In the United States Court of Federal Claims
OFFICE OF SPECIAL MASTERS
No. 12-312V

K.L.,	*	
	*	Filed: March 17, 2017
Petitioner,	*	
	*	Special Master Corcoran
v.	*	
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Decision; Human Papillomavirus ("HPV"); Epilepsy; Seizures; Cytokines.
	*	
Respondent.	*	
	*	

Paul Dannenberg, Huntington, VT, for Petitioner.

Robert Paul Coleman, U.S. Dep't of Justice, Washington, DC, for Respondent.

DECISION DENYING ENTITLEMENT[1]

On May 11, 2012, K.L. filed this action seeking compensation under the National Vaccine Injury Compensation Program (the "Vaccine Program"[2]). Petition ("Pet."), dated May 11, 2012 (ECF No. 1); Amended Pet., dated Mar. 11, 2013 (ECF No. 24). Petitioner alleges that she suffered a variety of injuries (including partial onset epilepsy, seizures, and migraine headaches) as a result of the human papillomavirus ("HPV") vaccine she received in February 2010. Amended Pet. at 1.

[1]This decision will be posted on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, Pub. L. No. 107-347, § 205, 116 Stat. 2899, 2913 (codified as amended, 44 U.S.C. § 3501 note (2006)). As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the published ruling's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen (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 in its current form. *Id.*

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3758 (codified as amended, 42 U.S.C. §§ 300aa-10 to 34 (2006)) [hereinafter "Vaccine Act" or "the Act"]. All subsequent references to sections of the Vaccine Act shall be to the pertinent subparagraph of 42 U.S.C. § 300aa (2006).

After considering the record as a whole, and for the reasons explained below, I find that Petitioner has failed to carry her burden in establishing causation, and therefore is not entitled to compensation under the Vaccine Program.

I. FACTUAL BACKGROUND

Early History and HPV Vaccinations

K.L. (born March 25, 1993) was a relatively healthy child for most of her early life. Throughout her childhood, however, she had recurring otitis media[3], anxiety disorder, reading difficulties, and a vasovagal attack with syncope.[4] Ex. 3 at 27-28, 34, 40-41, 145. In addition, K.L. has some family history of seizures, including three cousins on her father's side who experienced seizures at early ages—one of whom was formally diagnosed with epilepsy. Ex. 6 at 8. K.L.'s father had also once experienced a seizure after sleep deprivation. Ex. 3 at 150.

Petitioner routinely went to her primary care physician for yearly check-ups. At one such check-up on May 18, 2009, she received the first dose of the HPV vaccine, when she was 16. Ex. 2 at 1. She thereafter received the second and third doses of the HPV vaccine on August 18, 2009, and February 9, 2010, respectively. Ex. 2 at 4. The filed medical records reveal no complications or reactions to the first or second doses.

Onset of Seizures

On February 11, 2010 - two days after her third HPV vaccine dose - K.L. was transported by ambulance to the Copley Emergency Room ("ER") in Morrisville, Vermont, because of seizure activity and subsequent decreased mental status. Ex. 3 at 107. K.L.'s mother reported that before the seizure occurred she noticed K.L. having fine motor twitches in her right hand, followed shortly (within five minutes) by K.L. slumping over and hitting her head on a door handle. *Id*. K.L.'s mother then stated that she helped K.L. to the ground where "she had foaming at the mouth, was biting her tongue, and was somewhat blue around the mouth. This lasted about 4 minutes." *Id*. When the ambulance arrived a few minutes later, K.L. was conscious but confused, and had difficulty seeing what was in front of her. *Id.* Nonetheless, K.L. was able to help get herself onto the ambulance stretcher and was driven to Copley ER for evaluation, where she complained of a headache. *Id*.

[3] This recurrent condition resulted in K.L. having Sheehy PE tubes placed in her ears when she was about two and one-half years old (09/14/1995). Ex. 5 at 1. They fell out a year later and she had no further ear infections. Ex. 6 at 8.

[4] A vasovagal syncope is a transient vascular and neurologic reaction marked by pallor, nausea, sweating, bradycardia, and a rapid fall in blood pressure. It can result in loss of consciousness—and did for K.L. *Dorland's Medical Dictionary* 1818 (32nd ed. 2012) (hereinafter "*Dorland's"*).

K.L.'s intake report at Copley sets forth no underlying or concurrent symptoms - she had no fever, irregular heart rate, or respiratory distress. Ex. 4 at 52-53. She was noted to have an abrasion and swelling on the right side of her forehead, however, and K.L.'s mom reported that K.L. had recently had a cold. *Id*. at 52, 54. In fact, her mother informed initial treaters that prior to the seizure, K.L. had complained of ear pain, and received Benedryl and Sudafed at home. Ex. 3 at 107. K.L.'s doctor ordered a head and neck CT scan, CBC, and an EKG—all of which were normal.[5] Ex. 4 at 55.

K.L. was subsequently transported to Fletcher Allen Healthcare at the Vermont Children's Hospital ("FAHC"). Ex. 3 at 107. She was intubated and sedated, and treaters performed a lumbar puncture, MRI[6], and EEG. *Id.* K.L. was also evaluated for a central nervous system infection by looking at her cerebral spinal fluid ("CSF") testing from the lumbar puncture, but the results were negative. *Id*. She was treated with IV ranitidine for a stress ulcer prophylaxis.[7] *Id*. at 8. Two days after K.L. was initially sedated, she had her intubation tube removed, and she woke up and was transferred out of the pediatric intensive care unit. *Id*. Her doctors at this time proposed that the cause of her seizure was multi-factoral, "with potential contributors including a mild URI [upper respiratory infection], OTC pharmacotherapy with Benadryl and Sudafed, and recent HPV vaccine administration.[8]" *Id*. K.L. was discharged on February 13, 2010, and additional test results came back a few days later. Her MRI was normal, showing no signs of encephalitis, meningitis, or migrational anomaly or cerebral malformation, and her lumbar puncture was also normal. *Id*. at 113. Her EEG showed an impaired arousal mechanism, however. Ex. 12 at 16.

