In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 14-714V
(to be published)

L.M., *a minor by and through her parent and guardian*, CHAD MCCLELLAN, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	Special Master Corcoran Filed: July 23, 2019 Pneumococcal Vaccine; Seizure Disorder; SCN8A Genetic Mutation; Significant Aggravation; Epileptic Encephalopathy.

David C. Richards, Christensen & Jensen, P.C., Salt Lake City, UT, for Petitioner.

Ryan D. Pyles, U.S. Dep't of Justice, Washington, DC, for Respondent.

ENTITLEMENT DECISION[1]

Chad McClellan, as legal representative of his minor child, L.M., filed a petition on August 7, 2014, seeking compensation under the National Vaccine Injury Compensation Program ("Vaccine Program").[2] Pet. at 1 (ECF No. 1). Mr. McClellan initially alleged that L.M.'s seizure disorder was caused or significantly aggravated by the pneumococcal (Prevnar) vaccine administered on December 30, 2011. *Id.* at 2. L.M.'s family subsequently learned that she has a rare genetic condition: a mutation in the SCN8A gene. Petitioner therefore moved forward with a

[1] This Decision will be posted on the Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means that the Decision will be available to anyone with access to the internet.** As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen 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 whole 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, 42 U.S.C. §§ 300aa-10–37 (2012) (hereinafter "Vaccine Act" or "the Act"). Individual section references hereafter shall refer to § 300aa of the Act.

revised claim, asserting that the vaccine significantly aggravated L.M.'s epileptic encephalopathy/seizure disorder.

An entitlement hearing was held in this matter on September 10–12, 2018. After consideration of the record and testimony provided at hearing, I find that Petitioner is not entitled to a compensation award. As discussed in more detail below, Petitioner has not set forth a reliable theory explaining how the pneumococcal vaccine L.M. received on December 30, 2011, could have significantly aggravated her SCN8A-related seizure disorder, or that it in fact did so here.

I. Factual Background

Early History

L.M. was born by normal vaginal delivery on August 8, 2011, at Jordan Valley Hospital in West Jordan, Utah. Ex. 3 at 1, 3, 5, filed Jan. 12, 2015 (ECF No. 15). She received the Hepatitis B vaccination on that date, with no recorded reaction thereafter. *Id.* at 13.

Early in her life, L.M. began displaying behaviors and symptoms suggesting the existence of neurologic dysfunction. After birth, she experienced neonatal jaundice and abnormal involuntary movements. Ex. 3 at 2. At her newborn exam, she was jittery but otherwise normal, and she was discharged home on August 10, 2011. *Id.* at 3. Then, at an August 12, 2011 well-child checkup, L.M.'s pediatrician, Galina Hornyik, M.D., noted her jitteriness and jaundice, as well as myoclonus[3] in all extremities and mildly decreased tone in her upper extremities. Ex. 4 at 17–18, filed Jan. 12, 2015 (ECF No. 15). Dr. Hornyik assessed L.M. with possible hyperactive startle reflex. *Id.* By August 22, 2011, however, Dr. Hornyik noted that L.M.'s jerkiness and jitteriness appeared to have resolved, and that her jaundice was improving as well. *Id.* at 19. On September 14, 2011, L.M. received a prescription to treat gastroesophageal reflux disease due to her symptoms of spitting up, arching her back, acting fussy, and sleeping poorly. *Id.* at 23.

During her two-month checkup with Dr. Hornyik on October 12, 2011, L.M. experienced two episodes (lasting thirty to sixty seconds each) of myclonus or choreoathetotic-type movement,[4] during which her eyes rolled back and to the side. Ex. 4 at 25. Her mother reported that these episodes had been happening "since birth." *Id.* Dr. Hornyik opted to withhold vaccinations until L.M.'s condition was better understood, and she ordered L.M. to be transported to Primary Children's Medical Center ("PCMC") in Salt Lake City by ambulance for evaluation of her condition, which Dr. Hornyik characterized at that time as a movement disorder. *Id.*

[3] Myoclonus is characterized by "shocklike" muscle contractions. *Dorland's Illustrated Medical Dictionary* 1222 (32nd ed. 2012) (hereinafter "*Dorland's*").

[4] Choreoathetotic movement involves both choreic (irregular jerkiness) and athetotic (slow writhing) involuntary muscle movement. *Dorland's* at 172, 354, 1183.

Later that same day, L.M. had another "episode" at PCMC, during which her back arched, her head tilted right, her eyelids fluttered, and her arms stiffened. Ex. 6 at 49, filed Jan. 12, 2015 (ECF No. 15). The McClellans told providers at this time that L.M. had previously experienced episodes like this, especially after waking up, though the record does not reflect their frequency. *Id.* Neurologist Susan Benedict, M.D., diagnosed L.M. with "possible seizures" or a movement disorder, and noted that L.M.'s two documented episodes observed by Dr. Hornyik earlier that day "certainly sound like seizure." *Id.* L.M. underwent an electroencephalogram ("EEG"), which showed mildly abnormal results ("mild excess intermittent right posterior slowing of uncertain significance") but with no epileptiform features identified. *Id.* at 31–32. She was discharged from the hospital the following day (October 13, 2011). *Id.* at 55.

L.M. had a follow-up neurology appointment one month later, on November 14, 2011, at which time Dr. Benedict noted L.M.'s worsening head control and ongoing eye squinting, eyelid fluttering, and exaggerated startle reflex. Ex. 4 at 34. A developmental screen showed three-month-old L.M. to be at the one-month level for personal social skills, the two-month level for gross motor skills, the three-month level for fine motor skills, and the four-month level for language. *Id.* Dr. Benedict stated that she "ha[d] concerns" about L.M. at this time, and thus recommended that her parents contact a local early intervention program. *Id.*

L.M. received her two-month vaccinations, including Hepatitis B, Prevnar (pneumococcal), and Pentacel (diphtheria, tetanus, and acellular pertussis) on November 18, 2011. Ex. 4 at 29. Her medical records do not reflect any documented reaction to the November 18th vaccinations.

On November 21, 2011, L.M. underwent brain magnetic resonance imaging ("MRI") to determine whether a cause for her prior seizures could be identified. Ex. 6 at 101. However, the MRI showed normal results, revealing no explanatory anatomic abnormality. *Id.* On December 2, 2011, L.M.'s mother informed Dr. Hornyik via telephone of her view that a non-dairy diet had ameliorated L.M.'s neurologic symptoms. Ex. 4 at 31.

Seizure Activity Shortly Before the Relevant Vaccination

On December 14, 2011, L.M. was rushed to the PCMC emergency room ("ER") by ambulance after she experienced her most severe seizure to date. Ex. 6 at 121. L.M.'s mother reported that her arms had stiffened, her eyes had rolled back, her face had turned blue while she was sitting in a bouncy chair, and that L.M. had begun breathing independently only after her mother administered rescue breaths. *Id.* The episode lasted from one to five minutes, although by the time L.M. arrived at the ER, she appeared well. *Id.* Her temperature on examination was thirty-seven degrees Celsius, meaning that she did not have a fever. *Id.*; *Dorland's* at 1880 (normal body temperature is thirty-seven degrees Celsius). In the weeks prior, L.M. had not experienced any

documented neurologic episodes. Ex. 6 at 122. Tamara Pool, M.D., diagnosed the episode as a seizure and, because of L.M.'s past normal test results and her healthy appearance in the ER, discharged L.M. home with her parents. *Id.* at 123. On December 22, 2011, L.M. followed up with neurology and underwent an EEG, which showed normal results with no epileptiform activity. *Id.* at 124.

Two weeks later, on December 30, 2011, L.M. saw Dr. Hornyik for her four-month well-child visit. Ex. 4 at 46. L.M.'s mother reported that L.M. had now been having about one seizure a week since her December 14th seizure, with increasing seizure activity when she was sick with a fever (though it is not documented in the medical record when exactly L.M. had such a fever). *Id.* Concerns noted at this visit included L.M.'s inability to hold her head steady when sitting and a lack of advancement in motor control abilities. *Id.* Dr. Hornyik noted that L.M. seemed to be worsening and falling behind in development, though she had not yet lost any skills, and stated that it remained unclear whether her conditions stemmed from a neurologic abnormality. *Id.* at 46–48. At this point L.M. was not taking any antiepileptic medication, and her providers and parents planned to monitor her condition. *Id.* at 46.

Vaccinations and Alleged Reaction

L.M. received Prevnar, polio, haemophilus influenzae type B, and diphtheria-tetanus vaccinations at her December 30, 2011 checkup. Ex. 4 at 48. Dr. Hornyik withheld the pertussis vaccine, however, noting that L.M. "had worsening of [symptoms] earlier." *Id.*

The following day (December 31, 2011), L.M.'s parents brought her to PCMC due to increased seizure frequency. Ex. 6 at 149. Mr. and Mrs. McClellan reported that L.M. had seized at 6:00 A.M., 10:30 A.M., 12:30 P.M., and 3:30 P.M., and that she was very tired after each episode. *Id.* Although Mr. and Mrs. McClellan believed L.M. "felt warm," they had repeatedly taken her temperature and found no fever. *Id.* Admitting physician Lucy Hansen, M.D., examined L.M. and noted decreased tone throughout her extremities, very poor head tone, and that she was unable to hold her head up while sitting. *Id.* at 150. Dr. Hansen theorized that her vaccinations from the day prior "could be giving her low-grade temperatures," but recorded L.M.'s body temperature as 36.5 degrees Celsius, meaning that she did *not* have a fever. *Id.* Dr. Hansen also recorded L.M. as having an upper respiratory tract infection ("URI"). *Id.* at 151. L.M. was prescribed Keppra, an antiepileptic medication. *Id.* at 151. After evaluation by the neurology department, L.M. was discharged home on January 1, 2012, with instructions to continue Keppra and follow up with her primary care physician within the week. *Id.* at 172.

On January 3, 2012, L.M.'s mother called Dr. Hornyik with concerns that L.M.'s seizures had persisted, with four episodes the previous day. Ex. 4 at 176. At a follow-up visit the next day, Mrs. McClellan stated that L.M.'s demeanor was listless and disengaged, and that she had begun to lose skills such as strength and eye contact. *Id.* at 54. L.M.'s parents attributed this to the Keppra

she was taking, and they chose to stop administering it on the evening of January 3rd. *Id.* at 54–56.

On January 4, 2012, L.M. was assessed by Jordan Child Development Center. Ex. 4 at 59–60. On examination, she was found to demonstrate a two- to three-month delay in motor development, and qualified for early intervention services. *Id.*

At Dr. Hornyik's recommendation, L.M. was admitted to PCMC for a neurology workup and consult with a genetic specialist from January 11 to January 13, 2012. Ex. 6 at 146. At this time, the McClellans reported that L.M. had continued to have seizures with increasing frequency since December 31, 2011. *Id.* They also noted that L.M. appeared to be losing developmental milestones, which they attributed to Keppra (which they had discontinued after several days of apparently ineffective use). *Id.* An MRI taken at this workup showed no abnormality, while an overnight video EEG showed numerous seizures, indicating possible epileptiform encephalopathy. *Id.* at 147, 235.

In a neurological consult on January 30, 2012, Denise Morita, M.D., diagnosed L.M. with "epileptic encephalopathy," which she posited was likely due to genetic causes. Ex. 4 at 63–64. On February 13th, geneticist Nicola Longo, M.D. Ph.D., concluded that L.M.'s seizure disorder with normal brain imaging suggested a channelopathy, possibly Dravet syndrome,[5] and recommended a ketogenic diet. *Id*. at 75. Later testing excluded Dravet syndrome, however. *Id.* at 272.

L.M. began a ketogenic diet in March 2012. Ex. 4 at 79. She experienced seizures less frequently after the diet change, but continued to have very low muscle tone, was unable to hold her head up, and showed significant developmental delay. *Id.* at 79, 108. Providers followed L.M. for nutritional concerns and slow weight gain. *Id.* at 85. She tapered off Keppra, and her demeanor was generally more responsive but often distressed. *Id.* at 89. During a July 4, 2012 visit with Dr. Hornyik, L.M.'s parents requested a plan to take her off the ketogenic diet, and the doctor noted that, although seizures had not returned at this point, her development was nevertheless considerably delayed. *Id.* at 108.

Subsequent Treatment

On July 23, 2012, neurologist Francis Filloux, M.D. evaluated L.M. Ex. 4 at 259. The McClellans reported that she had been having seizures every two weeks, but that they believed she was making progress since discontinuing Keppra. *Id.* at 260. L.M. appeared to be in remission from active seizures at this point, and she displayed limited alertness and responsiveness. *Id.*

[5] Dravet syndrome is a rare seizure condition, also called Severe Myoclonic Epilepsy of Infancy, linked to mutations in the SCN1A gene. *Faoro v. Sec'y of Health & Human Servs.*, 127 Fed. Cl. 61, 63–64 (2016).

at 261. Dr. Filloux suspected epileptic encephalopathy and noted severe neurological impairments with global developmental impairment. *Id.* at 262. He stated that there was no unifying diagnosis for her condition, but that it was likely some kind of progressive neurological disease. *Id.* Dr. Filloux recommended genetic testing. *Id.*

An EEG taken on October 17, 2012, demonstrated abnormal activity, showing right multifocal cerebral disturbances and seizure tendency. Ex. 4 at 277. Background rhythms were excessively slow and disorganized, reflecting significant encephalopathy. *Id.*

L.M. was hospitalized in January 2013 for increased seizure activity, culminating in status epilepticus. Ex. 11 at 5, filed Jan. 12, 2015 (ECF No. 15). Dr. Filloux followed up with L.M. on March 8, 2013, noting her lack of neurodevelopmental progress and that her brain MRI showed a lack of cerebral growth and possible atrophy. Ex. 4 at 324–25. He stated that L.M. "probably has a neurodegenerative disease of some type," but that she still lacked a unifying diagnosis to explain her various conditions. *Id.*

Neurologist Kathryn Swoboda, M.D., recommended that L.M. undergo whole exome sequencing during a consult on January 3, 2014. Ex. 10 at 40, filed Jan. 12, 2015 (ECF No. 15). At a follow-up visit on March 7, 2014, Dr. Swoboda stated that L.M.'s primary diagnosis remained uncertain, but that she suffered from severe infantile parkinsonism and epileptic encephalopathy. *Id.* at 34.

Discovery of SCN8A Genetic Variant

L.M.'s whole exome sequencing results were reported March 6, 2015. Ex. 12 at 1, filed May 20, 2015 (ECF No. 19-1). The test revealed a likely pathogenic variant in her SCN8A gene. *Id.* The report noted that variants in the SCN8A gene, whose protein product "is one of the main sodium channels in the brain," "are associated with cognitive impairment . . . and with epileptic encephalopathy . . . [c]linical features . . . include hypotonia, seizures, epileptic spasms, intellectual disability, impaired coordination and balance, speech and language regression, and specific EEG findings." *Id.* at 1–2. SCN8A variants are associated with early infantile epileptic encephalopathy type 13 ("EIEE 13"). J. Malcomson, et al., *SCN8A Mutation in a Child Presenting with Seizures and Developmental Delays*, 2 Cold Spring Harbor Molecular Case Studies 1 (2016), filed as Ex. 69, June 9, 2018 (ECF No. 69-6) ("Malcomson").

After her genetic variant was discovered, L.M. became the subject of a case study—the very item of literature just referenced, Malcomson. *See generally* Malcomson. Malcomson's authors summarize L.M.'s clinical course over her first four years of life, as well as her current condition, which features idiopathic epilepsy (ten to fifteen seizures per day), cortical blindness, developmental regression, no language or motor skills, recurrent fevers, and osteopenia. *Id.* at 2. As they explain, L.M.'s specific SCN8A variant resulted in a leucine amino acid being exchanged

for serine, a substitution that has not been previously recorded in genetic databases. *Id.* at 7–8. Malcomson's authors identify a tentative link between the specific amino acid substitution and seizure activity, pointing out that a corresponding leucine substitution in SCN1A patients results in impaired channel inactivation, and that impaired channel inactivation is commonly seen in SCN8A patients with epileptic encephalopathy. *Id.* at 8. Malcomson acknowledges that L.M.'s seizure activity increased after her December 30, 2011 vaccinations, but does not propose a causal link between vaccination and symptom onset. *Id.* at 3. Its authors conclude that L.M.'s SCN8A variant "is considered to be a mutation that contributes to the phenotype described here." *Id.* at 7.

