142] published in 2001, also involving British children (Ex. P, Att. 60; Ex. JJ, pp. 94-95, 113-115); a study by DeWilde[143] and colleagues published in 2001, again involving British children (Ex. P, Att. 40; Ex. JJ, p. 96-97, 115; Ex. P, para. 106; Tr. 2545A-48); a study by Makela[144] and colleagues, published in 2002, involving Finnish children (Ex. P, Att. 108; Ex. JJ, pp. 100-01, 117; Ex. P, para. 107); and a study published by Takahashi[145] and colleagues in 2003, involving Japanese children (Ex. P, Att. 144; Ex. JJ, pp. 100-01, 117-18). All of those studies looked for an association between MMR vaccination and autism, or between autism and the *timing* of MMR vaccination. *And all of those studies failed to find such an association.*[146]

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[142]E. Fombonne, & S. Chakrabarti, *No Evidence for a New Variant of Measles-Mumps-Rubella-Induced Autism*, 108 PEDIATRICS 58 (2001). (Ex. P, Att. 60.)

[143]S. DeWilde, *Do Children Who Become Autistic Consult More Often After MMR Vaccination?* 51 BRIT. J. GEN. PRACT. 226 (2001). (Ex. P, Att. 40.)

[144]Annamari Makela et al., *Neurologic Disorders After Measles-Mumps-Rubella Vaccination*, 110 PEDIATRICS 957 (2002). (Ex. P, Att. 108.)

[145]Hiroshi Takahashi et al., *An Epidemiological Study on Japanese Autism Concerning Routine Childhood Immunization History,* 56 JAPANESE J. INFECTIOUS DISEASE 114 (2003). (Ex. P, Att. 144.)

[146]One additional study of this type was the Madsen study published in 2002, a very large retrospective cohort study involving Danish children born between 1991 and 1998. *See* Kreesten Madsen, et al., *A Population-Based Study of Measles, Mumps, and Rubella Vaccination and Autism*, 347 NEW ENG. J. MED.1477 (2002). (Ex. P, Tab 105; Ex. JJ, pp. 98-99, 115-117; Ex. P, p. 39; Tr. 2539A-41A.) The study compared children who had received MMR vaccines to children who hadn't, and found no association between vaccine status and the development of autism. (Tr. 2541A.) This study seems, therefore, to offer additional support to the conclusion of the nine other controlled observational studies discussed above. However, I have listed this 2002 Madsen study only in this footnote, for the following reason. I note that another study by Madsen, though with a largely different group of colleagues, was published in 2003; that study considered the possibility of a causal relationship between *thimerosal-containing vaccines* and autism. *See* Kreesten Madsen et al., *Thimerosal and the Occurrence of Autism: Negative Ecological Evidence From Danish Population-Based Data*, 112 PEDIATRICS 604 (2003). (Ex. P, Tab 106.) Both studies obtained information concerning the children's autism status from the Danish Psychiatric Central Research Register. (Ex.P, Tab 105, p.1478; Ex. P, Tab 106, p. 605.) In the article describing the 2003 study, the authors noted that a change in data recording in 1995, when outpatient autism diagnoses were first added to that Danish Register, may have exaggerated the rate of autism incidence in the year 1995 and thereafter. (Ex. P, Tab 106, p. 605.) A committee of the Institute of Medicine (IOM), in reviewing that 2003 study, noted that such problem "limits the study's contribution" to the causality analysis. (Ex. JJ, p. 53.) When discussing the separate 2002 MMR-related study by Madsen and the different group of colleagues, the IOM committee did *not* remark upon any similar analytical problem that might have been created by the 1995 change in the Danish data recording. Studying the two articles myself, I find it to be *unclear* whether there is any similar problem. But, because

(continued...)

ii. Ecological studies

Other epidemiologic studies fall within the category of "ecological" studies. Those studies, unlike the controlled observational studies discussed above, do not involve studying the records of individual children. Instead, they look at rates of autism in a particular population over time, in order to determine whether changes in immunization policy, such as the introduction or discontinuance of the MMR vaccination, had any effect on the rate of diagnosis of autism in that population. (Tr. 2532.) Several such ecological studies have been done, and, with one exception to be discussed below, those studies *failed* to find any association between MMR vaccination and autism.

For example, in 2004 Chen[147] and colleagues published a study of the British population covering the years 1959 through 1993. (Ex. P, Tab 28; Ex. P, para. 80; Tr. 2548-51A.) The study noted that when the monovalent measles vaccine (the measles vaccine given separately, not combined with mumps and rubella vaccines) was first introduced in Britain in 1968, there was no significant change in the incidence of autism. (Tr. 2550A.) Similarly, when the MMR vaccine was introduced in Britain in 1988, replacing the monovalent measles vaccine, again no significant "step-up" in the trend of autism diagnosis occurred. (Tr. 2550A.)

Another ecological study was published by Honda[148] and colleagues in 2005, analyzing data concerning Japanese children. (Ex. P, Att. 87; Ex. P, para. 82; Tr. 2557A-58A.) The MMR vaccine was introduced in Japan in the late 1980s, but, due to a tainted strain of vaccine, there was a decline in usage over the next four years, followed by a total discontinuance of the vaccine. Yet the study data showed that those changes in the MMR vaccine coverage of the population had *no effect* on the rate of diagnosis of autism during that period. (Tr. 2557A-58A.)

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[146](...continued)
of the possibility of a similar problem, in an abundance of caution, I have not included the 2002 Madsen study in my discussion above of "controlled observational studies."

My approach on this issue may or may not be overly cautious, but ultimately, it makes no difference to my overall analysis of the epidemiologic data. Even *excluding* the Madsen 2002 study from consideration, there are still *nine other* "controlled observational studies," from many different countries, enough to support the overall conclusion. And if, instead, there is no good reason to exclude the Madsen 2002 study from consideration, then there simply would be *one more* large study to support my general conclusion.

[147]W. Chen et al., *No Evidence for Links Between Autism, MMR and Measles Virus*, 34 PSYCHOLOGICAL MED. 543 (2004). (Ex. P, Att. 28.)

[148]H. Honda et al., *No Effect of MMR Withdrawal on the Incidence of Autism: A Total Population Study*, 46 J. CHILD PSYCHOLOGY & PSYCHIATRY 572 (2005). (Ex. P, Att. 87.)

Other similar ecological studies, which also found no correlation between MMR vaccination usage and the occurrence of autism,[149] include a study of Swedish children published by Gillberg and Heijbel[150] in 1998 (Ex. P, Att. 83; Ex. JJ, pp. 104-05, 121-22; Ex. P, p. 32); and another study of Swedish children published by Steffenburg[151] and colleagues in 2003 (Ex. P, Att. 140; Ex. P, p. 32).

iii. Summary concerning studies listed above

In sum, following the Wakefield article in 1998, which raised the issue of whether the MMR vaccination might be a contributing factor in causing autism, a number of research groups in several countries have devised several different types of studies to test the Wakefield hypothesis. Each of

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[149]Dr. Fombonne also pointed to three other studies as providing evidence against an association between MMR and autism: a British study, J.A. Kaye et al., *Mumps, Measles, and Rubella Vaccine and the Incidence of Autism Recorded by General Practitioners: A Time Trend Analysis*, 322 BRITISH MED. J. 460 (2001). (Ex. P, Att. 95; Ex. JJ, pp. 104-05, 120-21); a study of Canadian children, E. Fombonne et al., *Pervasive Developmental Disorders in Montreal, Quebec, Canada: Prevalence and Links with Immunizations*. 118 PEDIATRICS 139 (2006). (Ex. P, Att. 74; Ex. P, p. 33; Tr. 2552-56); and a study involving California children, L. Dales et al., *Time Trends in Autism and in MMR Immunization Coverage in California*, 285 JAMA 1183 (2001). (Ex. BB, Att. 18; Ex. JJ, pp. 102-103, 118-19; Ex. P, pp. 32-33; Tr. 2551A-52). However, I see a problem with this argument of Dr. Fombonne. (This point was never raised in the petitioners' briefs, but one of the petitioners' counsel seemed to raise it in questioning Dr. Fombonne (Tr. 2704-05), so I will discuss it here.) Those three studies, to summarize, each found that while MMR use was fairly steady during the studied time period (in Britain, Quebec, and California, respectively), the rate of autism diagnosis went up extremely rapidly at the same time. Dr. Fombonne pointed to those results as *refuting* the claim that MMR was associated with autism. However, Dr. Fombonne believes that the increase in autism *diagnosis* during those time periods in question was largely, if not completely, due to a broadening of the definition of autism, better awareness and case ascertainment, and other factors, rather than due to a *true increase* in the actual incidence of autism. But if Dr. Fombonne is correct in that regard, then those three studies would *not* offer evidence *against* the MMR/autism causation theory, since it would simply mean that while MMR coverage was steady, the *actual* incidence rate of autism (as opposed to the rate of *diagnosis*) *also* remained fairly steady. Of course, that would *not* mean that those studies could then be viewed as *positively* showing an association between MMR and autism, but the studies would then seem to be *neutral* concerning the issue of such an association, rather than constituting evidence *against* such an association.

Accordingly, in my analysis I have *not* viewed those three studies as among those constituting evidence *against* the petitioners' causation theory.

[150]C. Gillberg & H. Heijbel, *MMR and Autism*, 2 AUTISM 423 (1998). (Ex. P, Att. 83.)

[151]S. Steffenburg et al., *Autism Spectrum Disorders in Children with Active Epilepsy and Learning Disability: Comorbidity, Pre- and Perinatal Background, and Seizure Characteristic,* 45 DEVELOPMENTAL MED. & CHILD NEUROLOGY 724 (2003). (Ex. P, Att. 140.)

the studies discussed and enumerated above,[152] however, found *no* evidence that the MMR vaccination is associated with autism. To be sure, none of those studies is definitive by itself. While each of the study approaches has its strengths, each also has acknowledged limitations and weaknesses.[153] However, when all of the studies are considered *together*, the study results are highly significant. (*E.g.*, Ex. P, Att. 76, p. 156.) First of all, the studies show that medical researchers have *looked extensively* for any affirmative evidence that the MMR vaccine contributes 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 the MMR vaccination has played any significant role in the *overall* causation of autism since the introduction of the MMR vaccine. Of course, it is true that epidemiologic studies cannot prove definitively that Factor A *never* causes Condition B; such a study

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[152]An Institute of Medicine (IOM) report noted the existence of two additional studies that found no association between MMR vaccination and autism, which fell into a third category, *i.e.*, studies of "passive reporting data." (Ex. JJ, pp. 123-124.) Those were two Finnish studies: Annamari Patja et al., *Serious Adverse Events After Measles-Mumps-Rubella Vaccination During a Fourteen-Year Prospective Follow-Up*, 19 PEDIATRIC INFECTIOUS DISEASE J. 1127 (2000) (Ex. P, Att. 118); and Heikki Peltola et al., *Mumps and Rubella Eliminated From Finland*, 284 JAMA 2643 (2000) (Ex. P, Att. 120). However, as the IOM report described, those studies appear to be of quite limited value concerning the MMR/autism causation issue, because of the reliance on "passive reporting data" and other reasons. I have accorded no weight to those two studies.

[153]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 expert Dr. Fombonne, an expert extremely well-qualified concerning autism (see discussion at p. 109 above), described most of those studies, some at length, in both his expert report (Ex. P, pp. 31-48) and his hearing testimony (Tr. 2530-77). In addition, such studies are well-described by a comprehensive report issued by the Institute of Medicine (IOM) in 2004. (See Ex. JJ, pp. 65, 82-126.) (For a discussion of that 2004 IOM Report, see p. 124 below.)

Second, the petitioners in this case simply have *not contested* the descriptions and interpretations of those studies by the IOM committee and by Dr. Fombonne. That is, the petitioners have *not disputed* respondent's argument that the studies described above show clearly that the MMR vaccine does not play any 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 MMR vaccine contributes to *regressive autism*, rather than autism in general. The petitioners argue that regressive autism is a narrow subset of autism, and that none of the available studies have specifically studied the issue of whether the MMR vaccine causes *regressive* autism, so that the studies are simply *irrelevant* to cases involving regressive autism.

I have dealt in detail with this "irrelevancy" argument of the petitioners, at pp. 118-21 of this Decision. This footnote simply explains why I have not discussed each of the many individual epidemiologic studies in detail in this Decision.

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 whole, show very clearly that the MMR vaccine does 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 the MMR vaccination 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 MMR vaccines and autism at least *casts some doubt* upon the proposition that the MMR vaccine *ever* plays a role in causing autism.[154]

b. Studies by the Geiers and by Wakefield

As noted above, all of the studies that have addressed the MMR/autism causation issue published since the Wakefield article in 1998 have found *no association* between MMR vaccination and autism, with two exceptions. Both exceptions were studies published by the research team of Dr. Mark Geier and his son David Geier. (Ex. P, Att. 82; *Snyder* Ex. O, Tab 10;[155] Ex. JJ, pp. 23, 102-105, 119-20, 122-23; Ex. P, pp. 33-34.) To be sure, the petitioners in this case have *not* cited or relied upon those two studies, because, as I will discuss below (pp. 118-21), 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 two studies, to see if they afford any significant counterweight to the many contrary studies discussed above.

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[154]Another epidemiologic study was published in September of 2008. Mady Hornig et al., *Lack of Association between Measles Virus Vaccine and Autism with Enteropathy: A Case Control Study*, 3 PloS ONE e3140 (2008), *available at* www.plosone.org. Neither party has sought to make that study part of the record in this case, so I have not relied upon it. However, the abstract of that study states that the study "provides strong evidence against association of autism with persistent MV RNA in the GI tract or MMR exposure." Thus, it appears that the study would only add more weight to the conclusion that I have otherwise reached.

[155]D. Geier & M. Geier, *A comparative 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 P133 (2004). (Ex. P, Att. 82.)

Mark R. Geier & David A. Geier, *Pediatric MMR Vaccination Safety*, 18 INT'L PEDIATRICS 203 (2003). (*Snyder* Ex. 165.)

After careful consideration, I conclude that the Geiers' studies *cannot* be given any weight. Those studies were considered by the Institute of Medicine (IOM) committee that fully studied the entire MMR/causation issue in 2004 (Ex. JJ, pp. 102-05, 119-20, 122-23), and that committee concluded that the studies were so flawed as to be "uninterpretable" and to contribute nothing meaningful ("noncontributory") concerning the causation issue (Ex. JJ, pp. 119-120, 122-23). The committee noted that the studies were based on databases that themselves had "significant limitations" (*id*. at 120), and that the studies' methodologies had "serious methodological limitations" (*id*. at 120, 123). The committee added that the Geiers' articles describing the analytical methods were "not transparent" and omitted "important details," so that it was impossible to evaluate the studies. (*Id*.) Other specific points of deficiency in the studies were also discussed. (*Id*.)

In addition, Dr. Fombonne analyzed the Geier studies, and found them to be "seriously flawed in several respects." (Ex. P, para. 81.) None of the expert witnesses for the petitioners vouched for the reliability of the Geier studies.

I have reviewed the Geier studies, and I agree with the analysis of those studies set forth in the 2004 IOM Report and in Dr. Fombonne's report. I conclude that those two Geier epidemiologic studies are *not* reliable, and cannot be accorded any weight.

I also note that in listing and discussing the epidemiologic studies relevant to the MMR/autism causation issue, the IOM committee also mentioned the above-described original article published by Wakefield and colleagues in 1998. (Ex.P, Att. 152; Ex. JJ, pp. 108-09, 124-26.) The authors of that article examined the medical records of 12 children who each had a history of loss of developmental skills, and also had intestinal symptoms. Ten of the 12 seemed to have a disorder falling within the autism spectrum, and in most of those individuals the initial autistic symptoms were first noticed within two months after MMR vaccination. (Ex. P, Att. 152, p. 639; Ex. JJ, p. 125.) The authors concluded from these findings that they had possibly discovered a "unique disease process" or "syndrome" in which children had both developmental disorders and intestinal disorders, both potentially linked causally to the MMR vaccine. (Ex. P, Att. 152, pp. 639-41.)

That Wakefield article, however, *cannot* be considered to offer significant evidence concerning the MMR/autism causation issue. The article was intended to *raise a question* about a possible causal association--a question that would then be addressed in the future by large epidemiologic studies. (Such studies have in fact taken place, and have *failed* to find any evidence of association--see discussion at pp. 110-14 above). The study examined only 12 individuals, far too few to yield any strong evidence concerning causation. The 2004 IOM Report pointed out that "because of the overlap in timing between the typical age at which ASD symptoms are initially suspected and the [typical] schedule for MMR * * * vaccinations," it was hardly surprising that the Wakefield authors could find some children whose autistic symptoms were first noted within two months after MMR vaccination. (Ex. JJ at 126.) The IOM report concluded that the Wakefield article was simply "uninformative" concerning the MMR/autism causation issue. (*Id*.) Dr. Fombonne also pointed out deficiencies in the Wakefield article. (Ex. P, para. 62.)

I agree with the 2004 IOM Report that the 1998 Wakefield article is simply uninformative concerning the MMR/autism causation issue. I also note that, after Wakefield himself came under considerable professional criticism, ten of Wakefield's twelve co-authors on the 1998 article published a letter in which they clarified that a causal link between MMR vaccine and autism had *not* been established by their study. Furthermore, they formally "retract[ed]" the causation interpretation suggested in the original article. (Ex. T, Att. 125.)

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

As noted above, the petitioners have *not disputed* respondent's argument that the studies described above show that the MMR vaccine does not play any significant causal role in the causation of *autism overall*. Rather, the petitioners seem to argue that the studies pertain only to autism *in general*, and, should be considered as *irrelevant* to the issue of whether the MMR vaccine contributes to *regressive autism*.[156] The petitioners seem to argue that because regressive autism is a narrow subset of autism, and most of the epidemiologic studies have not specifically addressed the issue of whether the MMR vaccine causes *regressive autism*, the epidemiologic studies are therefore *irrelevant* to cases involving regressive autism.

First, I must define "regressive autism." 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 sometimes described as "autistic regression," and sometimes it is said that individuals who fall into this pattern have "regressive autism." (*E.g.*, Tr. 1054-55, 1287A-89A.) There have been various estimates as to what percentage of autistic individuals fall within this category, but many recent estimates have been near 20 percent. (Ex. P, para. 120; Ex. 61, p. 9; Ex. JJ, p. 33; Tr. 1054, 1290A.) Michelle Cedillo's autism has been described as regressive autism (although this point is, in dispute--see footnote 168 at p. 132 below), and it appears that many of the individuals who have filed Vaccine Act petitions grouped into the Omnibus Autism Proceeding have also been described as suffering from regressive autism. The theory advanced by the petitioners in this case, and by the Petitioners' Steering Committee (PSC) in the *Snyder* and *Hazlehurst* test cases, seems to be based upon the theory that "regressive autism" should be *considered separately* from other cases of autism for the purpose of determining causation.[157]

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[156]The petitioners did not address the topic of epidemiology in any detail in their post-trial briefs. Thus, the summary of their argument that I have stated above is my best guess as to what their argument is, based upon their brief quotation of Dr. Kinsbourne in their brief (P1, p. 123), other statements by Dr. Kinsbourne (Ex. 61, p. 10; Tr. 1059A-60), and questions asked and statements made by their counsel at the hearing (Tr. 2679-80, 2889).

[157]The petitioners' general causation theory, in its focus on "regressive autism,"seems to assume that regressive autism is such a distinct category of autism that the *causes* of regressive autism likely *differ* from those of other forms of autism. That assumption, however, is much in doubt. Petitioners have *not* supplied persuasive evidence indicating that regressive autism has a

(continued...)

Thus, the petitioners here seem to argue that all of the epidemiologic studies described above should be considered *irrelevant* to this case, and to all cases involving regressive autism, because, they suggest, such studies did not make any distinction between regressive autism and non-regressive autism.

It is true that *most* of the epidemiologic studies discussed above generally did *not* make any distinction between regressive and nonregressive autism. Thus, it is arguable that those epidemiologic studies, while providing very strong evidence that the MMR vaccination has not played any significant role in the *overall causation* of autism, do not necessarily *completely rule out* the possibility that the MMR vaccine might play some role in causing the *subset* of autism known as regressive autism.

But petitioners are wrong in contending that the epidemiologic studies are completely irrelevant. First, while those studies cannot *completely rule out* any possibility that the MMR vaccination might play some causative role in a subset of the overall autism cases, it seems to me that the failure of so many studies to find any association between MMR vaccine and autism at least *casts some doubt* on the proposition that the MMR vaccine *ever* plays a role in causing *any* type of autism, including regressive autism. Second, as Dr. Fombonne pointed out, five of the epidemiologic studies actually *did* make a distinction between regressive and nonregressive autism, and thus do have some *specific relevance* to the petitioners' "regressive autism only" theory.

