In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 17-0079V

(to be published)

* *	Chief Special Master Corcoran
LUKE CAREDIO *and* JAMIELEE CAREDIO *on behalf of their minor daughter,* D.C.,	
Petitioners,	Filed: July 30, 2021
v.	
SECRETARY OF HEALTH AND HUMAN SERVICES,	
Respondent.	
* *	

Michael A. Firestone, Marvin Firestone, MD, JD, & Assoc., San Mateo, CA, for Petitioners.

Terrence Mangan, U.S. Department of Justice, Washington, DC, for Respondent.

ENTITLEMENT DECISION[1]

On January 17, 2017, Luke and Jamielee Caredio, on behalf of their minor daughter, D.C., filed this action seeking compensation under the National Vaccine Injury Compensation Program (the "Program").[2] ECF No. 1. The Petitioners allege that an influenza ("flu") vaccine administered to D.C. on January 22, 2014, caused her to incur an autoimmune form of epilepsy, plus a number of secondary symptoms (anxiety and post-traumatic stress in particular). An entitlement hearing in the matter was held in Washington, D.C. on January 28-29, 2021.

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[1] This Decision will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means 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 published Ruling's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen (14) days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire Decision will be available to the public in its current form. *Id.*

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3758, codified as amended at 42 U.S.C. §§ 300aa-10 through 34 (2012) [hereinafter "Vaccine Act" or "the Act"]. Individual section references hereafter will be to § 300aa of the Act (but will omit that statutory prefix).

Having reviewed the record, all expert reports and associated literature, and listened to those witnesses and experts who testified at the 2021 hearing, I hereby deny an entitlement award. As discussed in greater detail below, Petitioners have not preponderantly established that the flu vaccine can cause autoimmune epilepsy, or that it did so to D.C. in the relevant timeframe, with onset no earlier than February 2014 (and thus within 10-14 days after vaccination)—but then evolving over the next three months before more completely manifesting.

I. Fact History

Pre-Vaccination Health

D.C. was born on December 6, 2011, via cesarean section, and she was described as a "vigorous, healthy infant." Ex. 6 at 1–3. Two months later, on February 2, 2012, Petitioners took D.C. to the emergency department at Memorial Hospital Los Banos because D.C. had "stopped breathing briefly [status post] immunizations today for approx[imately] 10 seconds." *Id.* at 117. Petitioners ultimately left the emergency department before D.C. was evaluated by a physician, however. *Id.* at 118. Throughout 2012, D.C. was seen by pediatricians for occasional sick visits. *Id.* at 146, 174–78, 204.

On January 6, 2013, D.C. was transported by ambulance to the Memorial Hospital Los Banos emergency department after she fell, hit her head, and lost consciousness for about a minute. Ex. 6 at 226–27, 244. She was also experiencing concurrent rhinitis and congestion. *Id.* at 227–28. D.C. was discharged, and her parents were given instructions to return if she developed symptoms of an acute head injury. *Id.* at 229. On January 13, 2013, D.C. experienced another fall, with loss of consciousness. Ex. 12 at 12. She was also evaluated around this same time by several physicians for a possible failure to thrive. Ex. 6 at 254; Ex. 7 at 132–33, 135–37. A number of laboratory studies were ordered to assess D.C.'s condition, but none of the findings were remarkable. Ex. 6 at 265–70.

Vaccination and Onset of Symptoms

When she was a little more than two years old, D.C. received the flu vaccine during a visit with her primary pediatrician, Dr. Michael Deldin, around noon on January 22, 2014. Ex. 11 at 2; Ex. 6 at 277. During this visit, Dr. Deldin noted that D.C. was "doing better," though he did not specify what condition had improved. Ex. 12 at 8.

At approximately 6:00 p.m. that same day, D.C. started "shaking" while at home, but remained conscious and talking throughout the episode, which lasted for approximately fifteen minutes. Ex. 6 at 277. At 7:09 p.m., Petitioners took D.C. to the hospital, and she was admitted to Memorial Hospital Los Banos emergency department with a fever of 103.8 degrees. *Id.* at 278. She was discharged the same evening, and Petitioners were instructed to monitor D.C.'s condition,

and to administer Tylenol and ibuprofen as needed. *Id.* at 280. Her diagnosis at the time of discharge was a fever, likely related to a viral infection. *Id.*

The following day, Petitioners took D.C. to the Valley Children's Hospital Central California emergency department where her chief complaint was listed as a fever. Ex. 7 at 127. She was evaluated by Soledad Raroque, M.D., who noted that D.C. "presents to the ED with fever and possible seizure episodes since yesterday. Patient received influenza vaccination after which she developed fevers. Mother reports shaking episodes with fevers yesterday. [P]atient remained awake and alert the whole time….Today mother reports patient having shaking episodes with fevers…." *Id.* At 3:06 p.m., D.C.'s temperature was recorded at 38.4 degrees Celsius (101.1 degrees Fahrenheit) and 37.4 degrees Celsius (99.3 degrees Fahrenheit) at 4:10 p.m. *Id.* at 127–28. Dr. Raroque's differential diagnoses at this time included gastroenteritis, intussusception, Otitis Media, Tonsillitis, UTI, viral illness, and "Other (febrile seizure)." *Id.* at 128. Based on Petitioners' description of the episode, Dr. Raroque was unable to determine whether D.C. had experienced a febrile seizure or simply fever-associated chills. *Id.*

The next month, on February 20, 2014, D.C. returned to Dr. Deldin. Ex. 12 at 8. He noted that D.C. was suffering a fever and a left earache. *Id.* She was again seen by Dr. Deldin on February 27, 2014 and April 21, 2014, but Dr. Deldin's hand-written records are nearly illegible, and it is not clear why D.C. was seen at this time. *Id.* at 7–8.

