IN THE UNITED STATES COURT OF FEDERAL CLAIMS
OFFICE OF SPECIAL MASTERS

No. 09-616V
Filed: September 28, 2012
To Be Published

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Alexis Henderson, by her mother ALISHA HENDERSON,	*	Prevnar; Autism; Acute and Static Encephalopathy; Acute Disseminated Encephalomyelitis;
Petitioner,	*	ADEM; Altered Mental Status;
v.	*	Pervasive Developmental Delay;
	*	Actual Causation; Expert
	*	Qualifications; Incorrect
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Diagnosis as a Basis for Expert Opinion; Molecular Mimicry
	*	
Respondent.	*	
* *		

DECISION[1]

Michael McLaren, Esq., Memphis, TN, for petitioner.
Alexis Babcock, Esq., and Voris Johnson, Esq. U.S. Dept. of Justice, Washington, D.C., for respondent.

Vowell, Special Master:

On September 21, 2009, Alisha Henderson ["Ms. Henderson" or "petitioner"] timely filed a petition for compensation under the National Vaccine Injury Compensation Program, 42 U.S.C. §300aa-10, *et seq*.[2] [the "Vaccine Act" or "Program"], on behalf of her minor daughter, Alexis Henderson ["Alexis"]. The petition alleged that Alexis suffered unspecified "developmental delays" as the result of a pneumococcal conjugate vaccine ["Prevnar"], administered on March 6, 2007. Petition, ¶¶ 2, 5.

[1] Because this decision contains a reasoned explanation for my action in this case, I intend to post this decision on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, Pub. L. No. 107-347, 116 Stat. 2899, 2913 (Dec. 17, 2002). As provided by Vaccine Rule 18(b), each party has 14 days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire decision will be available to the public.

[2] National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755 (1986). Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa.

The medical records reflect that Alexis has a diagnosis on the autism spectrum, as well as the developmental delays that often accompany an autism spectrum disorder ["ASD"] diagnosis.[3] Petitioner's Exhibit ["Pet. Ex."] 7, p. 14. Notwithstanding this diagnosis, petitioner contends that Alexis sustained an acute encephalopathy on March 11, 2007, which was caused by her Prevnar vaccination on March 6, 2007, and that as a result, she now suffers from a static encephalopathy manifesting as a pervasive developmental delay, rather than autism.[4]

In order to prevail in a Vaccine Act case, a petitioner must prove either a "Table" injury[5] or that a vaccine listed on the Table was the cause in fact of an injury. There is no Table injury associated with the Prevnar vaccine. Thus, petitioner must establish actual causation of Alexis's condition. To do so, she must demonstrate by preponderant evidence "(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." *Althen v. Sec'y, HHS*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *see also Grant v. Sec'y, HHS*, 956 F.2d 1144, 1148 (Fed. Cir. 1992); *Hines v. Sec'y, HHS*, 940 F.2d 1518, 1525 (Fed. Cir. 1991).

I hold that, although Alexis received a Prevnar vaccination as alleged in the petition, Ms. Henderson has failed to produce preponderant evidence that the Prevnar vaccine caused Alexis's current condition, which I find to be an autism spectrum disorder. *See* § 11(c)(1). I thus deny her petition for compensation.

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[3] "Autism spectrum disorder" is an umbrella term used interchangeably with "pervasive developmental disorder." The chapter of the DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS (American Psychiatric Association, 4th ed. text revision 2000) ["DSM-IV-TR"], which contains the diagnostic criteria for these developmental disorders is entitled "Pervasive Developmental Disorders." DSM-IV-TR, filed as Respondent's Exhibit ["Res. Ex."] C, Tab 1, at 69. However, the term "autism spectrum disorder" is commonly used in the medical community, and is expected to become the preferred term in the new version of the DSM being tested. In general, I employ the terms "autism spectrum disorder" or "ASD," rather than the term "pervasive developmental disorder," as the latter term is sometimes confused with "pervasive developmental disorder-not otherwise specified" ["PDD-NOS"], which, along with "autistic disorder," and "Asperger's disorder" are specific diagnoses found in Chapter 2 of the DSM IV-TR. *See* Tr. at 160-61, 163, 173-76; Respondent's Exhibit C, Tab 1.

[4] Encephalopathy is defined as "any degenerative disease of the brain." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY (32nd ed. 2012) ["DORLAND'S"] at 614. There are a number of specific types of encephalopathy, with a variety of causes ranging from infections such as HIV to mitochondrial disorders with neurologic manifestations. *Id.* at 614-15. The terms "acute encephalopathy" and "static encephalopathy" are discussed in some detail below.

[5] A "Table" injury is an injury listed on the Vaccine Injury Table, 42 C.F.R. § 100.3, corresponding to the vaccine received within the time frame specified. The pneumococcal conjugate vaccine is listed on the Table; however Alexis's medical condition is not an injury specified for compensation for that vaccine.

I. Procedural History.

After petitioner completed the filing of medical records, respondent filed her Vaccine Rule 4 report contending that the evidence failed to establish that Alexis's vaccine caused her developmental delay. Respondent's Report, filed May 4, 2010, at 18.

In response, on June 1, 2010, petitioner filed a motion to join the Omnibus Autism Proceeding ["OAP"].[6] The motion was granted, and the case was transferred to the OAP[7] and reassigned to me on June 21, 2010. Docket entries 16-17 (Orders issued June 21, 2010).

Petitioner filed an expert report and a curriculum vitae from Dr. J. Ivan Lopez[8] on December 10, 2010, as well as medical literature upon which Dr. Lopez relied. *See* Pet. Exs. 11-15. This initial report was inadequate in that it was unclear whether Dr. Lopez

[6] The Omnibus Autism Proceeding consisted of a large group of petitions alleging that certain childhood vaccinations cause or contribute to the development of a serious neurodevelopmental disorder known as "autism spectrum disorder" or "autism." To meet the burden of establishing vaccine causation of autism spectrum disorders, six "test cases" were tried under the two theories presented by the Petitioners' Steering Committee. The first three test cases presented the theory that a combination of the MMR vaccine and thimerosal-containing vaccines caused ASDs ["Theory 1"]. The second group of three test cases presented the theory that thimerosal-containing vaccines alone can cause ASDs ["Theory 2"]. The three special masters assigned to hear the test cases ruled that there was no reliable evidence that the vaccines caused ASDs. The courts that heard the appeals in the test cases all agreed with the special masters that there was no reliable evidence supporting vaccine causation.

[7] The practical effect of the transfer was to make available to the parties the substantial body of evidence filed in the OAP test cases. *Dwyer v. Sec'y, HHS,* No. 03-1202V, 2010 WL 892250 at *2 (Fed. Cl. Spec. Mstr. March 12, 2010). However, at the hearing, petitioner objected to my consideration of any OAP evidence to decide causation in this case. Tr. at 3-8. I address this issue in Section III (D) below. Petitioner also argued that this case was similar to another case, *Banks v. Sec'y, HH*S, No. 02-0738V, 2007 WL 2296047 (Fed. Cl. Spec. Mstr. July 20, 2007), and should be resolved similarly. *Id.* The *Banks* case is discussed in n.14, below.

[8] Doctor Lopez attended medical school in Mexico, in a six year program that combined undergraduate school and medical school. Tr. at 11-13. He moved to the United States in 1991, and completed a residency in neurology with special qualifications in child neurology at the University of South Alabama in Mobile, AL. He remained there until 1997. Tr. at 14-16. Thereafter, he worked in a private, primarily adult neurology practice with his father, and became board certified in neurology in 2002. Tr. at 16-18. He moved to Georgia for two years, again working in a private neurology practice, but one with more pediatric patients. Tr. at 18-19. He returned to the University of South Alabama and worked there for six years. Doctor Lopez then moved to the University of Alabama at Birmingham, where he is currently an associate professor of neurology and pediatrics. Tr. at 20. His clinical practice there includes both children and adult patients, and he has teaching responsibilities involving both medical students and residents. Tr. at 21-22. Doctor Lopez joined the Army Reserve in 2005, and, as an activated reservist, he has served in Iraq, Germany, and Washington, DC as a neurologist treating both soldiers and their family members. Tr. at 23-27. Doctor Lopez listed eight publications on his CV, none of which involves autism spectrum disorders. Pet. Ex. 15 at 6. His research experience focused on stroke treatment. *Id.* at 2-3.

thought Alexis suffered from acute disseminated encephalomyelitis ["ADEM"][9] or a similar condition. The report relied on evidence that viral vaccines and illnesses could cause ADEM, but failed to address how a non-viral vaccine such as Prevnar could do so. Additionally, the report failed to address explicitly the *Althen* factors. I therefore ordered petitioner to file a supplemental report from Dr. Lopez. Order, issued Jan. 7, 2011.

The supplemental report of Dr. Lopez was filed on February 3, 2011. Thereafter, respondent filed the report of Dr. Peter Bingham[10] on May 9, 2011. Pursuant to Vaccine Rule 5, I held a substantive status conference on May 18, 2011, addressing the strengths and weaknesses of the expert reports. During the status conference and in an order that followed it, I expressed concerns about Dr. Lopez's theory—that Alexis suffered a post-vaccination encephalopathy similar to ADEM caused by an autoimmune attack on her brain triggered by molecular mimicry.[11] I also expressed my concern that Dr. Bingham's report did not explain why Alexis's condition in March 2007 and her current condition were inconsistent with post-vaccinal encephalopathy or encephalitis.[12] I afforded the parties the opportunity to file reports from additional experts. On September 13, 2011, respondent filed the report of Dr. Max Wiznitzer.[13] Petitioner

[9] ADEM, or as it is sometimes called, post-infectious encephalomyelitis ["PIEM"], "is usually a monophasic, primarily inflammatory demyelinating disorder of the central nervous system." C. Mihai & B. Jubelt, *Post-infectious Encephalomyelitis*, CUR. NEROLOG. & NEUROSCI. REP. 5: 440-45, 440 (2005), filed as Pet. Exs. 12 and 17 ["Mihai & Jubelt"].

[10] Doctor Bingham attended medical school at Columbia College of Physicians and Surgeons and did postgraduate training at Children's Hospital of Philadelphia. Tr. at 74. He also completed a fellowship in neuromuscular diseases. *Id.* For the last ten years, Dr. Bingham has divided his time between clinical research and a general child neurology practice at the University of Vermont. Currently, 100% of his time is devoted to clinical duties, including teaching medical students, residents, and fellows. Tr. at 75. About 15-20% of Dr. Bingham's patients are autistic. He also sees and treats patients with ADEM or other post-infectious conditions. Tr. at 76.