The first such study was the Taylor 2002 study.[158] If the petitioners were correct that MMR is causing a significant amount of regressive autism but not nonregressive autism, then one would expect that the proportion of regressive autism with respect to overall autism would have *increased* with the introduction of the MMR vaccine. However, the Taylor 2002 study indicated that the ratio of regressive autism to overall autism remained about the same in Britain after the MMR vaccine was introduced in 1988. (Ex. P, para. 122; Tr. 2564A-66A.) Similarly, the 2001 Fombonne and

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[157](...continued)
distinct cause or set of causes. For example, there is no persuasive evidence indicating that regressive autism might be any less of a *strongly genetic* condition than other forms of autism. There has also been scattered discussion in the record concerning whether regressive autism should be considered a district "phenotype" of autism.

However, I find that it is *unnecessary* for me to resolve the *general* questions of whether regressive autism is a category likely to differ from other forms of autism as to causation, or whether regressive autism should be considered a separate "phenotype." Regardless of whether regressive autism is viewed separately for purposes of causal analysis, or is considered a separate "phenotype," the petitioners simply have failed, for all the reasons set forth above, to supply any persuasive evidence that the *MMR vaccine* plays any role in causing *any* kind of autism, regressive or not.

[158]Brent Taylor et al., *Measles, Mumps, and Rubella Vaccination and Bowel Problems or Developmental Regression in Children with Autism: Population Study*, 324 BRIT. MED. J. 393 (2002). (Ex. P, Att. 146.)

Chakrabarti study[159] also indicated that the proportion of regressive autism in British children remained the same after the introduction of the MMR vaccine. (Ex. P, para. 121; Tr. 2571A-72.) And yet another study involving British children, published by Smeeth and colleagues[160] in 2004, reached the same conclusion. (Ex. P, para. 123.)

Further, a 2006 study by Uchiyama and colleagues[161] showed that the *regression* rate was no higher among autistic Japanese children *exposed* to MMR than among those *unexposed*, contrary to what one would expect if the MMR vaccine caused regressive autism. (Ex. P, Tab 87; Ex. P, para. 124; Tr. 2566A-67.)

Finally, another epidemiologic study was designed specifically to compare autistic children with regression to those without regression, and to test whether the two groups were any different with respect to the *timing* of MMR vaccination. That study was published by Richler and colleagues[162] in 2006. (Ex. P, Tab 124; Ex. P, para. 113; Tr. 2572-76.) That study compared the regressive vs. nonregressive groups in several ways, and found no evidence of any difference between the regressive and nonregressive groups, and no evidence that the regressive autism had any association with the timing of MMR vaccination. (Tr. 2572-76.)

Accordingly, the petitioners are mistaken when they suggest that all of the published epidemiologic studies make no distinction between regressive and nonregressive autism. The five studies discussed above provide important evidence that the MMR vaccine is *not* associated with the specific subcategory of *regressive autism*. The petitioners' experts had an opportunity to rebut Dr. Fombonne's testimony regarding those studies, but failed to do so.

In sum, it is true, as a statistical matter, that the epidemiologic studies detailed at pp. 110-14 above, while showing clearly that the MMR vaccination could not be causing any *substantial portion* of the cases of *autism in general*, do not *completely rule out* the possibility that the MMR vaccine might be associated with some small subset of autism, such as regressive autism. Nonetheless, the balance of evidence from those studies weighs against the petitioners' causation theory. First, it is indeed an *exceedingly slight* point in the petitioners' favor for them to claim that these many studies

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[159]E. Fombonne & S. Chakrabarti, *No Evidence for a New Variant of Measles-Mumps-Rubella-Induced Autism*, 108 PEDIATRICS 58 (2001). (Ex. P, Att. 60.)

[160]Liam Smeeth et al., *MMR Vaccination and Pervasive Developmental Disorders: A Case-Control Study*, 364 LANCET 963 (2004). (Ex. P, Att. 137.)

[161]T. Uchiyama et al., *MMR-Vaccine and Regression in Autism Spectrum Disorders: Negative Results Presented from Japan*, 37 J. AUTISM & DEVELOPMENTAL DISORDERS 210 (2007). (Ex. P, Att. 149.)

[162]J. 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 & DEVELOPMENTAL DISORDERS 299 (2006). (Ex. BB, Att. 84.)

by different researchers in different countries have not *completely ruled out* the possibility of any merit to their 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 the MMR vaccine *does* likely cause 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 MMR vaccine and autism, while not *completely ruling out* a possible causal role with respect to a *subset* of autism, at least *casts considerable doubt* upon the proposition that the MMR vaccine *ever* plays a role in causing any kind of autism, including regressive autism.

Third, and most importantly, at least five studies *do* provide evidence *directly relevant* to the petitioners' "regressive autism only" argument. Those five studies, as detailed at pp. 119-20 above, provide significant evidence *against* the theory that the MMR vaccine plays a causal role even in the subset of autism known as regressive autism.[163]

d. 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 vaccination 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*. at 1325-26; *Althen v. Secretary of HHS*, 418 F.3d 1274, 1281 (Fed. Cir. 2005). That case law, of course, correctly recognizes the fact that with respect to many causation-in-fact claims raised in Program cases, the question of whether the *type* of vaccination 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

[163] Another argument that the petitioners seem to raise against the epidemiologic evidence advanced by the respondent is that the *non-American* epidemiologic studies involved children who, prior to receiving their MMR vaccinations in question, received fewer thimerosal-containing vaccines, and/or less total thimerosal, than U.S. children. Therefore, petitioners seem to argue, the fact that MMR has not been associated with autism in other countries should not be deemed relevant to *U.S. children*, whose immune systems, according to petitioners, are allegedly weakened by exposure to *higher* amounts of thimerosal prior to their MMR vaccinations. (Again, this point was *not* raised by petitioners' counsel in their post-hearing briefs. But see the questions asked by petitioners' counsel at Tr. 2640A-52.) Such an argument, however, must be rejected. As explained above (pp. 22-34), the petitioners have wholly failed to demonstrate any merit in their claim that the small amounts of mercury contained in thimerosal-containing vaccines have *any effect* on infants' immune systems. Therefore, there is no reason to disregard the MMR/autism studies from non-U.S. countries, simply because children in those other countries may have received amounts of thimerosal different from the amounts received by U.S. children.

whether such a vaccination could cause such an injury. 418 F.3d at 1280. In such a situation, where there 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. *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. 03-720V, 2008 WL 5068934, at *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. 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. Similarly, in *Andreu v. Secretary of HHS*, No. 98-817V, 2007 WL 2706157, at *28 (Fed. Cl. Spec. Mstr. Aug. 29, 2007), it was noted that special masters routinely use medical literature in order to evaluate causation theories.

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*, No. 98-910V, slip op. at 29 (Fed. Cl. Jan. 30, 2009); *Estep v. Secretary of HHS*, 28 Fed. Cl. 664 (1993); *Sharpnack v. Secretary of HHS*, 27 Fed. Cl. 457 (1993); *Sumrall v. HHS*, 23 Cl. Ct. 1 (1991).

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 of 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.

e. Summary concerning epidemiology

The numerous epidemiologic studies done over the past ten years, when taken together, make it *very unlikely* that the MMR vaccination has 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 the MMR vaccine might be associated with some small subset of autism, such as regressive autism. However, there are three reasons why 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 MMR vaccine and autism, while not *completely ruling out* a possible causal role with respect to a *subset* of autism, at least *casts considerable doubt* upon the proposition that the MMR vaccine *ever* plays a role in causing any kind of autism, including regressive autism. And, third, five studies provide evidence that is *directly relevant* to the petitioners' "regressive autism only" argument, supplying significant evidence *against* the theory that the MMR vaccine plays a causal role *even* in the subset of autism known as regressive 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.

9. Conclusions of the Institute of Medicine committees

Another part of the record in this case adds additional weight to my conclusion concerning this MMR/autism general causation issue. That is, two very well-qualified groups of medical experts have studied the issue of whether the MMR vaccine causes autism, and both groups have reached a conclusion *against* the proposition that the MMR vaccine causes autism.

I refer to two reports 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 Congress in 1863 to be a 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. (Ex. JJ, 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 Ex. JJ, p. 25.) Two of those reports are of direct relevance to the general causation issue involved in this case. (Ex. HH and Ex. JJ.)

In the first of those reports, issued in 2001, an expert committee selected by the IOM extensively examined all of the information then available concerning the same general causation controversy at issue here, *i.e.*, the question of whether the MMR vaccine can cause or contribute to autism. After a lengthy discussion, that 2001 IOM Committee reached the conclusion that "the evidence favors rejection of a causal relationship at the population level between MMR vaccine and ASD." (Ex. HH, p. 60.) 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. (Ex. HH, p. 19.)

By 2004, considerable additional evidence was available concerning the MMR/autism general causation issue, so the IOM assembled another committee to study the issue again. And once again, the 2004 IOM Committee, after studying the additional evidence that had become available since 2001 along with the earlier evidence, reached the same conclusion, that the evidence "favors rejection of a causal relationship between MMR vaccine and autism." (Ex. JJ, pp. 8, 126, 151-52.)

It is quite appropriate that I assign at least some evidentiary weight to the conclusions of those two IOM committees. 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, special masters should carefully consider those studies in deciding Vaccine Act cases.[164]

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[164]Respondent has also asserted that numerous other prestigious expert medical groups, beside the IOM committees discussed above, have also "rejected any link between vaccines and ASDs." (R1 at 61.) But, with two exceptions, respondent has not supplied *documentation* that such bodies have stated any such conclusions, so I cannot place any reliance on any alleged conclusions of any other scientific bodies. One exception is a report issued by the Medical Research Council (MRC) of the United Kingdom in December of 2001, which was filed as an attachment to Dr. Ward's report. Medical Research Council, *MRC Review of Autism Research: Epidemiology and Causes,* Dec. 2001, London. (Ex. BB, Att. 70.) The MRC appears to be the British counterpart to the United States' National Institute of Health or the Institute of Medicine. (Tr. 1246A.) The MRC (continued...)

Moreover, I note that during the 15-year history of the Vaccine Act, special masters have consistently relied upon the reports of the Institute of Medicine. *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) (affirming special master's reliance 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 (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. 99-103V, 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).

To be sure, I stress that I am certainly *not* allowing the judgment of the IOM committees to substitute for my own. The conclusion of those committees constitutes *only one item* of evidence, among many, concerning the general MMR/autism causation issue in this case. My own conclusion concerning this general causation issue would, indeed, be *exactly the same* if the IOM reports 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 conclusion here.

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[164](...continued)
concluded that the medical evidence available at that time did *not* support a causal relationship between the MMR vaccine and autism. (*Id*. at 3, 25, 28-31.)

The second exception is a report from the World Health Organization. That organization's Global Advisory Committee on Vaccine Safety conducted a review of the evidence, and concluded that "no evidence exists of a causal association between MMR vaccine and autism or autistic disorders." World Health Organization, *MMR and Autism - A Review for the Global Advisory Committee on Vaccine Safety*, WEEKLY EPIDEMIOLOGICAL RECORD (January 24, 2003). (Ex. TT, p. 1.)

The conclusions of those two committees supply yet another reason to reject the petitioners' general theory, advanced in this case, that the MMR vaccine can contribute to the causation of autism.

10. 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 the MMR vaccination can be a substantial factor in contributing to the causation of autism, in individuals suffering from regressive autism or any other type of autism. To the contrary, the evidence that I have reviewed makes it appear *extremely unlikely* that the MMR vaccine can contribute to the causation of autism.

C. Reasons for rejecting the claim that the MMR vaccine substantially contributed to Michelle Cedillo's autism

I must also reject the claim that the MMR vaccine substantially contributed to *Michelle Cedillo's* autism, for several reasons set forth below.

1. I have rejected the petitioners' "general causation" theory.

In the pages above, I have explained at length why I have rejected the petitioners' *general causation* theory, concerning how the MMR vaccine allegedly can contribute to the causation of 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 the autism of *Michelle Cedillo herself* was caused by her MMR vaccination.

2. Petitioners' theory depends upon the existence of a reliable laboratory test finding of persisting measles virus, which does not exist in Michelle's case.

Dr. Kinsbourne made it absolutely clear that his causation theory depended upon *assuming* the existence of a reliable laboratory test that finds persisting measles virus in an autistic child's body. He indicated that in *no case* could he opine that the MMR vaccine caused a person's autism in the absence of a reliable finding of persisting measles virus in the vaccinee's body. (*E.g.*, Tr. 1180A, 1183A, 1196A.) However, for the reasons already explained above, I have concluded that the Unigenetics laboratory result purporting to find persisting measles virus in *Michelle*'s case is *not* reliable. Therefore, petitioners' and Dr. Kinsbourne's conclusion that the MMR vaccine substantially contributed to *Michelle's* autism must be rejected for that reason alone.

3. Dr. Kinsbourne relied upon incorrect assumptions concerning the timing of Michelle's autism symptoms.

Dr. Kinsbourne also made it clear that, in offering his causation opinion in Michelle's case, he relied upon the certain assumptions concerning the *timing* of the onset of Michelle's symptoms of autism. He opined that Michelle was a normally developing infant, with no indications of autism, until the time of her MMR vaccination on December 20, 1995. (Ex. 61, p. 19; Tr. 1040.) He further testified that Michelle's first symptoms of autism then began quite abruptly about seven days after that vaccination, or within a few days thereafter. (Ex. 61, p. 3; Tr. 1041, 1175A-76, 1184A.) However, upon a complete analysis of the record, I conclude that these assumptions of

Dr. Kinsbourne were *not* correct. To the contrary, the evidence shows that (1) Michelle exhibited symptoms of autism *prior* to her MMR vaccination, and (2) Michelle did *not* experience an abrupt onset of autism symptoms shortly after her MMR vaccination.

a. Analysis of the record, especially certain videos, demonstrates that Michelle was exhibiting symptoms of autism even prior to the MMR vaccination in question.

i. Testimony of Dr. Fombonne and Dr. Wiznitzer

Respondent relied upon two experts who testified that there is much evidence that demonstrates that Michelle was exhibiting symptoms of autism *even prior* to her MMR vaccination of December 20, 1995. Those witnesses were Dr. Eric Fombonne and Dr. Max Wiznitzer.

Dr. Fombonne, as noted above, is a pediatric psychiatrist with extensive experience in examining and treating autistic children, and in studying the issue of the causation of autism. (Tr. 1239-62A.) Dr. Fombonne described several different categories of evidence that indicate the presence of autism in Michelle prior to the MMR vaccination. (Tr. 1328A.) First, he noted that Michelle's medical records contain notations indicating that Michelle was exhibiting signs of *social and language delay*, an important component of autism, prior to her MMR vaccination. One record indicated that Michelle did not smile until she was four to six months of age. (Tr. 1328A-29, Ex. 7, p. 3 (note that p. 3 of Ex. 7 is p. 2 of Dr. Roth's report).) Dr. Fombonne explained that children usually smile well before that time, so this would be evidence of a delay in social development. (Tr. 1329.) He further noted that some records indicated that Michelle had about 10 words by the age of 15 ½ months, when she received her MMR vaccination. (Tr. 1329; Ex. 7, p. 3; Ex. 4, p. 2.) Assuming that report to be accurate, Dr. Fombonne explained that most children have about 40 words by the age of 16 months, so that the report of only 10 words was an indication of delay in language development. (Tr. 1330A-31.)

Next, Dr. Fombonne pointed to the fact that Michelle's *head circumference* was abnormally large during her first year of life, which is typical of autism. (Tr. 1335-37; Ex. 8, pp. 7-8.)

Also, Dr. Fombonne noted that he had reviewed all of the Cedillo family *videos* of Michelle during the period prior to her MMR vaccination, and found many examples of autistic behavior. (Tr. 1337-50A.) During the evidentiary hearing, Dr. Fombonne displayed a number of examples of such videos, pointing out specific behaviors that, in his view, constituted autistic behavior by Michelle during the pre-vaccination period. Examples included Michelle failing to respond to her name, failing to make eye contact, failing to play with toys in a fashion typical of her age group, failing to use communicative gestures, failing to use any words, engaging in certain stereotypical "hand-flapping" movements, and tending to fixate exclusively on a non-human stimulus (in this case, a Sesame Street video) to the exclusion of social interaction. (Tr. 1340-50A.) He explained that all

of these behaviors were abnormal for children of Michelle's age, and all were indicative of autism.[165] (*Id*.)

Dr. Wiznitzer, a pediatric neurologist who also has had extensive experience in diagnosing and treating autistic children, also reviewed the videos of Michelle. (Tr. 1645, 1756, 1779.) He commonly uses videos in his clinical practice concerning autistic children, both for confirming the diagnosis of autism and for pinpointing the time of onset of the condition. (Tr. 1644-45, 1699-1700, 1757-58.) Dr. Wiznitzer testified that he found much evidence of autism on the videos of Michelle *prior* to her MMR vaccination of December 20, 1995. (Tr. 1647-67.) Like Dr. Fombonne,[166] Dr. Wiznitzer, during the evidentiary hearing, displayed a number of excerpts from those videos, and pointed to specific behaviors that he found to be clear examples of autistic behavior in Michelle, behaviors that would not be expected in children who are not autistic. (*Id*.)

Dr. Wiznitzer pointed to a video in which, when Michelle was nine months of age, she engaged in certain repetitive hand movements typical of autism, movements that later became even more defined when she was in her second and third years of life. (Tr. 1656-57A.) Dr. Wiznitzer pointed out many instances of the same types of behavior noted by Dr. Fombonne, including a lack of eye contact or the failure to sustain eye contact; a lack of social engagement with the adults around her; a marked tendency to prefer watching videos or examining objects to the exclusion of interacting with people; and the fact that it was much more difficult for adults to attract her attention than would be the case with typical children of that age. (Tr. 1651-67, 1781-82A.) Also like Dr. Fombonne, Dr. Wiznitzer testified that Michelle used no words in the videos, and for the most part did not even make non-verbal sounds in interaction with the people around her, as would be typical for a child of that age. (Tr. 1651, 1659A, 1661-62, 1780.) Dr. Wiznitzer explained that all of these behaviors were not typical of children of that age, and were indicative of autism. (Tr. 1647-67, 1781-82A.)

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[165]Dr. Fombonne also pointed to notations in the medical records indicating that Michelle had delays in *motor skills* prior to her MMR vaccination. He argued that Michelle was later than the average child in both sitting independently and walking. (Tr. 1332-34A, 1462-63; Ex. 7, p. 3.) Dr. Kinsbourne acknowledged that Michelle was relatively late in reaching those milestones, but suggested that Michelle was within the wide range of normal variability in those cases. (Tr. 1062A-63.)

As Dr. Kinsbourne acknowledged, Michelle was certainly slower than average in meeting these two motor skill milestones. However, the record of this case is not clear as to the limits of the range of normality in these areas, especially as to walking. Further, it is not clear to what extent motor skill delays are closely tied to autism. Therefore, I do *not* consider the evidence as to Michelle's possible delays in these *motor skills* as significant evidence of autism in Michelle predating the MMR vaccination.

[166]Dr. Wiznitzer testified that he reviewed the videos and reached his conclusions concerning them independently, without consulting with Dr. Fombonne or anyone else. (Tr. 1667, 1771A-72A.)

Dr. Wiznitzer also noted that Michelle's abnormally large head size during her first year of life was evidence of autism that pre-existed her MMR vaccination. (Ex. DD, p. 4.)

In this regard, both Dr. Fombonne and Dr. Wiznitzer emphasized that Michelle's parents were certainly *not* blameworthy in failing to recognize that those behaviors in Michelle constituted early evidence of autism. (Tr. 1362-64, 1667-71.) Indeed, Dr. Fombonne testified that it was quite common for even pediatricians to fail to recognize the earliest signs of autism. (Tr. 1453A-56A.)

ii. Petitioners' arguments and evidence

Concerning this point of possible pre-vaccination evidence of autism, the petitioners did offer some counter-evidence, which merits discussion. One witness in this regard was Michelle's mother, Theresa Cedillo, and several points that Mrs. Cedillo made are important. First, she offered an alternative explanation for a particular instance of Michelle's behavior in the video dated December 17, 1995, which Dr. Wiznitzer had interpreted as the autistic behavior known as "hand regard." (Tr. 2878A-79; see Tr. 1649-51A.) Mrs. Cedillo's explanation concerning this particular behavior seems plausible, so I have not placed any reliance upon Dr. Wiznitzer's particular point concerning the alleged "hand regard" behavior. Next, Mrs. Cedillo showed a photograph of Michelle smiling just prior to Christmas during her first year of life. (Tr. 2879-80.) That photograph and testimony seems to show that Michelle did smile by about age 3 ½ months, contrary to the medical record cited by Dr. Fombonne, which had estimated her first smile at age 4 to 6 months. (Tr. 1328A-29; Ex. 7, p. 3.) Therefore, I have not placed any reliance on Dr. Fombonne's particular point concerning late smiling.