K.L. had a follow-up visit with her primary care physician, Dr. Melissa Volansky, on February 15, 2010. At that time, she complained of headaches, vomiting, nausea, and dizziness. Ex. 3 at 16. After examination, Dr. Volansky concluded that K.L.'s recent seizure had an unclear etiology, speculating that although it "may have been effect of recent Gardasil and/or decongestants," it could also simply reflect new onset epilepsy. *Id*. at 17. She confirmed prior determinations that there was no sign of infection or brain trauma on imaging; K.L. did have elevated prolactin[9] but pituitary imaging was normal. *Id*.

On February 27, 2010, K.L. returned to the FAHC ER after complaints of twitching, arm

[5]CT stands for computed tomography. *Dorland's* at 440. CBC is a complete blood count. *Id*. at 310. EKG is an electrocardiogram. *Id*. at 597.

[6] MRI stands for magnetic resonance imaging. *Dorland's* at 1184.

[7] Ranitidine inhibits gastric acid and can be used as a prophylactic (a preventive measure) for stress ulcers. *Dorland's* at 1592.

[8] OTC means over the counter medication. *Dorland's* at 1350.

[9] Prolactin is a hormone that stimulates and sustains lactation. *Dorland's* at 1524.

jerking, and leg buckling. Ex. 3 at 97. While there, K.L. experienced an observed generalized tonic clonic seizure, which was treated with 1000 mg of Keppra and lorazepam.[10] *Id*. It was noted at this visit that K.L. had been suffering from a stomach bug for the last few days, but she had experienced no other seizures or illness since her February 11, 2010 hospitalization. *Id*. K.L. was discharged on February 28, 2010 and began a regimen of Keppra 500mg, with the instruction to follow up with a pediatric neurologist. *Id*.

Evaluation of K.L.'s Condition

K.L. was seen for that follow-up appointment on March 22, 2010, with Dr. Louisa Kalsner. Dr. Kalsner noted that K.L. had been seizure-free since February 28, 2010, but had been experiencing some difficulty using her right hand and recalling certain words. Ex. 3 at 150. K.L. also complained of headaches that she believed may have begun following the receipt of the third dose of the HPV vaccine. *Id*. at 149-50. Dr. Kalsner did record that it was notable that K.L.'s first seizure was two days after she received the third dose of the HPV vaccine. *Id*. Dr. Kalsner concluded the visit by prescribing K.L. Ativan, and recommending that she increase her Keppra dosage to 750 mg. *Id*.

In order to gain more insight into the basis and nature of K.L.'s condition, K.L. next saw Dr. Annapurna Poduri, a neurologist and epileptologist, at Children's Hospital in Boston, Massachusetts, on June 1, 2010. Ex. 3 at 143. Dr. Poduri reviewed K.L.'s records and symptoms progression, taking note of the illness that had occurred around the time of her first seizure, as well as K.L.'s receipt of the third dose of the HPV vaccine two days prior. *Id*. at 143. Dr. Poduri's notes also record facts suggestive that K.L. might have, in retrospect, experienced some related symptoms that predated the third HPV dose. Thus, K.L. informed Dr. Poduri that she recalled experiencing a dead feeling in her arm after throwing a baseball or writing prior to her first seizure, although she did not state precisely when. *Id*. at 144. In addition, she noted that a hand-twitching episode she had experienced in April (as recalled by her mother) may have been similar to prior experiences at earlier times. *Id.* ("[s]he admits that she may have had episodes like that in the past").

Dr. Poduri wanted to conduct a more detailed MRI study to make sure K.L. did not have a small area of abnormality in her brain. Ex. 3 at 146. Moreover, Dr. Poduri stated "given her [K.L.'s] past history of reading difficulties and the association between periventricular heterotopia and reading abnormalities and epilepsy typically at this age, I think it would be worth a very careful look at the periventricular region for small focal heterotopia as well." *Id*. at146-47. Based on this overall examination, Dr. Poduri's initial conclusion about K.L.'s condition was that she had experienced a juvenile onset form of idiopathic partial onset epilepsy. *Id*. at 147. Dr. Poduri

[10] Keppra is the brand name of a prescription medication (levetiracetam) used in the treatment of seizures. *Dorland's* at 978, 1051. Lorazepam is used in the treatment of anxiety as a sedative agent. *Id*. at 1074

reasoned that this was the most likely diagnosis, given the medical facts, K.L.'s family history, and her otherwise normal development. *Id*. She did not attribute K.L.'s seizures to the HPV vaccine.

Petitioner was re-evaluated by Dr. Kalsner on June 22, 2010. Ex. 9 at 10. Dr. Kalsner noted that K.L. had been seizure free for four and one-half months and was doing well on Keppra. *Id*. Dr. Kalsner acknowledged that there had previously been "concerns" about the HPV vaccine's connection to the first seizure, although she did not (in this record) propose a relationship. *Id*. Her notes also stated her awareness that K.L. had been taken to see "an epileptologist in Boston" (Dr. Poduri), but that the write-up from that visit had not yet been provided to her (and hence her analysis did not reflect any of Dr. Poduri's more specialized views). *Id.* Dr. Kalsner stated that K.L. was scheduled to receive another MRI shortly thereafter. *Id*.

A few days later, on June 30, 2010, K.L. returned to Dr. Poduri, who performed and reviewed the more detailed MRI. Ex. 3 at 140. She stated that the MRI was "an excellent quality study that shows a structurally normal brain. No abnormalities were noted." *Id*. The MRI results allowed Dr. Poduri to more conclusively propose, as she had initially speculated, that K.L. had "partial onset epilepsy that appears to be truly idiopathic." *Id*.