[11] The problems with Dr. Lopez's supplemental opinion centered on the lack of any scientific or medical support for a relationship between Prevnar and any of the conditions from which Alexis suffered. These problems are addressed in more detail below.

[12] In his hearing testimony, Dr. Bingham elaborated on his expert report, explaining why Alexis's clinical presentation was inconsistent with a post-vaccinal encephalopathy. Tr. at 78. The report of respondent's second expert, Dr. Wiznitzer, cured the other problem in Dr. Bingham's initial report by explaining why Alexis's autism spectrum disorder diagnosis was correct. Res. Ex. C at 7-8.

[13] Doctor Wiznitzer attended medical school at Northwestern University in a program that combined undergraduate school and medical school. Tr. at 118. He had three years of training in pediatrics at the Cincinnati Children's Hospital, followed by a year of training in developmental disorders, after which he attended a child neurology program at the Children's Hospital of Philadelphia. Tr. at 118-119. He then obtained grant funding for a fellowship in learning language and electrophysiology through the National Institutes of Health, during which he developed an interest in autism. Tr. at 119-20. Doctor Wiznitzer is board-certified in pediatrics, neurology with special qualifications in child neurology, and in neurodevelopmental disabilities through the American Board of Pediatrics and the American Board of Psychiatry and Neurology. Tr. at 120. He is currently a staff physician in the child neurology division at

declined the opportunity to respond to Dr. Wiznitzer's report. *See* Petitioner's Status Report, filed Dec. 13, 2011.

In a hearing on February 17, 2012, held in Washington, DC, all three experts testified in person. The parties opted against filing post-hearing briefs. *See* Joint Status Report, filed Apr. 12, 2012. The issues are now fully joined and ready for decision.

II. Medical History and Factual Findings.

A. Introduction.

This is not a complicated case. Petitioner presented a causation theory predicated almost entirely on the *ipse dixit* of her sole expert. As a pediatric neurologist, Dr. Lopez met the threshold qualifications to opine on the cause of a child's neurologic condition. He presented as a sincere and earnest witness who genuinely attempted to assist the court in resolving this case. However, the molecular mimicry theory he advanced was incompatible with the vaccine administered and the clinical features of Alexis's March 2007 illness.

Under other circumstances, his theory might serve to explain some neurological injuries,[14] but it was unavailing here, as it required me to find that Alexis had been misdiagnosed not once, but twice. Doctor Lopez opined that the Prevnar vaccination she received on March 6, 2007, was responsible for the symptoms that led to her hospitalization and ultimately for the symptoms that led to her autism diagnosis. When Alexis was hospitalized briefly in March 2007, her treating physicians settled on a diagnosis of "altered mental status." However, Dr. Lopez opined that she suffered

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the Rainbow Babies and Children's Hospital in Cleveland, OH. Tr. at 118. His primary focus is patient care, which includes reading EEGs and covering the epilepsy laboratory on a rotating basis. Tr. at 121. Additionally, he has both teaching and administrative responsibilities. Tr. at 121-22. Doctor Wiznitzer teaches medical students about autism. He belongs to several professional organizations focused on autism spectrum and other neurodevelopmental and movement disorders. Tr. at 122-23. He is currently conducting research on the use of medications to lessen the severity of autism spectrum disorders. He serves on the editorial boards of several medical journals, and has authored a number of articles and book chapters about various aspects of autism, including diagnosis and assessment of the condition. Tr. at 124, 126-27. He has been caring for children with autism spectrum disorders for almost 30 years. Tr. at 125.

[14] Petitioner's counsel argued that this case was similar to *Banks v. Sec'y, HHS*, 2007 WL 2296047, another case in which Dr. Lopez testified on behalf of petitioners, but one in which vaccine causation was successfully established. Tr. at 4-5. Not only am I not bound by the decision of another special master in another case (*Hanlon v. Sec'y, HHS*, 40 Fed. Cl. 625, 630 (1998)), there are marked factual differences between the two cases. In *Banks*, the child received a measles vaccine and was diagnosed with ADEM, a condition causally associated with the measles virus and possibly the measles vaccine, and sustained some permanent neurological injuries as a result. In contrast, Alexis received a vaccine not previously associated with ADEM, was never diagnosed with ADEM, was neurologically normal at the time of her hospital discharge, and was properly diagnosed with an ASD.

instead from an "acute encephalopathy," which he equated with ADEM, a serious and sometimes life-threatening condition. He stopped short of actually saying that Alexis had ADEM because she did not meet the diagnostic criteria for that condition (Tr. at 32), but the only support for his causation theory rested on evidence that some vaccines can cause ADEM. He concluded that Alexis had a "post vaccine encephalopathy" (Tr. at 29), which, coincidentally or otherwise, is very similar to other terms for ADEM.[15]

In the second part of his causation theory, Dr. Lopez drew a link between this "acute encephalopathy" and Alexis's subsequent diagnosis with an autism spectrum disorder. Tr. at 29-31. Once again, he redefined her diagnosis, because, as he testified (Tr. at 33), vaccines do not cause autism. He opined instead that Alexis was suffering from a "static encephalopathy" that caused her to exhibit behaviors that resembled those displayed by children with autism. Tr. at 30, 45-46. When asked to distinguish Alexis's condition from autism, clinically or otherwise, Dr. Lopez could not do so except by reference to a causal event in Alexis's case and the absence of any causal event in cases of autism. According to Dr. Lopez, Alexis does not have autism because there was a temporal connection between her March 2007 illness and her condition when seen by her primary care provider five months later. Because there was a vaccination, followed by an illness, followed by an autism diagnosis, Dr. Lopez concluded that the vaccine was responsible for the symptoms giving rise to that autism diagnosis. A better example of both circular and *post hoc, ergo propter hoc* reasoning would be difficult to find.

B. Medical History.

1. Medical Records and Histories Prior to March 2007 Hospitalization.

Alexis was born on November 26, 2005, and left the hospital on November 29, 2005. Pet. Ex. 3, p. 10. For reasons unexplained in the record, Alexis did not see a physician again or receive any vaccines until she was eight months old.

At her initial well-child appointment at Carolina Family Healthcare on July 13, 2006, per parental request,[16] Alexis received only two vaccinations at this visit, her first diphtheria, tetanus, and acellular pertussis ["DTaP"] and hemophilus influenzae type b ["Hib"] vaccines.[17] Pet. Ex. 4, p. 1. She received her second and third DTaP and Hib vaccines at her next two well child visits, at nine and twelve months of age. *Id*., pp. 4, 8.

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[15] *See* DORLAND'S at 613 (noting that ADEM is also called postvaccinal encephalitis).

[16] A chart entry at Alexis's second well child visit on September 7, 2006, indicated that Ms. Henderson "wants to perform immunizations on her own schedule." Pet. Ex. 4, p. 3.

[17] The Centers for Disease Control ["CDC"] website contains recommended vaccination schedules that indicate that children should receive three doses of the hepatitis B, DTaP, Hib, and polio vaccines by six months of age. http://www.cdc.gov/vaccines/recs/schedules/downloads/child/0-6yrs-schedule-bw.pdf (last visited Sept. 28, 2012).

Alexis was assessed as "well developed" at her seven-month visit and as having "appropriate" development at her one year visit.[18] At the nine-month visit, the records were more specific, reflecting not only that Alexis met "behavioral and developmental milestones," but also mentioning that she could pull herself up, transfer objects from hand to hand, drink from a cup, and babble three words. Pet. Ex. 4, pp. 1, 3, 6.

At a December 26, 2006 visit, Alexis was ill with a fever that had developed two days prior to the visit. The fever was described as "recurrent," coming and going intermittently. Alexis also had nasal congestion for three days prior to the office visit. Additional symptoms included decreased urination, decreased fluid intake, nasal discharge, fever less than 101° Fahrenheit, and poor appetite. Pet. Ex. 4, p. 9. Alexis was diagnosed with an acute upper respiratory infection. *Id.*, p. 10.

The medical records reflect four notes dated between the end of February and early in March 2007. It is difficult to tell from the partial nature of these notes how many telephone messages or conversations they document, but there was at least one.[19] Part of one note dated February 28, 2007, concerns giving Alexis fluids and Tylenol,[20] but the remainder is cut off. Later that same day, there is an entry reading "she can get it check (sic) out with next well child visit." Finally there were two notes dated March 1, 2007, indicating that Alexis was cutting a molar and had decreased appetite, and that Alexis was coming into the office on March 2, 2007. Pet. Ex. 4, p. 11. There is no record of an office visit on this date.

Alexis had her 15 month well child visit on March 6, 2007. Her mother reported that Alexis was teething, and her right lower molar was causing pain and a "low grade fever." She was described as a picky eater, but also as eating a variety of organic foods and soy milk. Pet. Ex. 4, p. 12. Alexis weighed 21 pounds, a gain of one pound since her one-year well child visit in December 2006.[21] The review of symptoms section of the computerized form contains an entry describing intermittent fever of two days

[18] If this medical practice used developmental checklists, they were not filed with the medical records.

[19] During the hearing, petitioner's counsel indicated that he did not believe these notations documented conversations or messages to or from petitioner. *See* Tr. at 111-12. However, if these notations were not documenting messages or telephone calls, there is little reason for them to appear in Alexis's medical records. For example, there would be no need to discuss giving Alexis fluids and Tylenol, unless the intent was to communicate that treatment plan to Alexis's parents. Likewise, Alexis's parents must have communicated the information that she was cutting a molar as there is no other way the office staff could have known that prior to her March 6, 2007 visit.

[20] Tylenol is commonly used to treat pain or fever. Tr. at 111.

[21] During her March 11-13, 2007 hospitalization, Alexis was reported to have gained no weight since she was 12 months old. Pet. Ex. 3, p. 79. This report was incorrect, based on these contemporaneous medical records.

duration, placing onset on or about March 4, 2007. Pet. Ex. 4, p. 12. On physical examination, Alexis had enlarged and injected tonsils, and her pharynx was also injected. *Id.*, p. 13. The assessment was "teething syndrome." Per her mother's request, Alexis received only a Prevnar vaccination at this visit. *Id*. If Alexis's development milestones were assessed, the results were not recorded.

2. The March 2007 Hospitalization.

In the early afternoon of March 11, 2007, Alexis experienced what a physician would later describe as a "bizarre episode." *See* Pet. Ex. 3, pp. 72, 77. The following accounts are drawn from the contemporaneous medical records and the histories provided by petitioner to the health care providers.

a. Alexis's Condition in the Two Weeks Preceeding the Episode.