Third, Mrs. Cedillo testified that Michelle used several words for a purpose, not in mere imitation, during the pre-vaccination period. (Tr. 2875A-76A.) Mrs. Cedillo seemed to have real memories of Michelle using those words, and this testimony does stand in contrast to the testimony of both Dr. Fombonne and Dr. Wiznitzer that, in all of the videos of Michelle that they reviewed, she never used any functional words. (Tr. 1460A-61A, 1651, 1659A, 1661-62, 1780.) It does seem surprising that if Michelle did use several words functionally, as Mrs. Cedillo described, that such usage was never captured on any of the family videos of Michelle. Yet I certainly do *not* doubt either that Mrs. Cedillo was honestly relating her memories, or that Drs. Fombonne and Wiznitzer were honestly and accurately describing what they saw on the videos. However, I do not need to resolve this anomaly in the evidence. While both Dr. Fombonne and Dr. Wiznitzer doubt that Michelle ever used ten words functionally, as the Cedillos later reported to her doctors (Ex. 7, p. 3; Ex. 4, p. 2), Dr. Fombonne testified that *even assuming* that Michelle *did* have such use of about 10 words, that would *still* be abnormally slow language development, since most children have about 40 words by age 16 months. Therefore, Michelle's limited word use would *still* be an indication of a delay in language development. (Tr. 1330A-31.)

The petitioners' other arguments concerning pre-vaccination evidence of autism are not persuasive. Concerning the issue of Michelle's abnormally large head circumference, petitioners' counsel have suggested that her head was not abnormally large compared to her height and weight,

which were both well above average. However, in both his expert report and his hearing testimony, Dr. Fombonne explained that even taking into account Michelle's length and weight, her head size still must be considered abnormal, a condition that is associated with autism. (Tr. 1456A-1460A; Ex. P, pp. 60-61.) Dr. Fombonne's testimony in this regard was not contradicted by any expert, and I found it to be persuasive.

Finally, petitioners' expert, Dr. Kinsbourne did state generally that he watched the videos of Michelle during the pre-vaccination period, and did not see any evidence of autism. (Tr. 1063-65.) I did not find this general testimony, however, to be of much value. Dr. Kinsbourne acknowledged that he has no experience reviewing videotapes as part of the treatment of autism (Tr. 1171), which contrasts with the extensive experience that Dr. Wiznitzer has with such review. (Tr. 1644-45, 1699-1700, 1757-58). Further, in the area of spotting evidence of autistic-like behavior, Dr. Kinsbourne is also obviously disadvantaged, since he has *no* experience in treating autistic children for the past 17 years. This contrasts strongly with the extensive experience of both Dr. Fombonne and Dr. Wiznitzer in treating autistic children during that time period. (Tr. 1163A, 1253A-54A, 1576A-77A.) And most importantly, both Dr. Fombonne and Dr. Wiznitzer, as described above, displayed a number of videos of Michelle during the hearing, and pointed out Michelle's *specific behaviors* that they deemed to be evidence of autism during the pre-vaccination period. Petitioners had the opportunity for rebuttal--*i.e.*, their counsel could have had Dr. Kinsbourne, or some other *expert* witness, exhibit the same videos and state any *disagreements* with Dr. Fombonne's and Dr. Wiznitzer's interpretation of Michelle's behaviors. Petitioners, however, presented no such rebuttal by any expert. Thus, the interpretations of Michelle's pre-vaccination behaviors presented by Drs. Fombonne and Wiznitzer, highly qualified witnesses whom I found to be honest and credible, stand unrebutted. I conclude that those behaviors were, in fact, evidence of autism in Michelle that predated her MMR vaccination.

iii. Summary concerning pre-vaccination evidence of autism

In short, for the reasons set forth above, I conclude that Dr. Kinsbourne was *mistaken* in his assumption that Michelle displayed normal development prior to her MMR vaccination of December 20, 1995. To the contrary, the evidence strongly indicates that Michelle was already showing evidence of brain abnormality and of autism *prior* to her MMR vaccination.

b. The medical records and testimony also contradict Dr. Kinsbourne's assumption that Michelle experienced an abrupt onset of autism symptoms about seven days post-vaccination.

Thus, as demonstrated above, Dr. Kinsbourne was wrong in his assumption that Michelle displayed no symptoms of autism *prior* to her MMR vaccination in question. But he also erred in a *second* assumption, *i.e.*, his understanding that Michelle's first symptoms of autism began *abruptly* about one week after her MMR vaccination on December 20, 1995, or within a few days thereafter. (Ex. 61, p. 3; Tr. 1041, 1175A-76, 1184A.) That is, Dr. Kinsbourne stated in his expert report that

Michelle experienced the onset of fever on December 27, 1995, and then the *very next day* she "stopped talking" and ceased to respond to her name. (Ex. 61, p. 3.) At the evidentiary hearing, Dr. Kinsbourne again indicated that Michelle abruptly "fell silent," ceased to "utter any words at all," and lost the desire to be held (Tr. 1041), although he was less clear as to *exactly* when that occurred. At one point he indicated that it occurred within seven days of the vaccination (Tr. 1184A); at another point he seemed to state that it occurred when Michelle's fever "abated," which would have been a few days later. (Tr. 1041.) In either event, however, Dr. Kinsbourne emphasized that Michelle's loss of speech and onset of other symptoms was "unusually abrupt" (Tr. 1175A) and "came on really fast" (Tr. 1176).

However, this assumption of Dr. Kinsbourne--*i.e.*, that Michelle suffered an *abrupt* loss of words, loss of reaction to stimuli, and loss of the desire to be held, occurring about seven days post-vaccination or within a few days thereafter--is *not* supported by the contemporaneous medical records. That is, a detailed record exists of Michelle's visit to her pediatrician on January 6, 1996, which was 17 days after the MMR vaccination of December 20, 1995. That record contains many details about Michelle's symptoms of the previous 17 days. Specifically, the pediatrician's note indicates that Michelle had a "fever and rash last week," and that the fever got better but then "spiked up" again. (Ex. 8, p. 1.) The record further indicates that Michelle's second episode of fever "started [with] cough yesterday [January 5]. Gagging to point of vomiting," and that by the following morning ("today"), Michelle's temperature, taken at home, was 105.7 degrees. (*Id*.) However, despite containing all those notations about various symptoms, that pediatrician's note makes *no mention whatsoever* of any symptoms that would seem to be symptoms of autism. The record does *not* mention any loss of speech or words, or that Michelle no longer responded to her name, or that she lost the desire to be held. Given the amount of detail in the pediatric note on that date, it seems likely that if Michelle's parents had, in fact, mentioned any such changes in behavior, the pediatrician would have recorded that in the note. But there is no mention of any such symptoms.

Significantly, the record of Michelle's next visit to the pediatrician, on March 15, 1996, contains a notation that Michelle "talks less since ill in Jan[uary]." (Ex. 8, p. 1.) This notation is very important since, with the benefit of hindsight, it would appear to be the first mention in the medical records of symptoms of Michelle's autism. But the notation indicates only a *reduction* in Michelle's speech, not that she abruptly ceased to speak altogether. The notation fails to mention either a lack of reaction to her name, or a loss of the desire to be held. In fact, the record states that Michelle "seems to hear well," which *contradicts* the assertion that she had ceased to respond to her name. Thus, this March 15 notation, indicating some type of *reduction* in speech over the two-month period since the January 6 visit, is a far cry from Dr. Kinsbourne's assumption that Michelle experienced, in late December or early January, an *abrupt* and *total* loss of speech, loss of reaction to her name, and loss of the desire to be held.

I do acknowledge that Michelle's mother, Theresa Cedillo, has provided statements at various times which offer at least some support to Dr. Kinsbourne's assumption that Michelle's first symptoms of autism occurred suddenly, shortly after Michelle's vaccination of December 20, 1995.

For example, in an affidavit prepared for this litigation, Ms. Cedillo suggests that in late December of 1995 Michelle suddenly stopped talking, stopped playing, stopped responding to her name. (Ex. 54, paras. 12, 14, 21.) However, as explained above, Michelle's medical records do *not* support those assertions. Further, during the evidentiary hearing in this case Mrs. Cedillo herself acknowledged that Michelle's behavior change came on *gradually* over the following year, rather than *abruptly* after the fever episodes. (Tr. 400-01A.) And this explanation by Mrs. Cedillo at the hearing is consistent with the fact that Michelle was never taken to any doctor during the year after the pediatric visit of March 15, 1996. Had there been an *abrupt*, *drastic* change in Michelle's behavior, Michelle's parents would not likely have waited another full year to seek further medical attention.

To be sure, I do *not* conclude that Mrs. Cedillo was ever, in her affidavits or her hearing testimony, intentionally failing to tell the truth as she remembered it at that time. After observing her testimony during the evidentiary hearing, I certainly have a favorable impression of her as an honest person. It is simply the case that human memories often become less accurate with the passage of time, especially with respect to emotionally-charged events. I conclude that the *most accurate* account of the progression of Michelle's early autism symptoms comes from (1) the records made during the pediatric visits in January and March of 1996, when Mrs. Cedillo's memory was fresh, and (2) the inferences that can be drawn from the lack of any further physician visits over the following year. *Cucuras v. Secretary of HHS*, 26 Cl. Ct. 537, 542 (1992).[167]

In sum, I conclude that Dr. Kinsbourne, in opining that the MMR vaccine contributed to the causation of Michelle's autism, based his opinion on another significant mistaken assumption of fact--his assumption that Michelle suddenly and abruptly lost all speech, ceased to react to her name, and lost the desire to be held, about seven days after her MMR vaccination. To the contrary, the overall record demonstrates that her family noticed symptoms of Michelle's autism *gradually* after the pediatric visit of January 6, 1996, and over the following year.[168]

I do note that this *particular* mistaken assumption by Dr. Kinsbourne does *not* by itself totally negate his causation opinion as to Michelle. That is, Dr. Kinsbourne did explain that he could *still* give a vaccine-causation opinion in an individual case, even where the first symptoms of autism took

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[167]I note also that respondent's expert Dr. Fombonne, who has much experience treating autistic children, explained that most parents of autistics report that the symptoms of autism appeared *gradually*, over a number of months. Parents usually cannot date the onset more precisely than that. (Tr. 1285A-87A.) This testimony supports my conclusion that the symptoms of *Michelle's* autism, like those of other autistic children, *gradually* became more evident over a period of months.

[168]As noted above, Dr. Kinsbourne also seemed to rely on the assumption that Michelle's condition falls within the category of "regressive autism." Respondent's witness Dr. Fombonne, however, argued that Michelle should not be considered as falling into the regressive category. It is unnecessary, however, to resolve this dispute. Whether Michelle's autism is considered "regressive" or not, petitioners have failed to demonstrate that regressive autism in general can be vaccine-caused, or that Michelle's own autism was vaccine-caused.

place up to *three months* (or perhaps even longer) after an MMR vaccination. (Tr. 1176-78A.) Therefore, this particular mistaken assumption of fact is not fatal to Dr. Kinsbourne's opinion by itself. But I mention it here because it demonstrates yet another erroneous assumption upon which Dr. Kinsbourne relied.[169]

4. No evidence of brain inflammation

Dr. Kinsbourne's hypothesis, as previously noted, is that the persisting vaccine-strain measles virus invaded cells in Michelle's brain, prompting an immune system response, and that the *inflammation* produced by that response disorganized critical circuits in her brain, thereby causing the autism. (Tr. 1098A-1100.) Petitioners, however, failed to supply any evidence of brain inflammation in Michelle. To the contrary, respondent's expert Dr. Wiznitzer, a well-qualified pediatric neurologist who has treated many autistic children, testified that Michelle "did not *show* any evidence of inflammation * * * [of] the brain on any medical testing." (Ex. DD, p. 2, emphasis added.) Respondent's expert Dr. Griffin noted that Michelle Cedillo's EEG result was normal, and was not characteristic of measles virus infection of the brain. (Tr. 2796.) And respondent's expert Dr. Ward stated that Michelle's repeated CT scans and MRI scan showed no sign of central nervous system ("CNS") inflammation. (Ex. BB, p. 8.)

Thus, the fact that the petitioners failed to demonstrate any evidence of brain inflammation in Michelle adds another reason to reject their theory that her autism was vaccine-caused.

5. Summary concerning causation of the autism of Michelle Cedillo

In sum, for all of the reasons stated above, I conclude that the petitioners have failed to demonstrate that the MMR vaccine received by Michelle Cedillo on December 20, 1995, contributed in any fashion to the causation of her autism.[170]

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[169]Also, Dr. Kinsbourne stated that Michelle started with *diarrhea* within two weeks of her MMR vaccination, and "from then on," up "to this present day," she had diarrhea. (Tr. 1042.) This reflects a gross misunderstanding of the actual record concerning Michelle's gastrointestinal symptoms. As I will explain in detail below (p. 149), the medical records demonstrate that Michelle's chronic *constipation* began many months *prior* to her MMR vaccination, while her chronic *diarrhea* did not begin until more than *three years after* that vaccination.

In this regard, Dr. Kinsbourne indicated that the fact that Michelle experienced *both* autism *and* chronic gastrointestinal symptoms after receiving the MMR vaccination was an important factor in his conclusion that Michelle's autism was vaccine-caused. (Ex. 61, pp. 12-14.) Thus, the fact that Dr. Kinsbourne so grossly misunderstood the record, as to the timing of Michelle's gastrointestinal symptoms, is yet another reason to reject his conclusion that the MMR vaccination contributed to the causation of Michelle's autism.

[170]At one point in their post-hearing briefs, petitioners state, without further elaboration, that
(continued...)

VIII

PETITIONERS HAVE NOT DEMONSTRATED EITHER THAT THE MMR VACCINE *CAN* CAUSE CHRONIC GASTROINTESTINAL DYSFUNCTION, OR THAT AN MMR VACCINATION *DID* CAUSE CHRONIC GASTROINTESTINAL PROBLEMS IN MICHELLE

In this case, the petitioners have contended, as a *general* matter, that the strain of the measles virus contained in the MMR vaccine sometimes persists in the gastrointestinal tissue of children, causing chronic gastrointestinal dysfunction. They also contend that Michelle Cedillo herself suffers from such a vaccine-caused chronic gastrointestinal condition. I conclude, however, that the petitioners have *failed* to demonstrate, to the level of "more probable than not," either that the MMR vaccine *can* cause chronic gastrointestinal dysfunction in general, or that an MMR vaccination *did* cause chronic gastrointestinal problems in Michelle.

A. Background information concerning the human gastrointestinal system

The following background information concerning the human gastrointestinal system may be helpful in understanding my discussion of the petitioners' allegations concerning "gastrointestinal dysfunction." The term "gastrointestinal" literally refers to the stomach ("gaster") and the intestines. (*Dorland's* at 756, 759.) However, the term "gastrointestinal tract" is used to refer to the *entire* system for digesting and voiding food, extending from the mouth to the anus. (This tract is also known as the "digestive tract.") It appears that the petitioners and their experts at times used the terms "gastrointestinal dysfunction" or "gastrointestinal symptoms" to refer to *any* type of problematic symptoms involving the digestion and defecation functions. I will use those terms in the same way. The parties and experts at times have used "GI" as short for "gastrointestinal," and I will also do so at times.

Once food is taken into the mouth and swallowed, it passes down through four major components of the gastrointestinal tract--the esophagus (a long tube from the mouth to the stomach), the stomach, the small intestine, and the large intestine--before being voided as stool. (Tr. 2099-2103A; R. Trial Ex. 15, p. 1.) The insides of those four components are lined with soft tissue, which can become inflamed for any of a number of reasons. (Tr. 2088A-89.) I will use the term

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[170](...continued)
"if the special master finds that Michelle was autistic before her MMR vaccine, he may certainly also find that the vaccine significantly aggravated an underlying condition." (P3, p. 14.) I have found, as noted above, that Michelle likely *was* autistic prior to her MMR vaccination. (See pp. 127-130 above.) However, in the record of this case I find no persuasive evidence that the MMR vaccine played any role in "aggravating" her autism. Indeed, Dr. Kinsbourne himself stated that if a child was "showing evidence of an emerging autistic disorder beforehand [*i.e.*, prior to vaccination], then I would not attribute causation to a vaccination." (*Snyder* Tr. 536A-536B.) Thus, there is simply no expert testimony that would support an "aggravation" contention.

"gastrointestinal inflammation" to refer to inflammation anywhere in those four components. The term "intestinal inflammation," on the other hand, will refer more narrowly to inflammation within the large and small intestines. The terms "bowel" and "gut" were often used, by the expert witnesses and in the medical literature, to refer to the intestines. (*Dorland's* at 244, 804.)

As will be discussed in detail below, the petitioners have alleged that Michelle Cedillo suffers from chronic gastrointestinal inflammation. Their expert has opined that Michelle has suffered from "inflammatory bowel disease," "Crohn's disease," and "enterocolitis."

"Inflammatory bowel disease," also known as IBD, is a term that encompasses a number of disorders involving *chronic inflammation* of the human digestive tract. (Tr. 428, 2088A; *Dorland's* at 536.) Although a number of disorders involving chronic inflammation of the digestive tract can fit within the category of IBD, the two most common disorders are Crohn's disease and ulcerative colitis. (Tr. 428, 2089.)

"Crohn's disease" is a particular type of chronic inflammatory condition, which can involve any part of the gastrointestinal tract, but most commonly involves the terminal ileum, a part of the small intestine. (Tr. 430A-31A, 2091A-92A; *Dorland's* at 531.)

"Enterocolitis" means inflammation of both the large intestine (the main part of which is known as the colon) and the small intestine. (Tr. 422, 2092.) I also note that the suffix "-itis" means inflammation, so that "esophagitis" means inflammation of the esophagus, "gastritis" means stomach inflammation, etc.

The experts have also discussed two types of conditions that have been found in Michelle's intestines. The first condition is "lymphoid nodular hyperplasia," also known as "lymphonodular hyperplasia" or "LNH." The experts explained that the lymphoid tissue in the lining of the digestive tract is formed into "lymph nodes" or "nodules," and when those nodules become enlarged, the condition is known as LNH. (Tr. 445A-46A, 2115-16, 2150A.) Reports of "nodularity," in descriptions of examinations of the intestines, refer to the presence of LNH.

The second condition is "aphthous ulcers," also known as "aphthous ulcerations," which occur in the lining of the gastrointestinal tract. One of respondent's experts explained that the term refers to a type of tissue erosion that can occur anywhere in the digestive tract. (Tr. 2120.) He testified that common "cold sores" or "canker sores," which people often experience in their mouths, are a type of aphthous ulcer, and that aphthous ulcers in the intestines are similar. (Tr. 2120, 2126-27.)

The experts differ regarding the *significance* of both LNH and aphthous ulcers, both in general and in Michelle's case. Respondent's experts view those conditions as common and not suggestive of inflammation, while petitioners' expert argues that they are signs of inflammation in Michelle's intestines. That issue will be addressed below.

B. Petitioners' evidence--Dr. Krigsman

Petitioners' sole witness in this *Cedillo* proceeding, concerning the issue of gastrointestinal dysfunction, was Dr. Arthur Krigsman, a pediatric gastroenterologist, who filed an expert report (Ex. 59), and testified orally at the evidentiary hearing (Tr. 408-574). In his expert report, Dr. Krigsman stated the opinion that Michelle's chronic gastrointestinal problems have been caused by her MMR vaccination. (Ex. 59, pp. 7-9.[171]) He wrote that the "most compelling factor" supporting that opinion "is the simple chronology of events"--*i.e.*, the fact that, as he understood the history, Michelle's chronic gastrointestinal symptoms began soon after her MMR vaccination and have continued since that time. (*Id*. at 6.)

Dr. Krigsman further noted, in his expert report, that he was relying on the "pattern of bowel inflammation" in children with both autism and gastrointestinal complaints, the pattern first reported in the 1998 Wakefield article. (*Id*. at 7-8.) He wrote that such pattern was supported by the Unigenetics testing[172] and the Walker study discussed above. (*Id*. at 7; see my discussion of the Unigenetics testing and the Walker study at pp. 42-44, 64-65 above.) He opined that Michelle's case fits that pattern, stating that her condition is a "classic" case of the "ASD-GI disease" pattern. (*Id*. at 8.)

In his hearing testimony, Dr. Krigsman further explained his opinion. He stated the view that where a laboratory test finds evidence of measles virus in the gastrointestinal system[173] of an autistic child who has experienced GI inflammation, the measles virus is the likely cause of that GI inflammation. (Tr. 488A, line 13, through 489A, line 6.) As a basis for that opinion, Dr. Krigsman pointed to the finding by the Unigenetics lab of "measles virus genome in the inflamed guts of autistic children who had bowel symptoms" (Tr. 489A, lines 10-21), combined with a "pattern of inflammation" in the bowels of these children "consistent with viral infection," and findings of "lymphoid hyperplasia" (Tr. 489A, lines 22 through 490, line 3). He further opined that *Michelle Cedillo's own* gastrointestinal condition, which he usually described as "enterocolitis" or "inflammatory bowel disease," falls into this pattern, and is, therefore, likely to be the result of the vaccine-strain measles virus which he believes to be persisting in her body. (Tr. 489A, lines 1-6.)