Increase in Observed Symptoms and Epilepsy Diagnosis

There is an almost three-month gap in the medical record before Petitioners again sought formal care for D.C. associated with the injuries alleged in this action. On May 13, 2014, D.C. was brought back to Dr. Deldin, who was informed that D.C. had been experiencing eye twitching, and also was told of a recent episode where her head rolled back. Ex. 12 at 7. Dr. Deldin recommended D.C. be taken to Valley Children's Hospital for evaluation of potential seizure activity. *Id.* There, D.C.'s history of present illness was reported as a "one-week history of abnormal eye twitching…started having episodes [on] the right side of her face…as well as her shoulder and then her hand" lasting about four to five seconds without loss of consciousness. Ex. 7 at 108. D.C. had no fever at this time. *Id.* A CT scan performed that day was normal, and D.C.'s clinical impression remained "seizure." *Id.* at 110, 112. It was recommended that D.C. be seen by her pediatrician the next day, and to have him schedule an outpatient electroencephalogram[3] ("EEG"). *Id.* at 110.

[3] An EEG is a diagnostic test that measures the currents emanating from nerve cells in the brain. The fluctuations in current are shown in waves, which correlate with different neurologic conditions. *Dorland's Illustrated Medical Dictionary* 594 (33rd ed. 2020) ("*Dorland's*").

The EEG was performed on May 21, 2014, and Dr. Andrew Mower, M.D. documented D.C.'s history of "episodes described as eye twitching beginning in the right then goes to the left. Episodes began about one month ago and occur randomly and are brief lasting...Parents also report in January, [D.C.] received a flu shot, [D.C.] began having stiffening and shaking of her arms lasting about 10 seconds. Patient appeared unresponsive and had a high temperature of 103 degrees." Ex. 7 at 73. The results of the EEG were abnormal, and deemed consistent with partial epilepsy. *Id.*

D.C. was subsequently evaluated by neurologist Dr. James Nelson on May 29, 2014. Ex. 7 at 4–6. In addition to describing D.C.'s post-vaccination episode of January 14th, Dr. Nelson's history from this evaluation also noted that D.C. had fallen, stiffened, and lost consciousness on two separate occasions when she was a year old (but prior to receiving the vaccine at issue). *Id.* at 5. Following a physical examination and review of D.C.'s medical history, Dr. Nelson diagnosed D.C. with partial epilepsy with impairment of consciousness, and prescribed an increased dose of Trileptal—an anti-epileptic medication. *Id.* at 6.

On June 12, 2014, D.C. experienced an episode of right-sided eye and mouth twitching that lasted approximately 15-20 seconds. Ex. 7 at 33. Because this episode lasted longer than usual—and at the recommendation of Dr. Nelson—Petitioners brought D.C. to Valley Children's Hospital emergency department on June 13, 2014, where she was evaluated by Michael Hauser, M.D. *Id.* He noted D.C.'s history of "having episodes of right-sided 'twitching' over the last few months . . . seem to be getting more frequent." *Id.* Dr. Hauser's physical examination of D.C. did not reveal any neurologic abnormalities, but he recommended D.C. be admitted for observation and EEG monitoring. *Id.* at 33–34.

EEG video monitoring revealed left temporal parietal seizure activity. Ex. 7 at 36. D.C. was prescribed Topamax—another anti-epileptic medication—and the Caredios were instructed to restart Trileptal. *Id.* The frequency of D.C.'s seizures decreased with the addition of this medication, but they did not completely resolve. *Id.* It was recommended that D.C. undergo an MRI to further evaluate her seizure activity. *Id.* D.C. was discharged from Valley Children's Hospital on June 16, 2014.

An MRI was performed on August 4, 2014, but its results did not provide a readily-apparent etiology for D.C.'s seizures —though nonspecific T2 hyperintensities in the frontal region of the centrum semiovale region of the brain were observed. Ex. 7 at 13. Approximately two weeks later, on August 22, 2014, D.C. was admitted to Stanford's Lucile Packard Children's Hospital. Ex. 5 at 3.

During this admission, treaters sought to identify the underlying etiology for what was now being described as epilepsia partialis continua ("EPC").[4] Ex. 5 at 3. Treaters identified several potential underlying/explanatory diagnoses, including Rasmussen's encephalitis,[5] autoimmune etiologies, and/or mitochondrial etiologies. *Id.* D.C. was also started on a three-day course of intravenous methylprednisolone, after which she began receiving prednisone and intravenous immunoglobulin ("IVIG") once daily for four days. *Id.* Due to an inability to tolerate the prednisone, D.C. was transitioned to prednisolone. *Id.* D.C. began to experience some improvements in her right eye with these treatments, but the seizure activity in her right cheek and shoulder remained unchanged. *Id.*

On August 23, 2014, D.C. underwent a repeat EEG, which now showed "diffuse slowing and left centro-temporal spike and wave." Ex. 5 at 144. These findings were consistent with "focal epilepsy with left posterior hemisphere focus, and possible epilepsia partialis continua (EPC)." *Id.* at 6. MRI and lumbar puncture studies were unrevealing. *Id.* at 5, 152–53, 160. Mitochondrial and autoimmune etiologies were suspected, though treaters, including neurologist Katherine Mackenzie, M.D., also continued to consider the possibility of Rasmussen's encephalitis. *Id.* at 3, 25. D.C. was discharged on September 3, 2014.

Petitioners returned to Lucile Packard Children's Hospital on September 19, 2014. Ex. 5 at 164. During this visit, D.C. was evaluated in the Neuroimmunology Clinic by Drs. Keith Patrick Van Haren (who testified in this matter) and Jennifer Frankovich. *Id.* at 164–70. During her review of D.C.'s medical history, Dr. Frankovich noted that D.C.'s partial seizures began in March 2014 but had worsened in August. *Id.* at 168. During the visit, D.C. received IVIG and experienced a dramatic decrease in the severity of her symptoms. *Id.* at 166. Thus, both Drs. Van Haren and Frankovich proposed in reaction that D.C.'s seizures were likely the result of an autoimmune process, given the effectiveness of the IVIG treatment. *Id.* at 166, 170. To confirm this assessment, Drs. Van Haren and Frankovich recommended a steroid taper and follow-up appointment.

Petitioners adopted this recommendation and agreed to initiate the steroid taper, which resulted in an almost immediate reduction in D.C.'s symptoms. Ex. 5 at 171. D.C. had been experiencing seven to nine episodes a day since starting her taper, but was now down to three or fewer while receiving the full steroid dose. *Id.* Dr. Van Haren thereafter cut the steroid taper trial short and instructed Petitioners to administer the full dose of IVIG, which further proved ameliorative. *Id.* D.C. later returned to the Neuroimmunology Clinic for a follow-up appointment with Dr. Van Haren, during which he discussed D.C.'s lack of response to antiepileptic

[4] EPC is a form of status epilepticus with focal motor seizures, marked by continuous clonic movements of a limited part of the body. *Dorland's* at 626.