According to histories provided by Ms. Henderson to physicians at an urgent care center and later at Carolinas Medical Center ["CMC"], Alexis had been experiencing fever (measured subjectively, because her parents did not have a thermometer) in the one to two weeks prior to the episode that led to her hospitalization.[22] She was also demonstrating some "pain" behavior, which had been attributed to teething; irritability; and loss of appetite for about two weeks. Pet. Ex. 3, p. 79. Alexis was also unsteady when walking, but it is difficult to tell from the history if the unsteadiness manifested earlier than March 11, 2007. *Id.*, p. 66. Her mother reported that on March 10, 2007, Alexis experienced a "significant fever." *Id.*, p. 72. She was quieter than usual that evening. *Id*.

b. The March 11, 2007 Episode.

On the morning of March 11, 2007, Alexis was fussier than usual when she woke up, but was otherwise behaving normally. After breakfast, she played and did not appear to be feverish. Pet. Ex. 3, p. 78. For a reason that does not appear in the records, she was given Tylenol at about 1:00 PM.

At some point in the afternoon, while Ms. Henderson was on the computer, she heard Alexis come up behind her. Alexis screamed, and when Ms. Henderson

[22] The history provided at the urgent care center at about 1:30 PM on March 11, 2007, and at the emergency department at about 3:15 PM indicated that Alexis had been experiencing fever off and on for about one week. Pet. Ex. 3, pp. 66, 86. The history taken when she was admitted to the Pediatric Intensive Care Unit ["PICU"] at CMC was the most extensive in the medical records, and in it, Ms. Henderson indicated that the fever had lasted for about two weeks. *Id.*, p. 79. Other histories taken in the hospital adopted the two week history. *See, e.g.*, *id.*, pp. 74, 78. I conclude that Alexis had been experiencing intermittent fevers for at least ten days prior to her hospitalization and for about a week prior to her receipt of the Prevnar vaccination, based on the entries in the medical records for February and March 2007.

approached her, Alexis was variously described as curled up in a "fetal position,"[23] looking confused and dizzy, and pulling away when her mother picked her up. *See* Pet. Ex. 3, pp. 66, 72, 78-79, 86. There were no symptoms such as shaking, stiffening, or eye deviation, common in seizures. *Id*., p. 78; PRINCIPLES OF NEUROLOGY (9th ed. 2009), at 306. Ms. Henderson put Alexis to bed, where she vomited. She was also reaching out in the air for things that were not present, appeared not to recognize her mother, and cried continually. Pet. Ex. 3, pp. 66, 72, 78-79, 86. She had a red, blotchy rash on her face. *Id.*, p. 78. Ms. Henderson bathed Alexis, and she vomited again. *Id*.

c. The Urgent Care Center.

After Alexis vomited for the second time, her parents took her to an urgent care center, where they reported that she had lost consciousness.[24] Pet. Ex. 3, p. 86. During the trip to the urgent care center, Alexis was lethargic and sleepy. *Id.*, p. 72. On examination at the urgent care center, she was described as possibly having a disconjugate gaze, mild pallor, and both as "unresponsive" and "respond[ing] to stimuli." *Id.*, p. 86. She was assessed as "probably post ictal"[25] and sent to CMC by ambulance. *Id*. En route to CMC, she became more awake and alert, and cried in the ambulance. *Id*., p. 72.

d. Evaluation and Treatment in the Emergency Department.

Although there was no indication that Alexis had a fever at the time of the episode in her home or on arrival at either the urgent care center or the emergency department, the chief complaint on arrival at the CMC emergency department was listed as "febrile seizures."[26] Pet. Ex. 3, p. 69. On initial exam at about 3:15 PM, she was described as irritable, with cyanosis due to crying, and a rash on her right temple. She had normal affect, tone, and range of motion, and there were no signs of meningitis. *Id*., p. 66.

[23] According to Dr. Bingham, a child experiencing a seizure would be unlikely to curl into a fetal position. Syncope (fainting) would be a more likely explanation for this position. Tr. at 114.

[24] Some of the histories did not describe a loss of consciousness at home (*see* Pet. Ex. 3, pp. 66, 86, 72), although they do indicate Alexis was staring off into space (*id*.). I note that the urgent care record incorrectly states that Alexis recently had a chicken pox vaccine, instead of Prevnar. A history form completed at the hospital also reflects receipt of a chicken pox vaccination. Pet. Ex. 3, p. 97.

[25] An "ictal" event is a seizure. "Post-ictal" refers to the confusion and lethargy that often follow a seizure. DORLAND'S at 1502.

[26] On arrival at the emergency department at around 2:35 PM on March 11, 2007, Alexis's temperature was 98.3, measured rectally. Pet. Ex. 3, p. 69. The comment about "febrile seizures" was a presenting complaint, not a diagnosis. *Id.* Alexis was never diagnosed with either seizures or a seizure disorder.

The examining physician, Dr. Robert Schafermeyer, ordered placement of an intravenous line, blood and urine testing, chest and abdominal x-rays, and a brain CT.[27] He also ordered the administration of Rocephin, an antibiotic. Pet. Ex. 3, pp. 63, 72-73. None of the tests indicated any reason for Alexis's condition. *See id*., pp. 127-28 (x-rays read as normal), p. 126 (brain CT read as normal); pp. 115-19 (blood tests and cultures; limited toxicology screen for alcohol, acetaminophen, and aspirin; and urine testing, all with results in the normal range).

Alexis cried inconsolably during the examination and during the IV placement and other procedures, but rested comfortably in her mother's arms a few minutes later. *Id*., pp. 70, 72. For reasons not entirely clear from the medical records, morphine was ordered at 6:30 PM and administered at 6:42 PM.[28] *Id.*, pp. 63, 70. At 7:32 PM on March 11, shortly before her admission to the PICU, Alexis was described as alert and playing with toys. *Id.*, p. 70.

e. Evaluation and Treatment in the PICU.

Alexis was admitted to the PICU at about 8:00 PM on the evening of March 11, 2007, with a diagnosis of "altered mental status," which is frequently abbreviated in the medical records as "AMS." Pet. Ex. 3, pp. 55-57; *see also* Tr. at 34-36, 44. During her PICU stay, Alexis was intermittently irritable and calm. She interacted appropriately with her parents and caregivers. In spite of some gait unsteadiness or loss of balance, which primarily occurred when she was upset and crying, Alexis stayed in the PICU less than 18 hours.

On arrival in the PICU, she was crying, but easily consolable by her mother. Pet. Ex. 3, p. 164. She was examined by Dr. Eaker, who reported that Alexis was alert, in no apparent distress, and that her neurological examination and tone were normal. *Id.*, p. 80. After Alexis was sedated, Dr. Eaker attempted a lumbar puncture, but she was unsuccessful.[29] *Id.*, pp. 89, 164.

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[27] A CT scan refers to a computed tomography scan of the brain, a test used to diagnose central nervous system disease, including tumors, aneurysms, and hemorrhages. It consists of a computerized analysis of x-rays of the brain. MOSBY'S MANUAL OF DIAGNOSTIC AND LABORATORY TESTS (4th ed. 2010) ["MOSBY'S"] at 1080-82.

[28] The nursing records indicate that morphine was given for "pain." Pet. Ex. 3, p. 70. Doctor Schafermeyer's notes do not indicate why morphine was ordered, but the history taken by Dr. Eaker upon Alexis's admission to the PICU described an incident in the ER involving Alexis arching her back and emitting a high-pitched cry, and then becoming somewhat sleepy. *Id.*, p. 78. This may have prompted the morphine order.

[29] Alexis received more morphine and Ativan, an anti-anxiety medication, before the procedure. Pet. Ex. 3, p. 89. Although some of the records indicate that the attempts were unsuccessful due to Alexis's lack of cooperation (*id*., p. 77), Dr. Eaker indicated that the needle was placed in the spinal column four times, but no cerebrospinal fluid was obtained on any attempt. *Id.*, p. 89.

At about 9:15 PM that evening, Alexis was crying and standing up in her crib. According to a nursing note, while crying Alexis became weak and sat down. The nurse consoled her by rocking her, and a few minutes later, Alexis was resting comfortably with her mother. By 10:00 PM, she was back in her crib. *Id.*, p. 164.

Alexis slept until 5:30 AM on March 12, 2007, when she awoke crying. She was unsteady on her feet and again lost her balance. A nursing note described Alexis as unconsolable unless she was being held and rocked by the nurse. She was placed back into her crib, resting quietly, at 6:15 AM. Pet. Ex. 3, p. 164. At 8:15 AM, Alexis was awake, interactive with her mother, and babbling. She had a slightly unsteady gait. *Id.*, p. 149.

Based on her condition the previous evening and examinations conducted the morning of March 12, plans were underway by 9:40 AM to transfer Alexis from the PICU to the general pediatrics ward. Pet. Ex. 3, pp. 49-51, 148-49. Doctor Shanks, a pediatric neurologist, noted that Alexis was irritable and difficult to examine because she was fussy, but he also described her as alert and interactive. Because Alexis would not leave her mother's lap, he was unable to assess her gait. *Id.*, p. 75. He described his findings as "non-focal" but noted that sedation would be necessary for a sleep-deprived EEG due to her "tremendous irritability." *Id.*, p. 61. Alexis was also assessed by Dr. Young, the PICU attending physician. He described her mental status on the morning of March 12, 2007 as normal, but indicated that she might be more clumsy than normal. He found no evidence of meningismus[30] or meningitis symptoms. *Id*., p. 77.

f. Remainder of Hospitalization.

Alexis was transferred from the PICU to the regular pediatric ward the afternoon of March 12, 2007, where she remained until her discharge on March 13, 2007. On arrival, she was crying but consolable. Pet. Ex. 3, p. 141. When examined by the staff pediatrician, she was afebrile, sleeping but easily arousable, fussy, and consolable. Her neurologic exam was normal. *Id.*, p. 60.

That afternoon and evening, Alexis was playing in the room and walking in the hallway with her father. She was "agitated" at 8:00 PM and given Tylenol for pain. She apparently slept from 11:00 PM until after 2:00 AM. At either 3:00 or 5:00 AM (the handwriting is difficult to read) on March 13, 2007, she was awake and alert at the nurses' station, with no signs of pain or distress. Alexis appeared to walk normally. *Id.*, p. 141.

While hospitalized, Alexis underwent several medical tests, including the unsuccessful attempt to obtain cerebrospinal fluid for analysis (*see* Pet. Ex. 3, pp. 89,

[30] Meningismus (meningism) is defined as the signs and symptoms associated with inflammation of the meninges, the membranes that envelop the brain and spinal cord. DORLAND'S at 1132.