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[171]Ex. 59 was not paginated as originally submitted by Dr. Krigsman. Accordingly, I will refer to the *electronic pagination* in the upper-right-hand corner, according to which the first page of his text is paginated as 2, the last page as 9.

[172]Dr. Krigsman cited the Uhlmann article, which describes the Unigenetics testing.

[173]At page 488A, line 24, the transcript contains the word "ileo". From the context, I conclude that Dr. Krigsman actually said "ileal," which is the adjectival form of the word "ileum," a part of the small intestine.

C. Respondent's evidence

Concerning the petitioners' allegations about gastrointestinal dysfunction, respondent relied primarily on the evidence supplied by four experts, Drs. Hanauer, Griffin, Gershon, and MacDonald.

1. Dr. Hanauer

Respondent's primary witness offered in response to Dr. Krigsman's testimony was Dr. Stephen B. Hanauer, a gastroenterologist. Dr. Hanauer provided both a written expert report (Ex. X) and hearing testimony (Tr. 2076-2200). He provided an extensive analysis of Michelle's own case, in which he detailed his disagreements with Dr. Krigsman's opinion. He went in detail through the medical records of the examinations of Michelle's gastrointestinal system, specifically of her multiple endoscopies and biopsies, pointing out how the results of those examinations are *inconsistent* with Dr. Krigsman's conclusions. (Tr. 2108A-43.) Dr. Hanauer also made it clear that he disagrees completely with Dr. Krigsman's *general opinion* that the MMR vaccine can cause chronic gastrointestinal dysfunction by persisting in a child's body.

I will discuss the *specifics* of Dr. Hanauer's analysis of Dr. Krigsman's general causation theory, and of Michelle's specific case, below.

2. Dr. Griffin

Respondent's expert Dr. Diane Griffin, as noted above (pp. 108-09), has extensive experience concerning the measles virus. Her expert report, while largely devoted to other matters, did offer brief instruction concerning the topic of whether the MMR vaccine can cause chronic GI symptoms. Dr. Griffin noted that while the measles virus sometimes does invade the GI system ("gut lymphoid tissue"--Ex. V at 2), it "does not usually cause gastrointestinal symptoms (*e.g.*, diarrhea or constipation)" (Ex. V at 2; *see also* Tr. 2864-65). I note that Michelle Cedillo's most prominent chronic gastrointestinal symptoms were diarrhea and constipation.

3. Dr. Gershon

Respondent filed a written report of Dr. Michael Gershon, a medical doctor specializing in neurogastroenterology, addressing the issue of the causation of Michelle's gastrointestinal symptoms. (Ex. T.) His analysis concerning Michelle's gastrointestinal symptoms is similar to that of Dr. Hanauer. (*Id*. at pp. 13-15, 20-22.) Like Dr. Hanauer, Dr. Gershon, after reviewing Michelle's medical records, found that Dr. Krigsman was not justified in concluding that Michelle suffered from chronic GI *inflammation*. Dr. Gershon concluded, contrary to Dr. Krigsman's view, that there exists no significant evidence that MMR vaccination leads to inflammatory bowel disease ("IBD"), and that there exists "no evidence that MMR caused Michelle Cedillo to acquire a gastrointestinal illness." (*Id*. at 22.)

Dr. Gershon did not testify during any hearing, so his opinion is of lesser importance than that of Dr. Hanauer, but Dr. Gershon's opinion does add additional support to the conclusion that I have reached.

4. Dr. MacDonald

Dr. MacDonald, a Ph.D. immunologist who specializes in the gastrointestinal immune system, testified in the *Hazlehurst* case that there is no valid evidence to support the "autistic enterocolitis" causation theory upon which Dr. Krigsman bases his own general causation theory. (*Hazlehurst* Tr. 629A-49A, 660A-63.) Dr. MacDonald also testified concerning "lymphoid nodular hyperplasia," also known as "LNH," a condition of the lining of the intestines, which Dr. Krigsman found to be indicative of intestinal inflammation. Dr. MacDonald explained that LNH does *not* indicate intestinal inflammation, and is not an abnormal finding in children. (*Id*. at 616A-19.)

D. Experience and background of the experts

One important factor, which influenced my analysis concerning this issue, is the experience and credentials of the experts who presented evidence concerning the alleged causation of gastrointestinal dysfunction by the vaccine-strain measles virus. The petitioners' expert, Dr. Krigsman, does have important credentials relevant to this issue. He is a board-certified pediatric gastroenterologist, and he has practiced pediatrics or gastroenterology since 1995, when he completed his gastroenterology fellowship. (Tr. 409; Ex. 60.)

However, there are problems with Dr. Krigsman's practice history and his resume that are relevant to the credibility of his expert opinion given in this case. Dr. Krigsman, after working as an attending physician at Lenox Hill Hospital in New York from 2000 to 2004, left that hospital's employ under questionable circumstances. (Tr. 499A-500, 558-560.) According to Dr. Krigsman's own testimony, the hospital restricted his privileges to perform endoscopies (an invasive procedure with some risks) in the belief that Dr. Krigsman was performing medically unwarranted endoscopies on children for research purposes.

Dr. Krigsman later joined a medical practice in Texas, with the same Dr. Andrew Wakefield whose 1998 article initiated the theory that the MMR vaccine can cause autism and GI symptoms. (Tr. 491-92A.) In 2005 Dr. Krigsman was fined $5,000 by the Texas State Board of Medical Examiners, apparently in part because the website of that medical practice had represented that he was available to see patients at a time when he was not yet licensed to practice medicine in that state; in part because of his "disciplinary action" by the Lenox Hill Hospital; and in part because of his "falsification" and "attempted concealment" of a prior disciplinary action by the Florida medical board. (Tr. 501-503; R. Trial Ex. 2, p. 2--"Applicant #391.")

There also were questions concerning Dr. Krigsman's *curriculum vitae* ("C.V."). The C.V. that petitioners introduced into this proceeding stated that he was an "Assistant Clinical Professor" at the New York University Medical School (Ex. 60, p. 3), but Dr. Krigsman acknowledged on

cross-examination that he has never taught a class there (Tr. 503). His C.V. also listed four items under the heading of "Publications" (Ex. 60, p. 4), but on cross-examination Dr. Krigsman acknowledged that only one of the four items represented an actual publication (Tr. 504-06).

On the other hand, the witnesses upon whom respondent relies, concerning this issue, have very impressive backgrounds. Dr. Hanauer is board-certified in both gastroenterology and internal medicine. (Tr. 2078A; Ex. Y, p. 1.) He is a Professor of Medicine at the University of Chicago, where he is the chief of the gastroenterology section. (Tr. 2077A; Ex. Y, p. 1.) His section sees about 6,000 patients per year, and he himself maintains an active clinical gastroenterology practice, performing about 12 or more colonoscopies each week. (Tr. 2082-83.) Within the field of gastroenterology, Dr. Hanauer subspecializes in an area extremely pertinent here, the area of gastrointestinal inflammation, or IBD. (Tr. 2079A.) He chaired the International Organization for Inflammatory Bowel Disease, and also chaired the Infections, Immunology, and Inflammatory Bowel Disease section of the American Gastroenterology Association. (Tr. 2079A; Ex. Y at 2.) For the past 14 years, he has been the Co-Director of the Inflammatory Bowel Disease Research Center at the University of Chicago. (Tr. 2085.) He has served as editor-in-chief of a publication known as the *Inflammatory Bowel Disease Monitor*, as a section editor of the *Inflammatory Bowel Disease Journal*, and as a member of the editorial board of twelve medical journals. (Tr. 2083-84; Ex. Y at 3.) Dr. Hanauer has published more than 280 articles related to gastrointestinal issues, virtually all related to GI inflammation, and has also published over 70 medical book chapters. (Tr. 2083; Ex. Y, pp. 4-31.)

Respondent's expert Dr. Griffin, as previously noted, has studied the measles virus for more than 30 years. (Tr. 2743-48.) She is a medical doctor specializing in molecular biology, immunology, and virology. (Tr. 2739A-41.) She is the chair of the Department of Molecular Microbiology and Immunology at the John Hopkins School of Public Health. (Tr. 2740-41.) She has been an editor or editorial board member of a number of scientific journals relating to virology. (Tr. 2742A-43A; Ex. F, p. 5.) She has written many book chapters and edited several textbooks concerning virology, and published more than 240 research articles in scientific journals. (Ex. F, pp. 18-37; Tr. 2746.) Even one of petitioners' experts, Dr. Kennedy, acknowledged Dr. Griffin's considerable expertise concerning the measles virus. (Tr. 851A.)

Respondent's third expert in this area, Dr. Gershon, also has impressive credentials. He is a medical doctor specializing in neurogastroenterology, and has studied immunology and bowel disorders since obtaining his medical degree in 1963. (Ex. T, p. 1.) He has authored nearly 350 scientific articles and book chapters, as well as a book concerning bowel function. (Ex. T, p. 2; Ex. U, pp. 4-31.) He has served on editorial boards of scientific journals, including the journal *Gastroenterology*. (Ex. T, p. 2.) He is a faculty member at Columbia University medical school, where he recently stepped down after serving as chair of that school's Department of Anatomy and Cell Biology. (Ex. T, p. 1.)

Finally, respondent's fourth expert, Dr. MacDonald, has excellent credentials as well. As noted above, Dr. MacDonald is a Ph.D. immunologist who, during a medical research career of more

than 30 years, has specialized in the immunology of the human gut (intestines). (*Hazlehurst* Ex. A, p. 1; *Hazlehurst* Tr. at 603-07A.) He is a Professor of Immunology and Dean for Research at the medical school of the University of London. (*Hazlehurst* Ex. A, p. 1; *Hazlehurst* Tr. at 603-04A.) He stated that he has had "a particular interest in the lymphoid tissue of the human gut" (*Hazlehurst* Ex. A, p. 1), which is the tissue involved in Dr. Krigsman's allegation of inflammation in Michelle Cedillo. He has published at least 158 articles concerning gut immunology, written a book on that topic, edited several other such books, written many book chapters, and served in editorial positions on a number of medical journals. (*Hazlehurst* Tr. 607A-09A.)

Thus, as was the case with the issues of the validity of the Unigenetics testing and the causation of *autism*, I again see a very significant difference, in the backgrounds of the parties' experts relevant to this gastrointestinal dysfunction causation issue. One difference is the fact that Dr. Krigsman specializes in *pediatric* gastroenterology, rather than general gastroenterology, so that in that one respect Dr. Krigsman does have an edge over the respondent's primary expert, Dr. Hanauer, a gastroenterologist who does not specialize in pediatric gastroenterology. In other respects, however, there is a vast difference in respondent's favor, as is made clear by the description of the experts' credentials above. Concerning the area of gastrointestinal *inflammation*, Dr. Hanauer has far more expertise than Dr. Krigsman. Dr. Griffin has much more expertise than Dr. Krigsman concerning the *measles virus*. All four of respondent's experts have much longer experience in their fields than does Dr. Krigsman in his. All four have high-ranking academic positions at prestigious universities, and have published very extensively, in contrast to Dr. Krigsman's single actual medical publication.

This very substantial difference in background and experience level, then, combined with the problems with Dr. Krigsman's practice history and resume detailed on pp. 138-39 above, is one factor leading to my conclusion that the respondent has presented a far more persuasive case concerning this causation issue.

E. Analysis concerning the petitioners' general theory that the MMR vaccination can cause chronic gastrointestinal dysfunction

After considering the evidence offered by Dr. Krigsman, along with the evidence offered by the respondent in response, I conclude that the petitioners have *failed* to demonstrate that it is "more probable than not" that the MMR vaccination can cause chronic gastrointestinal dysfunction. I found Dr. Krigsman's testimony to be quite unpersuasive, and to be substantially outweighed by the testimony of the respondent's experts, especially that of Dr. Hanauer. There are a number of reasons for this conclusion.

1. Dr. Krigsman's opinion was based upon an erroneous assumption concerning the reliability of the Unigenetics testing.

Dr. Krigsman's entire general causation approach was based upon an *erroneous assumption* concerning the reliability of the Unigenetics testing. Dr. Krigsman, in essence, based his general causation opinion on the following chain of reasoning: (1) The Uhlmann study performed by the Unigenetics laboratory, along with the Walker study, has demonstrated that the vaccine-strain measles virus often persists in the intestinal tissue of children with autism and chronic gastrointestinal problems. (2) It is likely that a persisting measles virus would cause chronic GI *inflammation*, in turn causing chronic symptoms such as abdominal pain, diarrhea, and constipation. (3) Therefore, if a child has been shown by a laboratory test to have a persisting measles infection in the GI tract after MMR vaccination, and has shown evidence of chronic inflammation and other chronic GI symptoms, and the chronic GI symptoms appeared within six months after an MMR vaccination, then it is reasonable to conclude that the chronic GI inflammation and other symptoms were *caused*, at least in significant part, by the MMR vaccination that introduced the measles virus into the body. (Ex. 59 at 7-9; Tr. 488A-90, 536A.)

Thus, Dr. Krigsman made it clear that both his *general causation* opinion, as well as his specific causation opinion in *any* case, depended upon the assumption of the reliability of the Unigenetics testing for the presence of measles virus. Dr. Krigsman is, in fact, relying on the Unigenetics testing in two different ways. First, in forming his *general causation theory*, he relied upon the general accuracy of the Uhlmann study. Second, in forming his *specific causation* conclusion in a particular case, he would depend upon the reliability of the *specific* laboratory test, again performed by Unigenetics, that allegedly found the presence of the measles virus in that person's intestinal tissue.

However, for the reasons set forth above (pp. 41-78), I have concluded that the Unigenetics testing for measles virus, in both the Uhlmann study and in the subsequent testing of individuals such as Michelle Cedillo, was *not* reliable.[174] Therefore, Dr. Krigsman's entire approach to general causation simply has no probative value, because it is based upon the *incorrect assumption* of the reliability of the Unigenetics testing.

2. Dr. Krigsman's theory lacks support, and is based upon the heavily-criticized "autistic enterocolitis" theory of Dr. Wakefield.

As explained above, Dr. Krigsman based his general causation opinion on the reliability of the Uhlmann study's *general conclusion* that children with both developmental disorders and gastrointestinal problems are often infected with measles virus in their intestines, while

[174]Dr. Krigsman also relied on the ongoing Walker study, in which he is one of the participating researchers, as supportive of the results of the Uhlmann study. However, I have already explained (p. 64-65 above) why I find that the "preliminary data" from the Walker study *cannot* be given any evidentiary weight.

developmentally normal children with GI problems are rarely so infected. However, as previously discussed, I have concluded that the Uhlmann study was unreliable. Therefore, with the Uhlmann study discredited, Dr. Krigsman's *general causation* theory is simply left without any evidentiary support.

Dr. Krigsman has not pointed to any *other* possible basis for his theory. For instance, Dr. Krigsman did not point to examples in medical history of *any* type of virus persisting in intestinal tissue and causing chronic GI symptoms. To the contrary, Dr. Hanauer, an expert well-qualified concerning GI inflammation, testified that he is unaware of *any* examples of viral persistence in intestinal tissue causing *chronic* inflammation. (Tr. 2093, 2161A.) Neither Dr. Krigsman nor any other expert for petitioners contradicted Dr. Hanauer on this point.

Moreover, in constructing his general causation theory, Dr. Krigsman clearly based his theory on the "autistic enterocolitis" theory that evolved from Dr. Wakefield's seminal 1998 article mentioned above. In his expert report, Dr. Krigsman indicated that he sees a causal connection between the MMR vaccine and a disease category that he described as "autistic enterocolitis." (Ex. 59, p. 7.) And at the evidentiary hearing, Dr. Krigsman again used the term "autistic enterocolitis" to describe the disease category that he believes to be MMR-caused. (Tr. 515, 519A, 523-24A.) Indeed, Dr. Krigsman's use of the term "autistic enterocolitis," along with his assertion that Michelle Cedillo's illness is a "classic" case of "ASD-GI disease," perhaps might create the impression that "autistic enterocolitis" is a *recognized* disease category, accepted by the medical community. That, however, is not the case.

To the contrary, Dr. Hanauer, very experienced in the specific area of inflammatory bowel disorders, testified that the term "autistic enterocolitis" is *not* utilized in any gastrointestinal textbook of which he is aware. (Tr. 2143.) Similarly, Dr. Gershon stated that both the terms "autistic enterocolitis" and "ASD-GI" are not recognized by "gastroenterologists as a scientific community." (Ex. T, p. 16.) Dr. Fombonne and Dr. MacDonald both testified that there exists no evidence to support such a diagnostic category. (Tr. 1416, 1423A-24A; *Hazlehurst* Tr. 662-63.) And Dr. Krigsman himself admitted that two leading textbooks on gastroenterology, which he acknowledges to be authoritative, do not use the terms "autistic enterocolitis" or "ASD-GI." (Tr. 522A-25A.)

Thus, it is clear that the diagnostic category of "autistic enterocolitis," developed by Dr. Wakefield and adopted by Dr. Krigsman, is *not* a medically-recognized category.

In fact, the record indicates that the term "autistic enterocolitis" evolved from Dr. Wakefield's above-mentioned 1998 article; the term appears in several articles published over the following years by Dr. Wakefield and a small group of his followers. (Ex. T, p. 16; *Hazlehurst* Tr. 634A.) One such article using the term "autistic enterocolitis" was published in 2000 by

Wakefield and colleagues.[175] (Ex. 61, Tab NNN, p. 13.) And it is clear that Dr. Krigsman, in developing his causation theory, was influenced by those articles. For example, Dr. Krigsman testified that his initial idea, that autistic children with gastrointestinal symptoms might be suffering from IBD, was triggered when he read that very Wakefield 2000 article.[176] (Tr. 415-16A.)

Given that Dr. Krigsman's general causation theory was influenced by the "autistic enterocolitis" theory developed by Dr. Wakefield and colleagues, it is fair to note that Dr. Wakefield's "autistic enterocolitis" theory, and his credibility in developing the theory, have come under severe criticism. For example, see the discussion at pp. 123-25 above concerning various committees of medical experts who have considered and rejected Dr. Wakefield's causation theory. Further, respondent's experts in this case provided much testimony relevant to the credibility of Dr. Wakefield's procedures in developing his theory.

For example, Nicholas Chadwick in 1996 was a Ph.D. student working in a London laboratory for Dr. Wakefield, performing PCR testing for measles virus. (Tr. 2283-84; Ex. QQ, pp. 1-2.) Chadwick's interactions with Dr. Kawashima's laboratory, which was collaborating with Wakefield in the area of measles detection, convinced Chadwick that Kawashima's positive results in measles virus testing were "false positives," the result of contamination. (Tr. 2286-87; Ex. QQ, paras. 10-11.) Chadwick related that conclusion to Dr. Wakefield. (Ex. QQ, para. 11, Tr. 2287.) Nevertheless, Wakefield submitted for publication a manuscript relying on the purportedly positive results from Kawashima's PCR testing. (Tr. 2290A; Ex. QQ, para. 14.) Chadwick asked that his own name be taken off the manuscript, because he was not comfortable with the data. (Tr. 2290A.)

Dr. MacDonald described the Wakefield 2000 article as "deception" (*Hazlehurst* Tr. 646A), in two respects. He opined that the article deliberately described normal findings in the intestines of the autistic children as "pathology"--*i.e.*, abnormality indicative of disease--in order to create the false impression that the autistic children had much more intestinal pathology than the non-autistic children in the study. (*Id*. at 644-46A.) Dr. MacDonald also testified that the article misrepresented a photograph of a child's cecum (a part of the large intestine) as being a photograph of the child's ileum (a part of the small intestine). (*Id*. at 647A-48A.) He opined that it was "highly unlikely" that this misrepresentation was a mistake, as opposed to deliberate deception. (*Id*. at 648A.)

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[175] Andrew Wakefield et al., *Enterocolitis in Children with Developmental Disorders*, 95 AM. J. GASTROENTEROLOGY 2285 (2000). (Ex. 61, Tab NNN.)

[176] Dr. Krigsman testified that the article that triggered his interest was "written by Professor John Walker Smith, amongst others" (Tr. 415), and was published in September of 2000 in the American Journal of Gastroenterology. (Tr. 416A.) The Wakefield 2000 article mentioned above was, in fact, published in the September 2000 edition of that journal, and included John Walker-Smith as a co-author.

Dr. Rima described an interaction with Dr. Wakefield, in which he informed Dr. Wakefield of a specific contamination error in Wakefield's measles detection efforts. Dr. Wakefield, however, did *not* retract his claim that measles material had been identified. (*Snyder* Tr. 843A-46A.)