K.L. had no subsequent seizure activity until January 2013, when her treating physicians attempted to reduce her dosage of Keppra in an effort to wean her off the medication. *See* Ex. 21 at 4. Because these efforts were unsuccessful, she was again placed on a higher dose of Keppra, and her seizures remained controlled thereafter. *Id*. Although K.L. remained seizure-free during this period, she began to have frequent headaches and vomiting. Ex. 3 at 129. She was diagnosed with migraines, prescribed medication, and her headaches began to gradually decrease in quantity and severity. *Id*. at 116. K.L. was also noted to have functional dyspepsia and gastroparesis, which was helped by eliminating dairy from her diet.[11] *Id*. at 19. In January 2012, K.L. was seen for complaints of anxiety and underwent a comprehensive educational evaluation due to difficulty she was experiencing in college. *Id*. at 3, *see generally* Ex. 17. K.L. was diagnosed with a language-based disorder of written expression, and advised to pursue tutoring along with a reduced course load. Ex. 7 at 12, 14. To help with her anxiety she was prescribed an anti-depressant and began seeing a psychiatrist. Ex. 3 at 6.

[11] Functional dyspepsia is the impairment of the power or function of digestion with no physical cause, usually resulting from nervousness or anxiety. *Dorland's* at 579. Gastroparesis is paralysis of the stomach, usually from damage to its nerve supply, so that food empties out more slowly. *Id*. at 765.

II. EXPERT TESTIMONY

Both sides offer their own neurologist expert. The opinions and testimony of the relevant experts are set forth below.

A. Dr. Beatrice C. Engstrand

Petitioner's expert, Beatrice C. Engstrand, M.D., provided an opinion for the theoretical causative role the HPV vaccine could play in seizures and other neurological conditions. She filed three expert reports in this case, and also testified at the hearing. *See* Ex. 23, filed on June 20, 2014 ("First Engstrand Rep."); Ex. 28, filed on December 12, 2014 ("Second Engstrand Rep."); Ex. 31, filed May 18, 2015 ("Third Engstrand Rep."); Transcript ("Tr.") at 6-42. In addition, after the hearing Dr. Engstrand filed an affidavit offering additional medical literature along with an explanation of their significance. *See* Ex. 40, filed on November 4, 2016 ("Engstrand Aff.").

Dr. Engstrand graduated from the Medical College of Pennsylvania in 1984 (after obtaining her bachelor's degree at Lehigh University). Ex. 24 at 4 (Dr. Engstrand's CV). She completed three residencies - one in medicine at the North Shore University Hospital, and two in neurology at The New York Hospital/Cornell Medical Center and SUNY Health Science Center. *Id*. at 3-4. Dr. Engstrand is board certified in neurology. *Id*. at 1. She currently works in private practice and is a Clinical Associate Professor of Neurology at the New York Medical College. *Id*. Her practice involves the treatment and evaluation of adolescents and adults who suffer from various forms of acute and chronic neurological conditions—20 percent of whom suffer from seizures. First Engstrand Rep. at 2, Tr. at 10. As she acknowledged at hearing, however, Dr. Engstrand lacks specialized expertise in the condition of epilepsy (whether in her education, or through research or study), other than from what she has learned from those patients she has seen with it. Tr. at 10.[12]

Dr. Engstrand opined that the HPV vaccine caused K.L.'s "persistent neurological sequelae, poor concentration, migraines, learning disorder, and seizure disorder." First Engstrand Rep. at 4. She initially proposed that the most likely mechanism for causation was "the release of the cytokine interleukin 1 beta in the course of the immune response to a[n] infectious agent such as a vaccine, [that] could in turn trigger a cluster of afebrile convulsions or seizures." *Id.* Specifically, she posited that this process created agitation in K.L.'s brain leading to right arm shaking and her generalized seizure. Tr. at 8.

In so opining, Dr. Engstrand relied on the fact that, as noted above, certain treater records initially included the third HPV vaccine dose in the differential diagnosis as a possible causative

[12] I also note that Dr. Engstrand is not an immunologist – although neither is Dr. Shinnar, for that matter. However, this lack of specific expertise on a matter relevant to the resolution of the case cuts more against Petitioner than Respondent, since Petitioner bears the initial, and ultimate, burden of proof. *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010).

factor. First Engstrand Rep. at 3. She also referenced a piece of literature involving observed adverse incidents from nearly 700,000 HPV vaccine doses given to females between the ages of 13 and 15 in Ontario, Canada from September 2007 to December 2011. T. Harris, *et al., Adverse Events Following Immunization in Ontario's Female School-Based HPV Program*, 32 Vaccine 1061, 1061-66 (2014), filed as Ex. 25 ("Harris"). Harris, however, specified only two instances of seizure following the HPV vaccine – and one involved an individual with a prior pediatric history of febrile seizures, as well as a pre-vaccination epilepsy diagnosis. Harris at 1063. Dr. Engstrand offered an additional article discussing autoimmune reactions to the HPV vaccine, although the article makes no reference to an autoimmune form of epilepsy (or any form, for that matter). P. Pellegrino, *et al., On the Relationship Between Human Papillomavirus Vaccine and Autoimmune Diseases*, 13 Autoimmunity Revs., 736, 736-41 (2014), filed as Ex. 27.

Dr. Engstrand's second report was aimed at addressing the informational categories identified in Special Master Moran's Order[13] pertaining to the use of expert reports as direct testimony, and therefore mostly responded to questions that the Order had indicated needed answers. *See generally* Second Engstrand Rep. Dr. Engstrand did, however, attempt to bulwark or add details to aspects of her opinion as expressed in her first report. Thus, she now emphasized that K.L. had displayed no seizure-like or other medical symptoms before her initial seizure on February 11, 2010. Second Engstrand Rep. at 1.

Dr. Engstrand also offered an additional article from a Spanish medical journal – M.A. Rodriguez-Galán, *et al., Adverse Reactions to the Human Papillomavirus Vaccine in the Valencian Community (2007-2011)*, 81 Anales Pediatria 303, 303-309 (2014), filed as Ex. 29 (the "Valencian Article"). The Valencian article was a retrospective study of reported adverse events (via a Spanish passive reporting system similar to the VAERS system[14] utilized in the United States) in a region of Spain after administration of 187,385 doses of the HPV vaccine to young females between September 2007 and December 2011. Valencian Article at 305. Out of 194 adverse reporting incidents reviewed, only six reported seizures – four of which were connected to syncope. *Id.* at 306-07.