II. Witness Testimony

A. Fact Witnesses

1. *Chad McClellan*

Mr. McClellan testified at hearing, describing L.M.'s course in a manner generally consistent with the medical records. *See* Tr. at 9–70. Although many records suggest that L.M. displayed concerning neurologic symptoms before the relevant vaccinations, Mr. McClellan characterized her pre-vaccination condition as consistently normal and healthy, with no cause for concern about L.M.'s development.

For example, when discussing records from L.M.'s November 14, 2011 visit with Drs. Benedict and Swoboda, Mr. McClellan stated that while L.M. was noted to have a floppy neck, he and his wife did not find this concerning, as their older daughter had displayed a similar condition as an infant. Tr. at 20 (discussing Ex. 4 at 32–35). Mr. McClellan was "quite sure . . . that nothing indicated any issues at that point." *Id.* at 24. With regard to notes from L.M.'s December 30th well-child visit, Mr. McClellan was unsure to what Dr. Hornyik's note of "increasing seizures" referred. *Id.* at 31 (discussing Ex. 4 at 46–49). He asserted that Dr. Hornyik's noted concern about L.M.'s neurologic problems likely referred only to her floppy neck. *Id.* at 34 (discussing Ex. 4 at 48). And to Mr. McClellan's recollection, L.M. did not have a URI when she was hospitalized for her seizures on December 31, 2011, though he allowed that she may have had "a clear runny nose" or clear discharge from her nose during a seizure. *Id.* at 40, 65.

Mr. McClellan also described the dramatic change in L.M.'s condition after her seizures became more prevalent around December 31, 2011. He recalled that "on December 30th, L.M. was a happy baby that would play with toys, and we could get her to giggle, and she would interact with her brothers and sister. After that, it never happened again, not even once . . . something was wrong . . . and it was as if she wasn't there in the room with us anymore, even though she was right there." Tr. at 45. L.M. stopped making eye contact, visually tracking, moving independently, and crying. *Id.* at 45, 52. He recalled a single instance after L.M.'s January 13, 2011 discharge from PCMC when she lifted her head and hands. *Id.* at 52–53. He also described the difference

between L.M.'s EEG tests, contrasting a normal EEG from November 2011 with a subsequent one performed on January 11, 2012, at which time doctors told Mr. McClellan that "it looked like World War II was going on in her brain" due to the abnormal seizure activity L.M. was experiencing. *Id.* at 20, 54 (discussing Ex. 4 at 34; Ex. 6 at 237).

Finally, Mr. McClellan described L.M.'s current condition and her need for constant care. Tr. at 57–61. She must be fed through a tube, requires enemas to relieve herself, vomits spontaneously, and makes no meaningful movements, only tremors. *Id.* at 57–58. She still experiences seizures, though their frequency varies depending on her diet and medication. *Id.* at 58–59. L.M. has cortical blindness and experiences occasional spontaneous bone fractures. *Id.* at 60–61.

2. *April McClellan*

L.M.'s mother, April McClellan, also testified at hearing, echoing her husband's view that L.M. was developing almost normally before her December 30, 2011 vaccinations (in contrast to what the record seems to indicate), then experienced a rapid and dramatic change for the worse the day after. Tr. at 369–93. Mrs. McClellan acknowledged that L.M. had displayed slight jitteriness in her early weeks of life, but stated that she did not find this concerning, as her three older children had shown similar symptoms during infancy. *Id.* at 370. And while Mrs. McClellan conceded that Dr. Hornyik had suggested that L.M. might be experiencing small seizures at an October 12, 2011 visit, she maintained that she did not understand the basis for this assessment. *Id.* at 371–72.

Although no reaction (including fever) was documented in the medical records following L.M.'s first round of vaccinations on November 18, 2011, Mrs. McClellan recalled that L.M. had in fact experienced a high fever after vaccination. Tr. at 376. L.M.'s demeanor was subdued and listless, and she was "foaming at the mouth." *Id.* Her fever resolved the following day, however, after her parents administered Tylenol and Ibuprofen and gave her a bath. *Id.*

Mrs. McClellan also provided detailed accounts of L.M.'s pre-vaccination seizures. She described the seizure L.M. experienced on December 14, 2011, as well as a subsequent seizure L.M. suffered in a Walmart some days later. Tr. at 379–80, 390. Mrs. McClellan recalled no additional seizures between December 14th and 31st, thus characterizing L.M.'s pre-vaccination seizure frequency somewhat differently than Dr. Hornyik, who had recorded that L.M. "[h]as had about 1 seizure a week since her first one 3 weeks ago" at L.M.'s December 30th checkup. *Id.* at 390; Ex. 4 at 46.

Consistent with her husband's testimony, Mrs. McClellan recalled that L.M. was referred to Jordan Development Center for her floppy neck, and that she did not have a runny nose or other URI symptoms when she received her vaccinations on December 30, 2011. Tr. at 388, 393. She also recounted the change in L.M.'s condition in a manner consistent with what her husband had

described. She confirmed that L.M. stopped crying, moving, or making eye contact after she was discharged from the hospital in mid-January, and stated that "it was like someone took my baby from me and handed me another baby." *Id.* at 387.

B. Petitioner's Expert Witnesses

1. *Dr. Marcel Kinsbourne*

Marcel Kinsbourne, M.D., testified at hearing and provided two reports on Petitioner's behalf. *See generally* Ex. 15, filed Aug. 31, 2015 (ECF No. 21-3) ("Kinsbourne First Rep."); Ex. 41, filed July 29, 2016 (ECF No. 33-1) ("Kinsbourne Second Rep."). Dr. Kinsbourne opined that L.M.'s dramatic post-vaccination decline could not be wholly attributed to her SCN8A variant, and that the close temporal connection and lack of alternate explanation meant that her December 30, 2011 vaccinations more likely than not were the reason for the evident worsening of her condition.

Dr. Kinsbourne is a pediatric neurologist, and as seen in his curriculum vitae ("CV"), he received his medical degree in England and has been licensed to practice medicine in North Carolina since 1967. Ex. 16 at 1–2, filed Aug. 31, 2015 (ECF No. 21-4). He has held a variety of academic positions over the course of his career, teaching and researching subjects including psychology, neurology, occupational therapy, pediatrics, and linguistics. *Id.* at 2–3. His clinical experience includes serving as a senior staff physician in Ontario from 1974–80 and as a clinical associate in neurology at Massachusetts General Hospital from 1981–91. *Id.* He has published hundreds of articles on various neurological issues, and he is on the editorial board of several medical journals. *Id.* at 4, 7–39. Importantly, however, Dr. Kinsbourne has not treated patients, pediatric or otherwise, for almost thirty years, and he has devoted the last several decades of his professional life to teaching subjects ranging from linguistics and cognitive science to behavioral neurology, as well as frequently serving as an expert witness. *Id.* at 3–4; Tr. at 145–46.

At hearing, Dr. Kinsbourne discussed L.M.'s pre- and post-vaccination medical records in depth. He acknowledged, as several points in her pre-vaccination record reflect, that L.M. displayed a degree of brain abnormality or hyperexcitability that was likely attributable to her SCN8A mutation. *See, e.g.*, Tr. at 80–81 (noting that abnormal movements and jitteriness at birth reflect hyperexcitability of the brain), 103–05 (discussing December 14, 2011 seizure). Dr. Kinsbourne otherwise characterized L.M.'s condition as an epileptic encephalopathy, which he defined as a seizure disorder that would affect multiple parts of the brain, resulting in damage to various mental processes. *Id.* at 136.

Overall, however, Dr. Kinsbourne described L.M.'s pre-vaccination condition as relatively mild, featuring a movement disorder and one full seizure attributable to her SCN8A variant. Tr. at 134–35, 141–43. After vaccination, by contrast, he opined that L.M. had suffered a catastrophic

and abrupt collapse. *Id.* at 143. He highlighted the difference between her December 22, 2011 EEG, which showed no epileptiform activity, and her January 11, 2012 EEG, which was severely abnormal. *Id.* at 128–30. He also noted her dramatic regression after vaccination, stating that before vaccination, L.M. was "developing normally or close to normally, acting like a normal baby in the way it interacts with the world and her parents and so on," whereas after vaccination, she became "a child who has regressed sharply to a state where she essentially is doing nothing, seems unable to do anything, expresses nothing." *Id.* at 134–35.

In light of this sharp decline, Dr. Kinsbourne opined that L.M.'s underlying genetically-caused seizure disorder had been significantly aggravated by her December 30, 2011 vaccinations. Tr. at 134–35. He found no reason to believe that she would have experienced such a collapse absent vaccination, and could identify no other possible trigger for her abrupt decline. *Id.* at 144–45. He expanded on this viewpoint in his written reports, discussing the concept of gene-environment interaction. Kinsbourne First Rep. at 8. Noting that individuals with SCN8A variations present with phenotypes of varying severity, he suggested that "other moderating variables seem to be at work," including environmental factors. *Id.* at 8–9. Because the severity of L.M.'s condition could not have been predicted by the existence of her SCN8A mutation alone, Dr. Kinsbourne concluded that "there is no evidentiary basis for discounting the dramatic aggravation caused by vaccine injury as being unrelated to the ultimate outcome." *Id.* at 9.

In his second report, Dr. Kinsbourne responded to a report filed by Respondent's expert, Gerald Raymond, M.D. Kinsbourne Second Rep. at 1. He now endorsed a more expansive view of gene-environment interaction, stating that "[a]ny seizure disorder, whether monogenetic or otherwise caused, is open and vulnerable to events capable of modifying it at any time during its course." *Id.* at 3. He also discussed the concept of a "two-hit" model, stating that this is a well-accepted mechanistic vehicle applicable in the context of epilepsy patients. *Id.* at 4. In L.M.'s case, he suggested that the vaccines she received on December 30, 2011, likely triggered production of pro-inflammatory cytokines, which then acted as a seizure-inducing "second hit," adversely impacting the course of her seizure disorder. *Id.* at 6.

On cross examination, Dr. Kinsbourne acknowledged that he is not an expert in genetics, nor did any of his prior neurology research focus on seizure disorders. Tr. at 147–48. He also acknowledged that he has not managed a seizure patient, young or old, in a hospital setting since 1991. *Id.* at 146–47. When asked about the literature that he relied on to support the contention that an exsting epileptic condition requires an environmental trigger, he pointed only to unpublished data contained in a written report filed in this case by Michael Hammer, Ph.D., on behalf of Petitioner. *Id.* at 158, 161 (discussing Ex. 18, filed Aug. 31, 2015 (ECF No. 21-6) ("Hammer Rep.")).

Dr. Kinsbourne maintained that he had seen literature supporting the view that SCN8A

mutation disorders are immune-mediated, but was unable to provide any specific citations on this point. Tr. at 164. He also was unable to reconcile his "two-hit" model with an SCN8A animal study showing that mice can seize spontaneously without any trigger. *Id.* at 171 (discussing J. L. Wagnon, et al., *Convulsive Seizures and SUDEP in a Mouse Model of SCN8A Epileptic Encephalopathy*, 24 Human Molecular Genetics 506 (2014), filed as Ex. U, Apr. 21, 2017 (ECF No. 50-4) ("Wagnon")). Dr. Kinsbourne also conceded that L.M.'s condition had been worsening *prior* to vaccination in December 2011. *Id.* at 156. And he agreed that literature documenting the trajectory of EIEE 13 patients shows two times of peak onset: one month old and four months old (roughly comparable to when L.M.'s increased seizure activity was observed). *Id.* at 166–67.

Finally, Dr. Kinsbourne was asked why, under his proffered theory, L.M. did not experience a seizure-triggering reaction to the earlier set of vaccinations she received in November 2011. Tr. at 178. In response, he theorized that this may have been due to her older age at the time of her December vaccinations, meaning that she was less protected by her mother's vaccinations, or that her dramatic worsening in December may have reflected a cumulative response to both sets of vaccinations. *Id.*

2. *Dr. Richard Boles*

Richard Boles, M.D., provided two written reports and testified for Petitioner at hearing. *See generally* Ex. 45, filed July 29, 2016 (ECF No. 36-1) ("Boles First Rep."); Ex. 46, filed Jan. 3, 2017 (ECF No. 43-1) ("Boles Second Rep."). Dr. Boles opined that L.M.'s condition would have been far less severe had the December 30, 2011 vaccinations not significantly aggravated it.

As reflected in his curriculum vitae, Dr. Boles received his B.S. from the University of Arizona and his M.D. from the University of California Los Angeles ("UCLA"). Ex. 45 Tab F at 2, filed July 29, 2016 (ECF No. 37). He completed a pediatrics residency at Harbor-UCLA Medical Center, followed by a genetics fellowship at Yale University. *Id.* Dr. Boles served as a professor of clinical pediatrics at the University of Southern California from 1993 to 2014. *Id.* He is board-certified in clinical genetics and clinical biochemical genetics. *Id.* at 1. He recently began working in private practice after spending several years as a researcher with Courtagen Life Sciences. Tr. at 240. Dr. Boles has experience with a wide selection of neurologic conditions, ranging from autism and developmental regression to depression. Boles First Rep. at 1. At present, his practice and research are focused on neurotransmitter disorders and channelopathies, which he defined as mitochondrial deficiencies in the ion channels. *Id.*; Tr. at 242.

Dr. Boles provided background information about L.M.'s SCN8A genetic variant. Tr. at 192, 203–06. Her variant is *de novo*, meaning that she did not inherit it from either parent. *Id.* at 206. She has a gain-of-function missense variant, meaning that it "causes a protein to have some additional function which it did not have before and that results in disease." *Id.* at 203. L.M.'s particular variant caused a leucine amino acid to be replaced with a serine amino acid. *Id.*

Dr. Boles also testified at length about the role genes play in disease. In his view, genetic variants do not *cause* disease; rather, they merely *confer risk*. Tr. at 197. As support for this proposition, he stated that some individuals with genetic variants thought to be disease-causing in fact never develop the associated disease. *Id.* In the context of pediatric neurological conditions linked to genetic variants, Dr. Boles stated that there is usually (though not always) a "trigger"—i.e., an environmental insult of some kind—which can either cause a condition to develop for the first time or worsen a preexisting condition. *Id.* at 198. He described a "three-legged stool" model of disease causation, identifying three factors that must be present for development of genetic diseases: (1) genetic susceptibility, meaning that an individual has a genetic variant that puts her uniquely at risk for a certain condition; (2) an environmental trigger; and (3) a vulnerable age, as individuals are more prone to develop certain conditions at different stages of development. *Id.* at 199.

Throughout his testimony, Dr. Boles reiterated his view of gene-environment interaction as well-accepted in the field of genetics today. Tr. at 200, 226, 260. Responding to criticisms from Respondent's geneticist, Dr. Raymond, that such an analytic framework was speculative, Dr. Boles described gene-environment interaction as the "bread and butter" of modern genetics. *Id.* at 226. He provided anecdotal examples of patients he has seen with the same genetic variant who experienced different outcomes due to environmental factors, such as a pair of twins who developed different degrees of intellectual disability after one suffered a more severe course of the stomach flu during infancy. *Id.* at 231–32.

Applying this gene-environment interaction framework to L.M.'s case, Dr. Boles opined that the mere existence of her SCN8A variant could not fully explain the severity of her condition. Tr. at 204–05. He based this determination on medical literature documenting a wide range of outcomes in SCN8A patients. Tr. at 214, 222–23 (discussing G. Anand, et al., *Autosomal Dominant SCN8A Mutation with an Unusually Mild Phenotype*, 20 European J. Paediatric Neurology 761 (2016), filed as Ex. 45 Tab A, July 29, 2016 (ECF No. 36-2)[6] ("Anand"); J. Larsen, et al., *The Phenotypic Spectrum of SCN8A Encephalopathy*, 84 Neurology 480 (2015), filed as Ex. 27, Aug. 31, 2015 (ECF No. 21-15)[7] ("Larsen")).

In Larsen, for example, only 40% of patients possessing the SCN8A genetic variant experienced regression (loss of previously-gained skills), which L.M. experienced after her seizures began in earnest on December 31, 2011. Tr at 214; Larsen at 4–5. In Dr. Boles's view,

[6] This same article was also filed by Petitioner as Ex. 51 (ECF No. 43-6).