Further, as noted above, after public criticism of the "autistic enterocolitis" theory, ten of Wakefield's twelve co-authors on the original 1998 article published a letter in which they formally "retract[ed]" the causation interpretation suggested in the original article.[177] (Ex. T, Att. 125.) At the same time, the British medical journal that published the 1998 article, the *Lancet*, reviewed allegations of impropriety by Dr. Wakefield and his co-authors in the submission of the article. (*Snyder* Ex. O.) The *Lancet* editors noted that some of the children described in the article were also part of the legal action against the vaccine manufacturers, in which Dr. Wakefield was also involved. (*Id*. at 1.) The editors concluded that this circumstance constituted a financial conflict of interest by Wakefield, which Wakefield should have disclosed to the *Lancet*, but did not. (*Id*. at 2.)

Dr. MacDonald, indeed, went so far as to opine that Dr. Wakefield's "autistic enterocolitis" theory was merely an "invention" created for litigation purposes. (*Hazlehurst* Tr. 662A.) Similarly, Dr. Rust summarized Wakefield's process of developing and disseminating his general theory, and described it as "scientific fraud."[178] (*Hazlehurst* Tr. 505A-06A.)

To be sure, the petitioners in this case have stressed that they rely upon *Dr. Krigsman* as their expert concerning the causation of GI symptoms, not Dr. Wakefield. Thus, they argue that criticisms of the *personal integrity* of Dr. Wakefield are not relevant here. However, because Dr. Krigsman's general causation approach clearly was strongly influenced by Dr. Wakefield's theory, criticisms of Dr. Wakefield's "autistic enterocolitis" *theory* are relevant, and criticisms relating to Dr. Wakefield's credibility in *developing* that theory are of relevance as well. Therefore, it is a noteworthy point that not only has that "autistic enterocolitis" theory *not* been *accepted* into gastroenterology textbooks, but that theory, and Dr. Wakefield's role in its development, have been strongly criticized as constituting defective or fraudulent science.[179]

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[177]Simon H. Murch et al., *Retraction of an Interpretation* (Letter) 363 LANCET 750 (2004). (Ex. P, Att. 114.)

[178]Respondent's counsel submitted Respondent's Trial Exhibit 7, representing that the document was a copy of a patent application filed by Dr. Wakefield for a new type of monovalent (measles only) measles vaccine. Respondent's counsel suggested that this demonstrated that Wakefield had a financial incentive to discredit the MMR vaccine, so that a market would be created for his new measles vaccine. (Tr. 1207.) The document does appear to be a part of a patent application submitted by Dr. Wakefield, but the document does *not* indicate precisely *what* patent Dr. Wakefield sought. From the document, I *cannot* determine if the patent was for a measles vaccine, or something else. Accordingly, I have *disregarded* that trial exhibit and respondent's representation as to its relevance.

[179]I note also that prior to his 1998 article initiating the theory that the MMR vaccine can
(continued...)

Finally, as explained above concerning the other causation theories of petitioners, I stress that I am *not* automatically rejecting Dr. Krigsman's causation theory simply because it has not met with widespread medical acceptance. At times novel theories can be persuasive. However, it is the *petitioners' burden* to demonstrate that there is sufficient supportive evidence to justify the adoption of a proffered new theory. In this situation, Dr. Krigsman has failed to point to any persuasive evidence for his theory.

3. Dr. Krigsman's opinion was contradicted by Dr. Griffin's testimony.

Next, I note that Dr. Krigsman's opinion also was contradicted by another of respondent's experts, Dr. Diane Griffin. As previously noted, Dr. Griffin has excellent credentials as an expert concerning the measles virus. In her expert report, Dr. Griffin noted that while the measles virus sometimes does invade the GI system ("gut lymphoid tissue"--Ex. V at 2), it "does not usually cause gastrointestinal *symptoms* (*e.g.*, diarrhea or constipation)" (*id*., emphasis added). This opinion obviously contradicts Dr. Krigsman's view that the MMR vaccine should be considered the likely cause of chronic GI symptoms in autistic children.

4. Dr. Krigsman's general lack of credibility as a witness

As explained above, Dr. Krigsman based his general causation theory squarely upon the Wakefield article and the Uhlmann study, which have been shown to be unreliable, and pointed to no other evidentiary support for his general theory. Thus, the only remaining support for Dr. Krigsman's general theory is whatever general credibility he personally has as an expert witness. However, I did not find Dr. Krigsman to be an expert upon whom I could reasonably rely for sound opinion and judgment.

There are several reasons for this conclusion concerning Dr. Krigsman. First, I note the problems concerning Dr. Krigsman's practice history and resume, set forth above at pp. 138-39. Second, I note that Dr. Krigsman's testimony concerning *Michelle's own case* put his general reliability as an expert into a poor light. As explained below at pp. 149-50, Dr. Krigsman based his testimony concerning Michelle's case on a grossly mistaken assumption as to the history of

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[179](...continued)
cause the combination of autism and gastrointestinal disorders, during much of the 1990s Dr. Wakefield had advocated a theory that the MMR vaccine caused *Crohn's disease* and/or other inflammatory bowel diseases. (*E.g.*, *Hazlehurst* Tr. 629A-33A; Ex. BB, p. 10; Ex. BB, Att. 89.) However, when that theory was examined by other scientists, it was not confirmed. One research group demonstrated a flaw in Wakefield's testing procedures for measles virus. (*Hazlehurst* Tr. 631A-32A; Ex. BB, p. 10; Ex. B, Att. 45, pp. 167-68.) Further, several research groups published studies indicating that, contrary to Wakefield's claims, measles virus was *not* present in the gastrointestinal tissue of Crohn's patients. (*Hazlehurst* Tr. 632A; Ex. BB, pp. 10-11.) The British Medical Research Council reviewed that theory of Dr. Wakefield, and issued a report pointing out problems with the theory. (*Hazlehurst* Tr. 631A.) Thus, the theory was "largely dismissed" by the medical community. (Ex. BB, p. 10.)

Michelle's chronic GI symptoms. Clearly, Dr. Krigsman presented an opinion concerning Michelle's case either without examining Michelle's medical records at all, or after badly misreading those records. Either way, such a mistake reflects poorly on the general reliability of his expert opinion.

Similarly, Dr. Krigsman's reliability as an expert witness was also damaged by his application of his general causation theory to Michelle's case. That is, while his stated theory involves chronic intestinal *inflammation* caused by a persisting measles virus, he applied his theory to an individual case--Michelle Cedillo--in which there exists no persuasive evidence of chronic intestinal *inflammation*, as opposed to other, noninflammatory, GI symptoms. I note that, in Dr. Krigsman's view, Michelle has suffered for many years, beginning about three weeks after MMR vaccination, from chronic intestinal *inflammation--i.e.*, chronic "enterocolitis," which means inflammation of both her large and small intestines--caused by a persisting measles virus infection. (*E.g.*, Ex. 59, p. 7; Tr. 489A.) However, on the issue of whether Michelle in fact has suffered from any form of chronic intestinal *inflammation*, I found that Dr. Krigsman's testimony was quite unpersuasive, and was substantially outweighed by a combination of the medical records and the testimony of Dr. Hanauer and respondent's other experts. Dr. Hanauer spent considerable time during his hearing testimony pointing out in detail how the results of Michelle's gastrointestinal examinations were *inconsistent* with Dr. Krigsman's conclusion that Michelle has suffered from chronic intestinal inflammation since her vaccination. (Tr. 2108A-43.) I have set forth a full discussion of the evidence concerning the issue of alleged intestinal inflammation at pp. 150-61, below. The general point here, however, is that while Dr. Krigsman stated a general theory involving intestinal *inflammation* ("enterocolitis"), in practice he seems to be willing to apply his theory to a case with *no* persuasive evidence of intestinal inflammation. He seems willing to apply his theory to any case involving *any* type of chronic GI symptoms, whether those symptoms involve evidence of intestinal *inflammation* or not.[180] In my view, this adds further reason to doubt Dr. Krigsman's general credibility as a witness, and, therefore, to doubt the validity of his general theory that the MMR vaccine can contribute to the causation of chronic GI symptoms.

5. Epidemiologic studies contradict petitioners' theory.

As described above, there have been many epidemiologic studies that have considered the issue of whether the MMR vaccine is associated with *autism*. In contrast, there have been only a few studies that are relevant to the issue of whether the MMR vaccine is associated with *gastrointestinal disorders*. But those few studies do afford some evidence relevant to the general issue of whether the MMR vaccine causes gastrointestinal dysfunction.

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[180]Dr. Krigsman seems highly inclined to diagnose the presence of gastrointestinal *inflammation* on the basis of almost any chronic GI symptoms. For example, he diagnosed Michelle with "inflammatory bowel disease" in July of 2003, before he had even met and examined her. (Ex. 28, p. 84; Tr. 515.)

First, three epidemiologic studies compared children with *regressive* autism to those with *nonregressive* autism. If, as petitioners theorize, the MMR vaccine causes chronic gastrointestinal inflammatory disorders in children with *regressive* autism, one would expect to see more chronic inflammatory GI disorders in the regressives. But that was not found in the studies. In two of the studies, there were no more chronic gastrointestinal symptoms in the children with regression than in the nonregressive children.[181] (Ex. P, Att. 112; Ex. P, Att. 60; Tr. 2572.) In the third study, the regressives did experience somewhat more chronic GI *symptoms*, such as chronic diarrhea, but did *not* experience more chronic GI "disorders," a category that included Crohn's disease and colitis.[182] (Ex. BB, Att. 124, pp. 11-12.)

Second, one study found *no temporal association* between MMR vaccination and the onset of gastrointestinal symptoms in children with autism.[183] (Ex. P, Att. 12.) If petitioners' theory were correct, one would expect to see GI symptoms often having their onset *soon after* MMR vaccination, but that was not the case in this study.

Finally, another study looked at the incidence of gastrointestinal problems in British children over long periods of time, both before and after the introduction of the MMR vaccination in Britain. It concluded that, after the introduction of the MMR vaccination, there was *no increase* in the percentage of autistic children who suffered from GI symptoms.[184] (Tr. 2565A; Ex. P, Att. 146.) That result, once again, is contrary to what one would expect if the MMR vaccine were causing gastrointestinal symptoms in autistic children; if that were the case, one would expect the percentage of autistic children with GI symptoms to have *increased* after the introduction of the MMR vaccination.

In sum, there are only a few epidemiologic studies relevant to the issue of whether the MMR vaccine causes *chronic gastrointestinal dysfunction*. However, the results of those studies make it

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[181]Cynthia A. Molloy & Patricia Manning-Courtney, *Prevalence of Chronic Gastrointestinal Symptoms in Children with Autism and Autistic Spectrum Disorders*, 7 AUTISM 165 (2003). (Ex. P, Att. 112); Eric Fombonne & Suniti Chakrabarti, *No Evidence for a New Variant of Measles-Mumps-Rubella-Induced Autism*, 108 PEDIATRICS e58 (2001). (Ex. P, Att. 60.)

[182]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 & DEVELOPMENTAL DISORDERS 299 (2006). (Ex. BB, Att. 84.)

[183]Corri Black et al., *Relation of Childhood Gastrointestinal Disorders to Autism: Nested Case-Control Study Using Data from the UK General Practice Research Database*, 325 BRIT. MED. J. 419-20 (2002). (Ex. P, Att. 12.)

[184]Brent Taylor et al., *Measles, Mumps, and Rubella Vaccination and Bowel Problems or Developmental Regression in Children with Autism: Population Study*, 324 BRIT. MED. J. 393 (2002). (Ex. P, Att. 146.)

seem *unlikely* that the MMR vaccine causes chronic GI problems. Accordingly, this factor adds *another* reason to reject the general causation theory of the petitioners.

6. Summary concerning general causation of gastrointestinal dysfunction

In short, I found that the evidence put forth by petitioners, concerning the general proposition that the MMR vaccine can contribute to the causation of chronic GI dysfunction, was very weak. [185] The petitioners' evidence was significantly outweighed by the persuasive testimony of respondent's experts, especially Dr. Hanauer. I conclude that petitioners have not made a persuasive case concerning this issue.

F. Analysis concerning Michelle Cedillo's gastrointestinal symptoms

Because I rejected above the arguments of the petitioners' expert as to the *general proposition* that the MMR vaccine can cause chronic gastrointestinal dysfunction, it is clear that, for the same reasons, I must also reject the petitioners' argument that *Michelle Cedillo's* chronic gastrointestinal problems were caused by her MMR inoculation. In addition, there are several more reasons to reject petitioners' specific contention concerning Michelle.

1. Dr. Krigsman's opinion was based on an erroneous assumption concerning the validity of the Unigenetics testing.

First, Dr. Krigsman, who gave the only opinion specific to *Michelle's own* gastrointestinal symptoms, made it clear that his opinion in Michelle's case relied upon the assumption that a reliable laboratory test had found evidence of persisting measles virus in Michelle's intestinal tissue. (*E.g.*, Tr. 531-33A, 538A.) However, I have concluded that the Unigenetics testing that purported to find evidence of persisting measles virus in Michelle's system was *not* reliable. Therefore, Dr. Krigsman's opinion concerning Michelle's GI symptoms is, obviously, entitled to no evidentiary weight.

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[185] Dr. Jean-Ronel Corbier, who testified for the petitioners in the *Hazlehurst* case, did indicate his view that a persisting measles virus could contribute to causing *gastrointestinal symptoms* as well as autism. However, in discussing the issue of *gastrointestinal dysfunction* in their post-hearing briefs, the petitioners have *not* specifically relied upon Dr. Corbier's opinion. Moreover, Dr. Corbier's testimony would not assist petitioners in any event. First, Dr. Corbier's opinion, like that of Dr. Krigsman, assumes that the Unigenetics testing for measles virus, reported in the Uhlmann study, was reliable (*Hazlehurst* Tr. 272A-73A, 278A-79A), but I have concluded otherwise. Second, Dr. Corbier, a neurologist, did not appear to have any particular expertise in gastroenterology. (*See*, *e.g.*, *Proveris Scientific Corp. v. Innovasystems, Inc.*, 536 F.3d 1256, 1268 (Fed. Cir. 2008) (the fact that a witness is qualified as an expert in one scientific area does not qualify that witness to opine in other areas); *Nimely v. City of New York*, 414 F.3d 381, 399 n. 13 (2d Cir. 2005) (same).) And third, I simply did not find Dr. Corbier to be a reliable expert in general, as explained at p. 106 above.

2. Dr. Krigsman's opinion was based on an incorrect assumption concerning Michelle's gastrointestinal symptom history.

It is also noteworthy that Dr. Krigsman seemed to have a *grossly mistaken* understanding of the history of Michelle's gastrointestinal symptoms. In his report, he wrote that the "most compelling factor" supporting his opinion in Michelle's case was "the simple chronology of events." (Ex. 59, p. 7.) Dr. Krigsman wrote that Michelle's diarrhea began about "18-20 days" after her MMR vaccination on December 20, 1995. (*Id*.) He later indicated that his understanding of Michelle's history was that Michelle experienced the *onset of chronic diarrhea* soon after her MMR vaccination, and that such diarrhea lasted for "a good year or two" (Tr. 509), followed by a period of chronic constipation and difficult stooling for another year or two, followed by another period of chronic diarrhea. (Tr. 509, 535A.)

However, a simple reading of Michelle's medical records demonstrates that Dr. Krigsman's understanding was clearly wrong. While it would be expected that virtually any infant might *occasionally* experience *temporary* periods of diarrhea associated with temporary infectious illnesses, the medical records from the period of 1996 through 1999 do not indicate the presence of any *chronic* or *persistent* diarrhea during that period. To the contrary, the record of a visit by Michelle to her pediatrician on March 15, 1996, about three months after Michelle's MMR vaccination, states that she was "stooling well," indicating an absence of diarrhea or any other stooling problem at that time. (Ex. 8, p. 1.) Further, Michelle's treating gastroenterologist, Dr. Ramon Montes, wrote a report on May 22, 2000, describing her *chronic* gastrointestinal symptoms; he noted that her "*initial* gastrointestinal symptoms" consisted of constipation, *not* diarrhea. (Ex. 44, p. 58, emphasis added.) Dr. Montes, in that same report, added that Michelle's chronic constipation subsided about "1 year ago," and that she "has not had any formed stools since;" this indicates that Michelle's *chronic diarrhea* (*i.e.*, a lack of "formed stools") began about one year prior to that visit of May 2000, or about *May of 1999*. (*Id*.) That report of Dr. Montes does not say when the chronic *constipation* began, but indicates that the constipation was associated with milk consumption (*id*.), and a record from June 2, 1995, long *before* Michelle's MMR vaccination, indicates that Michelle was "[e]xtremely constipated on 2% milk." (Ex. 8, p. 3.)

Similarly, a history form filled out on January 31, 2002, stated that Michelle's chronic diarrhea had continued for about "2 ½ years." That record confirms that the onset of her chronic diarrhea occurred in mid-1999. (Ex. 44, p. 7.)

In short, the medical records indicate that Michelle's chronic *constipation* may have begun many months *prior* to her MMR vaccination in question, and, more importantly, that her *chronic diarrhea* did not begin until mid-1999, more than three years *after* that vaccination.[186] Thus, those

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[186]Concerning Michelle's history of diarrhea, I acknowledge that there have been statements from Mrs. Cedillo that offer at least some support to Dr. Krigsman's assumption that Michelle's chronic diarrhea began soon after her MMR vaccination of December 20, 1995. (*See*, *e.g.*, Tr. 232A-
(continued...)

records show that Dr. Krigsman gravely misunderstood the temporal history of Michelle's gastrointestinal problems, so that the "most compelling factor" that he relied upon was simply wrong.[187]

3. Dr. Krigsman's opinion was based on an incorrect conclusion that Michelle experienced chronic gastrointestinal inflammation.

Dr. Krigsman's view of Michelle's case was that she has suffered for many years, beginning very soon after her MMR vaccination of December 20, 1995, from *chronic gastrointestinal inflammation*, specifically including inflammation of her *intestines*, which he believes to be caused by a persisting measles virus infection. At various times, Dr. Krigsman has alleged that Michelle has "inflammatory bowel disease," also known as "IBD," which encompasses a number of types of chronic inflammation of the digestive tract (*e.g.*, Ex. 59, p. 7; Tr. 427A), or that she has "Crohn's disease," which is a specific form of IBD (*e.g.*, Tr. 428, 470A-72A). He has also repeatedly characterized her as suffering from chronic "enterocolitis," which specifically means inflammation of both her large and small *intestines*. (*E.g.*, Ex. 59, pp. 7, 9; Tr. 422, 470A, 489A-90.) However, on the issue of whether Michelle has in fact suffered from chronic enterocolitis, IBD, Crohn's disease, or any form of chronic gastrointestinal *inflammation*, I found the testimony of Dr. Krigsman to be quite unpersuasive, and to be substantially outweighed by a combination of the medical records and the testimony of respondent's experts, especially Dr. Hanauer. The evidence demonstrates that while Michelle did have some inflammation of her esophagus and mild inflammation of her stomach in 2000, there has *never* been, despite multiple diagnostic procedures, any competent evidence of inflammation in her *intestines*, and there has been no evidence of chronic inflammation *anywhere* in her digestive system since the gastritis in 2000.

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[186](...continued)
33.) However, I cannot accept those particular statements of Mrs. Cedillo as *accurate*. As noted above, I certainly do *not* believe that Mrs. Cedillo was ever intentionally failing to tell the truth to the best of her memory. Perhaps Mrs. Cedillo does remember some episode of *temporary* diarrhea shortly after the MMR vaccination, though that episode is *not* noted in the medical records. And certainly the medical records absolutely support Mrs. Cedillo's memory that Michelle did suffer from *years* of chronic diarrhea. However, the medical records, as described above, indicate clearly that Michelle's extended period of *chronic* diarrhea did not begin *until mid-1999*. On this specific point, I find that the medical records are the best evidence.

[187]I note that respondent's initial brief pointed out the errors in Dr. Krigsman's understanding of Michelle's symptom history (R1, p. 38), yet, in their reply brief, the petitioners did *not* attempt to defend Dr. Krigsman's stated history.

a. Dr. Hanauer's analysis of Michelle's clinical symptoms

Dr. Hanauer, a specialist in IBD, explained persuasively that Dr. Krigsman was not justified in reaching a diagnosis of IBD or enterocolitis based on Michelle's chronic *clinical symptoms* of diarrhea and constipation. For example, he testified that while diarrhea can be caused by bowel inflammation, it can also be caused by many *other* factors. (Tr. 2100A-07.) He explained that Michelle's pattern of alternating diarrhea and constipation, combined with abdominal pain, could *not* justify a diagnosis of IBD, but would instead suggest another disorder known as "irritable bowel syndrome." (Tr. 2105A, 2107-08A.) He testified that the existence of Michelle's chronic constipation actually *precluded* a diagnosis of gastrointestinal inflammation. (Tr. 2107.)