In the spring of 2015, Dr. Engstrand filed her third report, which mainly sought to rebut points made by Respondent's expert, Dr. Shlomo Shinnar, in his report. Thus, she maintained that autoimmune-related epilepsy was more common than Dr. Shinnar allowed, and that it could manifest without evidence on an EEG and without a prior or concurrent fever. Third Engstrand

[13] As will be discussed in the procedural history section below, Special Master Moran presided over this case before it was transferred to me on April 2, 2014, and had previously ordered the parties to address specific topics in their written reports, so that those reports could be treated as direct testimony at hearing.

[14] VAERS is the Vaccine Adverse Event Reporting System, which allows doctors and patients to self-report any potential reactions to vaccines into a database. Centers for Disease Control and Prevention, *Vaccine Adverse Event Reporting System (VAERS)*, Vaccine Safety (last updated Aug. 28, 2015).

Rep. at 1. Indeed, she made the general assertion that some of K.L.'s observed symptoms, like migraines, could be associated with epilepsy, while denying the importance of the absence of other corroborative evidence usually associated with autoimmune diseases (for example, CSF testing revealing the presence of inflammation), which in her view did not conclusively rule out the existence of an autoimmune reaction. *Id.* at 2. She also offered additional literature which either provided further information about the risks of the HPV vaccine[15]or generally discussed the nature of epilepsy. *Id.* at 3-4.

At hearing, Dr. Engstrand refined components of her opinion as set forth in her expert reports. For instance, and in response to Dr. Shinnar's assertion that the IL-1 beta cytokine was predominantly associated with fever[16] – something K.L. had unquestionably not experienced at the time of her initial seizure – Dr. Engstrand stated that she no longer relied exclusively on IL-1 beta as the most likely mechanism of injury. Tr. at 19. Rather, she more generally stated that some "signaling cytokine would be the mechanism based on an immune response that she had to have seen." *Id*. In connection with this assertion, she further maintained that scientific literature existed that connected the HPV vaccine to afebrile seizures (although such literature had not been filed by Petitioner at the time of hearing). Dr. Engstrand also asserted that the Valencian Article provided additional evidence of instances of afebrile seizures following the HPV vaccine. *Id.* at 23-25. She admitted that in fact the reported instances of post-vaccination seizures in that article were silent on whether the individuals at issue had fevers at the time, but maintained that the Valencian Article would have reported this if so (and therefore it could be assumed from the omission of that fact that the seizures were afebrile). *Id.* at 26.

Dr. Engstrand admitted that she could not point to any testing results from K.L.'s initial hospitalization that confirmed K.L. had experienced an autoimmune reaction to the HPV vaccine. Tr. at 33-35. But she discounted the absence of such evidence (*see, e.g.*, Tr. at 35 ("[l]ike sometimes you could have inflammation show up on an MRI, but you don't always need it to show up")), or attributed the lack of corroborative proof to a failure to test for the proper autoimmune markers. *Id.* at 34. She did deem significant the evidence about changes in K.L.'s mental status post-vaccination (Tr. at 14-17), but agreed that to her the most telling proof that the HPV vaccine had caused K.L.'s seizure was the close temporal relationship between the two. *Id.* at 14 ("[s]he had never had a seizure prior to the vaccine and it was within the time frame two days later . . .").

As noted above, after the hearing Petitioner filed an affidavit from Dr. Engstrand

[15] For example, Dr. Engstrand offered L. Tomlijenovic, *et al., Too Fast or Not Too Fast: The FDA's Approval of Merck's HPV Vaccine Gardasil*, Conflicts Int. Prac. Med., 673, 673-81 (2012), an article exploring the risks of the HPV vaccine compared to its benefits.

[16] Dr. Shinnar's report had cited to literature that presented the well-accepted concept that IL-1 beta can trigger a febrile seizure. Gatti S, *et al.*, *Febrile Seizures* (Tallie Z. Baram, Shlomo Shinnar eds., Academic Press 2002) at 169-88, filed as Ex. M ("Gatti"), *see also* Ex. A at 7.

explaining the relevance of four additional items offered post-hearing in support of Petitioner's claim.[17] In particular, Dr. Engstrand offered an article that she represented further supported the possibility of afebrile seizures following the HPV vaccine. *See* N. Crawford, *et al., Syncope and Seizures Following Human Papillomavirus Vaccination: A Retrospective Case Series*, 194 Med. J. Austl., 16-18 (2011) filed as Ex. 41 ("Crawford"). Crawford, like the Valencian Article, involved a retrospective study of passive surveillance reporting of alleged vaccine adverse events, here based on the HPV vaccine's administration in Australia to young females. Crawford at 16. The majority of observed events involved a combination of syncope with seizure, with only three study subjects experiencing afebrile seizure without syncope – although all three instances involved individuals with a "confirmed underlying epilepsy disorder." *Id.*

Dr. Engstrand also offered an additional article to bulwark her opinion on the role cytokine production allegedly played herein. *See* G. Li, *et al., Cytokines and Epilepsy*, 20 Seizure 249, 249-56 (2011), filed as Ex. 42 ("Li"). The authors of Li reviewed studies involving cytokines's role in epilepsy. Li concluded that an array of different cytokines were involved – but more importantly (for present purposes), that the cytokines were activated only after the patient had suffered a seizure, as opposed to causing them, and it could not be fully ascertained in any event whether post-seizure cytokines exacerbated seizure activity. Li at 256 ("[cytokines] are activated by seizures, but their precise role in epilepsy is not yet clear"). And Dr. Engstrand filed S. von Spiczak, *et al., A retrospective population-based study on seizures related to Childhood Vaccination*, 52 Epilepsia, 1506, 1506-12 (2011) filed as Ex. 43 ("Spiczak"), which surveyed the German database of adverse events following vaccination (presumably similar to the VAERS database) for reported seizures in children up to the age of six. The study found that 17.8 percent of the children who experienced afebrile seizures had them within 7.5 days of vaccination - although none had been immunized by the HPV vaccine. *Id*.