[7] This same article was also filed by Petitioner *four more times* in this case: as Ex. 41 Tab E (ECF No. 33-6), Ex. 42 Tab A (ECF No. 34-2), Ex. 45 Tab C (ECF No. 36-4), and Ex. 53 (ECF No. 43-8). In the future, parties are encouraged to avoid the duplicative filing of exhibits.

the medical literature showed that *all* SCN8A cases featuring profound developmental delay involved congenital[8] onset of the disease. Tr. at 224–25. By contrast, L.M. experienced post-congenital onset, followed by sharp regression resulting in profound delay, making her "the only case ever" of that kind. *Id.* at 225. He also noted that, under his three-legged stool framework, infancy is a "vulnerable age," due in part to the high rate of brain growth during that time. *Id.* at 216–17. Thus, because L.M.'s condition worsened significantly during a vulnerable age, he concluded that she must have encountered an environmental trigger during that time. *Id.* at 220.

For early onset epileptic encephalopathies such as L.M.'s, Dr. Boles theorized that multiple triggers might be involved, even as many as four or five. Tr. at 199. In his own practice, Dr. Boles stated that he has witnessed a wide range of triggers, including breaking a bone, over-exercising, allergies, surgery with anesthesia, and (most commonly) immunologic triggers. *Id.* at 214–16. He deemed the December 30, 2011 vaccinations the most likely "primary trigger" for L.M.'s regression, though he refrained from identifying a particular vaccine as most likely causal. *Id.* at 219–20 ("I don't know which one, maybe it's not any of them, maybe it's the combination of all the vaccines, but I would say it's the vaccinations in the plural"). He based this assessment on the close temporal nexus between vaccination and L.M.'s increase in seizures, his own clinical observations of vaccine-triggered reactions, and the fact that gain-of-function sodium channelopathies are often associated with vaccine-linked deterioration (relying on the same Hammer Report that Dr. Kinsbourne had found significant). *Id.* at 220–22 (citing Hammer Rep.); Boles First Rep. at 8–9 (citing Larsen; Hammer Rep.). He could not rule out the possibility that a common cold might also have triggered her regression, though he had not personally seen a URI act as such a trigger in his own clinical practice. Tr. at 218.

Dr. Boles also opined that, absent vaccination, L.M. would have experienced only moderate developmental delays from her SCN8A variant. Tr. at 210–13, 232; Boles First Rep. at 12–13. As an adult, he stated that she might have had an intelligence quotient ("IQ") in the range of thirty-five to fifty, or an IQ of a child between four and seven years of age. Tr. at 211–13. She would therefore have been able to communicate, walk around, interact emotionally, and even hold a simple job. *Id.* at 213. Dr. Boles also opined that it was more likely than not that L.M. would *not* have encountered another regression-causing trigger during her infancy (a vulnerable age, under his theory), though he did not explain the basis for this statement, and on cross examination conceded that it would be impossible to predict the odds of L.M. encountering another such trigger. *Id.* at 233, 269–70. Also during cross examination, he acknowledged that L.M. exhibited some signs of delay and neurologic abnormality before vaccination. *Id.* at 248–50 (acknowledging L.M.'s pre-vaccination seizures and gross motor delay).

[8] Congenital means that a condition was present at or before birth. *Dorland's* at 403.

In his second report, prepared at my request, Dr. Boles outlined differences between the SCN8A variant and the *SCN1A* variant, whose association with Dravet syndrome has been extensively litigated in the Vaccine Program but found wanting.[9] Second Boles Rep. at 1. He noted that the two genes encode different proteins in different locations. *Id.* He pointed out that SCN8A is a gain-of-function variant, while SCN1A is a loss-of-function variant, meaning that the two variants cause disease by different mechanisms (even if they both can result in seizure disorders). *Id.* He also emphasized the wide variety of outcomes among SCN8A patients, though he declined to opine as to whether SCN1A patients present with similarly varied outcomes. *Id.* at 2. Finally, Dr. Boles argued that the two variants result in different diseases. *Id.* He did not expand upon the significance of these distinctions for purposes of a causation analysis, however. *See generally id.*

3. *Dr. Vera Byers*

Vera Byers, M.D., Ph.D., testified at hearing and provided four written reports for Petitioner. *See generally* Ex. 13, filed Aug. 31, 2015 (ECF No. 21-1) ("Byers First Rep."); Ex. 42, filed July 29, 2016 (ECF No. 34-1) ("Byers Second Rep."); Ex. 43, filed July 29, 2017 (ECF No. 35-1) ("Byers Third Rep."); Ex. 44, filed July 29, 2016 (ECF No. 35-6) ("Byers Fourth Rep."). Dr. Byers opined that the vaccinations L.M. received on December 30, 2011—in particular the Prevnar vaccine—led to excessive cytokine production, which ultimately triggered or worsened her underlying genetic condition.

Dr. Byers received her bachelor's degree, master's degree in microbiology, and Ph.D. in immunology from the University of California, Los Angeles. Ex. 14 at 1, filed Aug. 31, 2015 (ECF No. 21-2) ("Byers CV"). Before entering medical school, Dr. Byers completed two post-doctoral fellowships: one in protein chemistry at Abbott Labs in Chicago, Illinois, and the second in clinical and tumor immunology at the University of California, San Francisco ("UCSF"). *Id.* She then attended medical school and completed a three-year residency at UCSF, thereafter becoming a member of the faculty there. *Id.* at 1, 4.

Dr. Byers is presently a medical toxicologist and consulting medical director at Immunology, Inc. of Incline Village, Nevada, and she has frequently served as an expert witness in lawsuits over the past fifteen years, including Vaccine Program cases. Byers CV at 2; Tr. at 294. She has throughout her career maintained several positions as an allergist and immunologist performing research and clinical trials in a variety of different areas. Byers CV at 2–4. Although her CV includes an extensive list of publications, Dr. Byers has not published on the causes of seizures, nor on cytokine responses to vaccinations. *Id.* at 6–14; Tr. at 330. She also has not maintained a clinical practice for almost twenty years, and has not seen a pediatric patient since approximately 1987. Tr. at 328. At present, Dr. Byers does not have any hospital admitting

[9] The Vaccine Program decisions involving the SCN1A genetic variant and its relationship to seizure disorders are discussed in greater detail in § IV, *infra*.

privileges, academic positions, or research lab positions, and she derives the majority of her income from her work as an expert witness. *Id.* at 328–29.

In her first report and her hearing testimony, Dr. Byers attempted to lay out a theory explaining how vaccines could have aggravated L.M.'s seizure disorder. She explained that foreign nucleotides or proteins can interact with Toll-Like receptors[10] in the innate immune system, leading to the release of pro-inflammatory cytokines.[11] Byers First Rep. at 4. These cytokines include IL-1 beta, IL-6, and TNF-alpha. *Id.* at 4. Dr. Byers's views on the effect of these cytokines varied throughout her reports and testimony, as she alternatingly opined that their release (especially IL-1 beta, or the combination of IL-1 beta and IL-6) could either exacerbate, prolong, or outright cause seizures. *Id.* at 5; Tr. at 302–03. Her explanations for how cytokines could do this included, at various points, that they affect neuronal structure, impair sodium and/or calcium channels, break down the blood-brain barrier, and/or produce neurotoxicity. Byers First Rep. at 5; Tr. at 302–03, 309, 314, 354–55. When questioned for more clarity on this proposed pathogenic process, however, she only responded that cytokines "can both cause seizures, and they can cause fever," and that "it depends on, I guess, a lot of environmental and other factors of the host to decide which one they do." Tr. at 425.

Dr. Byers also discussed the relationship between fever and seizures in her testimony. She described the idea of febrile-induced seizures as a "myth," maintaining that fever itself does not cause seizures, but rather "the fever produces IL-1 beta, and it's the IL-1 beta then in the brain that produces the seizure." Tr. at 302–03. For this reason, Dr. Byers asserted that, while L.M. may not have experienced a fever before her seizures began on December 31, 2011, the seizures nonetheless could have been vaccine-induced, because (in her view) the vaccines could have triggered an outpouring of IL-1 beta or other seizure-inducing cytokines. *Id.* at 319, 348. When pressed further for evidence of a cytokine-driven reaction in L.M., Dr. Byers simply pointed to L.M.'s December 31, 2011 seizures, as well as the fact that L.M. had a fever after her *November* vaccinations (although there is no similar medical record evidence of a fever around the time of December 30th, nor did L.M. have a seizure following her November vaccinations). *Id.* at 430.

As laid out in her written reports, Dr. Byers's theory hinged largely on the idea that the initial manifestation of L.M.'s seizure disorder required a trigger. *See, e.g.*, Byers First Rep. at 7 ("It is clear that just having the genetic mutation does not cause symptoms. All disease must be triggered by something"); Byers Second Rep. at 1 (analogizing that, because (in her view) vaccines trigger manifestation of Dravet syndrome, which results from the SCN1A variant, EIEE 13 resulting from the SCN8A variant is similarly triggered by "strong[] environmental stressors"); Byers Third Rep. at 3 ("the fact [that] roughly 50% of all SCN8A patients have normal EEGs

[10] Dr. Byers defined Toll-Like receptors as receptors on the surface of cells in the innate immune system. Tr. at 313.

[11] Dr. Byers defined a cytokine as "a protein that allows cells to talk to each other." Tr. at 300.

before their first seizure proves that there has to be a trigger before the genetically associated disease presents"); Tr. at 352. While Dr. Byers maintained that vaccines triggered the onset of L.M.'s condition, she did not explain how vaccines could *aggravate* a preexisting condition with a genetic derivation. She also did not discuss how her theory could be harmonized with L.M.'s pre-vaccination symptoms, instead maintaining that she simply had no opinion about the cause of L.M.'s December 14, 2011 seizure (and not acknowledging the existence of one or more other pre-vaccination seizures). Byers First Rep. at 7; Tr. at 304–05.

Dr. Byers pointed to the vaccines L.M. received on December 30, 2011, as the most likely trigger for her subsequent increase in seizures due to their close temporal connection. Byers Second Rep. at 1. In particular, she identified Prevnar as most likely causal due to its purported association with increased production of IL-1 beta. Tr. at 299, 346. She conceded, however, that she could cite no scientific literature confirming that Prevnar stimulates excessive IL-1 beta production. *Id.* at 346. Dr. Byers nevertheless maintained that Prevnar is "more likely to produce seizures than other vaccines." *Id.* at 347. In support for this, she cited "VAERS" data,[12] as well as a post-licensure safety review of Prevnar (which also relied exclusively on VAERS data), though she maintained (without citing any additional evidence) that "[o]ther research confirms this clinical finding." Byers First Rep. at 6 (citing R. Wise, et al., *Postlicensure Safety Surveillance for 7-Valent Pneumococcal Conjugate Vaccine*, 202 J. Am. Med. Ass'n 1702 (2004), filed as Ex. 38, Aug. 31, 2015 (ECF No. 21-26) ("Wise")); Tr. at 344–48. When questioned, Dr. Byers asserted that animal studies confirmed the association between Prevnar and seizures, but that she could not recall which ones. Tr. at 424.[13]

In theory, Dr. Byers agreed that a URI could have triggered onset of L.M.'s condition, but she maintained that L.M.'s medical record showed no evidence of a URI before her frequent seizures began. Byers Fourth Rep. at 2. The documented runny nose and congestion at L.M.'s December 31, 2011 hospital visit instead were, in her view, proof of a post-vaccination inflammatory response. *Id.*

[12] "VAERS," or the Vaccine Adverse Event Reporting System, is a passive surveillance system maintained by the Center for Disease Control, in which anyone may file a report alleging that a vaccine caused a particular injury, illness, or death. As discussed by other special masters, the data provided by VAERS does not illustrate a causal connection; rather, VAERS exists to prompt further scientific investigation into potentially dangerous vaccines. *See, e.g.*, *Tompkins v. Sec'y of Health & Human Servs.*, No. 10-261V, 2013 WL 3498652, at *9 n.25 (Fed. Cl. Spec. Mstr. June 21, 2013), *mot. for review denied*, 117 Fed. Cl. 713 (2014). VAERS reports are informal and unverified, and should not be confused with formal case reports in medical literature. *Id.* at *9 n.26. For these reasons, other special masters have consistently declined to rely on VAERS data as probative with regard to vaccine causation. *See, e.g.*, *Analla v. Sec'y of Health & Human Servs.*, 70 Fed. Cl. 552, 558 (2006); *Ryman v. Sec'y of Health & Human Servs.*, 65 Fed. Cl. 35, 39–40 (2005).

[13] In her first written report, Dr. Byers cited animal studies to demonstrate the association between *IL-1 beta* and seizures (rather than Prevnar and seizures). Byers First Rep. at 5–6. It is unclear whether she meant to reference these studies or others when she testified at hearing about Prevnar's purported association with seizures.

4. *Dr. Michael Hammer*

Dr Hammer provided a written report for Petitioner, but did not testify at hearing. *See* Hammer Rep. Dr. Hammer is also the co-author of an article (filed in this case as Exhibit 52) which summarizes recent literature concerning the SCN8A variant. M. Hammer, et al., *SCN8A-Related Epilepsy with Encephalopathy*, GeneReviews (2016), filed as Ex. 52, Jan. 3, 2017 (ECF No. 43-7). This article discusses the range of phenotypic outcomes associated with SCN8A-related epilepsy, but makes *no* mention of vaccine-caused aggravation of the condition. *See generally id.* In a subsection entitled "Agents/Circumstances to Avoid," the authors record that several SCN8A patients experienced worsening of seizures when taking Keppra, citing Dr. Hammer's unpublished data; however, no mention is made of vaccines as a worsening agent. *Id.* at 9.

As detailed in his report, Dr. Hammer received his B.A. from Lake Forest College in Lake Forest, Illinois, followed by his Ph.D. in genetics from University of California-Berkeley. Hammer Rep. at 5. He is the head of a research laboratory at the University of Arizona, where he studies human evolution and the origins of humanity, as well as the genetic components of neurodevelopmental disorders and epilepsy. *Id.* at 5–8. Much of his research involves primates. *Id.* at 5–7.

In his three-page report,[14] Dr. Hammer explained that he is currently studying around sixty families with children who suffer from SCN8A-related epilepsy. Hammer Rep. at 1. He follows these families through a Facebook group, as well as a website through which the families can complete questionnaires about their children's condition and development. *Id.* Although Dr. Hammer did not provide all of his underlying data, he noted that seven of twenty-six participants in one survey (29%) responded in the affirmative to the following question: "Did your child experience initial or increased seizure activity within 48 hours after a vaccination?" *Id.* at 2. In a separate survey, twenty-two of forty-one respondents (54%) "indicated that their child suffered a loss of developmental skills in association with a particular event . . . well after the onset of the first detectable seizures," and of these twenty-two cases, five listed vaccination as a triggering event. *Id.* Of these five cases in which a vaccine was reported to be a regression trigger, three lost "nearly all previously gained skills." *Id.* Based on this data, as well as his review of the reports provided by Drs. Byers and Kinsbourne, Dr. Hammer concluded that L.M. is one of these three total-regression cases, "presumably as a result of an adverse reaction to the vaccine." *Id.*

5. *Dr. Nicola Longo*

Although he did not testify at hearing, treating physician Dr. Longo provided a letter in support of Petitioner's claim. *See* Ex. 19 at 1, filed Aug. 31, 2015 (ECF No. 21-7). Dr. Longo is a

[14] As discussed above, several of Petitioner's experts, including Drs. Kinsbourne and Boles, relied on the conclusions and data set forth in Dr. Hammer's report when forming their own opinions in this case.

professor of pediatrics and chief of the division of medical genetics at the University of Utah School of Medicine, and he has been treating L.M. since 2012. *Id.* In his one-page letter, Dr. Longo stated that L.M. was found to have the SCN8A variant, and that "[t]his condition, and similar ones, can be aggravated by inflammation, fever and illnesses, including the inflammatory state caused by standard immunizations." *Id.* Dr. Longo adopted by reference the opinions of Drs. Byers and Kinsbourne, concluding that L.M.'s seizure condition was significantly aggravated as a result of her "reaction" to the December 30, 2011 vaccinations. *Id.* The letter provided no independent support for its assertions.