[5] Rasmussen's encephalitis/Rasmussen's syndrome is a rare form of encephalitis featuring focal lesions in one hemisphere of the brain, and is characterized by epilepsy and hemiparesis (one-sided muscle weakness). *Dorland's* at 606, 827.

medications and the likelihood that her condition was the result of an autoimmune process. *Id.* at 172. In order to better evaluate the potential role of autoimmunity, however, Dr. Van Haren ordered a number of laboratory studies, while advising a continuation of IVIG and Solumedrol treatments. *Id.* at 173.

Treaters thereafter struggled, as before, to identify the source or nature of D.C.'s illness. Cerebral spinal fluid ("CSF") studies of neurotransmitter metabolites derived results within normal limits. Ex. 5 at 233. In addition, an initial Epilepsy-Autoimmune Evaluation performed on August 27, 2014, was unrevealing; although subsequent studies performed later that fall were positive for a single specific category of antibody, treaters attributed this finding to the IVIG treatments D.C. had received just prior to the evaluation. *Id.* at 232, 234, 298. Genetic testing revealed that D.C. was heterozygous for three different genetic variants with pathogenic correlates, including myoclonic epilepsy, episodic ataxia, familial hemiplegic migraine, and cerebral arteriopathy with subcortical infarcts. *Id.* at 243. The significance of these findings was questioned, however, because the seizures D.C. experienced differed from those caused by the identified variants. *Id.* at 243, 297–98. Mitochondrial genome sequencing was also completed, but again produced unclear findings. *Id.* at 298.

On the morning of December 23, 2014, D.C. woke up in her usual state of health, but shortly thereafter began experiencing seizures with increasing frequency. Ex. 5 at 204. Petitioners took D.C. to the Memorial Hospital Los Banos emergency department, and following a physical examination and review of D.C.'s medical history, she received a 175 mg dose of Solumedrol. Ex. 6 at 337, 341, 343. D.C. was then transferred by ambulance to Lucile Packard Children's Hospital for steroid pulse treatment. *Id.* at 344; Ex. 5 at 204. During her admission, the onset of D.C.'s symptoms was now reported as "[o]ne week after her [flu] immunization" and it was again noted that D.C. did not experience relief with antiepileptic medications. Ex. 5 at 204. The following day, December 24, 2014, pediatrician, Dr. Ian Chua, M.D., evaluated D.C. for "[EPC] with likely autoimmune involvement." *Id.* at 208. She was hemodynamically stable during this evaluation, and Dr. Chua noted that D.C. had remained seizure free since receiving the Solumedrol treatment at Memorial Hospital Los Banos. *Id.* at 211.

A neurology consultation was performed the same day by Dr. Susy Shu-Hsin Jeng, M.D. Ex. 5 at 213–20. Following a thorough evaluation, including a review of D.C.'s medical history, laboratory findings, and physical examination, Dr. Jeng determined that a reduction of D.C.'s steroid and IVIG dosage was the most likely explanation for the unexpected exacerbation of her condition. *Id.* at 219–20. Thus, it was determined that D.C. should receive three days of treatment with Solumedrol followed by a prednisone taper. *Id.* at 220.

Treatment in 2015 and Beyond

Not long after being discharged from the hospital in late 2014, D.C. began to experience seizures with increasing frequency. Ex. 5 at 204, 247. Rather than tapering D.C.'s steroid dose, it was doubled but without improvement. *Id.* at 247. After returning to Lucile Packard Children's Hospital for additional IVIG treatment in early January 2015, a repeat EEG was performed, the results of which were again abnormal. *Id.* at 269. Jin Hahn, M.D., who interpreted the EEG, noted that D.C. experienced "frequent epileptiform potentials from the left posterior hemisphere." *Id.* These findings were deemed consistent with focal/partial epilepsy with left posterior hemisphere focus. *Id.* Petitioners were instructed to continue administering three different antiepileptic medications, with a fourth to be considered if D.C.'s seizures persisted. *Id.* at 263.

On January 26, 2015, D.C. was admitted to University of California, San Francisco ("UCSF") for a repeat EEG and brain MRI. Ex. 35 at 1. Julian Villar, M.D. reviewed D.C.'s medical history, at which time he noted that the onset of D.C.'s EPC occurred after receiving the flu vaccine when she was two years old. *Id.* at 2. No seizures were noted during Dr. Villar's physical exam, but the repeat EEG revealed "worsening epileptiform burden" compared to prior EEG studies. *Id.* at 2, 5. D.C. was discharged home with instructions to follow-up with the Pediatric Epilepsy Clinic in two weeks. *Id.* at 5.

D.C. returned to the Pediatric Epilepsy Center on February 2, 2015. Ex. 8 at 289. She was evaluated by Joseph Sullivan, M.D. (the second treater who testified in this matter), who recorded the following note:

> "During this 60 minute visit I spent 40 minutes counseling about the perplexing nature of her IVIG responsive epilepsy. I explained that this response does not prove that her epilepsy has an autoimmune component but I will leave the additional autoimmune evaluation up to Dr. Van Haren. While she has EPC her clinical presentation does not fit with Rasmussen syndrome, although I would be very interested to repeat her brain MRI to see if there has been any gradual, subtle left hemispheric changes. At this point I would not escalate her therapy as she seems to be responding to the IVIG. I will be very interested to see if my colleague Dr. Porter has any other diagnostic considerations and the family will keep us informed."

Ex. 8 at 289.

On February 16, 2015, D.C. again returned to Lucile Packard Children's Hospital due to increasing seizure frequency and prolonged duration presumed to be autoimmune in etiology. Ex. 5 at 277, 283. She was admitted for a three-day course of IVIG treatment as well as an MRI with spectroscopy to evaluate for lesions associated with Rasmussen's syndrome/encephalitis. *Id.* The MRI, which was conducted on February 18, 2015, showed "a few nonspecific T2 and FLAIR

hyperintense spots within the centrum semiovale bilaterally, unchanged compared to prior study." *Id.* at 321. The study was otherwise unremarkable, and D.C. was discharged on February 19, 2015. *Id.* at 321, 277–82.