B. Dr. Shlomo Shinnar

Dr. Shinnar filed a single report in this case on behalf of Respondent, along with 20 pieces of medical literature. *See generally* Report, dated August 25, 2014, filed as Respondent's Exhibit A (ECF No. 56) ("Shinnar Rep."). He contested Dr. Engstrand's theory in its entirety, maintaining that there is no evidence persuasively linking the HPV vaccine to epilepsy, that K.L. had not experienced an autoimmune reaction, and that the most likely proper diagnosis for her was

[17] Dr. Engstrand's affidavit attributes the late filing of these items to personal problems she was dealing with relating to a family member's sick care. Engstrand Aff. at 1. Putting aside the fact that sixteen months had passed from the date of her last report, however, none of the articles were recently-published – indeed, all four were published in 2011, before this case was even filed. Although I permitted these items into the record and have considered them in reaching my decision, Petitioner has offered no persuasive explanation for their dilatory filing, and it is reasonable to assume that the items in question were not deemed sufficiently important by Petitioner or Dr. Engstrand to have included in any of her first three reports filed prior to hearing.

idiopathic epilepsy. *Id*.

Dr. Shinnar completed his medical degree at the Albert Einstein College of Medicine in the Bronx, New York (after completing his undergraduate degree from Columbia College). Ex. B (Dr. Shinnar's CV). He went to Johns Hopkins Hospital in Baltimore, Maryland and served as an assistant Resident and Fellow in Pediatrics followed by a Residency and Fellowship in Neurology. *Id*. at 1. Dr. Shinnar is board certified in Neurology with special competence in Child Neurology and added qualifications in Clinical Neurophysiology and Epilepsy. Shinnar Rep. at 1. He currently works as a Professor of Neurology, Pediatrics and Epidemiology, and Population Health at Albert Einstein College of Medicine. *Id*. Dr. Shinnar serves as the Hyman Climenko Professor of Neuroscience Research and the Director of the Comprehensive Epilepsy Management Center at Montefiore Medical Center and the Albert Einstein College of Medicine. *Id*. Moreover, as the Director of the Comprehensive Epilepsy Management Center, he has treated and supervised the treatment of thousands of children suffering from seizure disorders. *Id*. Dr. Shinnar has also been awarded grants by the National Institutes of Health to research childhood afebrile seizures as well as childhood onset epilepsy. *Id*.

Dr. Shinnar's report provides a detailed review of K.L.'s medical history relevant to her illness herein. Shinnar Rep. at 2-5. Based upon that review, Dr. Shinnar concluded (consistent with treaters like Dr. Poduri) that K.L. suffers from idiopathic epilepsy. *Id.* at 6. Dr. Shinnar agreed that K.L. had epilepsy based on her clinical presentation of two or more unprovoked seizures more than 24 hours apart. *Id.* at 7-8. Dr. Shinnar noted that he was particularly persuaded by the reports written by Dr. Poduri, as she is a "renowned epilepsy expert," making her opinions about the etiology of K.L.'s epilepsy more trustworthy than K.L.'s other treaters (who were more general neurologists). Tr. at 67.[18]

Dr. Shinnar contrasted K.L.'s condition, as revealed in the medical records, with autoimmune epilepsy. In his explanation, autoimmune epilepsy is a rare condition characterized by intractable seizures[19] and a markedly abnormal and encephalopathic EEG, along with epileptiform activity[20], all of which he contended were not present in K.L. *Id*.; s*ee also* Tr. 65, 72-74. K.L.'s normal EEG, MRI, and lumbar puncture all failed to support the conclusion that K.L. had experienced an immune-mediated encephalopathy, given the absence of evidence of

[18] As a possible explanation for K.L.'s epilepsy, Dr. Shinnar proposed at hearing that her family history might suggest an underlying susceptibility, or the preexisting viral syndrome she was reported to be suffering from at the time of her first hospitalization. Tr. at 44. He did not, however, elaborate at length upon either of these possible alternative explanations.

[19] Intractable seizures are those that are resistant to cure, relief or control. *Dorland's* at 953.

[20] J. Suleiman, *et al., Autoimmune Epilepsy in Children: Case Series and Proposed Guidelines for Identification*, 54 Epilepsia 1036, 1039 fig. 1 (2013) filed as Ex. L.

inflammation and other autoimmune red flags. *Id*. at 8.

Beyond outlining the nature of K.L.'s condition, Dr. Shinnar opined that the HPV vaccine could not affirmatively be linked to epilepsy. In support, he cited a large population study of young girls in Denmark and Sweden. *See* L. Arnheim-Dahlstrom *et al.*, *Autoimmune, Neurological and Venous Thromboembolic Adverse Events after Immunization of Adolescent Girls with Quadrivalent Human Papillomavirus Vaccine in Denmark and Sweden: Cohort Study*, BMJ (Aug. 28, 2013), http://www.bmj.com/content/347/bmj.f5906?tab=related#webextra filed as Ex. S ("Arnheim-Dahlstrom"). That study found no increased risk for autoimmune or neurological events among the nearly 300,000 patients who received multiple doses of the HPV vaccine. *Id*. at 1. In contrast, Dr. Shinnar noted, the study found that the seizure rate was higher in the girls that did not receive the HPV vaccine. Tr. at 53.

Dr. Shinnar took particular issue with Dr. Engstrand's theory that the cytokine IL-1 beta was the mechanism for injury. As he noted, there is strong scientific support for the concept that IL-1 beta is the chief cytokine that mediates fever and has been associated with febrile seizures, but not afebrile seizures like K.L. experienced. Shinnar Rep. at 8; *see also* Tr. at 43 ("you cannot have an IL-1 beta mediated reaction that does not involve a fever"); Gatti at 171.