6. *Dr. Francis Filloux*

Petitioner filed a second letter from a treating physician who did not testify at hearing, Dr. Filloux. *See* Ex. 17 at 1, filed Aug. 31, 2015 (ECF No. 21-5) ("Filloux Rep."). Dr. Filloux is a professor of pediatrics and neurology, as well as the division chief of pediatric neurology, at the University of Utah School of Medicine. *Id.* In his one-page letter, Dr. Filloux endorsed the opinions of Drs. Byers and Kinsbourne, agreeing that L.M.'s condition was significantly aggravated by her December 30, 2011 vaccinations. *See id.* He noted that L.M.'s condition is "closely analogous to that with occurs in patients with SCN1A mutations causing Dravet syndrome," and asserted that in the context of Dravet syndrome patients, "it is well known that immunizations and febrile illnesses can trigger episodes of prolonged status epilepticus and seizures that then result in additional harm to the child's developing brain." *Id.* He deemed it probable that "a similar pathophysiological chain of events occurred in L.M.'s case." *Id.*

C. Respondent's Expert Witnesses

1. *Dr. Gerald Raymond*

Dr. Raymond testified at hearing and provided two reports on behalf of Respondent. *See* Ex. C, filed Dec. 30, 2015 (ECF No. 28-1) ("Raymond First Rep."); Ex. J, filed Apr. 17, 2017 (ECF No. 47-1) ("Raymond Second Rep."). Dr. Raymond, a specialist in pediatric neurogenetics, opined that the vaccines L.M. received on December 30, 2011 did not significantly aggravate her preexisting SCN8A-related EIEE 13.

Dr. Raymond received his B.S. from Fairfield University in Connecticut, followed by his M.D. from the University of Connecticut. Tr. at 433; Ex. F at 1, filed Dec. 30, 2015 (ECF No. 28-4) ("Raymond CV"). He completed an internship and residency in pediatrics at Johns Hopkins Hospital, followed by a neurology residency at Massachusetts General Hospital in Boston. Raymond CV at 1. Thereafter, he completed two fellowships, the first in developmental neuropathology at the Université Catholique de Louvain in Brussels, Belgium, and the second in genetics and teratology at Massachusetts General Hospital. *Id.* Dr. Raymond subsequently became

a professor of neurology at Johns Hopkins University School of Medicine, where he was also the division director of neurogenetics research. *Id.* at 2; Tr. at 434. In 2013, he became director of pediatric neurology at the University of Minnesota School of Medicine, and in 2017, he moved to the Penn State College of Medicine. Tr. at 434–35.

Dr. Raymond is board-certified in child genetics, as well as in neurology with a special qualification in child neurology. Tr. at 435; Raymond CV at 13. He spends most of his time on clinical work, focusing predominantly on neurogenetics, which he defined as the overlap of neurology and genetics, or how genes can cause brain abnormalities, progressive neurogenetic disorders, and more. Tr. at 435–36. He regularly sees patients with EIEE, and about 80% of his patient population is pediatric. *Id.* at 437–38. His published articles and book chapters focus on neurogenetics, including some discussion of sodium channels. *Id.* at 437.

In both his written reports and hearing testimony, Dr. Raymond provided background information about the SCN8A variant and its relationship to EIEE 13. The SCN8A gene, he explained, "encodes a portion of the voltage-gated sodium channel Na_v 1.6 which controls the transport of sodium molecules across cell membranes." Raymond First Rep. at 4. The variant, he explained, results in a change of amino acid within the body's sodium channels. *Id.* at 5; Tr. at 451. Sodium channels are "highly conserved," meaning that they have existed consistently in mammals throughout the evolutionary process and thus have very low tolerance for genetic variation. Raymond First Rep. at 5; Tr. at 451. The specific amino acid change is one factor that geneticists would consider when determining the likelihood that a particular variant is pathogenic. Tr. at 452. L.M.'s variant caused leucine, "a large amino acid with a hydrophobic side chain," to be replaced with serine, "a small polar, uncharged amino acid." Raymond First Rep. at 5. As reflected by literature filed in this case, L.M. is the only reported SCN8A patient with a leucine to serine amino acid change (*see* Malcomson at 7–8), and Dr. Raymond theorized that the structural differences between these two amino acids would likely cause significant physiochemical changes in the resulting molecule, thus causing harm to the structure and function of the resulting protein. Raymond First Rep. at 5; Tr. at 452.

Dr. Raymond explained that certain missense mutations[15] in the SCN8A gene cause EIEE 13. Raymond First Rep. at 3. In general, EIEEs are a group of genetic disorders characterized by early onset seizures, as well as intellectual and behavioral disability. *Id.* EIEE 13 specifically features seizure onset between birth and twelve months of age, with median onset at four months of age. *Id.*; Tr. at 458–59. Febrile seizures are rare for EIEE 13 patients. Raymond First Rep. at 3. Roughly half of EIEE 13 patients have a normal EEG at or near the time of their seizure onset, but have abnormal EEGs in the months thereafter. *Id.* Additionally, most regularly have normal MRIs. *Id.* Before seizure onset, roughly half of EIEE 13 patients have normal development, with developmental regression common after seizures begin. *Id.* at 4. Movement disorders and cortical

[15] A missense mutation is a genetic mutation that results in the coding of a different amino acid. *Dorland's* at 1214.

blindness are distinctive features of EIEE 13. *Id.*; Tr. at 460. Dr. Raymond identified several pieces of medical literature that supported his overall view that SCN8A variants regularly result in profound disability. Tr. at 465–70 (discussing Larsen; Anand; J. Wang, et al., *SCN8A Mutations in Chinese Patients with Early Onset Epileptic Encephalopathy and Benign Infantile Seizures*, 18 BMC Med. Genetics 104 (2017), filed as Ex. 64, June 9, 2018 (ECF No. 69-1); C. G. F. de Kovel, et al., *Characterization of a De Novo SCN8A Mutation in a Patient with Epileptic Encephalopathy*, (2014), 108 Epilepsy Res. 1511, filed as Ex. 22, Aug. 31, 2015 (ECF No. 21-10)).

Dr. Raymond discussed L.M.'s pre-vaccination medical history at length, explaining how her course was consistent with what would be expected for someone with an SCN8A alteration. Tr. at 438–49. Her jitteriness at birth, abnormal movements at two months old, and noted hypotonia were in his view all consistent with early presentation of EIEE 13. *Id.* Her post-vaccination history was similarly consistent with the expected course of someone with an SCN8A variant, including her seizure onset at around four months of age, cortical blindness, developmental regression, microcephaly, physical dysmorphia, intellectual disability, and movement disorder. *Id.* at 460–64. Her test results similarly conformed to what would be expected for EIEE 13 patients, including her normal EEG before seizure onset, her subsequent abnormal EEG, and her consistently normal MRI readings. *Id.* at 462–63; Raymond First Rep. at 6. Overall, Dr. Raymond emphasized that sudden regression and developmental decline such as what L.M. experienced has been "previously and consistently reported" in patients with SCN8A variants. Tr. at 456–57.

Based on his knowledge of EIEE 13 and his review of L.M.'s medical records, Dr. Raymond opined that vaccines did not cause or exacerbate her condition. Tr. at 456–57, 485–86; Raymond First Rep. at 10. He deemed her course completely consistent with what would be expected in light of her genetic variant, and stated further that environmental factors such as vaccines are not known to play any role in causing or aggravating EIEE 13. Tr. at 470–71. While some genetic conditions might be influenced by environmental factors, Dr. Raymond found no evidence that such factors could affect the course of an EIEE 13 patient. *Id.* He discussed a mouse study of the SCN8A variant, which showed that environmental factors do not affect the condition's course. *Id.* at 472–73 (discussing Wagnon). He also discussed the comparable SCN1A variant, which is believed by the medical community to result in Dravet syndrome, and explained that this condition has been clearly shown *not* to be affected by outside factors such as vaccinations. *Id.* at 479–81; Raymond Second Rep. at 2 (citing A. McIntosh, et al., *Effects of Vaccination on Onset and Outcome of Dravet Syndrome: A Retrospective Study*, 9 Lancet Neurology 592 (2010), filed as Ex. E, Dec. 30, 2015 (ECF No. 28-3) ("McIntosh")).

In his second report, Dr. Raymond responded to Dr. Boles's assertion that medical literature establishes the possibility of vaccine aggravation of the SCN8A variant, disputing that the cited literature in fact so indicates. Raymond Second Rep. at 2–4. Anand, for example, which discusses milder phenotypic presentations of the SCN8A variant, hypothesized only that some

patients experience a less severe presentation of the variant due to the presence of other genetic variants (or "modifier mutations") that lessen its pathogenicity. *Id.* at 4 (discussing Anand at 4). Furthermore, the patients studied in Anand did not have EIEE 13, but rather a different condition: benign familial infantile epilepsy. *Id.* at 4. The same was true of the patients discussed in another article cited by Dr. Boles, authored by Gardella, et al. *See generally* E. Gardella, et al., *Benign Infantile Seizures and Paroxysmal Dyskinesia Caused by an SCN8A Mutation*, Am. Neurological Ass'n 428 (2016), filed as Ex. 45 Tab B, July 29, 2016 (ECF No. 36-3) ("Gardella"). Dr. Raymond also did not place great significance in the existence of varying phenotypes for the same mutation, noting that variants in a particular gene commonly result in different phenotypes, a phenomenon which is "very well-recognized in the channelopathies." Raymond Second Rep. at 4. Dr. Boles's reliance on data from Anand and Gardella was therefore misplaced, he concluded. *Id.* And while the article by Larsen did describe a range of presentations among individuals with the SCN8A variant, Dr. Ramond maintained that L.M.'s course was consistent with results reported in that article—in particular with regard to her age of seizure onset, developmental regression, and test results. *Id.* at 3.

Dr. Raymond also criticized the scientific value of Dr. Hammer's report (which several of Petitioner's experts relied on), highlighting its reliance on self-reported survey data. Raymond First Rep. at 7–8; Tr. at 471. In particular, he pointed out that "Dr. Hammer indicates that it is data from two self-reporting surveys, but given the number of individuals he indicates are represented on the SCN8A Facebook page, there must be overlap." Raymond First Rep. at 7. He also noted that the survey instruments used therein have not been validated. *Id.* Finally, he stated that it is uncertain whether these survey reports had been confirmed by medical records, and that it is unclear how post-vaccination development was assessed in the surveys. *Id.* at 8. In addition, Dr. Raymond unpacked the VAERS data for Prevnar, which was relied on by Petitioner's experts and discussed in the Wise article. *Id.* at 9. He explained that, by its own terms, VAERS data does not establish causality, but rather observes reported adverse event incidences above the background rate. *Id.* This data showed that, of the 31.5 million doses of Prevnar administered in its first two years of post-market surveillance, only 393 post-vaccination seizures were reported. *Id.* (citing Wise). Yet the first ninety-eight of the reported seizure instances showed that "the majority were febrile or individuals with previous history of seizures and therefore were not unexpected in occurrence." *Id.* (citing Wise).

On cross examination, Dr. Raymond agreed that L.M.'s condition worsened notably the day after vaccination. Tr. at 512. He also conceded that he found certain aspects of Dr. Boles's theory about gene-environment interaction plausible, but maintained that he strongly disagreed with Dr. Boles's analytic construct that genes only confer risk and therefore cannot cause disease on their own. *Id.* at 514–15. He agreed, however, that an environmental trigger might be possible for some genetic variant conditions. *Id.* at 516.

Finally, Dr. Raymond disputed Dr. Byers's statement that there is no meaningful distinction between febrile and afebrile seizures. Although he did not testify in detail about the difference between the two, he explained that they are the result of entirely different mechanisms. Tr. at 457–58. He stated that there was strong evidence that L.M.'s seizures beginning on December 31, 2011, were *not* febrile in nature. *Id.* at 457. He also noted that illness, including a URI, is well-understood to exacerbate seizures in patients with seizure disorders such as EIEE 13. *Id.*

2. *Dr. Neil Romberg*

Neil Romberg, M.D., provided two written reports and testified for Respondent at hearing. *See* Ex. A, filed Dec. 16, 2015 (ECF No. 25-1) ("Romberg First Rep."); Ex. I, filed Mar. 22, 2017 (ECF No. 45-1) ("Romberg Second Rep."). Overall, he deemed L.M.'s response to the December 30, 2011 vaccinations to be normal, and did not see any evidence that she had experienced an abnormal immune response that could have significantly aggravated her underlying genetic disorder.

Dr. Romberg received his B.S. from the University of Michigan, followed by his M.D. from Pennsylvania State College of Medicine. Ex. B at 1, filed Dec. 16, 2015 (ECF No. 27-9). He completed a residency in pediatrics at the New York University School of Medicine and a fellowship in allergy and clinical immunology at Yale University. *Id.* Dr. Romberg worked for several years as an assistant professor of pediatric immunology at Yale University School of Medicine, where he was also the director of the Yale Pediatric Primary Immune Deficiency Clinic. *Id.* At present, he works at the Children's Hospital of Pennsylvania and is an assistant professor of pediatrics at the University of Pennsylvania School of Medicine. Tr. at 550–51. His clinical practice centers on pediatric immunology, though he spends most of his time on research, focusing specifically on monogenic immune system diseases. *Id.* at 551–53. Dr. Romberg is board-certified in allergy and clinical immunology. *Id.* at 551.

Dr. Romberg began his testimony with some discussion about the kind of immunologic reaction that a vaccine can trigger, and the association of that reaction to a seizure. He agreed with Dr. Byers that vaccinations can occasionally trigger a systemic response (as distinguished from a purely local response). Tr. at 566. In the case of such a response, IL-1 beta could bind to receptors in the central nervous system, thereby lowering the seizure threshold of a person genetically predisposed to seizures. Romberg First Rep. at 4. Evidence of a systemic response would include fever, loss of appetite, dizziness, and weakness, as well as an increased white blood cell count and a "left shift," which he defined as a change in the composition of white blood cells, featuring more myeloid cells and fewer lymphocytes. Tr. at 566–68. In the case of such a systemic response to vaccination, one would also expect to see clear evidence of an immune response at the site of injection. *Id.* at 570.

However, Dr. Romberg testified that he could see no evidence of such a systemic response to L.M.'s December 30, 2011 vaccinations based upon the relevant medical records. Tr. at 563–64, 573–74; Romberg First Rep. at 6. Around that time, L.M. did not experience a fever, any noticeable local response at the site of vaccination (her thigh), a loss of appetite, an increased white blood cell count, or a left shift. Tr. at 573–74; Romberg First Rep. at 4. Thus, Dr. Romberg concluded that L.M. had not likely experienced a significant or abnormal innate immune response to her December 30th vaccinations. Romberg First Rep. at 4. Absent evidence of such a heightened immune response, Dr. Romberg could see no evidence of any vaccine-related process by which L.M.'s seizure threshold could have been lowered. *Id.*

Moreover, even if L.M. had experienced an abnormal immune response contemporaneous with her seizure onset despite the lack of record evidence of it, Dr. Romberg was skeptical that such a response could be attributed to the vaccinations she received on December 30th. *See* Romberg Second Rep. at 2–4. Given the short time period between vaccination and L.M.'s decline, any immune event would necessarily involve the innate immune system, not the adaptive immune system. *Id.* at 3; Romberg First Rep. at 3. While researchers have succeeded in "training" the innate immune system to respond "more exuberantly to future infections," such "training" is not analogous to the pathogen-specific memory of the adaptive immune system, also known as "adaptive recall response." Romberg Second Rep. at 2–3 (citing J. van den Meer, et al., *Trained Immunity: A Smart Way to Enhance Innate Immune Defence*, 68 Molecular Immunology 40 (2015), filed as Ex. I, Tab 4, Mar. 22, 2017 (ECF No. 45-5)). The cells of the innate immune system are genetically identical, unlike the cells of the adaptive immune system, which are diverse and respond with specificity to particular pathogens. *Id.* The cells of the innate immune system thus cannot be trained to respond more aggressively to a given pathogen. *Id.* In light of this lack of specificity, Dr. Romberg concluded that even if evidence showed that L.M. experienced a significant inflammatory response on December 30–31, 2011, "a vaccine booster would <u>not</u> be more likely than other immune stimuli to be the cause." *Id.* at 3 (emphasis in original).

3. *Dr. Rajesh Sachdeo*

Respondent also provided one written report from Rajesh Sachdeo, M.D., who did not testify at hearing. *See* Ex. G, filed Jan. 29, 2016 (ECF No. 29-1) ("Sachdeo Rep."). As reflected in his CV, Dr. Sachdeo received his undergraduate and medical degrees in India. Ex. H at 1, filed Jan. 29, 2016 (ECF No. 29-2). He completed a a residency at V.A. Hines and Loyola University Medical Center in Maywood, Illinois, followed by a fellowship in neurophysiology and epilepsy at Rush-Presbyterian St. Luke's Medical Center in Chicago. *Id.* at 1–2. He has been a professor of neurology at the University of Medicine & Dentistry of New Jersey since 1982, and he serves as an attending physician at three New Jersey hospitals. *Id.* at 1–2. His dozens of published medical articles largely center on epilepsy and related conditions. *See id.* at 9–13.