In April 2015, D.C. was evaluated by neurologists Heather Olsen, M.D., and Leslie Benson, M.D., at Boston Children's Hospital. *See* Ex. 2. Both Drs. Olsen and Benson described the onset of D.C.'s illness as abruptly occurring approximately one or two weeks after receiving the flu vaccine (although the record is not fully consistent with that history). *Id.* at 1–2, 28. Notably, both physicians distinguished the "fever and tremulousness" D.C. experienced within hours of receiving the vaccine from the "onset of focal seizures in February 2014." *Id.* at 1–2, 28. Following thorough examinations and complete reviews of D.C.'s family and medical history, Drs. Olson and Brenson both opined that the etiology of her EPC remained unclear. *Id.* at 7, 33. While Dr. Brenson continued to consider Rasmussen's encephalitis and autoimmune triggers, Dr. Olson opined that D.C.'s clinical picture was largely inconsistent with Rasmussen's, and thus focused on the possibility of metabolic and/or genetic etiologies. *Id.* at 4, 8, 33. Both agreed that D.C. should continue receiving MRIs in addition to undergoing more extensive genetic and autoimmune testing, plus an addition course of IVIG. *Id.* at 8, 34.

On June 24, 2015, D.C. returned to UCSF where she was admitted and evaluated by Dr. Brian Gin, M.D. of the Pediatric Epilepsy Center for concerns relating to "facial seizures, hallucinations, sudden fear with dyscognitive features." Ex. 35 at 30–32, 43. Based upon the history provided to him by Petitioners, Dr. Gin documented the onset of D.C.'s EPC as occurring in "February 2014 when she developed irregular facial movements and eye twitching that was sometimes also associated with dropping objects." *Id.* at 43. During this admission, D.C. underwent repeat EEG and MRI studies. *Id.* at 30–32. The results of the EEG again demonstrated "frequent left posterior parietal epileptiform discharges." *Id.* at 33, 55–56. D.C. was discharged on June 25, 2015 with instructions to follow-up on September 30, 2015 with Dr. Sullivan. *Id.* at 65.

For the remainder of 2015, D.C. continued to receive repeat EEGs and IVIG therapy at UCSF throughout 2015. Ex. 35 at 101, 217, 344, 507. She also continued to demonstrate symptoms of EPC, corroborated by abnormal EEG results. *Id.* at 101, 144, 156, 233, 251, 347. Though the etiology for D.C.'s illness remained elusive, her responsiveness to IVIG treatment was consistently cited by treaters as evidence of an immune-mediated process. *Id.* at 120, 122, 135, 226–29, 372. Additional evaluation and testing performed in late 2015 was again inconsistent with a Rasmussen's diagnosis or an autoimmune-oriented disease. Ex. 35 at 507, 509, 528.

Testing performed in the first half of 2016 confirmed the presence of focal motor seizures and worsening epileptiform burdens. Ex. 3 at 4; Ex. 35 at 596, 600. Additional seizure activity occasionally required additional hospitalization, but EEG readings did not always reveal evidence of significant increases in activity. Ex. 3 at 4. By the second half of 2016, however, D.C. began to

receive psychological treatment for behavior difficulties associated with her condition and the intrusive treatments she was compelled to undergo. *See, e.g.*, *Id.* at 66. Her anxiety was deemed connected to the trauma of her seizure treatments. *Id.* at 70. On August 11, 2016, Dr. Sullivan stated in a letter that D.C. had an unexplained, immune-mediated epilepsy that appeared to present after a vaccination. Ex. 10. He wrote that it was in her best medical interest not to receive any further vaccinations for the rest of the school year. *Id.*

Later on that fall, D.C. seemed to improve somewhat, leading treaters to cease IVIG treatment. Ex. 35 at 849. She was now given the diagnosis of EPC, "initially IVIG-responsive." *Id.* By the summer of 2017, additional follow-up EEGs revealed further reduction in seizure activity. *Id.* at 918. Indeed, a record from a November 2017 telehealth visit with Dr. Sullivan states that D.C. remained off her EPC medication at that time, but was stable in terms of overall seizure activity, leading him to conclude that additional EEG testing was unnecessary at that time, although he did wish to follow up with her in six months. Ex. 42 at 1. A record from a subsequent visit with Dr. Sullivan in August 2020 was consistent in evaluating her EPC as largely stable. Ex. 46 at 1. And in a September 2020 letter (prepared and filed after this action's initiation), Dr. Sullivan opined that D.C. had experienced treatment-resistant epilepsy, and that "[d]espite an exhaustive work-up the etiology of her epilepsy and EPC remains unknown." Ex. 47 at 1.

II. Witness Testimony

A. Fact Witnesses

1. *Luke Caredio* – D.C.'s father was the first fact witness to testify. Tr. at 6-54. As he explained, D.C. is the older of the two Caredio children, and was a happy and active infant prior to receipt of the flu vaccine. *Id.* at 7–8. The Caredios initial felt it wise to make sure D.C. was vaccinated due to concerns at the time in the San Francisco Bay region of influenza outbreaks. *Id.* at 8. Mrs. Caredio therefore brought D.C. to the pediatrician on January 22, 2014, around noon. *Id.* at 9. D.C. had no evident symptoms before vaccination. *Id.* at 10.

That evening, however, after arriving home from work, Mr. Caredio recalls (around 6 p.m.) seeing D.C. look at him "with a kind of dazed look, glazed eyes," and appearing nonresponsive. Tr. at 11. D.C. did not seem warm in a febrile way. *Id.* In the process of trying to comfort her, Mr. Caredio noticed D.C. was shaking and continued to seem nonresponsive, with the shaking lasting for 15 minutes. *Id.* at 11–12. Mr. Caredio felt that something was likely wrong with D.C., and he and his wife made the decision to take her to the ER. *Id.* at 12.