Dr. Shinnar also noted that K.L.'s seizure after being weaned of her medication was consistent with the conclusion that she suffered only from adolescent onset epilepsy, which is often easier to control but can relapse when the patient's dosage is reduced. Shinnar Rep. at 8. Petitioner attacked this assertion at hearing, in an attempt to suggest that because K.L. was still on her medication at the time of that seizure, the medication was not effective against her condition, and thus it was less likely that K.L.'s epilepsy was idiopathic. Tr. at 48. But Dr. Shinnar maintained his position, rejecting the argument that weaning K.L. off Keppra was the same as treating her with the full dose. Tr. 48, 52. In his view, K.L.'s seizures were fully controlled on her full dose; when that dose was reduced, it naturally caused her to have a seizure, but once she was back on her full dose she remained seizure-free, and therefore the results of weaning did not undermine his conclusions. *Id*.

Dr. Shinnar ended his testimony by rejecting the Valencian Article offered by Dr. Engstrand as unreliable support for Petitioner's theory. After attacking the overall prestige of the medical journal in which the item was published, Dr. Shinnar observed that the Valencian Article relied on self-reported adverse events (which could be incorrect), in comparison to more trustworthy retrospective epidemiologic studies like Arnheim-Dahlstrom, which examined actual diagnosed reactions after vaccination. Tr. at 68. He also pointed to the range for the rate of seizures observed in the Valencian Article, which was from minus .3 to 1.1; because statistics are bound by zero (since there cannot be a rate of seizures lower than 0) the range cast doubt on the overall validity of the researchers' calculations. *Id*. at 69.

III. PROCEDURAL BACKGROUND

After initiating this action in May 2012, K.L. began filing medical records in support of her claim, completing the process approximately one year later. Respondent's Rule 4(c) Report was then filed in June of 2013. ECF No. 30. Petitioner was ordered to file an expert report by March 31, 2014 but subsequently requested numerous extensions of time to do so, accomplishing the task by mid-June of 2014 (and thereby allowing another year to pass). ECF No. 54. In the meantime, the matter (originally before Special Master Moran) had been assigned to me on April 2, 2014.

Over the next year, both parties filed additional expert reports and medical literature as noted above, and on October 13, 2015 the matter was set for hearing on September 27, 2016 in Washington, D.C. See Prehearing Order, dated October 13, 2015 (ECF No. 88). Importantly, the matter remained subject to an earlier order entered by Special Master Moran providing (in an effort to expedite the case's adjudication if heard at trial) that each side's expert's reports would be considered their direct testimony, thereby allowing their testimony to begin with cross-examination.[21] *See* Scheduling Order dated Jan. 15, 2014 (ECF No. 42).

The hearing went forward as scheduled, and the parties elected to file simultaneous post-hearing briefs, and they did so on November 14, 2016. See ECF No. 114,115. This matter is now ripe for a decision.

IV. APPLICABLE LAW

A. Petitioner's Overall Burden in Vaccine Program Cases

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury" – *i.e.*, an injury falling within the Vaccine Injury Table – corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[22]

[21] Application of this order did not appreciably hinder my ability to understand Petitioner's theory of the case, nor would have hearing the full direct testimony aided my ruling on this matter. To the contrary - it was helpful in streamlining the parties' argument, to the extent it directed the parties to address certain topics highly relevant to the case's resolution. It also assisted in reducing overall trial time.

[22] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Human Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Human Servs.*, 59 Fed. Cl. 121,

In this case, Petitioner does not assert a Table claim.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Human Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Sec'y of Health & Human Servs.,* 418 F.3d 1274, 1278 (Fed. Cir. 2005) : "(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 proximate temporal relationship between vaccination and injury." *Althen,* 418 F.3d at 1278.

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence

124 (2003), *aff'd* 104 F. App'x 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Human Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Human Servs.*, 121 Fed. Cl. 230, 245 (2015) ("[p]lausibility . . . in many cases *may* be enough to satisfy *Althen* prong one" (emphasis in original)), *vacated on other grounds*, No. 2015-5097 (Fed. Cir. Jan. 3, 2017). But this does not negate or reduce a petitioner's ultimate burden to establish his overall entitlement to damages by preponderant evidence. *W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted).[23]

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs*., 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct – that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence also present in the record – including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Caves v. Sec'y of Dept. of Health & Human Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 Fed. App'x 765 (Fed. Cir. 2012).

[23] Although decisions like *Contreras* suggest that the burden of proof required to satisfy the first *Althen* prong is less than the other two, there is ample contrary authority for the more straightforward proposition that the first *Althen* prong, like the overall test itself, simply applies a preponderance standard when evaluating if a reliable and plausible causal theory has been established. *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1350 (Fed. Cir. 2010).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 2013 WL 1896173 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. Law Governing Analysis of Fact Evidence

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Human Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

Medical records that are created contemporaneously with the events they describe are presumed to be accurate and "complete" (i.e., presenting all relevant information on a patient's health problems). *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Human Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd*, *Rickett v. Sec'y of Health & Human Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). This presumption is based on the linked propositions that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible,

so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Human Servs.*, No. 11-685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Human Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms.").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Human Servs*., No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony – especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Human Servs*., 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, there are situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Human Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Human Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Human Servs*., No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *La Londe v. Sec'y of Health & Human Servs*., 110 Fed. Cl. 184, 203-04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous

medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. Analysis of Expert Testimony

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Human Servs*., 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594-96 (1993). *See Cedillo v. Sec'y of Health & Human Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Human Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592-95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial for a (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Human Servs*., 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742-45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts of her own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 91997)); *see also Isaac v. Sec'y of Health & Human Servs*., No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot.*

for review den'd, 108 Fed. Cl. 743 (2013), *aff'd*, 540 Fed. App'x 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325-26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Human Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. Consideration of Medical Literature

Both parties filed medical and scientific literature in this case, but not all factor into the outcome of this decision. While I have reviewed all of the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case – just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Human Servs.*, No. 2015-5072, 2016 WL 1358616, at *5 (Fed. Cir. Apr. 6, 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. v. Sec'y of Health & Human Servs.,* 527 F. App'x 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to – and likely undermines – the conclusion that it was not considered").