164), an unsuccessful attempt at an electroencephalogram ["EEG"][31] (*id*., p. 60), and a sleep-deprived EEG, which was read as normal (*id*., pp. 59, 130). Alexis was scheduled for a head MRI and another lumbar puncture while under sedation to rule out ADEM, but her parents opted for the MRI to be performed on an outpatient basis.[32] The MRI and lumbar puncture were never performed, as Alexis's parents did not keep either the appointment made for testing or a follow up appointment with one of her treating physicians at CMC.

g. Summary of Hospital Course and Discharge.

In summary, no cause for the March 11, 2007 episode was ever identified by the treating physicians. One of her physicians called the episode at home a "[s]pell of possible alteration of consciousness of unclear nature. Possible ictal [seizure] event would be in the differential as would non-ictal events potentially associated with the irritability." *Id.,* p. 76. He went on to describe her clinical presentation during her hospitalization: "[N]o evidence to suggest metabolic derangement. She also has ongoing irritability, which has no overt neurologic appearance, and the possible etiologies are many." *Id*. The nursing notes and records of examinations by several physicians during the hospitalization reflect that Alexis was intermittently irritable and calm and interacting appropriately with her mother and hospital personnel. Other than some balance problems during episodes of crying and a slightly unsteady gait noted on one occasion, Alexis was neurologically normal every time she was assessed.

Alexis was discharged on March 13, 2007 with a discharge diagnostic code of 780.97, altered mental status (*id.*, p. 46), not any of the diagnostic codes associated with encephalopathy.[33] She was in a normal neurological state at the time of her discharge. *Id.*, p. 84; Tr. at 83.

3. Post Hospitalization Sick Child Visit.[34]

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[31] An EEG, or electroencephalogram, records the electrical activity of brain cells. DORLAND'S at 600.

[32] *See* Pet. Ex. 3, p. 47 (cancelling inpatient MRI scheduled for March 13, 2007); p. 135 (indicating parental preference for the outpatient procedure).

[33] *See* Diagnosis and Procedure Codes (Centers for Medicare & Medicaid Services, version 29), http://www.cms.gov/ICD9ProviderDiagnosticCodes/06_codes.asp (last visited Sept. 28, 2012).

[34] Two of the experts disagreed about the reliability of this medical record. Doctor Lopez, noting that the computerized record was generated from a template, indicated that he would not rely on this record in his own practice. Tr. at 56-59. He felt the lack of reliability extended even to entries that reflected the caregiver's observations and examination. Tr. at 58. On the other hand, Dr. Bingham thought the record was reliable. Tr. at 83. To the extent that this record reflected reports about Alexis's hospitalization that conflicted with the actual hospital records, I rely on the hospital records. However, with regard to the entries that reflect the observations of the caregivers, I see no good reason to reject this record in its entirety, in spite of Dr. Lopez's concerns.

On March 15, 2007, two days after her discharge from the hospital, Alexis was seen by her primary care provider for recurrent and random fevers with temperatures to 102.5°, with onset either three or five days earlier (both periods are mentioned in the record, placing onset on either March 10 or 12, 2007 and thus during her hospitalization).[35] Pet. Ex. 4, p. 15. Ms. Henderson reported that Alexis seemed better the evening prior to the visit, with a lower fever after being given Tylenol, but the fever "spiked" again that morning and she was lethargic. *Id.* The intake note indicated that her parents had left the hospital "AMA,"[36] an acronym for "against medical advice," because her mother was "angry that she did not receive any answers and left." Pet. Ex. 4, p. 15.

On examination, Alexis was lethargic and irritable but consolable. Pet. Ex. 4, p. 16. Her tonsils were enlarged and her pharynx was slightly red. Tests for influenza and strep infections were negative. *Id.* Ms. Henderson agreed to take Alexis back to the hospital for the MRI and lumbar puncture that had been scheduled. *Id*., p. 16. She never did.

There are no contemporaneous medical records reflecting Alexis's health and development between this visit and one on August 20, 2007, where petitioner expressed concern about possible autism.[37] In her second affidavit, Ms. Henderson acknowledged that Alexis did not see any health care providers between the March and August 2007 appointments with her primary care physician. Pet. Ex. 20, filed June 17, 2011, at 1.

4. Autism Symptoms and Diagnosis.

a. Primary Care Physician's Visits.

On August 20, 2007, five months after her hospital discharge, Alexis, then 22 months of age, returned to Carolina Family Healthcare. One of the two reasons for the

[35] It is impossible to reconcile the history of fever Ms. Henderson provided with Alexis's hospital records, as there is no mention of fever at the time Alexis was discharged from the hospital on the afternoon of March 13, 2007, and none of the hospital records of her vital signs reflect elevated temperature during her stay. *See* Pet. Ex. 3, p. 47 (discharge order written at 3:05 PM on March 13, 2007), pp. 144, 153, 170 (vital signs from March 11, 12 and 13). *See also id.,* pp. 58, 60, 65-66, 69, 75, 77, 80, 86, 88, 160 (hospital records reporting a normal temperature or noting that Alexis was afebrile).

[36] The hospital records do not reflect that Alexis left against medical advice. Rather, they indicate that her parents were given the option of her remaining hospitalized until the lumbar puncture and MRI could be performed or having the MRI done on an outpatient basis. They opted for the latter. Pet. Ex. 3, p. 135. Also, the records indicate a follow up appointment with Dr. Shanks was scheduled on March 28, 2007, after the MRI scheduled for March 21, 2007. *See id.*, pp. 84, 96.

[37] There is a parent questionnaire form completed by Ms. Henderson that describes some of Alexis's development during this period. *See* Pet. Ex. 24, pp. 3, 9-14. This questionnaire is discussed in more detail, below.

visit was a concern about "possible autism, only speaks two understandable words, covers ears when load (sic) noises, very quiet, isolated play." Pet. Ex. 4, p. 18.

Alexis returned to her primary care provider's office on August 30, 2007, for a "DAN visit."[38] The chief complaint was "no words." Alexis was reported to use "mama" and "dada" occasionally, and to babble a lot. By history, she had good eye contact, but was sensitive to sounds and noise. She would occasionally refuse to eat and "toe walked." Pet. Ex. 4, pp. 20-21.

In a questionnaire completed for the DAN! visit, Ms. Henderson indicated that she first noticed a problem with Alexis's development when she was 16 or 17 months of age. Pet. Ex. 24, p. 3. At that time, Alexis had "limited babbling vocabulary," which had not improved. *Id*. She reported that Alexis had been sensitive to sounds or noise and had been toe walking for about ten months, placing onset of these behaviors around October-November, 2006. *Id*., pp. 11, 13. Ms. Henderson also indicated that Alexis was a picky eater. She had been refusing some foods for about five months, and would self feed only dry foods. *Id*., p. 12. Ms. Henderson did not appear to associate Alexis's symptoms with her March 2007 vaccine or illness, as one of the questions on the form that did not contain any answer was "Was there any event or illness that you or others think brought on your child's symptoms?" *Id.*, p. 3.

The remaining records from Carolina Family Healthcare reflect visits for a sore throat and diarrhea (Pet. Ex. 4, pp. 22-23, 26-27) and one acute visit on January 31, 2008, for delayed speech, resulting in a referral to a neurologist and a diagnosis of "Developmental Dyslexia" (*id.*, pp. 24-25).

b. Specialist Evaluations.

On March 13, 2008, Alexis was evaluated by a neurologist who referred her to Mecklenburg County Children's Developmental Services ["CDS"]. Pet. Exs. 6, pp. 2-3; 7, pp. 10, 15. Alexis was evaluated by CDS in April and May 2008, when she was about 30 months old.[39] Pet. Ex. 7, pp. 10, 15. The evaluation disclosed delays in fine

[38] Alexis's primary care physician was Dr. Dino Kanelos. In addition to his more conventional medical practice, Dr. Kanelos is also a Defeat Autism Now ["DAN!"] physician, who continued to care for Alexis after her autism spectrum disorder diagnosis. Pet. Ex. 4, pp. 20-21. DAN! physicians subscribe to treatment protocols developed by the Autism Research Institute. These treatments may include chelation and other therapies not vetted as efficacious by controlled clinical studies. *Dwyer*, 2010 WL 892250 at *20, 178.

[39] The medical history set forth in the evaluation contains some inaccuracies. In particular, it indicates that Alexis received three meningitis vaccinations, and that she became ill at one year of age after her first pertussis vaccination. Pet. Ex. 7, p. 16. Alexis actually received three Hib and DTaP vaccinations (which include a pertussis component) before the Prevnar vaccination at 15 months of age, after which she became ill and was hospitalized. Pet. Ex. 4, pp. 1, 4, 8.

motor skills, self-help, and communication skills,[40] and "scattered cognitive abilities." *Id.*, p. 10. Additionally, it noted Alexis was "obsessed" with water, would only finger feed herself dry foods, and refused to eat white or green foods. *Id*., pp. 16-17. Alexis did not respond to her name or follow simple directions during the evaluation. *Id.*, p. 11.

According to the evaluator's observations and a history provided by Ms. Henderson, Alexis did not play appropriately with toys. When the evaluator arrived at the Henderson home, Alexis did not seem to notice her, and continued to line up objects on the floor. Ms. Henderson indicated that Alexis generally either lined things up or sorted objects by characteristics. For example, Alexis tended to line up her blocks by putting all the pictures on one side. She preferred to play alone and was described as "self-directed." She had tantrums when transitioning from a preferred activity or when a preferred item was taken away. During the evaluation, Alexis brought her mother a bowl, indicating she was hungry, and Ms. Henderson reported Alexis would bring a cup or a bottle to her when thirsty. Alexis did not engage in pretend play. She did not like people to talk to her or to look her in the face. Pet. Ex. 7, pp. 11-12.

On a test of cognitive development, Alexis scored in the extremely low (1st percentile) range. *Id.*, p. 12. She scored in the low range for adaptive behavior on the Vineland II scale, which measures communication, daily living skills, socialization, and motor skills. *Id.*, p. 13. On the Childhood Autism Rating Scale ["CARS"], Alexis received a score of 39.5, placing her in the severely autistic range. *Id*., p. 14.

C. Findings Regarding Disputed Factual Matters.

Most of the facts surrounding Alexis's March 2007 Prevnar vaccination and subsequent illness are not in conflict. The primary factual conflicts involve: (1) the severity of and diagnosis for Alexis's condition in March; (2) the sequelae, if any, she displayed after her discharge from the hospital; and (3) whether Alexis was properly diagnosed with autism or has another neurological condition that manifests with autism-like symptoms.