In his ten-page report, Dr. Sachdeo asserted that L.M.'s December 30, 2011 vaccinations played no role in the course of her EIEE 13. Sachdeo Rep. at 9–10. He emphasized that L.M. demonstrated neurological abnormality consistently prior to vaccination, a point which he believed Petitioner's experts attempted to minimize or disregarded entirely. *Id.* at 5–9. Dr. Sachdeo also noted that L.M. experienced certain conditions, including infantile Parkinsonism and microcephaly, that could not be fairly attributed to a mere worsening of her seizures after vaccination. *Id.* at 9–10. Rather, such conditions more likely arose due to her SCN8A variant. *Id.* Therefore, Dr. Sachdeo concluded that "[v]accination had absolutely nothing to do with her ultimate clinical outcome." *Id.* at 9.

III. Procedural History

As previously noted, Petitioner initiated this claim on August 7, 2014. Respondent filed his Rule 4(c) Report on December 5, 2014 (ECF No. 12). Extensive medical records were filed, including documentation of L.M.'s SCN8A variant after it was discovered in 2015. Over the course of 2015–17, each party filed several expert reports. At my direction, the parties later filed briefs addressing the relationship between the SCN1A genetic variant—which has been extensively litigated in the Vaccine Program—and L.M.'s SCN8A genetic variant. *See generally* Pet'r SCN8A Br., filed Jan. 3, 2017 (ECF No. 43); Resp. SCN8A Br., filed Apr. 21, 2017 (ECF No. 51). I thereafter determined that there was enough of a difference between the two variants to justify a hearing in this matter, despite my reservations that some of the law generated in litigating SCN1A cases might bear on the present outcome. *See* Order at 1–2, dated June 22, 2017 (ECF No. 58).

The parties filed prehearing briefs in the summer of 2018. *See generally* Pet'r Pre-Hrg. Br., filed June 9, 2018 (ECF No. 67); Resp. Pre-Hrg. Br., filed July 11, 2018 (ECF No. 70); Pet'r Pre-Hrg. Reply, filed Aug. 11, 2018 (ECF No. 71). A three-day entitlement hearing took place on September 10–12, 2018. The parties subsequently filed post-hearing briefs. *See generally* Pet'r Post-Hrg. Br., filed Dec. 20, 2018 (ECF No. 84); Resp. Post-Hrg. Br., filed Mar. 11, 2019 (ECF No. 87); Pet'r Post-Hrg. Reply, filed Apr. 19, 2019 (ECF No. 90). This matter is now ripe for resolution.

IV. Motions to Strike Exhibits

There are two evidentiary matters still pending in this case to be resolved.

First, on January 3, 2017, Petitioner filed Exhibit 48 (subsequently re-filed on August 11, 2018, as Exhibit 88), an expert report from Andrew Escayg, Ph.D. (the "Escayg Report"), originally filed in another Vaccine Program case, *Fischer v. Secretary of Health & Human*

Services, No. 11-202V, 2015 WL 4498811 (Fed. Cl. Spec. Mstr. June 18, 2015).[16] Respondent moved to strike the Escayg Report on April 21, 2017, citing Section 12(d)(4)(A) of the Vaccine Act, which requires express written consent of the litigant from a different case who initially filed the document in question. Resp. SCN8A Br. at 20. Petitioner subsequently filed Exhibit 87, a consent form from the petitioner in *Fischer* authorizing the use of Dr. Escayg's report in the present matter.

At hearing, Respondent renewed his objection to admission of the Escayg report, noting that the *Fischer* petitioner affidavit only authorized use of the report itself, as opposed to otherwise opening the *Fischer* case record entirely, and was thus an improperly selective waiver of Vaccine Program confidentiality. Tr. at 4–7. I reserved ruling on the motion at that time (*id.* at 8), and Respondent again renewed his motion to strike the Escayg Report in his post-hearing brief. Resp. Post-Hrg. Br. at 28. Petitioner countered that he has satisfied all applicable requirements for bringing the report into evidence. Pet'r Post-Hrg. Reply at 17.

Because Petitioner has submitted an affidavit from the petitioner in *Fischer*, he has met the minimum of the standard under Section 12 of the Act.[17] Accordingly, Petitioner has established grounds for admission of the Escayg Report in this case.

However, my admission of the Escayg Report will not alter the balance of evidence otherwise, as I give it little to no weight. This is primarily due to statements contained in the report itself, which underscore its limited value herein. For, as Dr. Escayg wrote in his report, "my opinion on this specific case *should not be extended to other cases*." Escayg Report at 1 (emphasis added). Furthermore, *Fischer* awarded compensation to its petitioner based on a stipulation between the parties in which Respondent did *not* concede that a vaccine caused or significantly aggravated the petitioner's injuries. *Fischer*, 2015 WL 4498811, at *1–2. Accordingly, this single item of evidence has extremely limited value to the present matter.

In addition, an expert opinion on SCN1A mutations, and the purported propensity of vaccines to interfere with the disease course they initiate, that Petitioner deems favorable to his argument must be considered in light of numerous existing Program decisions—the vast majority of which have determined that seizure disorders produced by this mutation cannot be significantly aggravated by vaccines. *See Faoro v. Sec'y of Health & Human Servs.*, No. 10-704V, 2016 WL

[16] *Fischer* involved a child with the SCN1A genetic variant and the associated Dravet syndrome, and the claim asserted therein was settled without Respondent's concession as to the legitimacy of the claim. *Fischer*, 2015 WL 4498811, at *2.

[17] Arguably, the waiver may be too narrow, since a proper waiver would likely apply to *all* filings from *Fischer*. Permitting a petitioner to decide on an ad hoc basis what documents from another matter can or cannot be disclosed is the kind of selective privilege waiver that federal courts generally do not countenance. However, because I do not find that the Escayg Report merits significant weight in this matter, I will not devote further analysis to whether the proper standard for its admission was met in this case.

675491 (Fed. Cl. Spec. Mstr. Jan. 29, 2016), *mot. for review denied*, 128 Fed. Cl. 61 (2016) (vaccines including pneumococcal and diphtheria-tetanus-acellular pertussis ("DTaP") did not significantly aggravate child's SCN1A mutation resulting in seizures and developmental delay); *Barclay v. Sec'y of Health & Human Servs.*, No. 07-605V, 2014 WL 7891493 (Fed. Cl. Spec. Mstr. Dec. 15, 2014) (DTaP vaccine did not significantly aggravate Dravet syndrome otherwise attributable to SCN1A mutation), *mot. for review denied*, 122 Fed. Cl. 189; *Snyder v. Sec'y of Health & Human Servs.*, No. 07-59V, 2011 WL 3022544 (Fed. Cl. Spec. Mstr. May 27, 2011), *mot. for review granted*, 102 Fed. Cl. 305 (2011), *rev'd*, 553 F. App'x 994 (Fed. Cir. 2014) (same). Accordingly, the Escayg Report swims against the stream of too many contrary and well-reasoned decisions to have an appreciable positive impact in this case.

Second, along with his post-hearing brief, Petitioner filed six additional exhibits – all scientific/medical articles - on December 20, 2018. He discusses these items of literature in his post-hearing brief, citing them for the proposition that vaccines can cause afebrile seizures and criticizing Dr. Romberg for "ignor[ing]" such evidence. Pet'r Post-Hrg. Br. at 26. Respondent subsequently moved to strike these articles in his post-hearing brief, arguing that it is "patently prejudicial" for Petitioner to rely on articles filed after the deadline for submitting new evidence when criticizing Respondent's expert. Resp. Post-Hrg. Br. at 28. Respondent notes further that none of the filed literature directly supports the position that any of the vaccines administered to L.M. can cause afebrile seizures. *Id.* In response, Petitioner argues that he did not file these articles before hearing because the capacity of vaccines to cause afebrile seizures is a point "so broadly accepted that it was a surprise to Petitioner when raised as a debatable issue at hearing." Pet'r Post-Hrg. Reply at 17. Petitioner re-filed the six exhibits at issue with pertinent passages highlighted as Exhibits 97–102 on April 19, 2019.

I will also allow these exhibits into evidence, keeping in mind the Vaccine Program's emphasis on permitting petitioners every opportunity to prove their case—even where filings are made that would be rejected outright in virtually any other federal civil litigation context. However (and although I discuss the substantive merits of these newly-filed articles below), I will also give them less weight, both due to their untimely filing and because they were filed without leave of the Court or Respondent's consent. I will also disregard Petitioner's contention that Dr. Romberg "ignore[d]" this evidence, given that it was not filed at any time that would have allowed him to review it while preparing an expert report or before testifying at hearing, nor will I accept at face value Petitioner's contention of the "self-evident" capacity of vaccines to trigger afebrile seizures.

V. Applicable Legal Standards

A. Claimant's 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 and also occurring 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; *see also Shalala v. Whitecotton*, 514 U.S. 268, 270 (1995) (quoting Section 11(c)(1)(C)(i)); *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).[18] Petitioner in this case asserts only a non-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). 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).

For a non-Table claim, proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs*., 931 F.2d 867, 873 (Fed. Cir. 1991). In such circumstances, 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 asserting a non-Table claim must satisfy all three of the elements established by the Federal Circuit in *Althen v. Secretary of Health & Human Services*: "(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." 418 F.3d 1274, 1278 (Fed. Cir. 2005).

[18] 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, 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).

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, the 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 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), *vacated on other grounds*, 844 F.3d 1363 (Fed. Cir. 2017).

In discussing the evidentiary standard applicable to the first *Althen* prong, many decisions of the Court of Federal Claims and Federal Circuit have emphasized that petitioners need only establish a causation theory's biologic plausibility (and thus need not do so with preponderant proof). *Tarsell v. United States*, 133 Fed. Cl. 782, 792–93 (2017) (special master committed legal error by requiring petitioner to establish first Althen prong by preponderance; that standard applied only to second prong and petitioner's overall burden); *Contreras*, 121 Fed. Cl. at 245 ("[p]lausibility . . . in many cases *may* be enough to satisfy *Althen* prong one" (emphasis in original)); *see also Andreu*, 569 F.3d at 1375. At the same time, there is contrary authority from the Federal Circuit suggesting that the preponderance standard applied when evaluating a claimant's overall success in a Vaccine Act claim also bears on the first *Althen* prong. *See, e.g.*, *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1350 (Fed. Cir. 2010) (affirming special master's determination that expert "had not provided a 'reliable medical or scientific explanation' *sufficient to prove by a preponderance of the evidence a medical theory* linking the [relevant vaccine to relevant injury]") (emphasis added). Regardless, one thing remains: petitioners always have the burden of establishing their Vaccine Act claim *overall* with preponderant evidence. *W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted); *Tarsell*, 133 Fed. Cl. at 793 (noting that *Moberly* "addresses the petitioner's overall burden of proving causation-in-fact under the Vaccine Act" by a preponderance).

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 Health & Human Servs.*, 100 Fed. Cl. 119, 136 (2011), *aff'd*, 463 F. App'x 932 (Fed. Cir. 2012); *Veryzer v. Sec'y of Health & Human Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review denied*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 F. App'x 765 (Fed. Cir. 2012).

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." *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. denied 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 denied* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. Standard for Significant Aggravation Claims

In this matter, Petitioner maintains that the relevant vaccines significantly aggravated L.M.'s preexisting SCN8A mutation. Where a petitioner so alleges, the *Althen* test is expanded, and the petitioner has additional evidentiary burdens to satisfy. *See generally Loving v. Sec'y of Health & Human Servs*., 86 Fed. Cl. 135, 144 (2009). In *Loving*, the Court of Federal Claims combined the *Althen* test with the test from *Whitecotton v. Secretary of Health & Human Services*, 81 F.3d 1099, 1107 (Fed. Cir. 1996), which related to on-Table significant aggravation cases. The resultant "significant aggravation" test has six components, which are:

> (1) the person's condition prior to administration of the vaccine, (2) the person's current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person's current condition constitutes a 'significant aggravation' of the person's condition prior to vaccination, (4) a medical theory causally connecting such a significantly worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) a showing of a proximate temporal relationship between the vaccination and the significant aggravation.

Loving, 86 Fed. Cl. at 144; *see also W.C.*, 704 F.3d at 1357 (holding that "the *Loving* case provides the correct framework for evaluating off-table significant aggravation claims"). In effect, the last three prongs of the *Loving* test correspond to the three *Althen* prongs.

Subsumed within the *Loving* analysis is the requirement to evaluate the likely natural course of an injured party's preexisting disease, in order to determine whether the vaccine made the petitioner worse than he would have been but for the vaccination. *Locane v. Sec'y of Health & Human Servs.*, 685 F.3d 1375, 1381–82 (Fed. Cir. 2012) (upholding special master's determination that petitioner had failed to carry her burden of proof in establishing that her preexisting injury was worsened by the relevant vaccine); *Hennessey v. Sec'y of Health & Human Servs.*, No. 01-190V, 2009 WL 1709053, at *41–42 (Fed. Cl. Spec. Mstr. May 29, 2009), *mot. for review denied*, 91 Fed. Cl 126 (2010). The critical point of examination is thus "whether the change for the worse in [petitioner's] clinical presentation was aggravation or a natural progression" of the underlying condition. *Hennessey*, 2009 WL 1709053, at *42.[19] The Federal Circuit has upheld the

[19] The legislative history of the Vaccine Act strongly supports interpreting "significant aggravation" as requiring a claimant to establish that a vaccine rendered a preexisting condition qualitatively worse than it would have been otherwise—not simply that the affected individual experienced a post-vaccination symptom that contrasts with the individual's comparatively better pre-vaccination health. *See* H.R. Rep. No. 99-908, at 15 (1986) ("This [significant aggravation] provision does not include compensation for conditions which might legitimately be described as pre-existing (e.g., a child with monthly seizures who, after vaccination, has seizures every three and a half weeks), *but is meant to encompass serious deterioration* (e.g., a child with monthly seizures who, after vaccination, has seizures on a daily basis" (emphasis added)).

determinations of special masters that worsening was not demonstrated by a petitioner in connection with establishing her overall preponderant burden of proof for a non-Table causation-in-fact claim. *See, e.g.*, *Snyder/Harris v. Sec'y of Health & Human Servs.*, 553 F. App'x 994, 999–1000 (Fed. Cir. 2014); *Locane*, 685 F.3d at 1381–82.[20]

Application of *Loving*'s "worsening" requirement has been the occasion for some disparate holdings by special masters as well as the Court, especially due to the problems posed when evaluating the impact of a preexisting genetic condition that likely played *some* role in an injured party's post-vaccination health. In some cases, the mere fact that an injured party was literally "worse" than she was immediately prior to the vaccination at issue has been viewed as sufficient to satisfy this prong. *See, e.g.*, *Paluck v. Sec'y of Health & Human Servs.*, 113 Fed. Cl. 210, 232 (2013), *aff'd*, 786 F.3d 1373 (Fed. Cir. 2015).

In other instances, however, the mere fact a vaccine might "trigger" a transient negative response in an individual with an underlying condition has not been deemed proof of worsening if that individual would be expected to experience a similar overall course regardless. *Faoro*, 2016 WL 675491, at *27 (finding that "the vaccinations would not have changed her clinical course and thus, the vaccinations did not significantly aggravate her preexisting condition"). This point has been emphasized in a subcategory of Program cases involving the claim that a child's Dravet syndrome was significantly aggravated by vaccination. *Id.* at *1. In such cases, special masters have repeatedly determined that petitioners failed to show that a child's expected outcome would have been different but-for the vaccination—even though it was not disputed that the child's first major seizure had been triggered by vaccination. *Id.* at *2 ("[a]lthough H.E.F.'s vaccinations may have caused a low-grade fever or otherwise triggered her first seizure, neither the initial seizure nor her vaccinations caused or significantly aggravated her Dravet syndrome and resulting neurological complications"); *see also Snyder/Harris*, 553 F. App'x 994 (special master was not arbitrary in finding that petitioners' expert failed to show that the child's outcome would have been different had he not received the vaccinations at issue).