ANALYSIS

Petitioner has not carried her burden of proof in this case. Beyond the close temporal relationship between K.L.'s receipt of the third dose of Gardasil and onset of her first diagnosed seizure, the medical record does not support the conclusion that her epilepsy was vaccine-caused. More fundamentally, she has not established a reliable scientific theory that the HPV vaccine could cause epilepsy of the kind experienced by Petitioner.

A. *Althen* Prong One

Through Dr. Engstrand's testimony, Petitioner proposes that an autoimmune response can occur when the HPV vaccine encourages the production of various cytokines in the body, which can in turn cause inflammatory signaling to the brain, making it hyper-excitable and resulting in a generalized seizure. Tr. 6-7. This causation theory has a number of self-evident deficiencies.

An overarching problem with Petitioner's theory is the extent to which it exceeds the expertise of Dr. Engstrand to espouse. As a general neurologist who sees patients with seizures

(about 20 percent of her patients), Dr. Engstrand was sufficiently qualified to testify about the general nature of K.L.'s condition, but she has no demonstrated competence or skill as an immunologist. As a result, my embrace of the core of Petitioner's theory requires acceptance of her expert's curatorial decisions in selecting various pieces of literature to support the theory – despite the fact that Dr. Engstrand herself lacks expertise in the specific components of that theory, such as studying cytokine upregulation and impact on the neurologic system. Despite the above, I have given the theory consideration - but it did not gain persuasiveness simply because Dr. Engstrand offered it.

Beyond Dr. Engstrand's qualifications, there is the issue of the reliability of the scientific basis for Petitioner's theory. While the individual articles offered proved reasonable and reliable individually, taken as a whole they do not assist Petitioner's case. Thus, much of the literature offered either involved autoimmune forms of epilepsy (which are irrelevant under the facts of the case), different vaccines, or involved the relationship between the HPV vaccine and febrile seizures, which K.L. unquestionably never experienced. The epidemiologic evidence, such as the Valencian Article, Crawford, and Spiczak, offered to suggest that afebrile seizures are also possible not only involved VAERS-like passive surveillance (which is inherently less trustworthy than a retrospective study observing actual diagnosed instances of illness or conditions like epilepsy following vaccination)[24] but was commonly distinguishable when examined closely.

The proposed mechanism in this case – the impact of cytokines to cause neurologic injury, first by impairing the blood-brain barrier, and then by attacking the brain and causing an afebrile seizure - was an especially weak link in the theory. Although petitioners are not obligated to prove a mechanism posited as a component of their causation theory (*Knudsen*, 35 F.3d at 548-49), the evidence a claimant offers in support of that theory may reasonably be scrutinized. *Althen*, 418 F.3d at 1278. But the authority Dr. Engstrand offered to establish the scientific grounding for this mechanism was insufficiently related to vaccines, or did not even facially support the concept. Li, for example – an article that Petitioner only filed late in the case despite its prior availability – involved the upregulation and impact of cytokines after, or in reaction to, a seizure – and thus tells us nothing about whether they could cause a seizure in the first place. Li at 256.

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[24] As another special master has commented in connection with the evidentiary value of VAERS reports,

> VAERS is a stocked pond. It only contains reports (many of which are unverified or incomplete) of adverse events after vaccinations. VAERS contains no reports or data about the relative rate of these same events in individuals who have not been vaccinated. Thus, the number of specific adverse events . . . reported after any vaccine, is meaningless without information about the background rate of that adverse event and information about the number of vaccines administered.

Tompkins v. Sec'y of Health and Human Servs., No. 10-261V, 2013 WL 3498652, at *16 (Fed. Cl. Spec. Mstr. June 21, 2013), *review denied sub nom., Tompkins v. United States*, 117 Fed. Cl. 713 (2014); *see also Analla v. Sec'y of Health & Human Servs.*, 700 Fed. Cl. 552, 558 (2006) ("[t]he Court uniformly has upheld . . . concerns about the reliability of VAERS data") (citations omitted).

Dr. Engstrand's effort to rehabilitate her opinion after its modification also reveals the weakness at the theory's heart. In her initial report, Dr. Engstrand proposed that cytokine IL-1 beta was the primary cytokine involved in her proposed causation mechanism. First Engstrand Rep. at 4. In response, Dr. Shinnar noted that this cytokine was associated with fever – but K.L. unquestionably had experienced an afebrile seizure, making it impossible for that particular cytokine to have been involved in the alleged process by which the HPV vaccine causes K.L.'s seizure. Ex. 4 at 52-53; Shinnar Rep. at 7; Tr. at 43. Dr. Shinnar further supported his position with medical literature establishing that a wide number of cytokines beyond IL-1 beta would likely cause fever if upregulated. *See* Gatti at 171.

After the filing of Dr. Shinnar's report, Dr. Engstrand attempted to bolster her opinion with medical literature that purportedly showed instances of afebrile seizures following the HPV vaccine, but on close inspection these were largely unpersuasive. The Valencian Article, for example, makes no mention of whether the few reported instances of seizure were afebrile, leading Dr. Engstrand to argue that they must have been because the authors would otherwise have affirmatively noted the presence of a fever – a somewhat unreasonable inference. Tr. at 25. She similarly referenced Li, which speaks more of the causative effect seizures have on the upregulation of cytokines than the other way around, thus further undermining Dr. Engstrand's efforts to restore credibility to her theory after abandoning her initial opinion about the role of the IL-beta cytokine.

Respondent, by contrast, offered far more reliable and credible medical and scientific articles suggesting the HPV vaccine would not likely cause injuries of the kind experienced by K.L. Studies like Arnheim-Dahlstrom were more scientifically reliable (both given the larger population groups studied, as well as the fact that they involved observed cases rather than simply reported reactions) and more persuasively demonstrated no link between a number of neurological events, including epilepsy, and receipt of the HPV vaccine. Arnheim-Dahlstrom at 4, 10 (Fig. 1). In fact, Arnheim-Dahlstrom found that there was a higher incidence of seizure in those girls who did not receive the HPV vaccine. *Id*. at 4, 8 (Table 2).