Because Dr. Lopez's expert opinion on vaccine causation depends on his diagnosis of an acute encephalopathy leading to a static encephalopathy manifesting with autism-like symptoms, the resolution of these conflicts is the threshold and dispositive issue in this case. *See Locane v. Sec'y, HHS,* 685 F.3d 1375, 1381 (Fed. Cir. 2012); *Broekelschen v. Sec'y, HHS,* 618 F.3d 1339, 1349 (Fed. Cir. 2010) (noting it is appropriate to determine first a petitioner's injury before evaluating if vaccine

[40] Ms. Henderson expressed concerns about her expressive and receptive language skills. Alexis was reported to understand the word "no" and to follow some household rules, but did not consistently respond to her name or to simple directions. She babbled, but did not talk, and would growl to indicate her displeasure. Pet. Ex. 7, p. 15.

causation has been established). If Alexis did not have an acute encephalopathy in March, Dr. Lopez's theory that Prevnar caused an acute encephalopathy via molecular mimicry falls by the wayside. If Alexis has autism, rather than a static encephalopathy with autistic like symptoms, Dr. Lopez's theory lacks a factual basis because he unequivocally testified that vaccines do not cause autism. Tr. at 33.

To resolve these conflicts, I rely on the contemporaneous medical records documenting Alexis's condition and treatment, including the opinions of her treating physicians; the opinions of the experts; and the medical literature filed to support those opinions.

There is an additional factual issue pertaining to Dr. Lopez's causation theory. He asserted that the Prevnar vaccination caused the symptoms Alexis experienced by a mechanism known as molecular mimicry. That theory requires that the vaccine contain proteins or amino acids that share sequences (homology) with central nervous system proteins. The unrebutted evidence establishes that Prevnar does not contain either proteins or amino acids, and thus cannot cause injury by the postulated mechanism of molecular mimicry.

1. Conflicts in Diagnosis for March 2007 Illness.

Doctor Lopez variously characterized Alexis's condition during her hospitalization as an "acute encephalopathy" and as a "post-vaccinal encephalopathy." Tr. at 29-30. He defined "acute encephalopathy" as a vague term used to indicate irritability or decreased alertness."[41] Although he stopped short of testifying that Alexis actually had ADEM,[42] his initial expert report equated ADEM with acute encephalopathy.[43] While Alexis displayed some symptoms that could be consistent with ADEM or a similar neurological condition, notably her unsteadiness,[44] her tremendous irritability, and the

[41] As reflected below, both Drs. Bingham and Wiznitzer disagreed with Dr. Lopez's definition for acute encephalopathy, indicating that a sustained period of impaired neurologic function was required.

[42] As explained in Section II(C)(3) *supra*, Alexis was never diagnosed with ADEM. The diagnostic criteria require either histopathological findings, or specific clinical manifestations plus an MRI demonstrating demyelination. *See* J. Sejvar, et al., *Encephalitis, myelitis, and acute disseminated encephalomyelitis (ADEM): Case definitions and guidelines for collection, analysis, and presentation of immunization safety data,* VACCINE 25:5771-92, 5778-79 (2007) ["Sejvar"], filed as Res. Ex. C, Tab 6; W. Huynh, et al., *Post-vaccination encephalomyelitis: Literature review and illustrative case*, J. CLIN. NEUROSCI. 15: 1315-22, 1319 (2008) ["Huynh"], filed as Pet. Ex. 14. Doctor Lopez agreed that the lack of an MRI precluded an ADEM diagnosis. Tr. at 32.

[43] Pet. Ex. 11, filed Dec. 10, 2010, at 1. His supplemental report equated ADEM with post-vaccination encephalopathy. Pet. Ex. 16, filed Feb. 3, 2011, at 1.

[44]Doctor Lopez characterized Alexis's loss of balance and unsteady gait as "ataxia," which he defined as "incoordination." Tr. at 31-32. Ataxia is among the presenting symptoms for ADEM, and may reflect some degree of neurological impairment or encephalopathy. *See* M. Stonehouse, et al., *Acute disseminated encephalomyelitis: recognition in the hands of general paediatricians*, ARCH. DIS. CHILD 88:

loss of consciousness that precipitated her presentation to the urgent care center, I find that her condition was never as severe as Dr. Lopez suggested and thus that his diagnosis of an acute encephalopathy is incorrect.

I base this conclusion on Alexis's clinical course during her hospitalization, the treatment she received, the observations of the treating physicians, and the opinions of Drs. Bingham and Wiznitzer, which are well-supported by the medical literature filed. I rely heavily on the medical records prepared by Alexis's treating physicians and nursing notes in determining the nature and severity of Alexis's symptoms during her hospitalization. *Andreu v. Sec'y, HHS,* 569 F.3d 1367, 1376 (Fed. Cir. 2009). Treating physicians and other health care providers are also in the best position to observe subtle signs and symptoms that may not be fully elucidated in the records. Here the records clearly reflect that Alexis, while quite irritable at times, was neurologically normal on every examination performed.

As Dr. Lopez acknowledged, during Alexis's stay in the PICU, there were no signs of seizure activity or abnormal neurologic status. Tr. at 49. After less than 18 hours of observation there, she was transferred to a regular pediatric ward. A neurologist who treated her found "no overt neurologic appearance" to Alexis's symptoms and characterized her as having "normal mentation." Pet. Ex. 3, p. 58. Doctor Lopez explained that this meant Alexis's behavior and interaction with her environment were normal. Tr. at 49, 52. Alexis was discharged in what Dr. Bingham called a "normal neurologic state" about 24 hours after her transfer to the regular pediatric ward. Tr. at 83; Pet. Ex. 3, pp. 84-85.

While hospitalized, Alexis received antibiotics, but she did not receive any treatment commonly administered to children with ADEM or other autoimmune encephalopathies. ADEM treatment is predicated on its probable autoimmune origin. It involves administration of steroids such as methylpredisolone, plasma exchange, and intravenous immunoglobulins. Mihai & Jubelt, Pet. Ex. 12, at 444. Alexis received none of these treatments.

122-24, 122 (2003), filed as Pet. Ex. 19. Doctor Lopez relied on the descriptions in the medical records regarding loss of balance and unsteady gait as evidence for his conclusion that Alexis was experiencing an acute encephalopathy. *See* Tr. at 48, 52. On the other hand, Dr. Bingham indicated that Alexis's unsteadiness on the evening of March 11 and morning of March 12 might well have been caused by the two doses of morphine and the Ativan she received on the evening of March 11, 2007. Tr. at 81. Doctor Lopez agreed that morphine could cause unsteadiness, but thought that the morphine would have left her system fairly quickly. Tr. at 51. Doctor Bingham disagreed. Tr. at 80-81. It is noteworthy that Alexis was not described as having any unsteadiness or ataxia in the afternoon of March 12 and was walking normally on March 13, the date of her hospital discharge, lending some support to Dr. Bingham's testimony. Furthermore, the two times she lost her balance in her crib in the PICU, she was upset and crying. The unsteady gait she experienced in the hospital was slight and only occurred on the morning of March 12 and was thus not persistent or sustained. Pet. Ex. 3, pp. 62, 149. However, Alexis was reported to have had some unsteadiness in walking on March 11, before administration of the morphine. *See id.*, p. 66.

Although ADEM was considered as a possible diagnosis at points during her hospitalization (*see* Pet. Ex. 3, pp. 48, 58, 60-61, 76), she was never diagnosed with it. She was never diagnosed with an encephalopathy of any type by her treating physicians, who included a pediatric neurologist and a pediatric intensive care specialist. There were a number of references by treating physicians regarding Alexis's normal neurological examinations and her interaction with her mother and others, and the lack of meningismus. *See, e.g.*, Pet. Ex. 3, pp. 75-77, 80, 149.

Respondent's experts convincingly explained why no diagnosis of an acute encephalopathy was made. Doctor Bingham testified that Alexis's clinical presentation during her hospitalization was inconsistent with ADEM or encephalomyelitis. Both of these conditions present with a sustained decrease in responsiveness, hemiparesis, vision changes, and possibly seizures. Alexis did not present with a sustained altered mental status or decreased responsiveness. *See* Tr. at 81-82, 100-01; Sejvar, Res. Ex. C, Tab 6, at 5776, 5778 (defining encephalopathy as "depressed or altered level of consciousness, lethargy, or personality change lasting > 24h[ours]").[45] Doctor Bingham emphasized the 24-hour requirement, noting that Alexis had only transient symptoms. *See* Tr. at 81-82. Doctor Wiznitzer also indicated that Alexis had only a transient impairment of consciousness, not lethargy, stupor, or coma persisting for more than 24 hours. Tr. at 149.

Other than the probable loss of consciousness observed by petitioner on March 11 and Alexis's initial presentation at the urgent care center, Alexis appeared to be fully conscious throughout her waking hours during the period from March 11-13, 2007. Although Dr. Wiznitzer's report reflected that a loss of consciousness qualified as an encephalopathy, he explained during his testimony that Alexis's loss of consciousness at home was temporary and brief and therefore did not constitute an acute encephalopathy. Res. Ex. C at 7; Tr. at 164, 171-72.

None of the other evidence petitioner filed supports Dr. Lopez's assertion that Alexis experienced an acute encephalopathy. Petitioner's medical journal articles provide useful background information on ADEM's clinical presentation, sequelae, presumed causes, and treatment. However, they primarily serve to cement the conclusion that Alexis did not have ADEM or any form of encephalomyelitis. At best, the medical journal articles filed by petitioner establish that Alexis had some symptoms

[45] The Sejvar article, Res. Ex. C, Tab 6, was co-authored by Dr. Wiznitzer. It represents consensus definitions formed by a diverse group of health care professionals as part of the Brighton Collaboration. The mission of the Collaboration includes developing and publishing case definitions used in research worldwide regarding adverse events following immunization. The definitions developed are endorsed by the World Health Organization, and are recommended for use by the U.S. Food and Drug Administration and the Centers for Disease Control and Prevention. *See* https://brightoncollaboration.org/public/what-we-do/standards/case-definitions.html (last visited Sept. 28, 2012). The Sejvar article describes the clinical manifestations of ADEM as including global cerebral dysfunction, multifocal neurologic findings, and meningismus. Res. Ex. C, Tab 6, at 5775.

consistent with ADEM at the time of her hospitalization, most notably altered mental status and possible ataxia, but none of those symptoms were present on a sustained basis. Even her irritability and altered gait were intermittent, not sustained over time.

Based on the record as a whole, I find inadequate evidence from which to conclude that Alexis suffered an acute encephalopathy during March 11-13, 2007, and therefore reject Dr. Lopez's attempt to re-diagnosis Alexis's condition as an acute encephalopathy.