In *Barclay*, however, the Court of Federal Claims called into question whether *Loving* was the appropriate framework in cases where a genetic basis for an injured party's disease is undisputed. There, Judge Bruggink discussed the fact that "how the genetic abnormality is taken into account" heavily impacted application of the *Loving* factors. *Barclay*, 122 Fed. Cl. at 193. The Court noted that in a case where a child unquestionably possessed a preexisting genetic mutation associated with a particular outcome (in *Barclay*, the SCN1A mutation and its association with

[20] This is consistent with the fact (well recognized by controlling precedent) that evidence of "worsening" relevant to Respondent's alternative cause burden may reasonably by evaluated by a special master in determining the success of a petitioner's prima facie showing. *Snyder/Harris*, 553 F. App'x at 1000 (quoting *Stone*, 676 F.3d at 1380 ("no evidence should be embargoed from the special master's consideration simply because it is also relevant to another inquiry under the statute")); *see also Bazan*, 539 F.3d at 1353 ("[t]he government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the petitioner's evidence on a requisite element of the petitioner's case-in-chief").

Dravet syndrome), the petitioner would logically seek to argue that the vaccine at issue had aggravated the child's pre-vaccination condition (which in *Barclay* involved *no* manifestation of seizure activity at all prior to vaccination) by attempting to prove that the vaccine had made the child's future seizures and developmental delay "more severe." *Id.* at 198. The alternative was untenable; the genetic factor was too persuasively associated with seizure activity to rule it out, and the fact that the vaccine (through causing a fever due to its stimulation of the innate immune system) might have directly caused initial seizure activity was "insufficient to establish liability" based simply on the fact that the child thereafter recovered (if briefly) from it. *Id.*

As a result, *Barclay* suggested that the *Loving* analysis might actually not be an "ideal fit" for cases involving a genetic mutation. Instead, a better way to approach such a case would simply be to evaluate Respondent's success in carrying his counter-burden of establishing that a "factor unrelated" to the vaccine was the cause of injury. *Barclay*, 122 Fed. Cl. at 193 (citing *Knudsen*, 35 F.3d at 547). Doing so would avoid requiring a petitioner to establish a disease prognosis in light of the preexisting genetic mutation (which *Barclay* deemed to constitute a heightening of the Petitioner's underlying burden of proof). *Id.* at 198–99.

C. Law Governing Factual Determinations

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 a 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"); *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 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms. It is equally unlikely that pediatric neurologists, who are trained in taking medical histories concerning the onset of neurologically significant symptoms, would consistently but erroneously report the onset of seizures a week after they in fact occurred").

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*, 968 F.2d 1226 (Fed. Cir.), *cert. denied sub nom. 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 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 over contrary testimony, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

D. 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 Pharmaceuticals, 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 fora (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 his 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, 618 F.3d at 1347 (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 (1997)); *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 denied*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. App'x 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339).

E. Consideration of Medical Literature

Both parties relied on a significant number of medical and scientific articles to support their respective positions. I have reviewed all of the medical literature submitted in this case, although my decision does not discuss each filed article in detail. *Moriarty v. Sec'y of Health & Human Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 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).

ANALYSIS

For the reasons set forth below, I find that Petitioner has failed to meet his burden of showing that the vaccines at issue (primarily, though not exclusively, the pneumococcal vaccine) significantly aggravated L.M.'s preexisting SCN8A mutation-related seizure disorder. I address the *Loving* factors below in order of their significance to my decision, rather than in their ordinal sequence.

A. *Loving* Prong Four: Petitioner Did Not Establish a Reliable Causation Theory

In this case, the existence of L.M.'s EIEE 13 disorder is accepted by both sides, along with the undeniability of its relationship to her preexisting SCN8A mutation (the effects of which manifested *before* she received the December 30, 2011 vaccinations, although the parties dispute the severity of her prior symptoms as well as what they predicted about her likely future course). In addition, Respondent does not contest the chronology of events, including the damaging seizures L.M. began experiencing more regularly after December 30th. The case mostly does not turn on disputes regarding the tragic facts of L.M.'s early existence.

Because of the above, Petitioner was tasked with setting forth a reliable and persuasive causal theory—rooted in accepted medical or scientific evidence, as explained by properly-credentialed experts with demonstrated knowledge of pediatric seizure disorders and their connection to genetic mutations—establishing that the vaccines at issue could provoke an immunologic response damaging enough to worsen the effects of a child's existing genetic

mutation. This Petitioner did not accomplish, despite the efforts of several experts and treaters. Rather, the three primary testifying experts offered opinions that were overly generalized and vague, persuasively rebutted by Respondent's experts, and/or unsupported by reliable medical literature. Although Petitioner's experts took efforts to stay within their professional "lanes," their individual opinions did not mesh into an overall reliable theory sufficient to meet Petitioner's preponderant burden.

Dr. Byers was intended to provided Petitioner with immunologic expertise, laying out a theory explaining how one or more of the vaccines L.M. received (although she unquestionably stressed the pneumococcal vaccine) could have aggravated L.M.'s EIEE 13, but her explanations were inconsistent, vague, and based on poor-quality data. At various points, Dr. Byers equivocated in her explanation of how vaccines could induce seizures, theorizing that cytokines released as a result of vaccination could (a) affect neuronal structure, (b) impair sodium or calcium channels, (c) break down the blood-brain barrier, or (d) produce neurotoxicity—thereby all allegedly causing seizures, but without specifying which of these mechanisms was most likely herein. Byers First Rep. at 5; Tr. at 302–03, 309, 314, 354–55. In her written reports, Dr. Byers emphasized vaccination as the trigger for the onset of L.M.'s condition, but when confronted with L.M.'s undisputed *pre-vaccination* seizures and other neurological abnormalities at hearing (which occurred outside the immediate dates in which L.M. had previously received vaccines), she made no attempt to reconcile her theory with this contradictory evidence. *Compare* Byers First Rep. at 7 ("[i]t is clear that just having the genetic mutation does not cause symptoms. All disease must be triggered by something") *with* Tr. at 305 ("I think I have no opinion as to what caused that December 14th seizure").

In addition to the vagueness and inconsistency in her explanations, Dr. Byers did not adequately support her assertions with reliable evidence. Some of the medical literature cited by Dr. Byers facially did not support her contentions. For example, Dr. Byers cited an article in support of her contention that the pneumococcal vaccine, when administered through the nose, can instigate seizures. Byers First Rep. at 6–7 (citing T. Zwijnenburg, et al., *IL-1 Receptor Type 1 Gene-Deficient Mice Demonstrate an Impaired Host Defense Against Pneumococcal Meningitis*, 170 J. Immunology 4724 (2003), filed as Ex. 40, Aug. 31, 2015 (ECF No. 21-28) ("Zwijnenburg")). However, not only was the document filed by Petitioner only an abstract, but it also does not appear that Zwijnenburg discusses seizures at all. *See* Raymond First Rep. at 9 (explaining that Zwijnenburg does not discuss seizures, but instead explains the role of cytokine IL-1 beta in a mouse's defense against pneumococcal meningitis).

Otherwise, the only data Dr. Byers was able to point to in support of her view that Prevnar could induce seizures was VAERS data, which has regularly been rejected in the Vaccine Program when offered to establish a causal connection.[21] *See Analla v. Sec'y of Health & Human Servs.*, 70

[21] *See supra* note 12.

Fed. Cl. 552, 558 (2006) ("the Court [of Federal Claims] uniformly has upheld the Chief Special Master's concerns about the reliability of VAERS data") (citations omitted); *Bender v. Sec'y of Health & Human Servs.*, No. 11-693V, 2018 WL 3679637, at *31 (Fed. Cl. Spec. Mstr. July 2, 2018), *mot. for review denied*, 141 Fed. Cl. 262 (2019). Ultimately, her contention that the pneumococcal vaccine was integral to L.M.'s subsequent seizure course was simply not borne out by any independent evidence, nor was it bulwarked by anything Dr. Byers could draw upon from her own experience (since she has little demonstrated background in studying the relationship of vaccines to pediatric seizures).

Dr. Byers's testimony was as unpersuasive and disorganized in this case as in many prior Vaccine Program actions. Her theories have been regularly rejected in Vaccine Program decisions due to their speculative and confusing nature, as well as the lack of medical literature offered in their support. *See, e.g.*, *Bender*, 2018 WL 3679637, at *31 (characterizing Dr. Byers's testimony as haphazard, confusing, facially contradictory, and overly reliant on general theories "that were at best loosely connected to the record evidence"); *Rego v. Sec'y of Health & Human Servs.*, No. 04-1734V, 2008 WL 1990844, at *10 (Fed. Cl. Spec. Mstr. Jan. 30, 2008) ("Dr. Byers's testimony was confusing, speculative, and frankly suspect as it [was] not supported by the record in this case or other reliable sources"); *Tosches v. Sec'y of Health & Human Servs.*, No. 06-192V, 2008 WL 440285, at *8–12 (Fed. Cl. Spec. Mstr. Jan. 31, 2008) (Dr. Byers cited literature that did not actually support her arguments). Here, as before, she failed to provide a coherent explanation, rooted in reliable evidence, of the immunologic process by which *any* vaccination, let alone the pneumococcal vaccine, could cause or aggravate an infant's preexisting EIEE 13 seizure disorder.

Dr. Byers's reliance on the idea that the initial, innate immune reaction can trigger seizures (even in an individual who already is predisposed to experience them due to a genetic mutation—and indeed who has experienced some within the month preceding vaccination) through the upregulation of pro-inflammatory cytokines was particularly unfounded. *See, e.g.*, Byers First Rep. at 4; Tr. at 319. Program claimants frequently invoke the concept of vaccine-triggered cytokine production in an attempt to explain how a particular vaccine could cause a certain illness or injury. However, as I have discussed in many previous decisions, the idea that vaccines stimulate cytokine production, while scientifically correct by itself, amounts to nothing more than an explanation of how vaccines generally are expected to function. *Palattao v. Sec'y of Health & Human Servs.*, No. 13-591V, 2019 WL 989680, at *36 (Fed. Cl. Spec. Mstr. Feb. 4, 2019); *Olson v. Sec'y of Health & Human Servs.*, No. 13-439V, 2017 WL 3624085, at *20 (Fed. Cl. Spec. Mstr. July 14, 2017), *mot. for review denied*, 135 Fed. Cl. 670 (2017), *aff'd*, 758 F. App'x 919 (Fed. Cir. 2018). It does not explain how the initial innate response becomes pathologic.

As a result, a claimant arguing that cytokine production due to vaccination could worsen a preexisting EEIE 13 condition needs to expand on the contention, referencing reliable evidence, such as literature connecting the upregulated cytokines to the condition at issue or some

comparable autoimmune illness. Petitioners cannot merely invoke the general concept of cytokine upregulation in the innate immune responsive process after vaccination to show causation. *Palattao*, 2019 WL 989680, at *36; *Olson*, 2017 WL 3624085, at *20. Dr. Byers's discussion of the subject did little to advance a persuasive theory of causation in this case.

Dr. Kinsbourne's opinion was no better in terms of reliability or persuasiveness. As a threshold matter, beyond his neurologic expertise, Dr. Kinsbourne has no demonstrated recent (i.e., in the past twenty years) experience (a) treating pediatric patients, (b) treating individuals of any age with a seizure disorder, or (c) studying seizure disorders and their potential triggers. Tr. at 146–48.[22] Although (in contrast to Dr. Byers) he provided a more coherent and understandable opinion, bulwarked by what literature he could lay his hands on to support it, he was unable to leverage his unquestionable neurologic learnedness into a persuasive opinion on vaccine causality for genetic-related seizure disorders.

In this case (as in many recent cases I have presided over), Dr. Kinsbourne appears to have been retained in large part on the basis of his experience as a Vaccine Program expert,[23] well versed in the requirements of testifying before a special master, and hired to perform research targeted at the medical or scientific issue in dispute for the purpose of offering a causation opinion. But although there is some benefit to having erudite medical or scientific professionals explain the complex issues raised by a particular Vaccine Act case, to be persuasive an expert *must* do more. A persuasive expert opinion will arise from the expert's *own expertise* in the field relevant to the disputed issues—whether due to clinical exposure to treating the illness in question, or knowledge derived from his own research. Dr. Kinsbourne's opinion, by contrast, arose from neither. As a result, his opinion and testimony were far less useful than what Respondent offered in rebuttal from Dr. Raymond—a currently-practicing pediatric neurologist with immediate, demonstrated expertise in the relevant subject matter.

Ignoring these admittedly-facial deficiencies, the substance of Dr. Kinsbourne's opinion was itself unpersuasive and unreliable. First, he downplayed L.M.'s pre-vaccination neurologic abnormalities and developmental delay, asserting that she was "developing normally or close to normally," while disregarding medical records showing that this was not the case. Tr. at 134. He thus made incorrect factual suppositions, rendering his views less persuasive than those of other

[22] I have previously criticized Dr. Kinsbourne for lacking up-to-date expertise on the medical issues about which he testifies. *See, e.g.*, *Pope v. Sec'y of Health & Human Servs.*, No. 14-078V, 2017 WL 2640503, at *21 n.29 (Fed. Cl. Spec. Mstr. May 1, 2017) (noting Dr. Kinsbourne's lack of current expertise on relationship between vaccines and neurologic injury or mitochondrial disease).

[23] In making these comments, I do not seek to disparage Dr. Kinsbourne's oft-demonstrated professionalism or gainsay his courteous service on behalf of Program petitioners, who unquestionably often find it difficult to find a proper expert for a given case. But petitioners still must strive to employ experts with sufficient qualifications on the topics at issue if they wish to prevail in a Vaccine Act case. Dr. Kinsbourne's expertise in neurology rendered him adequately qualified to *testify* in this case regarding the issues in dispute (unlike a dentist, for example), but that does not mean that this testimony would prove also to be reliable and persuasive, simply because it came from a neurologist's mouth.

experts. *Dobrydnev v. Sec'y of Health & Human Servs.*, 556 F. App'x 976, 992–93 (Fed. Cir. 2014) (giving little weight to expert opinions based on erroneous factual assumptions) (citing *Brooke Group Ltd. v. Brown & Williamson Tobacco Corp.*, 509 U.S. 209, 242 (1993) ("[w]hen an expert assumes facts that are not supported by a preponderance of the evidence, a finder of fact may properly reject the expert's opinion")).

Second, Dr. Kinsbourne made conclusory assertions that he could not back up with reliable scientific or medical evidence. As he conceded, his opinion that L.M.'s worsening could be attributed to vaccination relied on two suppositions: that her rapid increase in seizure activity required a trigger, and that the close temporal nexus between vaccination and increased seizures made vaccination the most likely culprit. *See* Kinsbourne First Rep. at 9. However, without evidence supporting his supposition that L.M.'s condition would not have changed for the worse but for an external trigger, or that such a trigger was enough to create the conditions for a worsened trajectory, I cannot credit his conclusions. Certainly he offered no reliable evidence regarding what medical science would expect might worsen a preexisting genetic condition like EIEE 13.

This raises another deficiency bearing on Petitioner's overall causation theory: whether a vaccine can trigger an afebrile seizure in an individual with a preexisting genetic disorder. Past Vaccine Program cases have determined that vaccination may trigger a fever, which in turn can provoke *febrile* seizures. *See, e.g.*, *Adams v. Sec'y of Health & Human Servs.*, 76 Fed. Cl. 23, 41 (2007) (finding an infant who developed febrile seizures within twenty-four hours after pneumococcal vaccination entitled to compensation); *Tembenis v. Sec'y of Health & Human Servs.*, No. 03-2820V, 2010 WL 5164324, at *15–16 (Fed. Cl. Spec. Mstr. Nov. 29, 2010) (finding entitlement where child experienced febrile seizure following DTaP vaccination, which resulted in epilepsy and child's subsequent death). However, while the McClellans suspected that L.M. might have had a fever around the time of her late-December vaccinations, her medical records consistently reflect that her temperature was normal when her seizures began more frequently on December 31, 2011. Ex. 6 at 149–50. L.M.'s seizures after her December vaccinations thus appear to have been afebrile.

Although (primarily via facially unpersuasive statements by Dr. Byers) Petitioner half-heartedly attempted to dispute the significance of the lack of record evidence in this case of a febrile seizure by denying the medical and scientific evidence mostly associating seizure with fever (*see, e.g.*, Tr. at 302 (Dr. Byers deeming as "myth" the distinction between febrile and afebrile seizures)), he later attempted to maintain that in fact vaccine-caused seizures can be afebrile. In support, he cited a past Vaccine Program decision. Pet'r Post-Hrg. Br. at 26 (citing *Graves v. Sec'y of Health & Human Servs.*, 109 Fed. Cl. 579, 595 (2013)).