Petitioner attempted to rebut such evidence with a few pieces of additional literature filed post-hearing, but as already noted such items did not appreciably aid her case. Crawford, for example, not only relied on data from a passive reporting system, but involved instances of post-HPV vaccination afebrile seizures experienced by individuals with a "confirmed underlying epilepsy disorder," thus greatly reducing the probative quality of such findings when applied to K.L., whose epilepsy is alleged to have begun only post-vaccination. *Id*. at 16. Spiczak, which found that a statistically meaningful number of studied vaccinated individuals experiencing afebrile seizures did so within approximately a week following vaccination (Spiczak at 1508), was

distinguishable because it did not involve the HPV vaccine. *Id.*[25] Thus, the fact that other vaccines can cause afebrile seizures provides weak proof for the proposition that the HPV vaccine did so in this case – especially given the many other deficiencies in Petitioner's theory already discussed.

Vaccine Act claimants are not required to prove a causation theory to a scientific certainty, but the theory must be based on "sound and reliable medical or scientific explanation." *Knudsen*, 35 F.3d at 548. I do not find that Petitioner has satisfied this standard.

B. *Althen* Prongs Two and Three

Given my finding above, it is unnecessary to discuss Petitioner's showings under the other two *Althen* prongs. *See, e.g., Veryzer v. Sec'y of Health & Human Servs.*, No. 06–522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *aff'd*, 100 Fed. Cl. 344 (2011). I will nevertheless briefly consider the evidentiary showing made by Petitioner for each of them.

First, K.L. has not successfully demonstrated with preponderant evidence that the HPV vaccine did cause her initial seizure as alleged, and thus has not satisfied the second *Althen* prong. K.L.'s medical records indicated no signs of an autoimmune process occurring contemporaneous with her initial hospitalization, or the kind of biologic markers that would reflect the cytokine upregulation that Dr. Engstrand opined was happening herein. Rather, her test results throughout treatment were normal, including an MRI and multiple EEGs. Dr. Shinnar also effectively distinguished K.L.'s presentation with that of a patient with autoimmune epilepsy, who would likely have displayed abnormal EEG results demonstrating the presence of a neurologic injury, while at the same time being resistant to treatment. Tr. at 63. In addition, particularly trustworthy treaters with significant epilepsy expertise, like Dr. Poduri, were aware of the vaccine's administration but concluded, based on their review of the developing medical record, that more likely than not K.L.'s epilepsy was idiopathic. Ex. 3 at 17, 107, and 143, Ex. 9 at 11. Such evidence was more persuasive than Dr. Engstrand's statements to the contrary, and could not be rebutted by contrary treater opinions that the vaccine was likely connected to K.L.'s epilepsy.

Resolution of the third *Althen* prong is less easily accomplished. Dr. Engstrand's theory proposed that the cytokine upregulation would occur in the two-day timeframe at issue herein. It is of course insufficient simply to rely on the temporal association between vaccine and injury to satisfy this aspect of *Althen*. *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992) ("a proximate temporal association alone does not suffice to show a causal link between

[25] Rather, Spiczak involved a number of common childhood vaccines— diphtheria- tetanus- acellular- pertussis, Hep. B, measles, mumps, rubella, and the inactivated polio vaccine. Although Petitioner filed this medical literature as Exhibit 43, she did not include the relevant supplemental references that were necessary for me to determine the vaccines administered in the study. I consequently accessed the literature online and filed the supplemental information as Court's Exhibit 1.

the vaccination and injury"). Dr. Engstrand was confronted with this at hearing, but confirmed that her opinion did in fact place great weight on the temporal relationship. Tr. at 34.

In addition, Dr. Engstrand offered little authority to support Petitioner's conclusion that this timeframe is "medically appropriate." Indeed, the medical literature that Petitioner did offer on this point is largely irrelevant to K.L. For example, Dr. Engstrand noted that the study in Crawford had three participants that had experienced afebrile seizures between four hours and two days after vaccination. Those three subjects, however, had an underlying epilepsy disorder, and neither vaccine nor cytokine causation was proposed. Crawford at 16. Dr. Engstrand also presented the Spiczak study, which reported that 17.8% of the children studied experienced afebrile seizures with a median onset period of 48 hours. *See* Court's Exhibit 1, fig. S1. But Spiczak did not include the HPV vaccine, or patients above the age of seven for that matter. *Id*. At the same time, however, I acknowledge that a two-day period between vaccination and seizure has been deemed medically acceptable in other Program cases involving epilepsy (albeit not the HPV vaccine). *L.A. v. Sec'y of Health & Human Servs.*, No. 12-629, 2016 WL 7664473, at *15 (Fed. Cl. Spec. Mstr. Dec. 15, 2016) ("no difficultly in ascribing causation in a two-day interval" between receipt of Flumist and the onset of seizures and encephalitis leading to a brain injury).

None of the above constitutes particularly robust support for Petitioner's proposed timeframe – even though that timeframe is consistent with both the evidence and Petitioner's theory. Yet even were I to find that the balance of evidence on this matter barely favored K.L., that determination would not alter my ultimate decision about causation, because Petitioner's causation theory itself is too deficient, and unsupported by the actual medical history. *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008) (The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement)); *see also, Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 2013 WL 1896173 (Fed. Cir. 2013). At bottom, Petitioner's theory is itself too unreliable to put stock in the fact that timing as evidenced by the facts herein is consistent with that theory.

CONCLUSION

The Vaccine Act permits me to award compensation only if a Petitioner alleging a "non-Table Injury" can show by medical records or competent medical opinion that the injury was more likely than not vaccine-caused. Here, the weight of the evidence does not support Petitioner's causation theory and there is insufficient evidence to support an award of compensation, leaving me no choice but to hereby **DENY** this claim.

In the absence of a timely-filed motion for review (see Appendix B to the Rules of the Court), the Clerk shall enter judgment in accord with this decision.

IT IS SO ORDERED.

/s/ Brian H. Corcoran
Brian H. Corcoran
Special Master