By the time the Caredios reached the hospital, D.C. was no longer shaking, but had a fairly high temperature. Tr. at 13. They informed treaters of D.C.'s strange behavior they had witnessed, and Mr. Caredio compared her shaking to having the chills or straining for a bowel movement. *Id.* at 12. Although a contemporaneous record from this hospital visit stated that D.C. was "alert and talking the whole time," Mr. Caredio recalled that she was awake but largely unresponsive and

silent. *Id.* at 15. She had no other symptoms of illness at this time, however, although Mr. Caredio recalled his concern that D.C. may have had a vaccine reaction. *Id.* at 16. Treaters proposed she had experienced a febrile seizure, and instructed the Caredios to use over-the-counter pain relievers, releasing the family to go home. *Id.* at 13.

That night, D.C. continued to run a temperature above 100 degrees, although it was lower than what she had displayed earlier at the hospital, and she was restless. Tr.at 13–14. The next day, while Mr. Caredio was at work, Mrs. Caredio called him to say that D.C. had experienced another shaking episode and that she was taking her back to the hospital. *Id.* at 14, 17. By this point, Mr. Caredio was concerned that D.C. was experiencing a vaccine reaction, especially in light of warnings given about how vaccines could cause fever and other transient symptoms. *Id.* at 16. The Caredios were advised by treaters to use over-the-counter pain relievers and monitor D.C. further. *Id.* at 18.

Mr. Caredio's next recollection of any noticeable symptoms he observed in D.C. was the beginning of an eye twitch/flutter in February 2014, in response to fear or anxiety. Tr. at 18. D.C. would display the twitch once a day on average, but her pediatrician informed the Caredios that it was not of concern. *Id.* at 18-19. The following month (March), when the Caredios were out to dinner, Mr. Caredio recalled that D.C. displayed a hand jerking while holding food in her hand—a new behavior. *Id.* at 20-21. The Caredios did not seek treatment or evaluation of this behavior at this time, however. *Id.* at 48-49. In fact, as Mr. Caredio acknowledged, D.C. was not taken to any treater between her January 2014 ER visits and the May visit—nearly four months—to evaluate the symptoms he testified to observing in the interim time period. *Id.* at 49-50.

Then, in May 2014, Mrs. Caredio phoned Mr. Caredio to inform him that D.C. had another hand twitch incident while eating causing her to drop her food, along with her eyes rolling back, and that this was observed also by Mrs. Caredio's mother, Debra Townsend. A few days later, on May 13, 2014, Mrs. Caredio again called Mr. Caredio to tell him she had observed a more pronounced version of the same behaviors. *Id.* at 22. In response, the Caredios took D.C. back to the hospital, and were told by treaters D.C.'s behavior might be attributable to a seizure. *Id.* By this time, D.C. was also more regularly displaying face twitches and shoulder hunching. *Id.* at 24. However, Mr. Caredio acknowledged that the medical record from this visit did not reflect or memorialize any reported symptoms from the prior months he had allegedly witnessed (although he reiterated his recollection of being told D.C.'s initial eye twitching was merely a tic). *Id.* at 51-52.[6]

A CT scan was performed, but it showed nothing concerning. *Id.* at 23. D.C. was no prescribed anti-seizure medication, although the side effects it caused (face swelling in particular) led the Caredios to request that the medicine be suspended. *Id.* at 26-27. Mr. Caredio also recalled

[6] Mr. Caredio attempted to differentiate the tempo of symptoms increase in May 2014 from February, explaining that the eye twitching he and his wife had previously noticed was infrequent/sporadic, whereas in May the frequency had increased over the week prior to the Caredios seeking medical intervention for D.C. Tr. at 51, 52-53.

that D.C. underwent an EEG, the results of which supported an epilepsy diagnosis. *Id.* at 27. This led to further hospitalization and anti-seizure treatment, but also the recommendation that the Caredios seek further treatment with more qualified neurologic specialists. *Id.* at 27-28.

To that end, the Caredios took D.C. to Stanford Children's Health. Tr. at 28-29. Treaters initially informed Mr. Caredio that D.C.'s epilepsy was not the worst kind they could think of EPC, only to state after review of an EEG that in fact that was the proper diagnosis. *Id.* at 29. The process of testing that D.C. underwent at this time was very difficult to endure for the Caredios and was very comprehensive. *Id.* at 30. D.C. was now on multiple medications, none of which seemed to be effective, while D.C.'s health and presentation deteriorated. *Id.* at 31-32. But one of D.C.'s treating neurologists, Dr. Cho told Mr. Caredio that immune-modulating therapies (in particular, steroids or IVGV) might be effective if in fact D.C.'s condition was an autoimmune response to her January 2014 vaccination. *Id.* at 32; Ex. 5 at 53. And in fact, D.C. responded positively to these treatments, leading the Caredios to approve periodic IVIG courses going forward. *Id.* at 34-36.

After D.C. had a seizure incident in December 2014, the Caredios decided they would again look for even more qualified expertise, leading them to visit the Neurology Depaartment at Boston Children's Hospital. Tr. at 36-37. Based on the evaluation received there, however, the Caredios concluded that the care D.C. was already receiving in California was competent, although they subsequently opted to move her care from Stanford to UCSF, where she could receive periodic IVIG treatments (although the distance to the Caredios's home in Los Banos, California was still significant). *Id.* at 38. D.C. also began to require some speech therapy due to stuttering associated with her epilepsy. Tr. at 41.

Today, Mr. Caredio testified, D.C. is largely doing better, and her seizure activity is under control (although she occasionally has one or a related flare-up). Tr. at 42-43. She also displays some memory issues. *Id.* at 44.

2. *Jamielee Caredio* – Mrs. Caredio's testimony was consistent with that of her husband. *See generally* Tr. at 54-99. D.C. had no evident symptoms on the day she received the flu vaccine in January 2014, and seemed otherwise healthy. *Id.* at 57. But later that day, she recalled, her husband informed her of D.C.'s shaking incident and febrile seizure, leading the Caredios to take her to the hospital. *Id.* at 58-59. At the hospital, she had a fairly high temperature, which she had not displayed when the seizure incident had begun at home. *Id.* at 60. After leaving the hospital, D.C.'s temperature moderated, but "never fully dropped." *Id.* at 61. The next day, Mrs. Caredio personally witnessed the second shaking episode that prompted her to take D.C. back to the hospital. *Id.* at 61-62.