2. Alexis's Condition between March 13 and August 20, 2007.

Assuming, arguendo, that Alexis did experience an acute encephalopathy during her hospitalization, Dr. Lopez's theory of an acute insult that persisted is at odds with Alexis's normal neurological condition at the time of her hospital discharge and her condition when seen a few days after her hospitalization at her primary care physician's office. Doctor Lopez's theory is even more difficult to reconcile with her parent's gradual recognition of developmental delays over the ensuing five months between visits to her primary health care provider. The descriptions of Alexis's behavior at the August 20, 2007 sick child appointment, the August 30, 2007 DAN! visit, and in the questionnaire completed for the DAN! visit are simply not consistent with a persisting encephalopathic state during the five months after Alexis's discharge from the hospital.

At the March 20, 2007 post-hospitalization visit, Alexis was described as lethargic and irritable, but consolable. Her mother reported she had been experiencing intermittent fever, with temperatures as high as 102.5°.[46] Notably, there were no notes indicating an encephalopathic state, and none prescribing treatment or recommending an immediate return to the hospital. Although Ms. Henderson indicated that she would keep the scheduled MRI and follow up appointments at CMC, she failed to do so. This suggests that Alexis was not manifesting encephalopathic symptoms in the first weeks after her discharge from CMC, as a caring and concerned parent would likely seek medical treatment for persisting neurological symptoms consistent with an encephalopathy.

The next time Alexis saw a doctor, she had a runny nose. That August 20, 2007 visit was an "Acute Office Visit," one requested to deal with an acute illness. Symptoms consistent with autism were listed secondarily on the complaints/concerns section of the notes.

In the questionnaire completed for the follow up August 30, 2007 DAN! visit, Ms. Henderson did not describe a sustained encephalopathic state. Rather, she listed

[46] I have no reason to doubt that Alexis experienced a fever the evening of March 19, 2007, before she was brought to her primary care provider, but, in view of the normal temperatures recorded in the hospital, I cannot credit the report of intermittent fevers occurring during the time she was hospitalized. Her temperature was normal on admission and normal throughout her hospital stay.

individual symptoms and various time frames when she first noticed or became concerned about them. Ms. Henderson noted Alexis's failure to progress in language development, rather than any loss of language. Based on the questionnaire, it appears that Ms. Henderson became concerned about language when Alexis was 16-17 months of age, placing the onset of her concern within one to two months of the March hospitalization. However, the medical records and histories contained in the records reflect that Alexis's vocabulary had not improved since she was nine months old, when she was reported to babble three words (Nana, Mama, and Dada). Pet. Ex. 4, p. 3. During her hospitalization at fifteen months of age, her mother indicated that Alexis had one or two words, although a checklist on a hospital form reflects that Alexis had between three and six words.[47] I place more reliance on the detailed history Ms. Henderson provided to Dr. Eaker, in which Ms. Henderson indicated that Alexis had one to two words (Pet. Ex. 3, p. 79), but even accepting the checklist as an accurate reflection of her vocabulary, Alexis had about as many words at 15 months as she spoke at 9 months of age (*id.*, p. 98).

Even if I accept the checklist entry as more accurate than the detailed history, Alexis had between three and six words during her hospitalization. At the time of the DAN! visit, Alexis only spoke two understandable words. Thus, it appears that Alexis's language development had not improved much, if at all, between nine and fifteen months of age, and it did not improve after her hospitalization. She spoke just a few words at 9, 15-17, and 20 months of age.

None of these records indicates the existence of a persistent encephalopathic state or a static encephalopathy during the five months between Alexis's Prevnar vaccination and her first autism evaluation by Dr. Kanelos. The record of the initial DAN! visit notes a possible seizure six days after the vaccination, but a normal EEG. The record does not reflect any concerns that Alexis's behavior had altered after her March vaccination and illness, nor does it describe any continuing or persisting symptoms consistent with an encephalopathy. Doctor Kanelos noted "? autistic characteristics," rather than describing any specific behaviors he observed. Pet. Ex. 4, pp. 20-21.

Based on the DAN! questionnaire, I conclude that Alexis had, at a time prior to her hospitalization, some behaviors consistent with a diagnosis of autism. Toe walking, the failure to develop additional language, and her picky eating and aversion to certain food textures, all symptoms listed on the questionnaire, are symptoms that children with ASD often display. Tr. at 128-31. While not sufficient for a diagnosis of autism or PDD-NOS, they nevertheless suggest the subtle and insidious onset of ASD at a time prior to the allegedly causal vaccine.

[47] It is unclear whether hospital staff or Ms. Henderson completed the form.

3. Current Diagnosis: Static Encephalopathy or Autism Spectrum Disorder?

Although Dr. Lopez testified unequivocally that vaccines do not cause autism (Tr. at 33), he opined that Alexis's Prevnar vaccine nevertheless caused her pervasive developmental delay. He explained away this apparent conflict by defining her condition as a "static encephalopathy" resulting from an acute encephalopathy, not autism. Tr. at 30-31. However, he was unable to explain how the clinical appearance of this static encephalopathy could be distinguished from autism, except by reference to a temporally related neurological event. Tr. at 65-66. He believed it reasonable to conclude that when a child displays signs and symptoms of a neurologic injury after a vaccination, and goes on to develop other neurological problems, such as Alexis displays (referring to her cognitive and behavioral problems), then the earlier event caused the subsequent problems. *Id*. He testified that what distinguished Alexis's case from autism was "the distinct temporal relationship and what happened immediately after the vaccines." Tr. at 66.

Based on the medical records, testimony, and medical literature, I conclude that Alexis was properly diagnosed with an autism spectrum disorder. It is not necessary to conclude whether the precise diagnosis is autism or PDD-NOS,[48] as both diagnoses are contained in the umbrella terms "pervasive developmental disorder" and "autism spectrum disorder."

a. Diagnosing Autism.

There are no biochemical tests diagnostic of autism. *See* S. Spence, et al., *Autism Spectrum Disorder: Screening, Diagnosis, and Medical Evaluation*, SEMIN. PEDIATR. NEUROL. 11: 186-95, 191 (2004) ["Spence"], filed as Res. Ex. C, Tab 2. Behavioral symptoms qualitatively different from those displayed by typically developing children are used to make an ASD diagnosis. A diagnosis of an autism spectrum disorder requires that a child display "severe and pervasive impairments in several areas of development: reciprocal social interaction skills, communication skills, or the presence of stereotyped behavior, interests, and activities." DSM-IV-TR, Res. Ex. C, Tab 1, at 69.

To be diagnosed with autistic disorder, symptoms must include qualitative impairments in six of 12 behavioral functions, with at least two in the social interaction domain, at least one in the communication domain, and one in the restrictive and stereotyped behavior, interests, or activities domain. DSM-IV-TR, Res. Ex. C, Tab 1, at 75. Delays or abnormalities in functioning in either social interaction, language use in

[48] In his report, Dr. Bingham indicated that Alexis had PDD-NOS. Res. Ex. A at 4. Doctor Wiznitzer testified that Alexis fully met the diagnostic criteria for autism. Tr. at 138, 140-44. He also explained that discrepancies among evaluators in placing children in specific diagnostic categories within the autism spectrum were one of the problems that the new DSM-V was designed to correct. Tr. at 132-34.

social communication, or symbolic or imaginative play must occur before a child is three years old for an autism diagnosis. *Id.*

A diagnosis of PDD-NOS is made when there is a severe and pervasive impairment in the social interaction domain, plus at least one impairment in either the communication or restrictive/stereotyped behavior domain. DSM-IV-TR, Res. Ex. C, Tab 1, at 84; Spence, Res. Ex. C, Tab 2, at 188.

b. Diagnosing Alexis's Condition.

Doctor Wiznitzer, the witness with the most expertise in diagnosing autism spectrum disorders, opined that Alexis was appropriately diagnosed with an autism spectrum disorder. Tr. at 138. Doctor Bingham concurred. Tr. at 85. Doctor Wiznitzer provided a detailed recitation of the behavioral symptoms leading to his conclusion. *See* Tr. at 140-48 (highlighting points from Alexis's evaluations, such as her not noticing visitors, avoidance of eye contact, lining objects up on the floor, having limited play skills, and an obsession with certain TV shows, and associating them with specific aspects of the DSM-TR-IV diagnostic criteria). A comparison of his testimony to the diagnostic criteria reflects that Alexis had the requisite behavioral symptoms to warrant the autism diagnosis. His assessment coincided with the diagnostic testing performed in May 2008 by personnel with the Mecklenburg County Children's Developmental Services. The CARS diagnostic test placed Alexis in the "severely autistic" range, not in the borderline area.

c. Problems with Dr. Lopez's Rediagnosis of Alexis.

Doctor Lopez's opinions reflect a fundamental misunderstanding of autism. In his report, Dr. Lopez asserted, without support, that if another cause for autistic symptoms is present, an autism diagnosis is not appropriate.[49] Quite simply, Dr. Lopez is wrong. As Dr. Wiznitzer pointed out, the DSM-IV-TR itself indicates than an autism diagnosis should be made, even when another co-morbid condition contributes to or causes autism.[50] Tr. at 137-38. The DSM-IV-TR states: "The Pervasive

[49] Doctor Lopez asserts that the term "autism" should be used only when the cause for a person's pervasive development delay is unknown. As an example, Dr. Lopez asserted that individuals with tuberous sclerosis should not receive an autism diagnosis, even if they have symptoms consistent with an autism diagnosis. Pet. Ex. 16 at 1. The DSM itself indicates otherwise, indicating that autism may be observed in association with other medical conditions, which should be noted on Axis III. DSM-IV_TR, Res. Ex. C, Tab 1, at 72. Axis III of the diagnostic assessment used in the DSM reflects physical conditions that may impact on Axis I disorders. *See* Tr. at 133. Doctor Wiznitzer emphatically disagreed with Dr. Lopez's assertion that autism should be diagnosed only when no other reason for the condition can be found. Tr. at 137-38.

[50] There are two exceptions contained in the DSM-IV-TR. An autism diagnosis is not made when a diagnosis of Childhood Disintegrative Disorder or Rett's Disorder is more appropriate. DSM-IV-TR, Res. Ex. C, Tab 1, at 75. Both of these diagnoses appear in the same chapter (Pervasive Developmental Disorders) of the DSM as autism.