In addition, Dr. Hanauer explained how chronic diarrhea can be a result of constipation. He testified that when a person is constipated, a large amount of fecal material can build up and stretch the rectum, leading to diarrhea that flows around the build-up.[188] (Tr. 2103A-04A.) And, in Michelle's case, the medical records offer support to a conclusion that such a phenomenon might explain Michelle's diarrhea. For example, there are notations of "fecal impaction," meaning a collection of hardened feces in the rectum (*Dorland's* at 915), accompanied by diarrhea. (*E.g.*, Ex. 36, p. 9.) There are also notations of "overflow diarrhea," again suggesting diarrhea flowing around a fecal obstruction in the rectum. For example, one record describes Michelle's "underlying constipation" and "recurring bowel impaction," then notes that "her diarrhea is actually overflow diarrhea." (Ex. 28, p. 241.) Another record states that Michelle's diarrhea "is overflow diarrhea around a massive fecal impaction." (Letter of Dr. Schneider filed on 10-31-00.) Thus, those medical records, along with Dr. Hanauer's testimony, indicate that Michelle's chronic diarrhea may be related to her constipation, rather than having anything to do with GI inflammation.

b. Specific analysis of the records of Michelle's endoscopies, biopsies, and the PillCam study

An even more important factor, contradicting Dr. Krigsman's notion that Michelle has had chronic gastrointestinal *inflammation*, is the evidence concerning the *examinations* of Michelle's gastrointestinal system, specifically of her multiple endoscopies and biopsies. (Tr. 2108A-43.) Dr. Hanauer pointed out in detail how the results of those examinations were inconsistent with Dr. Krigsman's conclusion that Michelle has enterocolitis or IBD. He noted that the results of those tests were generally considered *normal* by Michelle's actual treating physicians, with no evidence of inflammation in her intestines. Dr. Hanauer explained that it was incorrect for Dr. Krigsman to diagnose IBD without pathological evidence of intestinal inflammation, especially in light of multiple tests in which *no* inflammation of her intestines was found. (*E.g.*, Tr. 2098A-99.)

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[188]One of respondent's experts' in the *Hazlehurst* case, Dr. MacDonald, also described the same phenomenon of "overflow diarrhea" resulting from a fecal impaction. (*Hazlehurst* Tr. 674A.) Dr. MacDonald, like Dr. Hanauer, distinguished this overflow diarrhea from the diarrhea that a person would get with gastrointestinal inflammation. (*Id.*)

Specifically, Dr. Hanauer discussed in detail the results of the five occasions upon which Michelle underwent endoscopies and biopsies, along with an additional set of images of her digestive system taken by a "PillCam." There are two types of endoscopies that were performed on Michelle at various times. In an "upper endoscopy," a tiny camera attached to a flexible cable is passed through the mouth and down through the esophagus and stomach into the top part (duodenum) of the small intestine. In a "lower endoscopy," also known as a "colonoscopy," the camera is passed through the anus into the large intestine, also known as the colon, and then into the lower part ("ileum") of the small intestine. During such procedures, the endoscopist visually examines the tissues for signs of disease or other abnormality. In addition, during either type of endoscopy, biopsies of tissue may be collected for microscopic study. (Tr. 2096.)

On each of the five occasions when endoscopies were performed on Michelle, the gastroenterologist generated a written "surgical report" describing what was seen through the camera. In addition, biopsies (tissue samples) were collected during each procedure, and on each occasion, those biopsies were microscopically examined by a specialist, resulting in a "pathology report." During his testimony, Dr. Hanauer reviewed each of those reports concerning Michelle's endoscopies and biopsies, explaining why those reports were *inconsistent* with Dr. Krigsman's conclusion that Michelle suffered from chronic gastrointestinal inflammation.

Dr. Ramon Montes, a pediatric gastroenterologist in Phoenix, Arizona, performed an "upper endoscopy" on Michelle on June 12, 2000. Dr. Montes generated a written report concerning that "esophagogastroduodenoscopy," which is the more precise name of the procedure. (Ex. 44, pp. 64-65.) His report notes that Dr. Montes observed "erosive esophagitis" in the esophagus and "gastritis" in the stomach (*id.* at 65), but that the "duodenum," a part of the small intestine, was "normal except for mild nodularity"[189] (*id.* at 64). Biopsies were collected during that endoscopy, and the resulting pathology report indicates that the two samples from the duodenum were normal ("no histopathologic findings"), while in the esophagus and stomach ("gastric antrum") there were mild increases in white blood cells ("eosinophils"). (Ex. 21, p. 3.) Dr. Montes commented on those pathological findings in the esophagus and stomach in his next written report concerning Michelle, a letter that he wrote after examining Michelle on October 3, 2000. (Ex. 44, pp. 31-33.) In that letter, Dr. Montes described the "histologic evidence" from the June 12 endoscopy--*i.e.*, the pathology report--as showing "gastroesophageal reflux disease in addition to focal gastric antral inflammation." (*Id.* at 31.) During his hearing testimony, Dr. Hanauer explained that "gastroesophageal reflux disease," also known as "GERD," is a condition in which stomach acid inappropriately moves up through the esophagus, thereby causing the "erosive esophagitis" noted in the surgical report. (Tr. 2110-11A.)

[189] "Nodularity" refers to "lymphoid nodular hyperplasia," also known as "LNH." As will be discussed below (p. 157), intestinal findings of LNH are common, and do *not* indicate inflammation.

Concerning that endoscopy of June 12, 2000, in both the surgical report (Ex. 44, pp. 64-65) and the October 3 letter (Ex. 44, pp. 31-32), Dr. Montes did *not* mention inflammatory bowel disease, or any form of inflammation of the *intestines*.

Michelle underwent a follow-up endoscopy, also performed by Dr. Montes, on December 11, 2000. (Tr. 2113A; Ex. 44, pp. 41-42.) The chief observation made during that endoscopy, as reported in the surgical report, was that the "erosive esophagitis," which had been observed during the endoscopy of June 12, 2000, had now "resolved." (Ex. 44, p. 42.) Further, in the stomach Dr. Montes could see "no nodularity nor ulceration" (*id.* at 41), and the duodenum appeared "normal" (*id.* at 42).

A pathology report describes the microscopic evaluation of the tissue biopsied during the December 11 endoscopy. (Ex. 44, pp. 43-44.) The pathologist examined the tissue from the esophagus and found it to be unremarkable. (*Id.* at 43, 44.) In the stomach, the pathologist found evidence of "mild superficial chronic gastritis," which was "non-specific." (*Id*. at 43, 44.) Thus, the one abnormality found in the December 11 endoscopy was the microscopic evidence of "gastritis"--*i.e.*, inflammation in the stomach--that was characterized as "mild," "superficial," and "non-specific." (*Id*.) And that microscopic finding followed a visual finding by Dr. Montes of "gastritis" in the endoscopy on June 12, 2000. (Ex. 44, p. 65.) However, Dr. Hanauer explained that the gastritis observed in Michelle during those two endoscopies was *not* evidence of inflammatory bowel disease. (Tr. 2111A-12A, 2114A-15.[190]) Further, in his letter of June 4, 2001, Dr. Montes, who performed both endoscopies, indicated that the important finding of the second endoscopy was that Michelle's former "erosive esophagitis" was healed, adding that the results of the microscopic examination of the biopsies indicated "*only* a mild, nonspecific chronic gastritis." (Ex. 44, p. 5, emphasis added.) This use of the words "only" and "mild" indicate that Dr. Montes, like Dr. Hanauer, did not find the nonspecific gastritis to be a significant finding.

On January 31, 2002, Dr. Montes performed both an upper endoscopy and a lower endoscopy (colonoscopy) on Michelle. (Ex. 44, pp. 13-15.) According to the surgical report, the upper endoscopy found the stomach and the upper part of the small intestine, the duodenum, to be "unremarkable," meaning normal (*id.* at 13). The colonoscopy found the lower part of the small intestine (the "terminal ileal mucosa") to be "normal, without signs of inflammation" (*id.* at 14). The surgical report described "mild nodularity" in the small intestine and "excessive nodularity" in the large intestine (*id.* at 14). Dr. Hanauer and Dr. Krigsman explained that such "nodularity" describes "lymphoid nodular hyperplasia," also known as "lymphonodular hyperplasia" or "LNH." They explained that the lymphoid tissue in the lining of the digestive tract is formed into "lymph nodes" or "nodules," and when those nodules become enlarged, the condition is known as LNH. (Tr. 445A-46A, 2115-16, 2150A.) Dr. Hanauer stressed that LNH is a common, normal finding in children,

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[190]I note an error in the hearing transcript in this regard. In his letter of October 3, 2000, Dr. Montes wrote that the June 12 endoscopy showed "focal gastric antral inflammation." (Ex. 44, p. 31.) Respondent's counsel quoted that phrase from that letter during the examination of Dr. Hanauer, but the word "antral" was mistranscribed as "entero." (Tr. 2112A, line 22.)

and is *not* indicative of gastrointestinal *inflammation*. (Tr. 2115-16, 2150A.) And Dr. Krigsman himself stated that the 2002 colonoscopy, despite its findings of "nodularity" in both intestines, was "normal." (Tr. 426, 510.)

The pathology report for those 2002 upper and lower endoscopies found all of the biopsied tissue, from the esophagus and both the large and small intestines, to be "unremarkable"--*i.e.*, normal, without inflammation. (Ex. 44, p. 17; Tr. 2117.) In addition, biopsy samples from those 2002 endoscopies were also sent to a pathologist in Britain for examination. The samples from the esophagus and small intestine were found to be completely normal ("no histological abnormalities"). (Ex. 28, p. 178.) The samples from the large intestines were found to have "features that would be in keeping with colonic lymphoid nodular hyperplasia," but the pathologist added that in spite of such features, there was "no evidence of active inflammation" in any of the samples. (*Id*.) This apparently indicates that that pathologist, like Dr. Hanauer, did not find the presence of lymphoid nodular hyperplasia to be evidence of *inflammation*. (*Id*.)

Michelle's next set of endoscopies were performed by Dr. Krigsman himself.[191] Dr. Krigsman performed both upper and lower endoscopies on Michelle on September 25, 2003. (Ex. 28, pp. 454-56.) The surgical report concerning the upper endoscopy describes certain findings in the esophagus and the stomach that Dr. Hanauer was not able to interpret (see Tr. 2124-25), but makes no mention of any abnormalities in the duodenum portion of the small intestine. (Ex. 28, p. 455.) In describing the lower endoscopy (colonoscopy), Dr. Krigsman wrote that the only significant findings were "lymphonodularity hypoplasia" (sic[192]) and "multiple sigmoidal aphthous ulcerations." (*Id*.)

Dr. Hanauer discussed Dr. Krigsman's findings concerning the 2003 endoscopies. He explained that the observation of aphthous ulcers in the intestines on endoscopy does *not* justify a conclusion that the individual has intestinal *inflammation*. (Tr. 2125-28A.) He testified that common "cold sores" or "canker sores," which people often experience in their mouths, are a type of aphthous ulcers, and that aphthous ulcers in the intestines are similar. (Tr. 2120, 2126-27.) He stated that aphthous ulcers can be caused by many different factors, including the preparation of the bowel for the endoscopy, or the taking of certain nonprescription medications. (Tr. 2126, 2128A.) They can also be "part of the normal intestinal lining." (Tr. 2126.) Thus, Dr. Hanauer explained, Dr. Krigsman erred in concluding that Michelle's intestines had inflammation based on the presence

[191]Michelle's mother testified that she did research via the Internet concerning possible causes of autism and gastrointestinal symptoms. (Tr. 251A-52A.) She read about Dr. Krigsman, contacted him, and eventually took Michelle to New York, where Dr. Krigsman practiced, to be examined by him in September of 2003. (Tr. 252A-53, 256-57A, 322-23, 326A-27.)

[192]Dr. Krigsman's report did say "lymphonodularity hypoplasia." Presumably, he meant to say "lymphonodular hyperplasia."

of aphthous ulcers. Further, Dr. Hanauer explained that findings of "lymphonodular hyperplasia" in the intestines are also common, and do *not* indicate intestinal inflammation. (Tr. 2115-16, 2149-50A.)

In addition, a pathology report concerning the endoscopies of September 2003 was prepared, and was reviewed by Dr. Noam Harpaz, a pathologist described by Dr. Hanauer as "one of the world's authorities on inflammatory bowel disease." (Ex. 28, pp. 407-08; Tr. 2129A.) That pathology report concluded that all of the biopsied material from the intestines was "within normal limits," the only irregularity on any tissue being some "mild chronic nonspecific gastritis" in the stomach. (Ex. 28, pp. 707-08.)

Michelle underwent one more set of endoscopies, both upper and lower, on June 8, 2006, performed by Dr. Dana Ursea. The surgical report concerning the upper endoscopy states that it was a "normal examination." (Ex. 49, p. 20.) The surgical report for the lower endoscopy indicates, at its "assessment" line, an "abnormal examination." (*Id.* at 23.) However, Dr. Hanauer indicated that the "abnormalities" observed by Dr. Ursea did not indicate *inflammation*. (Tr. 2134A-35.) The surgical report indicates that two of the four sections of the colon yielded a "normal exam." (Ex. 49, p. 23.) The report further indicates that a third section of the colon, the "transverse" portion, had "one aphthous ulcer." (*Id.*) Also, in the fourth section of the colon, the "sigmoid" portion, it appears that aphthous ulcers[193] were also observed. (*Id.*) Dr. Hanauer, however, reiterated that aphthous ulcers are *not* indicative of bowel inflammation, so that those "abnormal" findings in two sections of the colon do *not* indicate inflammation. (Tr. 2134A-35, 2174A-75.) Further, in her "comments" after finishing the colonoscopy, Dr. Ursea herself wrote "no gross colitis" (Ex. 49, p. 24), seemingly indicating *Dr. Ursea's own view* that the aphthous ulcers that she reported were *not* evidence of "colitis" (*i.e.*, inflammation of the colon).

The pathology report from those endoscopies of June 8, 2006, once again indicated no intestinal abnormalities. Specifically, the report states that for all of the biopsies collected from the intestines (colon, duodenum), there was "no pathologic diagnosis." (Ex. 49, p. 82.) Dr. Hanauer noted that this means that the tissue was normal. (Tr. 2135.)

Finally, at the time of her last biopsies, in June of 2006, Michelle also underwent another diagnostic procedure, known as a "wireless capsule imaging," "capsule endoscopy," or "PillCam study." In that procedure, a pill with a camera in it went down through her digestive system, wirelessly sending back images of her digestive tract. (Tr. 455-62.) The parties have not identified, in the medical records filed in this case, any written report describing the results of that PillCam study. However, during his hearing testimony, Dr. Krigsman showed some images from that study, arguing that they supported his conclusion that Michelle has experienced chronic intestinal inflammation. (Tr. 456-468.)

[193]The report states "absent ulcers," apparently a transcription error. (See Tr. 2134A-35.)

Dr. Hanauer, however, analyzed the same images, and explained why they do *not* indicate intestinal inflammation. Dr. Hanauer described the features of Michelle's intestines, on which Dr. Krigsman's testimony had relied, as "mucosal breaks," very shallow erosions of the intestinal walls, similar to "aphthous ulcers" but shallower. (Tr. 2135-36A.) He stated that about 15% of normal intestines have such features. (Tr. 2136A.) Most importantly, Dr. Hanauer then showed images of intestines with actual Crohn's disease, and pointed out that such images were quite *different* from the images of Michelle's intestines taken by the PillCam. (Tr. 2137-41.) He noted, for example, that the lesions in Crohn's disease were 10 to 50 times as deep as the erosions noted in Michelle's intestines. (Tr. 2138A.) I found this particular testimony of Dr. Hanauer, concerning the PillCam images, to be very persuasive. Petitioners did not present testimony from Dr. Krigsman, or any other expert, to rebut that testimony of Dr. Hanauer.

To summarize, the medical records show that Michelle had upper endoscopies on five occasions, and lower endoscopies on three occasions. Each of the five upper endoscopies involved examination of the "duodenum," the upper part of her small intestine. Each of the three lower endoscopies involved examination of both her large intestine (colon) and the lower part (ileum) of her small intestine. Yet *none* of those procedures yielded any significant evidence of intestinal *inflammation*. None of the *pathology* reports ever indicated *any* inflammation of either the large or small intestines. None of the *surgical* reports ever indicated a diagnosis of IBD, enterocolitis, Crohn's disease, or any other diagnosis of inflammation of either intestine.

It is true that Michelle's first endoscopy, in June of 2000, indicated "erosive esophagitis," which had resolved by her second endoscopy in December of 2000. Further, both of those 2000 endoscopies indicated evidence of "gastritis." But both the esophagitis and the gastritis did not involve Michelle's *intestines*, which is crucial because Dr. Krigsman alleges chronic *enterocolitis*, which specifies *intestinal* inflammation. Further, all of the pathology reports for the three upper endoscopies performed after 2000 indicate *no* finding of inflammation of either the stomach or esophagus, other than "mild nonspecific" gastritis in one part of the stomach in 2003, and "mild" esophagitis in one part of the esophagus in 2006. Those pathology results, thus, indicate that there was no sustained, chronic inflammation of even the esophagus or stomach. And, to repeat, none of the pathology reports *ever* indicated any inflammation of either of the *intestines*.

In addition, there were reports of "nodularity" or "aphthous ulcers" in the intestines in several of the surgical reports of the endoscopies, as noted above. And Dr. Krigsman also interpreted some of the images from the PillCam study to indicate aphthous ulcers or lymphoid nodules. (Tr. 456-468.) However, Dr. Hanauer persuasively testified that such symptoms are common observations, and are *not* indicative of intestinal *inflammation*. (Ex. X, p. 2; Tr. 2115-16, 2125-28A, 2134A-36A, 2149-50A, 2174A-75.)

Therefore, I conclude that the medical records of Michelle's endoscopies, biopsies, and the PillCam study strongly support Dr. Hanauer's conclusions (1) that Michelle has never been shown to suffer from *intestinal* inflammation of any kind, and (2) that while Michelle did have some inflammation of her esophagus and stomach in 2000, and one finding of "mild" inflammation in each

of those areas since, she has not suffered from *chronic* inflammation of even those parts of her GI tract.

c. Additional discussion concerning issue of gastrointestinal inflammation

In addition, certain other parts of the record furnish additional support to my conclusion that Michelle likely did *not* suffer from *chronic* gastrointestinal *inflammation*, nor any *intestinal* inflammation.

First, a pediatric gastroenterologist, Dr. Ramon Montes, treated Michelle from 2000 to 2002, and performed the endoscopies in June 2000, December 2000, and January 2002. Dr. Montes *never* diagnosed Michelle to be suffering from IBD, or any intestinal inflammation. To the contrary, after examining the ileum section of Michelle's small intestine in 2002, Dr. Montes wrote that it "appeared normal without signs of inflammation." (Ex. 44, p. 14.)

Second, there were a number of tests on Michelle which looked for evidence of leukocytes in Michelle's stool samples, which would have indicated GI inflammation, but such testing was always negative. (Tr. 2142, 2172, 2191B-93A.)

Next, I reiterate that Dr. Krigsman during the hearing in this case repeatedly pointed to two types of findings in Michelle's intestines, lymphoid nodular hyperplasia ("LNH") and aphthous ulcerations, and opined that those findings supported a conclusion that she was suffering from intestinal inflammation. (Tr. 443-468.) However, Dr. Hanauer explained persuasively that those findings do *not* constitute evidence of inflammation. (Ex. X, p. 2; Tr. 2115-16, 2125-28A, 2134A-36A, 2149-50A, 2174A-75.) In addition, respondent's expert Dr. Gershon, a neurogastroenterologist who studied Michelle's records, confirmed that intestinal findings of LNH and aphthous ulcers on endoscopy are very common and do *not* support a conclusion of intestinal inflammation, in general or in Michelle's case. (Ex. T, pp. 8, 13, 15, 22.) Further, another of respondent's experts, Dr. MacDonald, a Ph.D. immunologist who specializes in the human gastrointestinal immune system, also testified that LNH is not indicative of GI inflammation. (*Hazlehurst* Ex. A, p. 7; *Hazlehurst* Tr. 616A-19.) He testified that LNH is especially common in children (*Hazlehurst* Tr. at 616A), and that a good endoscopist when seeing LNH will note its presence, but the finding will still be of "no diagnostic significance" (*id*. at 619). Dr. MacDonald also testified that LNH can be caused by constipation, which is important because Michelle suffered from chronic constipation for years. (Tr. 670A.) I found the presentations of Drs. Hanauer, Gershon, and MacDonald to be persuasive in this regard. Moreover, Michelle's treating gastroenterologist in 2002, Dr. Montes, wrote that Michelle's ileum "appeared normal without signs of inflammation and only mild nodularity." (Ex. 44, p. 14.) This notation clearly indicates that Dr. Montes, too, found the presence of some "nodularity" in Michelle's small intestine to be "normal," and not to be a sign of inflammation.[194]

[194]Similarly, the British pathologist who found features of LNH in Michelle's colon tissue (continued...)