At this second visit, Mrs. Caredio recalled that D.C. was "awake," and literally alert (in that her eyes were open), but she was not verbalizing either. Tr. at 64. After discharge, Mrs. Caredio first began to suspect that D.C. symptoms might be vaccine-related, given the temporal

association and the fact (as Mr. Caredio also stated) that pediatricians had warned that vaccination could produce a fever. *Id.* at 65. She also testified that she later (in February) mentioned to D.C.'s pediatrician, Dr. Deldin, that Mr. Caredio had noticed the eye twitch, and that Dr. Deldin had proposed to watch its development. *Id.* at 65-66. Mrs. Caredio acknowledged there was no reference to such discussions in Dr. Deldin's written notes from pediatric visits with D.C., but she observed that Dr. Deldin's notes were illegible, and also that in her experience he was not the kind of treater who would necessarily write everything down said to him. *Id.* at 66-67, 90-92.

Mrs. Caredio testified she first personally noticed D.C.'s eye fluttering on May 13, 2014, during dinner, when D.C. repeatedly dropped pizza from her hand while it jerked. Tr. at 67-68. She also witnessed D.C.'s eyes rolling back on the 19th. *Id.* at 89. However, she also alleged to have noticed what seemed like a nervous "quick little blink" before, in February of that year. *Id.* at 68, 69.[7] This blinking/eye twitch did not, however, concern Mrs. Caredio prior to May, until it evolved in nature and began occurring more frequently. *Id.* at 69, 92-93. After the May 13th incident, she contacted her husband then Dr. Deldin, who instructed the Caredios to take D.C. to the hospital, where she was given anti-seizure medication. *Id.* at 69-70. D.C. also around this time underwent an EEG that suggested to treaters she had epilepsy. *Id.* at 70-71.

After this time, Mrs. Caredio recalled, D.C.'s seizures worsened, eventually leading the Caredios to seek specialized expertise at Stanford. Tr. at 71-72. Like her husband, Mrs. Caredio recalled the pain of learning that D.C. suffered from a severe form of epilepsy. *Id.* at 72-73. This began an extended period of treatment at Stanford, with little working until IVIG was tried. *Id.* at 73-76. After that, the Caredios brought D.C. back to Stanford every few weeks for more IVIG, which was helpful until December 2014, when D.C. experienced some more severe seizure flares. *Id.* at 76-79. Mrs. Caredio also echoed her husband's testimony about their effort to obtain a second opinion in Boston, and subsequent determination to establish care at UCSF. *Id.* at 81-82.

Overall, D.C. displays great anxiety in addition to her seizures. Tr. at 82-83. The anxiety can flare up in tandem with increased seizure activity. *Id.* at 83. She can also be more emotionally sensitive during symptomatic flares, and did previously require some speech therapy to address seizure-induced stuttering. *Id.* at 84-85. And she displays memory issues as well. *Id.* at 86. Mrs. Caredio also reviewed with Petitioners' counsel a number of photos of D.C. over the course of her treatment, at Stanford and UCSF. *Id.* at 95-99.

3. *Sharon Caredio* – Mr. Caredio's mother Sharon, grandmother to D.C., testified about her observations of D.C.'s symptoms. Tr. at 114-33. She recalled D.C. being a happy playful child in their interactions (and she saw D.C. fairly regularly because she lives in the same town as Petitioners). *Id.* at 115. She recalled learning from her son about D.C.'s initial post-vaccination reaction, but also testified that she had personally seen D.C.'s eye blinking/twitching,

[7] In their affidavit, Petitioners more specifically state that D.C.'s blinking and right eye fluttering began three weeks after her initial seizure that resulted in an ER visit at their local hospital on January 22, 2014. *See* Affidavit, filed Jan. 26, 2017 (ECF No. 6-2) ("Caredio Aff."). Petitioners state "[w]e initially thought it might be a nervous twitch." *Id.*

in the time period after vaccination (although she could not precisely say when). *Id.* at 116-18, 128. She did not, however, observe D.C.'s May 2014 eye-rolling or hand-flutter incidents. *Id.* at 119. She did visit D.C. when hospitalized after May, and witnessed there D.C.'s seizure behaviors as well as her attendant anxiety. *Id.* at 119-21. And she was familiar with other sequelae of D.C.'s condition, although (in part due to the Pandemic) she had not recently seen D.C. in person. *Id.* at 122-27.

4. *Deborah Townsend* – Mrs. Caredio's mother (and D.C.'s maternal grandmother) also testified about her knowledge and observations of D.C.'s seizure course. Tr. at 132-52. Like Sharon Caredio, Mrs. Townsends lives near the Caredios and personally saw her daughter almost every day, and therefore had opportunities to observe directly D.C.'s behavior and symptoms. *Id.* at 134-35. D.C. before vaccination had been a happy, loving child. *Id.* at 134-35. Mrs. Townsend learned from Mrs. Caredio about the immediate post-vaccine ER visit and associated shaking/febrile seizure, but had directly seen instances (which she recalled she first noticed a few weeks after the January febrile seizure incident, although she could not be precise) in which D.C. displayed an eye twitch that was more pronounced when she was anxious. *Id.* at 136-38, 149-50. The twitch was not present pre-vaccination. *Id.* at 139.

Thereafter, Mrs. Townsend recalled, D.C. frequently displayed similar twitching, often in response to fatigue or anxiety, although she could not recall if it happened on a daily basis. Tr. at 139. She learned from her daughter that the twitching had become worse, however – and she was present at the initial May incident in the car with D.C. and Mrs. Caredio when D.C. displayed the seizure-like hand movement when holding some food. *Id.* at 140-41. She later learned about D.C.'s lengthy treatment course, and even had the opportunity to see her at Stanford or UCSF, where she observed D.C.'s fearful reactions to the medical interventions she endured. *Id.* at 141-44.