Developmental Disorders are sometimes observed with a diverse group of other general medical conditions (e.g., chromosomal abnormalities, congenital infections, structural abnormalities of the central nervous system). If such conditions are present, they should be noted on Axis III." DSM-IV-TR, Res. Ex. C, Tab 1, at 69-70. It also indicates that autism "is sometimes observed in association with a neurological or other general medical condition (e.g., fragile X syndrome and tuberous sclerosis)." *Id.*

Several of Dr. Wiznitzer's own peer reviewed publications involve explorations of co-morbid diagnoses of tuberous sclerosis and ASD. *See, e.g.,* M. Wiznitzer, *Autism and Tuberous Sclerosis*, J. CHILD. NEUROL. 19: 675-79 (2004), filed as Res. Ex. C, Tab 3. *See also* Spence, Res. Ex. C, Tab 2, at 188 ("Because the clinical nature of the diagnostic criteria does not preclude a diagnosis of ASD in the presence of other neurologic or genetic conditions, it is often important to provide the ASD diagnosis (in addition to their other condition) in cases where specific autism-related services could improve a patient's functional status.")

Ultimately, Dr. Lopez's testimony was based on his own unsupported and unique opinions. He acknowledged the lack of support for his theory that could connect an acute encephalopathy, followed by normal mentation, to the later development of a pervasive developmental disorder. Tr. at 71. There was likewise no support for Dr. Lopez's assertion that a static encephalopathy could mimic autism, but not actually be autism. In contrast, Drs. Bingham and Wiznitzer provided considerable support for their testimony that Alexis was correctly diagnosed with an ASD. I find that Alexis has an ASD, not some unspecified encephalopathy that mimics one.

4. Prevnar and Molecular Mimicry.

Even if I resolved all of three of the foregoing factual disputes regarding Alexis's diagnoses in favor of Dr. Lopez's assertions, there still exists a fundamental factual problem with Dr. Lopez's causation theory. Doctor Lopez asserted that Prevnar could cause ADEM via molecular mimicry, and that it could therefore cause a similar neurological condition in Alexis by the same biological process. If the molecular mimicry aspect of the medical theory is fallacious, then petitioner has failed to establish that Prevnar could be responsible for her hospitalization, and Dr. Lopez's causal chain breaks down at the first postulated link.

Doctor Lopez opined that Alexis's March 2007 illness reflected an autoimmune process triggered by molecular mimicry between components of her central nervous system and components of the Prevnar vaccine.[51] The factual underpinning for his

[51] He testified:

> Q: Now, in your report, you said that the biological mechanism for this is molecular mimicry?
>
> A: That's correct. [….]

theory is lacking, as the composition of the Prevnar vaccine precludes the causal mechanism postulated.

Doctor Lopez provided a very general explanation for how pathogens or vaccines cause ADEM. Tr. at 59-60. The medical literature petitioner filed indicates that molecular mimicry is considered the most likely causal explanation for ADEM. *See, e.g.*, Huynh, Pet. Ex. 14, at 1315-16 ("[t]he presumptive mechanism is immune-mediated demyelination, although immune-complex mediated vasculopathy has also been postulated"). A review of the other medical journal articles filed by petitioner indicates that the molecular mimicry theory is often cited as the probable method by which pathogens and vaccines cause ADEM.[52] *See, e.g.*, Mihai & Jubelt, Pet. Ex. 12, at 441; T. Menge et. al., *Acute Disseminated Encephalomyelitis*, ARCH. NEUROL. 62: 1673-1680 (2005), filed as Pet. Ex. 18, at 1675. Doctor Lopez asserted that Prevnar caused Alexis's acute encephalopathy by the same mechanism. *See* Pet. Ex. 16 (Petitioner's Supplemental Expert Report) at 1-2.

However, none of the filed medical literature connected Prevnar and ADEM via molecular mimicry.[53] A brief explanation of molecular mimicry is necessary to explain why Prevnar has not been so linked.

Molecular mimicry occurs when a pathogen or vaccine component shares amino acid sequences with a protein found in the central nervous system of the host. The sharing of amino acid sequences is known as homology. Homology may result in the cross activation of antigens not only against the pathogen or vaccine component, but against the host tissue as well. If these autoreactive cells enter the central nervous

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Q: So were you saying this was autoimmune in nature?

A. I would say so, yes.

Q: Is it an ongoing process? Does Alexis still have an autoimmune disease?

A. Well, this happens once. The child is exposed to this foreign protein. There is this theory of the molecular mimicry, but it's not continuously happening. It doesn't happen the rest of the child's or the individual's life. It happens then and there. The child has that acute insult, and what we're looking at now is the consequences of that.

Tr. at 59-60.

[52] There are other theories as well, although petitioner did not advance them. Vaccines that contain or were developed using central nervous system tissue are more likely to be causally associated with ADEM than vaccines that do not. Menge, Pet. Ex. 18, at 1675; Huynh, Pet. Ex. 14, at 1318. This suggests that the central nervous system components in vaccines are responsible for provoking the autoimmune response.

[53] Although Dr. Lopez testified that the Prevnar vaccine has been linked in medical literature as causal of ADEM and indicated that he would supply the citation to the court (*see* Tr. at 60-61), he failed to do so.

system, and encounter the homologous protein in the myelin (a substance that coats parts of nerve cells much like insulation coats electrical wires), an autoimmune reaction can occur, resulting in damage to the myelin sheaths. Huynh, Pet. Ex. 14, at 1318. This demyelination produces the MRI findings used to diagnose ADEM.[54]

There are numerous problems with Dr. Lopez's molecular mimicry theory of causation. The first, and most fundamental, is that the Prevnar vaccine does not contain any proteins or amino acids, and thus cannot be homologous with protein or amino acid sequences found in the central nervous system. Tr. at 79 (testimony of Dr. Bingham); *see also* PHYSICIAN'S DESK REFERENCE ["PDR"] (61st ed. 2007), at 3463. Prevnar is a sterile solution of polysaccharides (sugars) derived from the coating of seven strains of pneumococcal bacteria, attached to a diphtheria toxoid, and including an aluminum adjuvant. It contains no viral or bacterial proteins or amino acids. PDR at 3463; Tr. at 152-53. In the absence of any evidence to the contrary regarding the nature of this vaccine, molecular mimicry is unavailing as a theory of causation.[55]

5. Use of Expert Opinions in Determining Facts.

In concluding that petitioner has failed to establish the factual predicates for her causation theory, I have weighed and evaluated the experts' opinions, applying the factors identified in *Daubert v. Merrell Dow Pharmaceuticals, Inc*., 509 U.S. 579 (1993).

In Vaccine Act cases, special masters are frequently confronted by expert witnesses with diametrically opposed positions. When experts disagree, many factors influence a fact-finder to accept some testimony and reject other contrary testimony. As the Federal Circuit noted, "[a]ssessments as to the reliability of expert testimony often turn on credibility determinations, particularly in cases . . . where there is little supporting evidence for the expert's opinion." *Moberly v. Sec'y, HHS*, 592 F.3d 1315, 1325-26 (Fed. Cir. 2010). Objective factors, including the qualifications, training, and experience of the expert witnesses; the extent to which their proffered opinions are supported by reliable medical research and other testimony; and the factual basis for their opinions are all significant factors in determining what testimony to credit and what to reject.

[54] ADEM produces perivenous demyelination in the brain and infiltration of lymphocytes and macrophages. Sejvar, Res. Ex. C, Tab 6, at 5775. The demyelination is observable on MRI. The Mihai & Jubelt article indicated that the underlying infection and a secondary autoimmune response cause the central nervous system demyelination. Pet. Ex. 12 at 441.

[55] Vaccines prepared using central nervous system ["CNS"] tissue (specifically, one type of rabies vaccine) have been suspected of causing ADEM via molecular mimicry. Huynh, Pet. Ex. 14, at 1317. Although Dr. Lopez did not specifically assert this theory, he acknowledged during cross-examination that the Prevnar vaccine was not manufactured using CNS tissue, and that the manufacturing process for Prevnar did not permit CNS contamination. Tr. at 60.

All three experts in this case are board certified pediatric neurologists and thus possess the requisite qualifications to opine in a case of this nature. However, there were significant differences in their expertise in diagnosing and treating children with neurological disorders, including autism spectrum disorders. In general, I found respondent's experts to be more qualified to opine, and their opinions to be consistent with those of the treating physicians and better supported by the medical literature and the medical records filed in this case. I note that both Drs. Bingham and Wiznitzer have considerable experience in diagnosing and treating autism spectrum disorders; Dr. Lopez does not diagnose ASDs and no longer treats patients with ASDs. Tr. at 63, 76, 125. Additionally, Dr. Wiznitzer has a special qualification in neurodevelopmental disabilities, and frequently teaches, writes, and lectures about autism spectrum disorders. *See* Tr. at 120-27. Doctor Bingham has diagnosed and treated ADEM and similar disorders and about 15% of his patients have ASDs. Tr. at 76.

When one of the questions before the court is whether a diagnosis of an autism spectrum disorder is correct, experts who are familiar with making such diagnoses have a significant advantage. I have thus relied more heavily on the testimony and expert reports provided by Drs. Bingham and Wiznitzer than those provided by Dr. Lopez.

III. Law and Analysis.

Because the factual underpinning for Dr. Lopez's causation theory is absent, rendering his theory unreliable per se, it is unnecessary to examine the *Althen* factors in depth in this case. However, a brief analysis is provided.

A. Law Governing Off Table Causation Cases.

In a Vaccine Act case, a petitioner is not required to establish identification and proof of specific biological mechanisms, as "the purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof of how vaccines affect the human body." *Althen*, 418 F.3d at 1280. The petitioner does not have to show that the vaccination was the sole cause, or even the predominant cause, of the injury or condition; showing that the vaccination was a "substantial factor"[56] and a "but for" cause of the injury are sufficient for recovery. *Shyface*,165 F.3d at 1352; *see also Pafford v. Sec'y, HHS,* 451 F.3d 1352, 1355 (Fed. Cir. 2006) (petitioner must establish that a vaccination was a substantial factor and that harm would not have occurred in the absence of vaccination).

[56] The Restatement (Third) of Torts has eliminated "substantial factor" in the factual cause analysis. § 26 cmt. j (2010). Because the Federal Circuit has held that the causation analysis in Restatement (Second) of Torts applies to off-Table Vaccine Act cases (*see Walther v. Sec'y, HHS*, 485 F.3d 1146, 1151 (Fed. Cir. 2007); *Shyface v. Sec'y, HHS,* 165 F.3d 1344, 1352 (Fed. Cir. 1999), this change does not affect the determination of legal cause in Vaccine Act cases: whether the vaccination is a "substantial factor" is still a consideration in determining whether it is the legal cause of an injury. *See Stone v. Sec'y, HHS,* 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[T]he causation standard in off-Table Vaccine Act cases is to be applied consistently with the principles set forth in the Second Restatement of Torts.").