It is also noteworthy that Dr. Krigsman himself stated that Michelle's 2002 colonoscopy, which found "excessive nodularity" in the large intestine (Ex. 44, p. 14), was "normal." (Tr. 426, 510.) Given that admission that a finding of "excessive nodularity" is a "normal" one, Dr. Krigsman's claim that observations of "nodularity" in *other* endoscopies demonstrates intestinal inflammation becomes even less credible.

Dr. Krigsman also pointed to the results of certain testing done on Michelle--*i.e.*, that she had an elevated "c-reactive protein count," an elevated "sedimentation rate," and an elevated "OmpC count"--as evidence that Michelle had chronic intestinal inflammation. (Tr. 432-33A.) Dr. Hanauer testified, however, that there were other reasons for those test results, and that those results did not justify a conclusion that Michelle suffered from intestinal inflammation, in light of the repeated endoscopy and biopsy results which did not find inflammation. (Tr. 2130-32A.) Dr. Gershon, too, explained that the elevated "OmpC count" did not indicate gastrointestinal inflammation. (Ex. T, pp. 13-14.)

Dr. Krigsman also pointed to the fact that Michelle has experienced both arthritis and uveitis, inflammatory conditions of the joints and eyes, as evidence that Michelle also had inflammation of her intestines. (Tr. 471A.) Dr. Hanauer, however, testified that such an inference was not justified. (Tr. 2130; Ex. X, p. 3.)

Finally, Dr. Krigsman indicated that his opinion that Michelle had chronic bowel inflammation was based on a *combination* of a number of symptoms--*i.e.*, the endoscopic findings of aphthous ulcers and LNH, *plus* her history of diarrhea and abdominal pain, and the test results and presence of arthritis and uveitis mentioned in the previous two paragraphs. (Tr. 470A-72A.) Dr. Hanauer, however, opined that this constellation of symptoms described by Dr. Krigsman did *not* justify a diagnosis of intestinal inflammation, in light of the lack of evidence of inflammation in the *biopsies* collected during her multiple endoscopies. (Tr. 2172.)

d. Medical record notations cited by petitioners

With regard to this issue of whether Michelle experienced chronic GI *inflammation*, in their initial post-hearing brief petitioners pointed to a number of medical records which noted that Michelle had suffered from "inflammatory bowel disease," "colitis," "Crohn's disease," or "enterocolitis," all of which would indicate some form of gastrointestinal inflammation. (P1, pp. 38-59.) However, Dr. Hanauer discussed the issue of those medical record notations. (Tr. 2194A-96A.) *All* of those notations were made *after* Dr. Krigsman wrote a letter on July 10, 2003, diagnosing Michelle with "inflammatory bowel disease" and "entercolitis." (Ex. 28, p. 84.) And almost all of those notations were in records of physicians who were not *gastroenterologists*, and

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[194](...continued)
nevertheless found those samples to be free from "active inflammation," indicating that such pathologist *also* found LNH *not* to be a sign of inflammation. (Ex. 28, p. 178.)

thus not qualified to diagnose gastrointestinal inflammatory disease.[195] Dr. Hanauer indicated that such notations did *not* represent *independent* conclusions of such physicians that Michelle in fact suffered from gastrointestinal inflammation; rather, those physicians were merely noting that they had *read or been told* of a report by a previous treater, Dr. Krigsman, which stated that Michelle had chronic GI inflammation. (Tr. 2194A-96A.) Dr. Hanauer noted that such reports of diagnoses frequently "get carried over" from one physician to another, "without any level of review" or "without any re-check or evident review of primary data." (*Id*. at 2195A-96A.)

I found that testimony of Dr. Hanauer to be persuasive. In reviewing medical records in Program cases for nearly 20 years, I have often noted the phenomenon that Dr. Hanauer described, in which physicians during a visit note in a medical record what they have been *told* about *prior* diagnoses of the patient. It seems likely that many physicians, being told that a gastroenterologist (Dr. Krigsman) had diagnosed IBD, would simply write in their notes that Michelle carried a diagnosis of IBD.

Notations by two physicians, however, do merit additional discussion, since those notations were recorded by *gastroenterologists*. First, Dr. Sharon Taylor saw Michelle on October 16, 2003, and wrote that Michelle had a "diagnosis" of "Crohn's disease," and that she had "suffered in the past from enterocolitis, gastritis," and other conditions. (Ex. 28, p. 9.) However, that record seems to indicate that Dr. Taylor was consulted on that occasion specifically because Michelle was having trouble with her feeding tube, which needed prompt attention. (Ex. 28, pp. 9-11.) Dr. Taylor's role was simply to examine Michelle to devise an immediate solution for the tube problem. (*Id*.) There is no indication that Dr. Taylor performed any of the type of testing or "work-up" that likely would be performed by a gastroenterologist before diagnosing Crohn's disease or enterocolitis. My conclusion from those circumstances, thus, is that Dr. Taylor was not making *her own* diagnosis of Michelle, but was simply stating that she had been *told* by Michelle's parents that Michelle had a diagnosis of Crohn's disease and/or enterocolitis. I note that Dr. Taylor mentioned those conditions in the very first sentences of her note concerning the visit, which is the obvious place for a physician to record statements from the family describing the patient's background.

Similarly, petitioners also point to records made by Dr. Dana Ursea, another gastroenterologist, when she saw Michelle on February 2, 2006, and April 19, 2006. (P1, pp. 56, 58.) According to the records that I have identified among the medical records filed in this case, Dr. Ursea actually saw Michelle on at least four occasions. Dr. Ursea consulted on Michelle's case in the hospital in October of 2005, when Michelle was hospitalized for a broken leg (Ex. 49, pp. 62-66); saw Michelle at her office on February 2 and April 20, 2006 (Ex. 27, pp. 222-227); and then

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[195]Dr. Hutter, hematologist (P1, p. 38); Dr. Crawford, pediatrician (P1, p. 40); Dr. Sheets, rheumatologist (P1, pp. 42-44); Dr. Keller, rheumatologist (P1, p. 44); Dr. Kay, orthopedic surgeon (P1, p. 46); Dr. Posever, rheumatologist (P1, p. 48); Dr. Peare, apparently orthopedic surgeon (P1, p. 50); Dr. Saunders, emergency room physician (P1, p. 51); Dr. Howard, rheumatologist (P1, p. 52); Dr. Szer, rheumatologist (P1, p. 56); Dr. O'Halloran, opthalmologist (P1, p. 56); Dr. Scher, opthalmologist (P1, p. 59).

performed the above-described endoscopies and PillCam study on Michelle on June 8, 2006 (Ex. 49, pp. 20-24). In the notes of her encounters with Michelle, Dr. Ursea wrote in October of 2005 that Michelle had a "history of Crohn's disease." (Ex. 49, p. 62.) She wrote in February of 2006 that Michelle had a "history of chronic antral colitis." (Ex. 27, p. 226.) Lastly, she wrote in April of 2006 that Michelle had "multiple medical problems * * * including inflammatory bowel disease like enterocolitis (*sic*)." (Ex. 27, p. 222.)

Based on those records, however, I *cannot* conclude that Dr. Ursea ever made her *own independent* diagnosis that Michelle had chronic gastrointestinal inflammation of any kind. Dr. Ursea was first consulted when Michelle entered a hospital in October of 2005 for a broken leg, and experienced diarrhea during that hospitalization. (Ex. 49, p. 62.) During that consultation, Dr. Ursea spoke by telephone with Dr. Krigsman, describing him as "[Michelle's] gastroenterologist for the past two years." (*Id*.) Clearly, Dr. Ursea was told by *Dr. Krigsman* that Michelle had a "*history* of Crohn's disease." (*Id*., emphasis added.) Similarly, the letter that Dr. Ursea wrote concerning her office visit with Michelle in February of 2006 reported that Michelle had a "*history* of chronic antral colitis." (Ex. 27, p. 226, emphasis added.) And in the letter describing the April 2006 visit, when Dr. Ursea wrote that Michelle had "multiple medical problems including autism, seizure disorder and inflammatory bowel disease like enterocolitis" (Ex. 27, p. 222), Dr. Ursea clearly was summarizing Michelle's medical *history*, not herself *diagnosing* autism, seizure disorder, or inflammatory bowel disease.

Thus, I conclude that in her medical record notations describing Michelle as having had "Crohn's disease," "colitis," and "inflammatory bowel disease," Dr. Ursea was not issuing her *own independent* diagnosis that Michelle was experiencing chronic intestinal inflammation, but was merely recording that *Dr. Krigsman* had diagnosed those conditions in the past.[196]

In sum, I have carefully studied the medical records cited by petitioners in their brief that describe Michelle as suffering from inflammatory GI conditions. I conclude that those records do not indicate that any physician other than Dr. Krigsman actually *independently diagnosed* Michelle with intestinal inflammation, or any *chronic* inflammation anywhere in her gastrointestinal tract. And I find that Dr. Krigsman was not a credible witness, so that his own diagnosis in that regard is not reliable.

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[196]Of course, Dr. Ursea then performed her own endoscopies on Michelle on June 8, 2006, as described above (pp. 155-56). The parties have not identified any records created by Dr. Ursea *after* those endoscopies, so I have no way of knowing what Dr. Ursea's opinion of Michelle's condition was after that examination. It is noteworthy, however, that Dr. Ursea found the results of her upper endoscopy of Michelle to be "normal" (Ex. 49, p. 20), and that in the lower endoscopy, despite the aphthous ulcers she found "no gross colitis" (*id*. at 24) ("gross" in this context likely means "visible"--*Dorland's* at 800), meaning no visible inflammation. Then, the *pathology* reports of those endoscopies came back *negative* for inflammation of the intestines. (Ex. 49, p. 82.) Thus, perhaps Dr. Ursea, after those endoscopies and pathology reports, might have concluded that Michelle did *not* have intestinal inflammation. We simply don't know what her impression was at that point.

Further, even if I were to conclude that Dr. Ursea (or some other physician) *did herself diagnose* chronic intestinal inflammation, that would *not* change my opinion concerning whether Michelle likely did experience chronic gastrointestinal inflammation. I am still impressed that the *strongest evidence by far*, concerning Dr. Krigsman's allegation of chronic GI inflammation, was Dr. Hanauer's testimony about the specifics of the *endoscopies* and *biopsies* of Michelle, in which he demonstrated that the results of those procedures were inconsistent with chronic GI inflammation. Dr. Hanauer, an expert extremely well-qualified in the area of GI inflammation, testified *in detail* why the results of those procedures were inconsistent with Dr. Krigsman's conclusion. On the other hand, the record of this case supplies *no explanation* of why Dr. Ursea (or any other physician) might have reached any contrary view. I conclude that Dr. Hanauer's testimony, supported by the above-cited evidence from Drs. Gershon,[197] MacDonald, and Montes (see p. 157 above), is far more persuasive evidence than the unexplained statements in the medical records of Dr. Ursea or the other physicians cited by petitioners. Therefore, the medical record notations cited by petitioners do *not* change my conclusion concerning this inflammation issue.

e. Summary concerning allegation of gastrointestinal inflammation in Michelle

Accordingly, while Dr. Krigsman based his conclusion--*i.e.*, that Michelle's gastrointestinal symptoms were vaccine-caused--on the premise that Michelle had chronic GI *inflammation* (*i.e.*, IBD or enterocolitis), the evidentiary record in this case actually makes it appear completely unproven, and very *unlikely*, that Michelle ever had any *intestinal* inflammation, or any *chronic* inflammation anywhere in her GI tract.[198]

G. Summary concerning causation of gastrointestinal symptoms

It is quite clear that Michelle Cedillo herself has, very unfortunately, suffered from many ongoing gastrointestinal symptoms, including constipation, diarrhea, gastroesophageal reflux, vomiting, abdominal pain, and others. Dr. Hanauer, for example, plainly acknowledged as much. (Tr. 2143, 2144A, 2153A.) Further, it is also true that children suffering from regressive autism, or other types of autism, have often suffered from chronic gastrointestinal problems. As noted above, the record of this case certainly does *not* contain a definitive explanation of exactly *to what extent* autistic children tend to have more GI problems than non-autistic children, or *why* autistic children might be more susceptible to GI symptoms. An Institute of Medicine committee noted that it is

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[197]In addition to his testimony concerning LNH and aphthous ulcers, discussed above, Dr. Gershon also indicated his view that the *pathologic evidence* from the biopsies is crucial. Like Dr. Hanauer, Dr. Gershon indicated that Dr. Krigsman is *not* justified in diagnosing IBD or enterocolitis or Crohn's disease in light of the fact that the pathologic reports from Michelle's biopsies were *uniformly negative* concerning inflammation of the intestines. (Ex. T, pp. 15-16, 21.)

[198]Moreover, I also note that after Dr. Hanauer presented at the hearing his detailed criticism of Dr. Krigsman's opinion, petitioners had the opportunity to respond with rebuttal testimony of Dr. Krigsman or any other witness, but petitioners did *not* present any rebuttal testimony concerning the issue of the causation of Michelle's gastrointestinal symptoms.

possible that autism leads to *behaviors*--*e.g.*, abnormal eating patterns--that may cause GI problems. (Ex. JJ, p. 128.) Two of respondents' experts, Dr. Wiznitzer and Dr. Fombonne, offered that same possible explanation. (Tr. 2716A-17A; *Snyder* Ex. Y, p. 4.)

However, it is not necessary for me to determine, in this case, to what extent autistic children have an increased risk for gastrointestinal dysfunction, or to determine why, in general, autism or regressive autism might be associated with excessive GI problems.[199] Rather, the issues relevant here concern whether the *MMR vaccine* plays a *causal* role concerning chronic GI symptoms in autistic children; specifically, whether the petitioners have been able to demonstrate (1) that the MMR vaccine *can*, *in general*, contribute to causing chronic gastrointestinal dysfunction in autistic children, and (2) whether an MMR vaccination *did* contribute to the causation of *Michelle's own* chronic GI symptoms. For the reasons set forth above, I conclude that the petitioners in this case have *failed* to make a persuasive case concerning either issue.[200]

IX

PETITIONERS' EVIDENCE CONCERNING THE *COMBINATION* OF REGRESSIVE AUTISM PLUS GASTROINTESTINAL DYSFUNCTION IS NOT PERSUASIVE

In their post-hearing briefs, the petitioners in this case have *separately* organized and presented their evidence concerning their theories (1) that the MMR vaccine can contribute to the causation of *autism*, and (2) that the MMR vaccine can contribute to the causation of chronic *gastrointestinal dysfunction*. Accordingly, in the sections of my opinion above, I have *separately* analyzed the evidence concerning those two theories.

However, I do recognize that, at a number of places in their expert reports and their hearing testimony, the petitioners' experts indicate that these two causation allegations are *closely intertwined*. For example, Dr. Kinsbourne explained that a major part of his reasoning involved the fact that Michelle Cedillo has experienced *both* chronic gastrointestinal problems *and* autism. He opined that because (1) the Unigenetics lab found evidence of persisting vaccine-strain measles virus in Michelle's intestine, (2) the measles virus is prone to invade both the intestines and the brain, and

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[199]Petitioners in their briefs have cited articles that indicate that children with regressive autism often have suffered from GI symptoms. (P1, p. 230; P2, pp. 8-9, 21.) But that much is *not* in dispute, as noted above. I have examined those articles, but I conclude that those articles provide no significant evidence that the *MMR vaccine can cause* chronic GI symptoms, in autistic children or anyone else.

[200]Petitioners have also alleged that Michelle's conditions of arthritis and uveitis were caused by her MMR vaccination. (P1 at 229.) However, this claim is based completely on the petitioners' theory that Michelle has chronic MMR-caused gastrointestinal inflammation. Having rejected that GI inflammation claim, I must also reject the claim that Michelle's arthritis and uveitis were vaccine-caused.

(3) Michelle has *both* chronic intestinal symptoms *and* autism, then the most reasonable conclusion is that a *single* causative agent--*i.e.*, the vaccine-strain measles virus--is the likely cause of *both* chronic conditions. (Ex. 61, pp. 12-14.) Similarly, Dr. Krigsman indicated the view that Michelle's autism and her chronic GI symptoms "in fact represent a single systemic disease," caused at least in part by the MMR vaccine. (Ex. 59, p. 2.)

As previously noted, this general idea, that there exists a group of children who suffer from *both* autism and chronic GI dysfunction, *both* caused by the MMR vaccine, derives directly from the 1998 article by Dr. Wakefield and colleagues. In that article, Wakefield posited the possible existence of a "unique disease process" (Ex. P, Tab 152, p. 639) or "syndrome" (*id*. at 641) involving a combination of chronic GI dysfunction and autism. Since then, proponents of that theory have often used the term "autistic enterocolitis" to refer to that theorized disease process.

Indeed, in this case Dr. Kinsbourne himself referred *first* to the 1998 Wakefield article in describing his above-mentioned theory concerning a "single cause" for both GI symptoms and regressive autism. (Ex. 61, p. 12.) Dr. Krigsman, as well, used the term "autistic enterocolitis," as well as the term "ASD-GI disease" (ASD meaning autism spectrum disorder), to describe the category of children in which he believes Michelle to fall. (Ex. 59, pp. 7, 9.) Similarly, Dr. Corbier, who testified in the *Hazlehurst* case, also propounded the theory that the *combination* of regressive autism and chronic GI dysfunction, coupled with the onset of symptoms relatively soon after MMR vaccination, supports a conclusion that the MMR vaccination played a role in causing *both* the autism and the GI dysfunction. (*E.g.*, *Hazlehurst* Ex. 26, pp. 8, 13-14; *Hazlehurst* Tr. 271A-72A, 303-04, 313A-14A.)

Accordingly, the purpose of this Section IX of this Decision is simply to point out that while in the pages above I have analyzed the autism and GI causation claims *separately*, as did the petitioners in their post-hearing briefs, I have *not* failed to consider the argument of Dr. Kinsbourne and the others that the *combination* of the two conditions in a child supports the conclusion that both conditions resulted, at least in part, from the MMR vaccine. I have considered that argument, but found it to be unpersuasive.

First, both Dr. Kinsbourne's and Dr. Krigsman's arguments, regarding a combination of the two types of conditions, are based, as stressed above, on the *assumption* of valid laboratory test results finding evidence of persisting vaccine-strain measles virus in the autistic children's intestinal tissue. However, since I have concluded above that the Unigenetics testing is *not* reliable, both the *general* causation arguments of Drs. Kinsbourne and Krigsman, and their *specific* causation opinions in Michelle's case, must fail for that reason alone.

Moreover, after considering the testimony of the petitioners' experts concerning this "combination" argument in the overall context of the evidence in this case, I simply do not find this argument to be at all persuasive. In the pages above, I have examined in detail both the petitioners' evidence concerning whether the MMR vaccine can contribute to the causation of *autism*, and the evidence concerning whether the MMR vaccine can contribute to the causation of chronic

gastrointestinal dysfunction, and I have concluded that the overall evidence strongly contradicts the petitioners' claims on *both* counts. The fact that some children have *both* types of conditions does *not* give me any more reason to conclude that either or both conditions were causally related to MMR vaccinations.

Accordingly, I reiterate that, after considering the argument of the petitioners' experts pointing to the *combination* of autism and GI dysfunction in a child as an indication that both conditions were vaccine-related, I must reject that argument.

X

PETITIONERS HAVE NOT DEMONSTRATED THAT MICHELLE'S MMR VACCINATION CONTRIBUTED TO HER MENTAL RETARDATION OR HER SEIZURE DISORDER

Petitioners also have suggested that Michelle's MMR vaccination contributed to the causation of her *mental retardation* and her *seizure disorder*. This argument is completely derivative of their theory that the MMR vaccine caused Michelle's *autism*. The petitioners note that both mental retardation and seizure disorders are statistically associated with autism--*i.e.*, persons with autism are more likely to suffer from those conditions than persons without autism. They also point out that both of those conditions, like autism, result from defective brain function. They theorize that whatever injured Michelle's brain, causing her autism, *also* likely caused her mental retardation and her seizure disorder.

The problem for petitioners in this regard, of course, is that they have failed to demonstrate that the MMR vaccine contributed to the causation of Michelle's *autism*, for the reasons detailed above. Therefore, their derivative argument, concerning the causation of Michelle's mental retardation and seizure disorder, must fail as well.