B. Petitioners' Experts/Treater Witnesses

1. *Keith Van Haren, M.D.* – Dr. Van Haren, a Stanford pediatric neurologist, treated D.C. from the fall of 2014 until the spring of 2015, and he testified about his resulting treatment observations. Tr. at 100-13. Dr. Van Haren is currently Assistant Professor in the Department of Neurology, Stanford University School of Medicine, Division of Child Neurology at Lucile Packard Children's Hospital. *See* Curriculum Vitae, filed Jan. 22, 2021 (ECF No. 63-2) ("Van Huren CV"). His clinical area of expertise is in pediatric neuroimmunologic disorders with a special focus on inherited etiologies. *Id.*; Tr. at 101.

Dr. Van Haren began seeing D.C. in the fall of 2014, at which time Petitioners were struggling to identify an effective treatment, since anti-seizure medications did not seem to be working. Tr. at 102. However, because (at the time of referral) it was thought that D.C.'s seizures "had begun in a setting of fever and post-vaccination"—a supposition not supported by the medical record, as reviewed above—it was suspected that she might have suffered from an autoimmune encephalitis. *Id.* at 102-03. By then, she was receiving both steroids and IVIG—and although both

impact immune function, the latter was especially understood to assist with individuals suffering from "an overactive immune system." *Id.* at 103, 104-05. Dr. Van Haren proposed to taper the steroids given their side effects—but since this was also likely to lead to an increase in seizure activity, it would confirm the immune-mediated character of her condition. *Id.* at 103-04.

D.C.'s response was as Dr. Van Haren expected, leading him to treat her monthly with IVIG—which in turn proved effective (other than her December 2014 flare). Tr. at 104. This prompted Dr. Van Haren to propose in his treatment records that a "focal autoimmune injury" to a small region on the left side of her brain could be the proximate reason for her epilepsy course. *Id.* at 105-06; Ex. 5 at 172. He ultimately agreed with an earlier treater assessment that D.C. suffered from drug-resistant "medically intractable EPC due to autoimmune disorder." *Id.* at 107-08.

On cross, Dr. Van Haren acknowledged he had not cared for D.C. from the time of her initial vaccination or during her May 2014 presentation of first seizures. Tr. at 109. He also noted that the records from his initial visit with D.C. suggested onset of neurologic symptoms in February 2014—and that histories provided by the Petitioners, rather than independent records, were the primary corroboration for that onset determination. *Id.* at 111-12. Dr. Van Haren offered no opinion as to whether the flu vaccine itself was causal of D.C.'s condition. *Id.* at 112, 113.

2. *Lawrence Steinman, M.D., PhD.* – Dr. Steinman, a neurologist and immunologist, was the sole non-treating medical expert to testify for Petitioners. Tr. at 155-83, Report, dated April 12, 2017 (ECF No. 11-2) ("Steinman First Rep."); Report, dated Jan. 4, 2018 (ECF No. 28-3) ("Steinman Second Rep."); Report, dated July 6, 2018 (ECF No. 35-2) ("Steinman Third Rep."). He testified that the flu vaccine likely caused D.C. to experience some form of autoimmune epilepsy.

Dr. Steinman is currently a professor at Stanford University, Departments of Neurology, Pediatrics and Genetics. Curriculum Vitae, filed July 6, 2018 (ECF No. 35-3) ("Steinman CV"). He has published over five hundred peer-reviewed publications on immunology and molecular mimicry. Steinman CV at 5-46. He has maintained a large research lab for the past forty-one years, particularly in the area of neuroimmunology, and he has published papers on Rasmussen's and other autoimmune epilepsies. Tr. at 156-57. Dr. Steinman is board certified in neurology and has received several professional awards and prizes in the specialty. Steinman CV at 1, 2. Dr. Steinman alleges that he maintains a clinical practice in inpatient child neurology, with the majority of these patients having epilepsy. Tr. at 161. Dr. Steinman recalled that he has diagnosed or treated "thousands" of patients with epilepsy,[8] although he has only ever seen four patients with Rasmussen's syndrome/encephalitis. *Id.* at 161-62.

[8] Dr. Steinman testifies frequently in the Program—and has often informed the special masters he appears before that, whatever the injury in question, he has *repeatedly* had occasion to treat or diagnose it. *See, e.g.*, *McGrail v. Sec'y of Health & Hum. Servs.*, No. 17-926V, 2021 WL 1728706, at *10 (Fed. Cl. Spec. Mstr. Apr. 23, 2021) (estimating he

Dr. Steinman began by discussing the different types of epilepsy, explaining that it is a broad classification containing several subsets. Tr. at 162. Some types of epilepsy are genetic, some metabolic, and some are due to other neurological injury or brain malformation. *Id.* at 162-63. Dr. Steinman's opinion also often touched on Rasmussen's encephalitis—a progressive, chronic encephalitis (inflammation of the brain) occurring mainly in children and impacting one side of the brain—using it as a comparable condition, given its known autoimmune pathology and the fact that it is characterized by seizures consistent with what D.C. experienced. However, Dr. Steinman acknowledged that in fact D.C. was never so diagnosed (and had not even received the biopsy necessary to confirm it (*Id.* at 180)), adding that at most her treaters had speculated that aspects of her clinical presentation were "Rasmussen's-like." *Id.* at 218, 235; *see also* Steinman First Rep. at 7 ("[h]er overall picture is not fully consistent with Rassmusen [sp] Encephalitis"), 8.

Dr. Steinman agreed that the medical record supported the conclusion that D.C. had "focal epilepsy" manifesting as EPC, which was likely autoimmune in etiology. Tr. at 167, 211. EPC usually begins in a focal manner (meaning specific to a particular location in the brain), but not necessarily with a "full-blown" seizure. *Id.* at 172. It is also often a manifestation of Rasmussen's syndrome. S. Varadkar et al., *Rasmussen's Encephalitis: Clinical Features, Pathobiology, and Treatment Advances*, 13 Lancet Neurology 1, 2 (2014), filed as Ex. 30 Ref. 15 on Apr. 12, 2017 (ECF No. 12-7) ("Varadkar"). Given Dr. Steinman's admission that D.C. likely did not have Rasmussen's syndrome, however, it becomes difficult to understand why so much of his expert opinion delved into that syndrome's features, other than the fact that it is believed to be autoimmune-driven.