As Petitioner correctly points out, the Court of Federal Claims ruled therein that "the existence of a fever as a talisman to causation can be error." *Graves v. Sec'y of Health & Human*

Servs., 101 Fed. Cl. 310, 332 (2011).[24] However, *Graves*—decided eight years ago, and hence before the more recent caselaw discussing the association between certain genetic mutations, like SCN1A, and seizure disorders—must be evaluated in light of more recent decisions from the Court of Federal Claims that have *affirmed* special masters' decisions noting the reduced likelihood that afebrile seizures are vaccine-caused (at least where, as here, the Petitioner maintains that the seizures were cytokine-mediated). *See, e.g., K.L. v. Sec'y of Health & Human Servs.*, 134 Fed. Cl. 579, 587 (2017) (finding that special master's decision to credit expert testimony "that scientific evidence strongly supports that interleukin–1 beta is the chief cytokine that mediates fever, and, thus, it has been associated with febrile seizures, but not afebrile seizures" was not arbitrary or capricious); *Dodd v. Sec'y of Health & Human Servs.*, 114 Fed. Cl. 43, 55–57 (2013) (finding special master's determination that evidence concerning febrile seizures had little bearing on alleged vaccine causation of afebrile seizures to be neither arbitrary nor capricious). Thus, while (mindful of *Graves*, as well as some other decisions in which afebrile seizures were deemed vaccine-caused[25]) I do *not* consider the existence of fever to be prerequisite to a finding of causation in this case, I embrace the reasoning found in past Program decisions distinguishing between febrile and afebrile seizures and the relevance of this distinction where a cytokine-driven response is a primary component of the petitioner's claim.

Petitioner also (via his post-hearing filings) sought to bulwark *Graves* with some literature that he maintained established medical/scientific acceptance of vaccine-induced afebrile seizures. Pet'r Post-Hrg. Br. at 26. However, these articles largely do not support Petitioner's contention.[26] One, for example, was offered to establish an association between afebrile seizures and the measles-mumps-rubella vaccine. *See* Pet'r Post-Hrg. Br. at 27 (citing I. Eckerkle, et al., *Serologic*

[24] The citation provided by Petitioner in his post-hearing brief is for a 2013 damages decision in the *Graves* matter, in which the court does not discuss afebrile seizures at length. *See generally Graves*, 109 Fed. Cl. 579. The most thorough discussion in *Graves* regarding vaccines' ability to cause afebrile seizures is found in a 2011 ruling finding entitlement from the Court of Federal Claims (101 Fed. Cl. 310), and it is this analysis that I consider above.

[25] For example, past Vaccine Program cases establish a potential causal link between the whole cell pertussis vaccine—which L.M. unquestionably did not receive—and afebrile seizures. *See, e.g., Andreu*, 569 F.3d at 1380–81 (finding infant's seizures, which may have been afebrile, to be more likely than not caused by diphtheria-tetanus-whole cell pertussis ("DPT") vaccine); *Almeida v. Sec'y of Health & Human Servs.*, No. 96-412V, 1999 WL 1277566, at *3, *70 (Fed. Cl. Spec. Mstr. Dec. 20, 1999) (finding causation where petitioner experienced an afebrile seizure on the evening she received a DPT vaccine). Neither *Andreu* nor *Almeida* involved a claimant with a genetic variant that could explain the origin of his or her seizures.

[26] Petitioner also cites an article concerning SCN1A and the associated Dravet syndrome in his post-hearing brief to support the contention that vaccines can cause afebrile seizures. Pet'r Post-Hrg. Br. at 27 (citing N. Verbeek, et al., *Effect of Vaccinations on Seizure Risk and Disease Course in Dravet Syndrome*, 85 Neurology 596 (2015), filed as Ex. 42 Tab C, July 29, 2016 (ECF No. 34-4) ("Verbeek")). Because literature and case law regarding the ability of vaccines to trigger seizures in SCN1A patients has been discussed in detail elsewhere throughout this decision, I will not discuss Veerbeek at length herein. I note, however, that Verbeek's authors do not provide data distinguishing febrile from afebrile seizure patients in their analysis, and that they conclude that their results "provide[] direct evidence that there is *no effect of vaccination-associated seizure onset on disease course*." Verbeek at 598, 600 (emphasis added).

Vaccination Response After Solid Organ Transplantation: A Systematic Review, 8 PLOS ONE (2013) filed as Ex. 91, Dec. 20, 2018 (ECF No. 84-3) ("Eckerle")). But, while Eckerle discusses many vaccines, it does so in the context of organ transplant patients and the efficacy of vaccines in protecting them against post-transplantation infectious diseases. *See generally* Eckerle. The article makes *no mention whatsoever* of seizures, afebrile or otherwise. *See generally id.*[27]

Petitioner referenced two other articles in support of the contention that afebrile seizures "are often related to minor infections in which the mechanism of action is biochemically identical to that of vaccine reactions." Pet'r Post-Hrg. Br. at 27 (citing W. Lee, et al., *Afebrile Seizures Associated with Minor Infections: Comparison with Febrile Seizures and Unprovoked Seizures*, 31 Pediatric Neurology 157 (2004), filed as Ex. 92, Dec. 20, 2018 (ECF No. 84-4) ("Lee"); T. Zhang, et al., *Are Afebrile Seizures Associated with Minor Infections a Single Seizure Category? A Hospital-Based Prospective Cohort Study on Outcomes of First Afebrile Seizure in Early Childhood*, 55 Epilepsia 1001 (2014), filed as Ex. 93, Dec. 20, 2018 (ECF No. 84-5) ("Zhang")). Admittedly, both Lee and Zhang are more apposite to present circumstances than Eckerle—but neither implicates vaccines as causative. *See generally* Lee; Zhang. Nor does either article explain how the "mechanism of action" would be "biochemically identical to that of vaccine reactions," as proposed by Petitioner in his post-hearing brief. *Id*.

Lee in particular is far less helpful to Petitioner's case than it might seem at first glance. Its authors describe three categories of seizures: febrile (those occurring while the patient has a fever), provoked (those occurring while the patient has an infectious disease but no fever), and unprovoked (those occurring while the patient has neither a fever nor an infectious disease). Lee at 157–58. But with regard to provoked seizures—the category relevant herein, consistent with Petitioner's assertion that a vaccine would be comparable in effect to a mild infection—the authors note not only that some patients may have a fever at some time during the course of their illness, but emphasize that "[a]ll patients with provoked seizures manifested symptoms and signs of infection such as cough, coryza, vomiting, diarrhea, or fever." *Id.* at 158–59. Such circumstances are not comparable here, where L.M.'s only documented symptom on December 31, 2011, was a runny nose (while Lee discusses gastroenteritis or a URI). Ex. 6 at 151; Lee at 159. Thus, although Lee offers some support for Petitioner's assertion, it is not sufficiently specific to the present circumstances to merit significant weight.

Finally, two of Petitioner's post-hearing filings involved the broader concept of the relationship between proinflammatory cytokines and seizures (consistent with Dr. Byers's overall

[27] Another article was inapposite because it addresses the capacity of afebrile seizures to trigger epilepsy in genetically-susceptible humans—not the capacity of *vaccines* to do so (and in a patient who is not simply susceptible, but whose preexisting, genetic propensity for a seizure disorder has *already manifested*). Pet'r Post-Hrg. Br. at 27 (citing J. Nakayama, et al., *A Nonsense Mutation of the* MASS1 *Gene in a Family with Febrile and Afebrile Seizures*, 52 Annals of Neurology 654 (2002), filed as Ex. 94, Dec. 20, 2018 (ECF No. 84-6)).

theory that an innate immune response after vaccination resulting in cytokine upregulation triggered the late-December seizures). Pet'r Post-Hrg. Br. at 27 (citing T. Ichiyama, et al., *Tumor Necrosis Factor-[Alpha], Interleukin-1[Beta], and Interleukin-6 in Cerebrospinal Fluid from Children with Prolonged Febrile Seizures: Comparison with Acute Encephalitis/Encephalopathy*, 50 Am. Acad. Neurology 407 (1998), filed as Ex. 90, Dec. 20, 2018 (ECF No. 84-2) ("Ichiyama"); J. Ha, et al., *Interleukin-4 and Tumor Necrosis Factor-Alpha Levels in Children with Febrile Seizures*, 58 Seizure 156 (2018), filed as Ex. 102, Apr. 19, 2019 (ECF No. 90-6) ("Ha")).

These two last, newly-filed items are no more persuasive than those already discussed.[28] As their titles suggest, both Ichiyama and Ha studied cytokine levels in patients with *febrile* seizures. *See generally* Ichiyama; Ha. In Ichiyama, patients with afebrile seizures were included in a control group, but are not otherwise analyzed. Ichiyama at 2. The study's main aim was to distinguish between cases of febrile seizures and acute encephalitis, neither of which L.M. experienced. *Id.* at 6. A group of afebrile seizure patients was analyzed at greater length in Ha, but it observed afebrile seizure patients to have cytokine levels (specifically, TNF-alpha and IL-4) *near or below* control group levels, and far below febrile seizure patient levels. Ha at 159. Thus, neither Ichiyama nor Ha supports the position that a patient with afebrile seizures (such as L.M.) would be expected to have above-average cytokine levels. At bottom, all of these late attempts to imbue with significance the afebrile nature of L.M.'s post-vaccination seizures were less reliable, and persuasive, than Respondent's arguments about the significance of febrile seizures, the absence of such evidence in this case, and the lack of other proof of an existing systemic inflammatory reaction after the late December vaccinations.

The remaining expert opinions offered in this case[29] were facially conclusory or unreliable. Dr. Hammer appears to have direct knowledge of SCN8A patients, but the study he conducted (which purports to connect the mutation to vaccine-related exacerbation) was self-evidently the product of selection bias, as discussed in more detail below, with none of the supporting data filed in this case. Dr. Longo's opinion was too conclusory to give it much weight (although it is evaluated as a treater opinion below).

Dr. Filloux's letter raised an interesting point lurking in the background of this case: the extent to which Program case law pertaining to SCN1A mutations applies herein. If anything, Dr. Filloux's letter *supports* such application, for he explicitly endorses the idea that the SCN1A and SCN8A mutations, despite their differences as elucidated at hearing, result in "closely analogous"

[28] I also take note of the fact that five of the six late-filed items were authored and published before the September 2018 hearing—suggesting their filing could have been accomplished well prior to that date. Although I permitted these items into the record, and considered them in reaching my resolution of the case, I typically give late-filed items less weight where a party has not demonstrated a justification for their dilatoriness—for example, because the item in question was only published after hearing.

[29] Dr. Boles's opinion primarily sought to establish that an individual with a preexisting SCN8A mutation would not have experienced a course as severe as L.M.'s but for an environmental insult, and thus his opinion is discussed below.

conditions. Filloux Rep. at 1. He goes on to maintain that the causal relationship between vaccines and Dravet syndrome is "well known"—although he does not mention the numerous Program cases finding that *even if* a vaccine precipitated a seizure in an infant with the SCN1A mutation, the patient's overall outcome and course could not be attributed to the vaccine. *Id.*; *Faoro*, 2016 WL 675491 (vaccines including pneumococcal and DTaP did not significantly aggravate child's SCN1A mutation resulting in seizures and developmental delay); *Barclay*, 2014 WL 7891493 (DTaP vaccine did not significantly aggravate Dravet syndrome otherwise attributable to SCN1A mutation); *Taylor v. Sec'y of Health & Human Servs.*, No. 05-1133V, 2012 WL 4829293 (Fed. Cl. Spec. Mstr. Sept. 20, 2012), *mot. for review denied*, 108 Fed. Cl. 807 (2013) (same); *Snyder*, 2011 WL 3022544 (denying entitlement on grounds that SCN1A mutation was likely the sole cause of petitioner's seizure disorder). This persuasive Program case law (as well as reliable literature such as McIntosh, although it clearly only involves the SCN1A mutation) strongly support the proposition that Dravet syndrome is *not* aggravated by vaccination—allowing for a reasonable inference that the same is true for SCN8A mutations, given the admitted similarities between the two mutations as far as outcomes go.

Respondent's experts, by contrast, persuasively rebutted Petitioner's theory of causation. As Dr. Raymond established, there is no evidence that environmental factors can adversely affect the trajectory of EIEE 13. Tr. at 470–73. In particular, he highlighted the Wagnon study, which demonstrated that mice injected with an SCN8A variant seize spontaneously, without any need for an environmental trigger. *Id.* at 472–73 (discussing Wagnon). He also explained how literature cited by Dr. Boles for the proposition that disorders resulting from the SCN8A variant can be aggravated by environmental factors, including Anand and Gardella, do *not* in fact support this key point. Raymond Second Rep. at 4. The authors of Anand hypothesize that less severe presentations of the SCN8A variant are due to "modifier mutations," making no mention of vaccines or other environmental factors. *See* Anand at 4. Moreover, the patients studied in both Anand and Gardella do not have EIEE 13, but rather benign familial infantile epilepsy, making both articles less relevant to L.M.'s case than Dr. Boles implied. *See generally* Anand; Gardella.

Overall, because critical components of Petitioner's causation theory were (a) persuasively rebutted by Respondent's experts, (b) based on poor-quality data, (c) unsupported by reliable scientific evidence pertaining to the mutation and condition at issue, and (d) set forth in expert opinions that were disjointed or not based on the expert's demonstrated command of the relevant scientific or medical field, I cannot find that Petitioner has offered sufficient reliable evidence to preponderantly establish that vaccination could cause an aggravation of an infant's preexisting EIEE 13 seizure disorder otherwise attributable to an underlying SCN8A mutation.

B. *Loving* Prong Five: Petitioner Did Not Successfully Show that the Vaccines at Issue Caused L.M.'s Condition to Deteriorate

The medical record in this case does not support the conclusion that the vaccinations L.M. received on December 30, 2011, precipitated a worsening of her SCN8A-derived seizure condition beyond what was already underway.

Petitioner's theory depended on L.M. having experienced a systemic innate immune reaction to the vaccines she received on December 30th. But as explained in depth by Dr. Romberg, the medical records show that L.M. likely did *not* experience such a reaction. She had no fever, loss of appetite, increased white blood cell count, left shift, or noticeable immune response at the site of vaccination (her thigh), all of which would be expected if Petitioner's causation theory were occurring in real time. Tr. at 566–70, 573–74. Dr. Byers could not identify other evidence of a systemic reaction from the record,[30] and ultimately pointed to L.M.'s seizures as evidence that she experienced a post-vaccination systemic innate immune response. *See* Tr. at 430. This type of circular reasoning (the fact of the post-vaccination injury proves causation) is unpersuasive, as I have previously stated in other cases. *See R.V. v. Sec'y of Health & Human Servs.*, No. 08-504V, 2016 WL 3882519, at *34 n.80 (Fed. Cl. Spec. Mstr. Feb. 19, 2016), *mot. for review denied*, 127 Fed. Cl. 136 (2016).

Admittedly, Petitioner offered two treater opinions in support of vaccine causation, a kind of evidence entitled to some weight. However, I am not compelled to accept such treater statements as sacrosanct, and in this case I do not credit them as evidence deserving of great weight in support of this particular *Loving* prong. Dr. Longo's opinion that an SCN8A-derived seizure disorder like EIEE 13 could be impacted by an inflammatory process is undercut by the absence of medical record evidence that L.M. in fact experienced such an inflammatory response following vaccination. Dr. Filloux's opinion, as discussed above, was greatly undermined by its analogy to the SCN1A mutation, and his implicit acknowledgement that what is known about SCN1A bears equally in SCN8A cases.

Furthermore, neither treater appears to have attributed L.M.'s increased seizure frequency and regression to her vaccinations *when they were treating her*. *See* Ex. 4 at 72–75 (Dr. Longo's visit with L.M. on February 13, 2012; recording Petitioner's recollection that L.M.'s seizure increase "had been associated with her 4 month-old vaccine update" but not opining about possible vaccine causation), 259–62 (Dr. Filloux's initial consult for L.M. on July 23, 2012; recording

[30] Just as the coherence of her theories has frequently been called into question, Dr. Byers has also been criticized in other Vaccine Program cases for failing to offer a concrete explanation of how her proffered theory could apply to the facts of the instant matter. *See, e.g.*, *Shepperson v. Sec'y of Health & Human Servs.*, No 05-1064V, 2008 WL 2156748, at *10 (Fed. Cl. Spec. Mstr. April 30, 2008) (describing difficulty in following Dr. Byers's responses to questions: "The primary problem is that she testifies theoretically, never applying her theories to the facts and circumstances of a given case").