XI

PETITIONERS' ARGUMENT CONCERNING NOTATIONS OF "TREATING PHYSICIANS"

Petitioners have also raised an argument concerning certain notations of physicians and other service-providers who examined or treated Michelle. (P1, pp. 191-98; P3, pp. 9-14.) Petitioners argue that those notations indicate that those individuals believed that Michelle's autism was vaccine-caused. In this regard, I note that in the *Capizzano* opinion, the U.S. Court of Appeals for the Federal Circuit stressed that "medical records and medical opinion testimony are favored in vaccine cases, *as treating physicians are likely to be in the best position to determine* whether 'a logical sequence of cause and effect shows that the vaccination was the reason for the injury.'" 440 F.3d 1317, 1326 (Fed. Cir. 2006) (emphasis added, citation omitted). Similarly, in several recent cases, judges of this court, in resolving Vaccine Act causation issues, have relied heavily upon the

statements of treating physicians contained in the vaccinee's medical records. *E.g., Zatuchni v. Secretary of HHS*, 69 Fed. Cl. 612, 623 (2006); *Kelley v. Secretary of HHS*, 68 Fed. Cl. 84, 100 (2005). Accordingly, I have carefully studied those notations cited by petitioners. However, I conclude that they do *not* offer any substantial support to the petitioners' contentions that Michelle's autism, or any of her other conditions, were vaccine-caused.

Specifically, the petitioners quote nine notations in Michelle's records from eight individuals, including four physicians who treated Michelle and four non-physicians who examined Michelle. (P1, pp. 192-97; P3, pp. 11-13.) Petitioners seem to urge that each of the notations indicates that the writer believed that Michelle's autism was vaccine-caused. However, a close look at the quoted notations indicates that in *none* of those nine notations was the writer indicating such a causation opinion.

First, in seven of the nine notations, the writer merely indicated awareness of a *temporal relationship*, between Michelle's period of fever after the MMR vaccination and the appearance of symptoms of Michelle's autism sometime thereafter. This is true of the notations from the records of the physicians Dr. Crawford and Dr. Lott; the first notation from the physician Dr. Gupta; and the notations by the non-physicians[201] Lisa Shigio (audiologist), Dr. Roth (psychologist), Catherine Brown (speech therapist), and Dr. Freeman (psychologist). None of those seven notations indicates the opinion that the vaccination played a role in *causing* the autism.[202]

The second quoted notation from Dr. Gupta is from a letter in which Dr. Gupta replied to a letter from Michelle's mother. In her letter, Mrs. Cedillo had apparently asked whether Michelle might be exempted from vaccination requirements, and Dr. Gupta merely wrote that such an exemption could be arranged. (Ex. 24, p. 36.) Again, Dr. Gupta's letter in no way indicates that Dr. Gupta believed that Michelle's MMR vaccination *caused* Michelle's autism, or any of her other conditions.

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[201] Petitioners refer to Ms. Ligio, Dr. Roth, and Dr. Freeman as "physicians" (P1, p. 198), but from the records it appears that the first is a non-physician audiologist who works for a physician, and the latter two are non-physician Ph.D. psychologists.

[202] To be sure, when a physician notes, in a medical record, the existence of a temporal relationship between a vaccination and a medical symptom, that physician may well be indicating a *question* in the physician's mind whether there is a causal relationship, or a *suspicion* that there might be a causal relationship. However, that is quite different from an indication that such physician has reached a *conclusion* concerning a causal relationship, or even believes such a relationship to be likely. In several Program opinions, judges and special masters have noted that the mere fact that a physician mentions a vaccination in a medical record, or notes that a symptom occurred soon after a vaccination, is *not* evidence that the physician causally attributed the symptom to the vaccination. *E.g.*, *Moberly v. Secretary of HHS*, No. 98-910V, slip op. at 39-40 (Fed. Cl. Jan. 30, 2009); *Caves v. Secretary of HHS*, No. 07-443V, slip op. at 8 (Fed. Cl. Spec. Mstr. Nov. 25, 2008); *Carter v. Secretary of HHS*, No. 04-1500V, 2007 WL 415185, at *22 (Fed. Cl. Spec. Mstr. Jan. 19, 2007).

Finally, one of the quoted notations, from the neurologist Dr. William Masland, *does* express the physician's *speculations* concerning the causation of Michelle's neurologic abnormality , but *not* an opinion that the *MMR vaccine caused* Michelle's autism. (P1, pp. 192-93.) Dr. Masland, writing after examining Michelle on May 2, 1997, noted that Michelle lost her speaking ability after her post-MMR fever episodes, and stated that "it would appear that there was some neurological harm done at the time of the fevers;" he added that "given the overall history, it would appear the neurological problem now is dependent upon the febrile episodes and is not a structural or systemic problem, such as a chromosomal abnormality or one of the inborn errors of metabolism." (Ex. 28, p. 207.) These statements do indicate that at that time, Dr. Masland was theorizing that Michelle's *episodes of fever* played a role in causing neurological harm to her. However, Dr. Masland added that "[w]hether this was a post-immunization phenomenon or a separate occurrence, would be very difficult to say." (*Id*.) That last statement, thus, indicates that Dr. Masland was unsure whether the fevers were caused by the *MMR vaccine* or by an unspecified "separate occurrence." (*Id*.) Further, at that point in time, Dr. Masland believed that Michelle was suffering only from an "impairment of auditory perception." (*Id*.) No one had yet diagnosed Michelle with *autism*.

Thus, while Dr. Masland definitely did suspect on May 2, 1997, that Michelle's "fevers" might have caused neurological harm, he did *not* necessarily attribute her "fevers" to the MMR vaccination.[203] Further, at that early point in time Dr. Masland did not even yet know that Michelle's condition constituted *autism*. Accordingly, those speculations of Dr. Masland hardly constitute significant evidence that Michelle's autism was vaccine-caused. We do not know what Dr. Masland's later opinion, once he had all the facts, would have been. And, in contrast, respondent in this case has presented the opinions of a number of experts with very impressive credentials concerning autism, who have studied not only *all the facts* of Michelle's case, but also the vast amount of evidence concerning the *general issue* of whether the MMR vaccine can cause autism. Those experts have stated unequivocally that the MMR vaccine did *not* cause Michelle's autism, and they have been willing to *defend* that opinion in open court, under oath and under cross-examination. It seems astonishing for petitioners to now suggest that Dr. Masland's extremely brief, unexplained speculations contained in his letter of May 2, 1997, should be held to outweigh the opinions of those experts of respondent.

In short, I have carefully evaluated this argument of petitioners concerning the cited notations in the medical records, but those notations do *not* change my conclusions concerning any of the causation allegations raised by the petitioners in this case.[204]

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[203]Note that the expert with the most impressive credentials in studying the measles virus and MMR vaccine, Dr. Griffin, opined that while Michelle's *first* post-MMR episode of fever likely *did* result from that vaccination, her *second* febrile episode, a few days later, likely was *not* a result of the MMR. (Tr. 2816A.) Thus, perhaps Dr. Masland's reference to a "separate occurrence" indicates that he, too, doubted that the second febrile episode was related to the MMR vaccination.

[204]In their above-cited discussions in their briefs concerning "treating physicians," the (continued...)

XII

PETITIONERS' ARGUMENT CONCERNING OTHER PROGRAM CASES

As another argument in their briefs in this case, the petitioners raise a contention entitled "Michelle is like other vaccine-injured children who have been compensated in the Program." (P3, pp. 37-42; P1, pp. 180-83.) That argument consists chiefly of a list of 22 Program cases in which a vaccinee's injury or condition was found to be vaccine-caused. Petitioners contend that Michelle is "like" those vaccinees who were compensated for their injuries, so that therefore Michelle should be compensated for her medical conditions.

I find no merit to this argument. Michelle's case bears no resemblance at all to most of the cited cases, except for the fact that each case involved an allegation of "causation-in-fact." It is true that seven of the cited cases involved *MMR* vaccines which were found to have caused various neurologic conditions, and that Michelle, too, suffers from a neurologic abnormality. However, the theories of proof involved in those seven cases bear *no resemblance whatsoever* to the petitioners' theory of causation in this case. Petitioners have not suggested any similarity in the theories of proof, and I have found none. None of those cases involved a theory that the vaccine-strain measles virus, or any vaccine-strain virus, can persist in the body and thereby cause chronic disturbances in the gut or the brain.

In effect, the logic of this final argument of the petitioners seems to be simply that because *some* injuries or conditions have been found by special masters of this court to be vaccine-caused,

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[204](...continued)
petitioners do not mention Dr. Krigsman. Dr. Krigsman, however, is a physician who did treat Michelle on at least one occasion in person, in September of 2003, and who supervised Michelle's gastrointestinal care by telephone and e-mail for some time thereafter. And Dr. Krigsman has opined that Michelle's gastrointestinal problems have been caused by the MMR vaccine.

However, it is noteworthy that Dr. Krigsman was *not* a physician who merely happened to treat Michelle in the ordinary course of her illness. Based on the statements of Michelle's mother (see Tr. 256, 322-27), it appears that Mrs. Cedillo sought Dr. Krigsman out, even flying cross-country to see him, *precisely because* Dr. Krigsman was a *known proponent* of the theory that the MMR vaccine can cause autism and gastrointestinal dysfunction.

It is not surprising that some parents, like the Cedillos, after becoming interested in vaccine-autism causation theories through their own Internet research, may seek out those physicians who have taken such a public stance. However, I do not find it likely that the judges who wrote the *Capizzano*, *Zatuchni*, *Kelley*, and similar opinions had *that type* of physician-selection process in mind when they wrote of the importance of the opinions of "treating physicians."

In any event, I have fully considered Dr. Krigsman's report and testimony, and I have simply found his presentation, "treating physician" though he may be, to be *very unpersuasive*, for reasons set forth above.

based upon expert testimony, temporal relationships, and other circumstantial evidence, then *all* "causation-in-fact" claims should be found meritorious. This contention is without merit. Petitioners neglect to mention that while it is true that a substantial number of "causation-in-fact" claims have been found meritorious over the 20-year history of the Program, it is also true that *many more* such claims, numbering in the thousands, have been *rejected* by special masters. The fact is, of course, that in each case the special masters must evaluate the *particular* evidence and the *particular* causation theory presented, and determine whether it is "more probable than not" that the vaccination in question contributed substantially to the causation of the injury alleged. In some cases the special master will find that a causal connection has been shown, to the necessary level of probability, and in some cases the special master will not.[205]

In this case, the petitioners have advanced a theory of causation quite unlike any causation theory that I have previously seen in the 20 years of the Program's history. I have carefully evaluated that theory. Based upon all of the evidence, I have found that theory to be without merit.

XIII

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 while the *Althen* test has been the subject of slightly varying interpretations, under *any* reasonable interpretation of *Althen*, the petitioners' causation evidence in *this* case would fall far short of satisfying the test.

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[205] I note that I myself have made findings in *favor* of causation-in-fact contentions in many Program cases, and have also *denied* many causation-in-fact claims.

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

One interpretative issue with the *Althen* test concerns the relationship between the first two elements of that test. 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, on their faces, 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 need demonstrate (1) that the *type* of vaccination in question *can* cause the *type* of injury in question, and also (2) that the *particular* vaccination received by the specific vaccinee *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 the MMR vaccine *can* cause autism, in general, and (2) that Michelle's particular MMR vaccination of December 20, 1995, *did* cause her own autism.) Thus, a number of judges and special masters of this court have concluded that Prong 1 of *Althen* is the "can cause" requirement, and Prong 2 of *Althen* is the "did cause" requirement. *See*, *e.g.*, *Doe 11 v. Secretary of HHS*, 83 Fed. Cl. 157, 172-73 (2008); *Nussman v. Secretary of HHS*, 83 Fed. Cl. 111, 117 (2008); *Zeller v. Secretary of HHS*, No. 06-120V, 2008 WL 3845155, at *25 (Fed. Cl. Spec. Mstr. July 30, 2008); *Banks v. Secretary of HHS*, No. 02-738V, 2007 WL 2296047, at *24 (Fed. Cl. Spec. Mstr. July 20, 2007). And, most importantly, the *Federal Circuit itself* confirmed that interpretation in *Pafford*, ruling 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* that petitioner must then demonstrate that the *particular* vaccination *did* cause the *particular* condition of the 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*. *E.g.*, *Doe 11*, 83 Fed. Cl. at 173-74; *Scott v. Secretary of HHS*, No. 03-2211V, 2006 WL 2559776, at *18 (Fed. Cl. Spec. Mstr. Aug. 21, 2006); *Nussman v. Secretary of HHS*, No. 99-500V, 2008 WL 449656, at *12-13 (Fed. Cl. Spec. Mstr. Jan. 31, 2008), *aff'd*, 83 Fed. Cl. 111, 117-19 (2008); *Fields v. Secretary of HHS*, No. 02-311V, 2008 WL 2222141, at *7 n.5 (Fed. Cl. Spc. Mstr. May 14, 2008). However, it is *not* necessary, in this case, to delve into any such potential interpretative issues, since under virtually any interpretation of *Althen*, the petitioners' causation evidence put forward in this case could *not* satisfy any of the prongs of the *Althen* test.

That is, as set forth in detail above, I have concluded that petitioners have fallen far, far short of demonstrating either that the MMR vaccination *can* contribute, in *general*, to the causation of either *autism* or *chronic gastrointestinal dysfunction*, or that her MMR vaccination *did* contribute to the causation of *Michelle Cedillo's* own autism and GI symptoms. Thus, petitioners' arguments concerning all 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 the MMR vaccine contributed to the causation of *either* Michelle's autism or gastrointestinal symptoms.

C. Application of Althen *Prong 3 to this case*

Finally, petitioners have also failed to satisfy the *third element* of *Althen*, as to either their autism claim or their claim concerning gastrointestinal symptoms.

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 Michelle's autism, and/or the first symptoms of her chronic gastrointestinal problems, occurred in a *time frame* that would be consistent with causation by the MMR vaccination in question.[206]

In this regard, I must again separate my discussion concerning the petitioners' two major causation claims, relating to (1) autism and (2) chronic gastrointestinal difficulties. Concerning the *autism* claim, as discussed above (p. 101), Dr. Kinsbourne's testimony failed to establish, even to the level of "more probable than not," what might be an appropriate *time period*, *in general*, between MMR vaccination and the onset of symptoms of autism, under his causation theory. To be sure, Dr. Kinsbourne did indicate that the onset of autism at any time within three months after vaccination would be an appropriate time period. (Tr. 1176-78A.) However, Dr. Kinsbourne also admitted that he really has no idea how long it would likely take, as a matter of pathologic process or physiologic process, for a measles virus entering the body via MMR vaccination to reach the brain. (Tr. 1146-47.) Thus, Dr. Kinsbourne, by acknowledging that he does not know how long it would take the measles virus to reach the brain after MMR vaccination, has, in effect, acknowledged that he really *doesn't know* what would be the appropriate time period for onset of an autism

[206]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).

condition caused by an MMR vaccination. He acknowledged, in effect, that he is merely *guessing* or *speculating* when he indicates that, as a *general* matter, the onset of autism symptoms anytime within three months after vaccination would be appropriate.

Moreover, as to *Michelle's own case*, Dr. Kinsbourne was simply shown to be *wrong* in his assumption that the *first* symptoms of Michelle's autism appeared in the first several weeks following her MMR vaccination. To the contrary, as explained above, I conclude that Michelle was already exhibiting signs of autism even *prior* to the MMR vaccination.[207] (See pp. 127-30, above.)

Accordingly, for both of the reasons described in the previous two paragraphs, Dr. Kinsbourne's testimony has failed to satisfy Prong 3 of *Althen* as to Michelle's *autism*.

Next, concerning the claim as to *chronic gastrointestinal symptoms*, again the petitioners have failed to show that the first symptoms of Michelle's chronic gastrointestinal symptoms occurred in a time frame that would be consistent with causation by Michelle's MMR vaccination. First, Dr. Krigsman never even attempted to state what would be an appropriate time period after vaccination, *in general*, for the onset of vaccine-caused gastrointestinal symptoms after MMR vaccination. Dr. Krigsman did testify that Michelle's *chronic diarrhea*, which he assumed to be the beginning of her chronic gastrointestinal symptoms, began about 18 to 20 days after her MMR vaccination, and then continued for years thereafter. (Ex. 59, p. 6; Tr. 509.) This seems to indicate that he believes that such a time frame, about 20 days post-vaccination, would be appropriate for the onset of MMR-caused gastrointestinal symptoms. However, as noted above, Dr. Krigsman was *completely wrong* in his assumption as to when Michelle's chronic gastrointestinal symptoms *actually did* begin, since, in fact, Michelle's extended period of *chronic diarrhea* actually did not begin until more than *three years later*. (See p. 149 above.) Therefore, petitioners have also failed to demonstrate that Michelle's *chronic gastrointestinal symptoms* began in a time frame that would be consistent with causation by the MMR vaccine, and thus have failed prong (3) as to that causation theory as well.

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

Accordingly, for the reasons explained above, I conclude that as to both of their causation theories, concerning Michelle's autism and Michelle's chronic gastrointestinal symptoms, petitioners clearly have failed to satisfy any of the three prongs of the *Althen* test.[208]

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[207]Dr. Kinsbourne made it clear that for him to provide a causation opinion, the first symptoms of the child's autism must appear during the time period soon *after* vaccination. He stated that if there were symptoms of autism *preceding* the vaccination, he could *not* attribute the autism to the vaccination. (*Snyder* Tr. 536A-37A.)

[208]Because the petitioners have not met their burden, pursuant to § 300aa-13(a)(1)(A), of demonstrating that any of Michelle's vaccinations played any role in causing any of her medical (continued...)

E. Legal arguments raised by petitioners

In their initial post-hearing brief filed in this case, petitioners set forth some general discussion of the legal considerations in a causation-in-fact case, under the Program statute and the *Althen* test. (P1, pp. 172-187.) Most of their points are correct statements of the applicable law. As 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 the vaccination was the *sole* cause or even a *predominant* cause of Michelle's conditions, but only that it was a "substantial factor" in causing any of her conditions, 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 alleging that the MMR vaccine was the *sole* cause of Michelle's disorders, but are alleging only that the vaccine *contributed* to the causation of her disorders, possibly in concert with an underlying genetic vulnerability. I have looked beyond the epidemiologic evidence to determine whether the *overall evidence*--*i.e.*, medical opinion and circumstantial evidence and other evidence considered *as a whole*--tips the balance even slightly in favor of a causation showing as to any of Michelle's conditions.

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, declined to consider the video evidence, and/or excluded the testimony of Dr. Bustin. The result would be the same if I restricted my consideration to the evidence originally filed into the record of this *Cedillo* case, disregarding the general causation evidence from the *Hazlehurst* and *Snyder* cases. The petitioners' evidence has been unpersuasive on many different points, concerning virtually all aspects of their causation theories, 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 substantial likelihood that Michelle's MMR vaccination contributed in any way to the causation of any of *Michelle's own disorders*. To the contrary, based upon all the

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[208](...continued)
conditions, the burden *never shifted* to respondent to establish an "alternative cause" for Michelle's conditions. *DeBazan v. Secretary of HHS*, 539 F.3d 1347, 1353-54 (Fed. Cir. 2008).

evidence that I have reviewed, I find that it is *extremely unlikely* that any of Michelle's disorders were in any way causally connected to her MMR vaccination, or any other vaccination.

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.

XIV

CONCLUSION

The record of this case demonstrates plainly that Michelle Cedillo and her family have been though a tragic and painful ordeal. I had the opportunity, in the courtroom during the evidentiary hearing, to meet and to observe both of Michelle's parents, and a number of other family members as well. I have also studied the records describing Michelle's medical history, and the efforts of her family in caring for her. Based upon those experiences, I am deeply impressed by the very loving, caring, and courageous nature of the Cedillo family. Those family members clearly have done a wonderful job of coping with Michelle's conditions, and in caring for her with great love. I admire them greatly for their dedication to Michelle's welfare.

Nor do I doubt that Michelle's parents and relatives are sincere in their belief that the MMR vaccine played a role in causing Michelle's devastating disorders. Certainly, the mere fact that Michelle's autistic symptoms first became evident to her family during the months after her MMR vaccination might make them wonder about a possible causal connection. Further, the Cedillos have read about physicians who profess to believe in a causal connection between the MMR vaccine and both autism and chronic gastrointestinal problems. They have visited at least one physician, Dr. Krigsman, who has explicitly opined that Michelle's own chronic gastrointestinal symptoms are MMR-caused. And they have even been told that a medical laboratory has positively identified the presence of the persisting vaccine-strain measles virus in Michelle's body, years after her vaccination. After studying the extensive evidence in this case for many months, I am convinced that the reports and advice given to the Cedillos by Dr. Krigsman and some other physicians, advising the Cedillos that there is a causal connection between Michelle's MMR vaccination and her chronic conditions, have been *very wrong*. Unfortunately, the Cedillos have been misled by physicians who are guilty, in my view, of gross medical misjudgment. Nevertheless, I can understand why the Cedillos found such reports and advice to be believable under the circumstances. I conclude that the Cedillos filed this Program claim in good faith.

Thus, I feel deep sympathy and admiration for the Cedillo family. And I have no doubt that the families of countless *other* autistic children, families that cope every day with the tremendous challenges of caring for autistic children, are similarly 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 vaccination. 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 Michelle's behalf.[209]

/s/ George L. Hastings, Jr.

George L. Hastings, Jr.
Special Master

[209] 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