Although a petitioner cannot be required to show "epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect,"[57] when petitioner files medical literature, a special master may weigh and evaluate that medical literature. When the filed literature fails to support the medical theory alleged, it can be an important factor in determining whether petitioner has met her burden to show vaccine causation. Causation is determined on a case by case basis, with "no hard and fast *per se* scientific or medical rules." *Knudsen v. Sec'y, HHS,* 35 F.3d 543, 548 (Fed. Cir. 1994). Close calls regarding causation must be resolved in favor of the petitioner. *Althen*, 418 F.3d at 1280; *but see Knudsen*, 35 F.3d at 550 (when evidence is in equipoise, the party with the burden of proof fails to meet that burden).

B. Analysis of the *Althen* Factors.

1. The Medical Theory Advanced is Unreliable.

Althen requires that a petitioner in an off-Table causation case present a reliable medical theory by which a vaccine can cause the injury in question. *Althen*, 418 F.3d at 1278. This first prong of *Althen's* three part causation test has also been characterized as the equivalent of the "Can it cause?" inquiry used in toxic tort litigation. *See Pafford v. Sec'y, HHS*, No. 01-165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004), *aff'd*, 64 Fed. Cl. 19 (2005), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2006).

The medical theory must be a reputable one, although it need only be "legally probable, not medically or scientifically certain." *Knudsen,* 35 F.3d at 548-49. The Supreme Court's opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, likewise requires that courts determine expert opinions to be reliable before they may be considered as evidence. "In short, the requirement that an expert's testimony pertain to 'scientific knowledge' establishes a standard of evidentiary reliability." 509 U.S. 579, 590 (1993) (footnote omitted). The Federal Circuit has stated that a "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly,* 592 F.3d at 1324.

Separate and apart from the predicate factual issue regarding Prevnar's composition addressed above, two other reasons compel a rejection of Dr. Lopez's molecular mimicry theory. First, Dr. Lopez acknowledged that he was unaware of any homology between the components of the Prevnar vaccine and central nervous system tissue that could occasion an autoimmune attack on the brain. Tr. at 60. Second, Dr. Lopez's theory was based on the commonly cited connection between ADEM and viral and bacterial illnesses and some vaccines. Relying on evidence that ADEM can be

[57] *Capizzano v. Sec'y, HHS,* 440 F.3d 1317, 1325 (Fed. Cir. 2006).

caused by some vaccinations, Dr. Lopez asserted that the Prevnar vaccine can cause ADEM, too.

However, the literature actually filed does not indicate that the Prevnar vaccine is causally associated with ADEM, nor with any ADEM-like encephalopathic condition. Although petitioner's medical journal articles support the proposition that ADEM is associated with viral infections, viral vaccines, and some bacterial infections, none of the articles mention the Prevnar vaccine or the natural strains of strep pneumonia bacteria from which the vaccine is derived as causally associated.

Furthermore, Dr. Wiznitzer testified that the type of bacterial infections the Prevnar vaccine protects against have not been causally associated with ADEM. He explained that if the natural bacterial infections do not provoke post-infectious encephalopathy, it would not make biological sense to conclude that a vaccine derived from these bacteria could do so. He was unaware of any medical literature indicating that the Prevnar vaccine could or did cause a post-vaccine encephalopathy. Tr. at 152-53. Doctor Bingham testified similarly. Tr. at 78-79.

Petitioner's Exhibit 14 (Huynh), which focuses on post-vaccination encephalomyelitis, is illustrative. It discusses the vaccines associated with the development of ADEM. Huynh at 1316. Prevnar is not listed. Even with regard to the listed vaccines, the authors carefully distinguish "associated with" from "caused by." *Id.* at 1317; *see also* Sejvar, Res. Ex. C, Tab 6, at 5772.

According to another article filed by petitioner, ADEM is only rarely associated with vaccines, primarily those made using neural tissue such as some versions of the rabies vaccine. Vaccines prepared from whole, killed organisms (pertussis and influenza) may cause reactions, but recovery is usually without sequelae. Vaccines prepared from live attenuated organisms can cause neurologic allergic reactions including encephalomyelitis, but at much lower rates than for natural infection. Mihai & Jubelt, Pet. Ex. 12, at 441. Prevnar falls into none of these categories. In summary, petitioner's exhibits do not support Dr. Lopez's assertion that Prevnar is causally linked to ADEM.

2. Lack of a Logical Connection.

Assuming, arguendo, that the vaccine was somehow responsible for the March 2007 illness, there is nothing in this record except Dr. Lopez's sincerely held opinions to connect that illness to Alexis's subsequent developmental and behavioral problems. Several factors militate against a logical connection between her March illness and symptoms diagnostic of autism.

The first is that Alexis experienced some of the symptoms present during her hospitalization prior to the allegedly causal vaccine. Ms. Henderson reported significant

irritability and “pain” behavior as present before her Prevnar vaccination. Pet. Ex. 4, p. 12.

Second, Alexis experienced something of a plateau in her language development between her nine-month well child visit and her hospitalization. Alexis had about three words at nine months of age, and had about the same number, per parental report, during her hospitalization. She had only a few words at 16-17 months of age, again, per parental report.

Third, as respondent’s experts pointed out, Alexis recovered from whatever it was that prompted her hospitalization. Her condition on discharge from the hospital was significantly improved over her condition on admission, and in spite of her primary care provider urging her mother to keep the follow up appointment scheduled later in March 2007, Ms. Henderson did not take Alexis back for the MRI or to the neurologist’s appointment. That might represent her pique at the hospital for failing to find an answer for Alexis’s condition, but if Alexis was experiencing significant symptoms of an acute or static encephalopathy during this period, it is likely that her parents would have sought medical advice sooner than August, 2007. Neither the report at her August 20, 2007 primary care visit for a runny nose and “possible autism” nor the information contained in the questionnaire completed for the DAN! visit on August 30, 2007 convey a sense of urgency or mention a persistence of the symptoms that prompted her hospitalization.

Fourth, according to respondent’s experts, Alexis’s presentation over the months between her hospitalization and her diagnosis with autism was typical of the way autism presents. Furthermore, according to Dr. Wiznitzer, the witness with the most experience in diagnosing autism spectrum disorders, some of the behaviors consistent with an autism diagnosis (picky eating, toe walking, and sensitivity to noise) were present even before the March 2007 hospitalization, based on the questionnaire petitioner completed for the DAN! visit. *See* Tr. at 178-89; Pet. Ex. 24, pp. 11-13.

Finally, there was no evidence, other than Dr. Lopez’s unsupported opinion, that ADEM or a similar neurologic condition can mimic ASD. A special master is not required to accept the *ipse dixit* of an expert. *Snyder v. Sec’y, HHS*, 88 Fed. Cl. 706, 742-43 (2009), citing *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997). A severe case of ADEM may result in persistent neurological problems, but none of the many articles filed identified autism or similar symptoms as possible sequelae.

3. Proximate Temporal Relationship.

Once the scientific underpinning for Dr. Lopez’s molecular mimicry theory is removed by the unrebutted testimony and other evidence concerning the lack of proteins or amino acids in the Prevnar vaccine, only the temporal connection between the vaccine and Alexis’s March 2007 illness remains. Merely showing a proximate temporal connection between a vaccination and an injury is insufficient, standing alone, to establish causation. *Grant,* 956 F.2d at 1148. A proximate temporal relationship,

even when coupled with the absence of any other identified cause for the injury, is not enough to demonstrate probable cause under the Vaccine Act's preponderance standard. *Moberly*, 592 F.3d at 1323 (citing *Althen*, 418 F.3d at 1278). In this case, Dr. Lopez did not identify any specific medically appropriate timeframe between Prevnar vaccination and onset of acute encephalopathy or static encephalopathy.

C. Use of OAP Evidence.

At the hearing, petitioner's counsel objected to my consideration of any evidence from the OAP in determining entitlement. Tr. at 3-8. I did not rule on the objection at the time it was made, but at the conclusion of the hearing, I noted that petitioner had affirmatively requested that her case become part of the OAP on June 1, 2010. Tr. at 183. It was unnecessary, in this case, to rely on any material filed in the OAP test cases, thus I need not rule on petitioner's objection. I note, however, that I do not consider petitioner's objection, in view of her affirmative request to join the OAP, to be either well founded or timely made.[58]

IV. Conclusion.

In summary, Doctor Lopez's opinion consisted of the following causal chain: (1) the Prevnar vaccine can cause ADEM, a neurological injury; (2) this neurological injury occurs as the result of molecular mimicry; (3) the Prevnar vaccine caused Alexis to develop an acute encephalopathy akin to ADEM through a similar process; (4) an acute encephalopathy can become a static encephalopathy; (5) Alexis's acute encephalopathy developed into a static encephalopathy over the five months in 2007 between her March hospitalization and her August visit to her primary care provider, manifesting with autistic-like symptoms.

Doctors Bingham and Wiznitzer logically and effectively demolished each step of Dr. Lopez's causation theory. They explained why molecular mimicry was not a possible—let alone a probable—causal mechanism in this case, given the lack of any amino acids or proteinsin the Prevnar vaccine, and thus why Prevnar is not a likely cause for ADEM or a neurological condition similar to ADEM in cause and symptoms. They persuasively explained why Alexis was not diagnosed with an acute encephalopathy, post-vaccinal or otherwise, during her hospitalization. They established that the appropriate diagnosis for her current condition is an autism spectrum disorder, not the sequelae of ADEM or a similar neurological injury. Thus, the necessary factual predicates for Dr. Lopez's causation opinions were not established. As the Court of Federal Claims has noted, an expert's "conclusions . . . are only as good

[58] A more appropriate time for the objection would have been in February 2011, when I ordered respondent to file her expert report and identify any OAP evidence she intended to rely upon. Order (non-pdf), issued Feb. 7, 2011. Petitioner's counsel had another opportunity to raise an objection in May 2011, either during the status conference I held in this case or after I ordered respondent to identify any background autism spectrum evidence from the OAP. Order, issued May 18, 2011.

as the reasons and evidence that support them." *Davis v. Sec'y, HHS,* 20 Cl. Ct. 168, 173 (1990). *See also Perreira v Sec'y, HHS,* 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) ("An expert opinion is no better than the soundness of the reasons supporting it.") (citations omitted).

I conclude that petitioner failed to demonstrate any of the *Althen* factors by preponderant evidence. Petitioner has not demonstrated that Alexis's pervasive developmental delay was either caused in fact or significantly aggravated by the Prevnar vaccination she received on March 6, 2007. The petition for compensation is therefore DENIED. The clerk is directed to enter judgment accordingly.

IT IS SO ORDERED.

s/Denise K. Vowell
Denise K. Vowell
Special Master