Petitioner's recollection that her condition worsened after vaccination but not attributing any causal role to vaccines; opining that L.M. "fits into the broad category perhaps of an epileptic encephalopathy without clear explanation"). Although a treater can certainly modify his opinion on causation over the course of his direct experience with a patient, it is reasonable to give a treater view reflected in the contemporaneous medical record (before thought of litigation has occurred) greater weight than a subsequent statement prepared specifically to support a Vaccine Act case. *Gerami v. Sec'y of Health & Human Servs.*, 127 Fed. Cl. 299, 305–06 (2014) (affirming special master's decision to credit contemporaneous medical records over letter prepared by treating physician for purposes of litigation).

C. *Loving* Prong Three: Petitioner Did Not Show that L.M.'s Post-Vaccination Course Was Sufficiently Worse to Constitute a Significant Aggravation of her Condition

Loving prong three requires a petitioner alleging a non-Table significant aggravation claim to demonstrate that his or her illness or injury was "significantly aggravated." Merely showing that the claimant's condition was objectively worse after vaccination than before does not satisfy this requirement, as a preexisting condition might be expected to independently cause a person's health to deteriorate over time. *Locane*, 685 F.3d at 1381–82; *Hennessey*, 2009 WL 1709053, at *42. Thus, to satisfy this *Loving* prong, a claimant must show that his or her course was worse than what would have been expected based on available knowledge about the claimant's condition. *Locane*, 685 F.3d at 1381–82; *Sharpe v. Sec'y of Health & Human Servs*., No. 14-65V, 2018 WL 7625360, at *36 (Fed. Cl. Spec. Mstr. Nov. 5, 2018, *mot. for review denied*, 142 Fed. Cl. 630 (2019), *appeal docketed*, May 31, 2019.

L.M.'s condition unquestionably became worse in the days following her December 30, 2011 vaccinations. The seizures she experienced were demonstrably worse in character than those prior to that time, as both sides acknowledged. *See, e.g.*, Tr. at 134–35 (Dr. Kinsbourne describing L.M.'s worsened condition after vaccination), 512 (Dr. Raymond agreeing that L.M.'s condition worsened notably the day after vaccination). Nevertheless, Petitioner has failed to preponderantly show that her overall decline, considering the period from her date of birth until mid-2012, was distinguishable from what would have been expected, given her underlying SCN8A variant and what is known about it. It is more likely than not that L.M.'s course would have progressively worsened into 2012, even absent vaccination.

Dr. Boles's testimony (relying in part on his demonstrated expertise as a geneticist) was critical to the success of Petitioner's showing on this particular *Loving* prong. He proposed a general analytic framework that posited the centrality of environmental factors in directing the course of a condition with a clearly-defined genetic origin. But Respondent's experts persuasively rebutted this concept, noting that medical science recognizes the existence of *many* diseases that are predominantly (and hence, for purposes of Vaccine Program evidentiary standards, "more likely than not") attributable to a genetic mutation. *See, e.g.*, Tr. at 519–20. Certainly in the

Vaccine Program (particularly with respect to SCN1A mutations, which are highly relevant herein) it is understood that the preexistence of such a mutation can defeat a causation showing even if an environmental factor like vaccination might transiently cause a temporary worsening. *See, e.g.*, *Faoro*, 2016 WL 675491, at *27; *see also* McIntosh.

Moreover, even if I ignore such baseline insufficiencies in Dr. Boles's analytic framework, the independent support he mustered for his opinion was far less robust than it appeared. For example, he deemed it well-accepted in the medical/scientific community that environmental factors play a central role in defining the course of EIEE 13. Boles First Rep. at 11 (citing M. Meisler, et al., *SCN8A Encephalopathy: Research Progress and Prospects*, 57 Epilepsia 1027 (2016), filed as Ex. 67, June 9, 2018 (ECF No. 69-4) ("Meisler")). But the authors of Meisler merely hypothesized that environmental factors *might* influence clinical presentation, and otherwise avoided making any conclusive statements on the matter. *See* Meisler at 6 (noting that "[p]atients with the identical genetic variant can differ in clinical severity, demonstrating an important role of genetic background, and *possibly environment*, in clinical outcome" (emphasis added); making no other mention of environmental factors elsewhere in article).

Dr. Boles similarly relied heavily on Dr. Hammer's study, and its underlying data, to support the contention that L.M.'s condition was significantly aggravated by vaccination, noting the reports of post-vaccination worsening memorialized therein. Tr. at 244.[31] However, the distinctly poor quality of Dr. Hammer's data makes it difficult to give weight to his conclusions. *See generally* Hammer Rep. As Dr. Raymond noted, that data consisted of uncorroborated parental survey responses rather than clinical and independent observation (Raymond First Rep. at 7–8)—a kind of factual input that results in self-selection bias, reducing the probative value of the study in question. *Johnson v. Sec'y of Health & Human Servs.*, No. 14-254V, 2018 WL 2051760, at *24 (Fed. Cl. Spec. Mstr. Mar. 23, 2018) (discussing problems with self-selection studies); *Evanson v. Sec'y of Health & Human Servs.*, No. 90-775V, 1991 WL 179085, at *4 (Fed. Cl. Spec. Mstr. Aug. 28, 1991) (discussing "major methodological problems" of studies based on self-reporting); *see also* Fed. Judicial Ctr., *Reference Manual on Scientific Evidence* 583–97 (3d ed. 2011) (discussing problems of selection bias and informational bias in self-selected studies, potential for confounding factors to erroneously imply existence of a causal relationship, and inferiority of self-selection studies to observational studies).

In addition, Dr. Hammer's report also has not been peer-reviewed or accepted for publication, and is unverified by medical records substantiating its survey results. At bottom, Dr. Hammer's conclusions, and the report he penned that reflects their purported applicability to this

[31] Drs. Byers and Kinsbourne also relied heavily on Dr. Hammer's report when concluding that L.M.'s condition was likely aggravated by vaccination. Tr. at 158 (Dr. Kinsbourne testifying that Dr. Hammer's report was his source for the view that EIEE 13 requires provocation from an environmental factor), 309–10 (Dr. Byers testifying that she was "relying primarily upon [Dr. Hammer's] interpretation of the data" regarding the adverse effects of vaccines on SCN8A-variant patients).

case, relies ultimately on the sort of *post hoc ergo propter hoc* reasoning about causation routinely rejected across many contexts in the Vaccine Program.[32] *See, e.g., Doe/34 v. Sec'y of Health & Human Servs.*, 2009 WL 1955140, at *10 (Fed. Cl. Spec. Mstr. Mar. 4, 2009); *Pafford v. Sec'y of Health & Human Servs.*, No. 01-165V, 2004 WL 1717359, at *9 (Fed. Cl. Spec. Mstr. July 16, 2004), *aff'd*, 64 Fed. Cl. 19 (2005), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2006).

Relying on Dr. Hammer's flawed report, an overstatement of Meisler's conclusions, and the full range of phenotypic outcomes for SCN8A mutations described in Larsen (which can admittedly vary from mild to severe), Dr. Boles opined that L.M. would likely have had only moderate developmental delay had she not been vaccinated on December 30, 2011. Tr. at 210–13, 232; Boles First Rep. at 12–13. However, Dr. Raymond testified persuasively in response that SCN8A patients typically experience significant seizure activity and skill loss even *without* external triggers, and that they see a downward progression of symptoms in the same timeframe experienced herein, suggesting that L.M. was likely to undergo the same regardless of vaccination. Tr. at 470–73, 485–86. The very medical record in this case corroborates this contention, as L.M. experienced pre-vaccination seizures (in November and December 2011) with no identifiable trigger, and her debilitating seizures manifested at the time in life predicted for children with EIEE 13 attributable to an SCN8A mutation. Dr. Raymond's position was more firmly grounded in reliable evidence than that of Dr. Boles.

Independent reliable literature, like Larsen, also supports the determination that L.M.'s outcome was not worsened by vaccination, as her symptoms fell within the range of foreseeable phenotypes (if admittedly on the more severe end). The mean and median age of seizure onset among the seventeen SCN8A patients documented in Larsen were five months and four months, respectively; L.M.'s frequent seizures began when she was four months and three weeks old. Larsen at 2. Twelve of the seventeen patients identified in Larsen also experienced developmental slowing or regression after seizure onset, as L.M. did. *Id.* Other patients experienced choreoathetosis and a loss of eye contact ability, as did LM. *Id.* L.M.'s test readings were similarly aligned with those of other SCN8A patients—at the time of seizure onset, her brain MRI was normal, as were the MRIs of nine of the thirteen patients with available data. *Id.* at 3. And at the time of onset, eight of fourteen patients with available data had normal EEGs, while fifteen of seventeen patients developed abnormal EEG readings over time—both of which accurately describe the progression of L.M.'s EEGs. *Id.* at 3, 5. Her outcome, while unquestionably tragic, is not unexpected under the circumstances.

[32] For example, Dr. Hammer asked survey respondents whether their child "suffered a loss of developmental skills in association with a particular event," and from this concluded that the triggering event (e.g., vaccination) was *responsible* for the loss of skills—without any intervening logic other than the temporal connection to link the two. Hammer Rep. at 2.

Petitioner's attempt to demonstrate that L.M.'s condition was significantly aggravated also relied on an unpersuasive effort to minimize the severity of her pre-vaccination condition. *See, e.g.*, Pet'r Pre-Hrg. Br. at 17 (highlighting Dr. Boles's statement that L.M. "went from being an essentially developmentally normal baby in terms of language and motor skills to loss of all previously-gained activities") (citation omitted); Pet'r Post-Hrg. Br. at 7 (characterizing Dr. Hornyik's reason for sending L.M. to PCMC on October 12, 2011, as "because L.M. exhibited some atypical physical movements at this pediatric visit"). L.M.'s medical records establish her apparent neurologic abnormalities, though mild, even in her first months of life. *See, e.g.*, Ex. 6 at 49 (Dr. Benedict deeming the "abnormal movements" that led Dr. Hornyik to send L.M. to PCMC on October 12, 2011, a probable seizure); Ex. 4 at 34 (November 14, 2011 developmental screen showing three-month-old L.M. to be at the one-month level for personal social skills and two-month level for gross motor skills, prompting referral from Dr. Benedict for early intervention services). Moreover, it is clear that her condition was understood to be deteriorating *even on the date of the vaccination at issue*, as noted by Dr. Hornyik at the December 30th visit: "Unfortunately, things seem to be worsening as [patient] now has seizures, and [development] is starting to fall behind." Ex. 4 at 48. While the record *does* support the conclusion that L.M.'s overall status was literally worse after vaccination, her developmental course was not benign before (as Dr. Boles admitted), making it further difficult to find that it truly "worsened" as the term is understood in light of *Loving. See* Tr. at 248–50 (Dr. Boles acknowledging L.M.'s pre-vaccination seizures and gross motor delay).

As reflected in numerous Vaccine Program cases, the weight of authority goes against the conclusion that a post-vaccination increase in seizure activity otherwise attributable to an underlying genetic condition can be deemed a vaccine-caused significant aggravation under *Loving*. *See, e.g.*, *Sharpe*, 2018 WL 7625360 (DTaP vaccine not found to significantly aggravate child's preexisting DYNC mutation); *Oliver v. Sec'y of Health & Human Servs.*, No. 10-394V, 2017 WL 747846 (Fed. Cl. Spec. Mstr. Feb. 1, 2017) (vaccines, including DTaP and pneumococcal, did not significantly aggravate underlying mutation associated with seizure disorder, even though fever attributable to vaccination was trigger for initial seizures), *mot. for review denied*, 133 Fed. Cl. 341 (2017), *aff'd*, 900 F.3d 1357 (Fed. Cir. 2018). These decisions do not compel the outcome in this case, any more than the numerous cases involving SCN1A genetic variants do—but they provide well-reasoned analyses with high relevance to the present circumstances. Petitioner has not otherwise demonstrated that such prior decisions are not analogous, even though the SCN1A and SCN8A mutations are not the same.

D. Other *Loving* Prongs

Loving prongs one and two require a comparison of the injured party's pre- and post-vaccination condition. There is no question that L.M.'s condition became worse in the days following her December 30, 2011 vaccinations—although her pre-vaccination history provides many hints that she had some underlying neurologic problem, even if her condition had yet to

manifest in full. In her first four months of life, she achieved some developmental milestones, but also demonstrated some initial, if mild, developmental delay. She experienced occasional seizures, but far less often than she did beginning on December 31st. And, as described in her parents' moving testimony, L.M. was a more interactive, mobile, and smiling child before her frequent seizures began, whereas now she is unable to make eye contact, does not make voluntary movements, and lacks the ability to interact meaningfully with her family. However, as discussed above, the fact that L.M. was qualitatively "worse" after vaccination does not lead to the conclusion in this case that her condition was significantly aggravated by vaccines, for the reasons discussed above.

Loving prong six evaluates whether, under a petitioner's theory of causation, the claimed significant aggravation occurred within a medically-acceptable time frame. Although Petitioner's theory here was difficult to comprehend given the confusing manner in which it was delivered by Dr. Byers, I find that (consistent with that theory) a systemic innate immune response would likely occur within the first day or so after vaccination, as agreed upon by both parties' experts. Byers First Rep. at 4; Romberg First Rep. at 3. Certainly the beginning of L.M.'s more severe seizures occurred in such a period of time—although they happened absent any evidence of an aberrant or excessive immune response. Thus, the timing of L.M.'s post-vaccination seizures conforms to Petitioner's theory—although the significant deficiencies of that theory overall deprive my finding of any great assistance to Petitioner's success in carrying his burden of proof.

E. Respondent Established that L.M.'s Condition Was Caused by a Factor Unrelated to Vaccination: her SCN8A Variant

As noted in my initial discussion of the legal standards for a significant aggravation claim, where a genetic mutation clearly underlies the injured party's symptoms, there is some support in the Court of Federal Claims for analyzing such claims as a "factor unrelated" case, under which circumstances Respondent would bear the burden of proof. *Barclay*, 122 Fed. Cl. at 193 (*citing Knudsen*, 35 F.3d at 547).[33] I do not find in this case that the burden of proof did shift to Respondent, since Petitioner's evidence did not rise to a preponderant level on many of the linchpin *Loving* prongs he needed to satisfy. In particular, he did not establish that a vaccine could, under the circumstances, trigger a non-febrile seizure sufficient to significantly worsen a preexisting seizure disorder with an unmistakable genetic origin.

However, even if I had found that the burden of proof had shifted, the facts of this case preponderantly support the conclusion that it was the SCN8A mutation that was the cause of Petitioner's seizures, independent of vaccination. All experts agreed it played at least *some* role in

[33] When a petitioner makes a *prima facie* showing sufficient to preponderantly establish that a vaccine caused or aggravated his injury, the burden of proof shifts to the respondent to show (also by a preponderance of the evidence) that the injury was caused in fact by a factor unrelated to the vaccine. *Knudsen*, 35 F.3d 543 at 547 (citation omitted).

her outcome. The medical record establishes that L.M. was already experiencing seizures before the December 30, 2011 vaccinations. The results from L.M.'s EEGs and MRIs, both before and after vaccination, are consistent with what is commonly seen among SCN8A patients, as demonstrated in Larsen. And her overall course, including her increase in seizures and loss of previously-gained skills, is also consistent with what is seen in other SCN8A patients at this time in an infant's life. Respondent persuasively established that L.M.'s SCN8A mutation is the cause-in-fact of her condition, while Petitioner's experts either lacked sufficient grounding in the relevant medical and scientific issues to make a persuasive case (Drs. Kinsbourne and Byers), or did not establish with reliable evidence that Petitioner's outcome is outside the scope of what a child with an SCN8A mutation would be expected to experience but for vaccination.

CONCLUSION

L.M.'s condition is heart-breaking, and I am deeply sympathetic to her family's sincere efforts to provide her with adequate care, and also to identify the basis for her condition. In a case such as this, where a child suffers from a severe and life-altering illness, it is extremely difficult to resist awarding damages, simply out of the desire to perform a good deed. But I am required to apply Vaccine Program law correctly, and doing so here leads me to conclude that Petitioner has not supported his claim with preponderant and reliable evidence. I therefore DENY entitlement in this case.

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.[34]

IT IS SO ORDERED.

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

[34] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by filing a joint notice renouncing their right to seek review.