Importantly, Dr. Steinman distinguished D.C.'s purported initial febrile seizure from what the Petitioners observed starting to occur a few weeks later—eye twitching—which he deemed the "undisputed beginning" of her EPC. Tr. at 211 ("I'm not necessarily drawing a bridge between the febrile seizure initially and what happened a few weeks later with the eye twitching"). Thus, Dr. Steinman did *not* connect D.C.'s febrile seizure *at all* to her subsequent disorder—and even if the vaccine had caused her to suffer a fever which in turn caused the isolated seizure possibly observed on January 22, 2014, Dr. Steinman *did not contend* that this seizure was the onset of her alleged vaccine-caused injury. *Id.* at 266-67.

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has treated hundreds of patients with transverse myelitis and similar neurological conditions such as multiple sclerosis and neuromyelitis optica); *Salazar v. Sec'y of Health & Hum. Servs.*, No. 15-817V, 2021 WL 319393, at *9 (Fed. Cl. Spec. Mstr. Jan. 5, 2021) (stating he has cared for hundreds of adults and children with various forms of brachial plexus injuries, peripheral neuropathy, and autoimmune neurologic conditions); *Taylor v. Sec'y of Health & Hum. Servs.*, No. 13-700V, 2018 WL 2050857, at *7 (Fed. Cl. Mar. 9, 2018) (estimating he has treated over 2,500 patients with multiple sclerosis, Guillain-Barré syndrome ("GBS"), or Acute Demyelinating Encephalomyelitis ("ADEM")); *Rolshoven v. Sec'y of Health & Hum. Servs.*, No. 14-439V, 2018 WL 1124737, at *6 (Fed. Cl. Spec. Mstr. Jan. 11, 2018) (stating he has treated over 1,000 patients with headaches during his 35 year career); *Blackburn v. Sec'y of Health & Hum.* Servs., No. 10-410V, 2015 WL 425935, at *7 (Fed. Cl. Jan. 9, 2015) (stating he has treated approximately 400 patients with GBS). But even accepting Dr. Steinman's overall competence and expertise in neurologic matters, the contention that he has vast deep background exposure to virtually *any* neurologic injury is exceedingly difficult to swallow.

Next, Dr. Steinman explained his theory associating the flu vaccine to a condition like EPC. Overall, he contended that D.C.'s EPC was the product of an aberrant adaptive immune response to the flu vaccine, driven by T cells. Steinman First Rep. at 9. He forthrightly acknowledged that he was unable to offer any literature connecting the flu vaccine to EPC (though he added that recognized medical authorities like the Institute of Medicine (the "IOM") had not yet *disproven* the possibility). Tr. at 240. Instead, Dr. Steinman's theory depended on a number of separate components he attempted to link together.

First, Dr. Steinman noted that certain types of epilepsy are driven by autoimmune disease processes. First Steinman Rep. at 9; National Institute of Neurological Disorders and Stroke, *Rasmussen's Encephalitis Information Page*, available at https://www.ninds.nih.gov/disorders/alldisorders/rasmussensencephalitisinformationpage (last visited Apr. 12, 2017), filed as Ex. 22, Ref. 7 on Apr. 12, 2017 (ECF No. 11-9). As a result, it was plausible a vaccine (which impacts the immune system) could play a role in initiating an autoimmune form of epilepsy.

Second, Dr. Steinman proposed that the flu vaccine could do so via the scientifically-recognized biological mechanism of molecular mimicry. Steinman First Rep. at 10. Antigenic components of the vaccine could, he proposed, stimulate the immune system to cross-react with self tissue structures due to similarity between the components and the amino acid sequences making up the structures (meaning the immune system response to the vaccine would secondarily lead to an autoimmune attack). *Id*. In fact, many neuronal antigens are linked to certain autoimmunity-driven diseases featuring seizures, like Rasmussen's syndrome, having been revealed to be targets for antibodies critical to these autoimmune disease processes. *Id.*; A. Nibber et al., *Antibodies to AMPA Receptors in Rasmussen's Encephalitis*, 20 European J. of Paediatric Neurology Society, 222-27 (2016), filed as Ex. 26, Ref. 11 on Apr. 12, 2017 (ECF No. 12-3) ("Nibber").

In Nibber, 52 patients with Rasmussen's syndrome were tested by cell-based assays for antibodies associated with Rasmussen's, and ten had evidence of antibodies to specific neuronal antigens. Nibber at 222. Other literature has suggested that the direct injection of known molecular mimics into animals can induce an experimental form of autoimmune disease. First Steinman Rep. at 17; A. Gautam et al., *A Viral Peptide with Limited Homology to a Self-Peptide Can Induce Clinical Signs of Experimental Autoimmune Encephalomyelitis*, 161 J. of Immunology 60-64 (1998), filed as Ex. 26, Ref. 12 on Apr. 12, 2017 (ECF No. 12-4). While Dr. Steinman acknowledged that it was not established by such literature that autoantibodies to neuronal antigens believed associated with human seizure-featuring conditions would *also* induce clinical neuroinflammation simply by their introduction, he nevertheless deemed the articles useful in understanding the nature of the autoimmune process that could explain causation in this case. First Steinman Rep. at 13.

To demonstrate how the flu vaccine specifically could cause the creation of cross-reactive autoantibodies central to such a proposed autoimmune process resulting in EPC, Dr. Steinman endeavored to show "homology," or antigenic similarity, between the vaccine's components and self neurologic structures. He did so via BLAST[9] searches. Steinman First Rep. at 13. Specifically, Dr. Steinman reviewed online databases, looking for homologies between antigenic components found in the 2013-14 version of the flu vaccine (which he deemed a reasonable comparable to the version received by D.C.) and NMDA-R[10] and GABA[11] neuronal receptors (among others) which are suspected to be targets for attack in certain autoimmune-driven epilepsies. Tr. at 243. In his estimation, the number of matched common amino acids in sequence (matches of more than five out of twelve) was enough to support the conclusion that the 2014 influenza vaccine could also stimulate a cross-reaction. *Id*. at 175; 221-23.

At trial, however, Dr. Steinman admitted that demonstrating a theoretical basis for homology is only the first step to establishing a possible causal association. Tr. at 223-24. Indeed, he went so far as to acknowledge that his contentions about the plausibility of a vaccine-induced cross reaction attributable to molecular mimicry was *the most* he could offer in support of his contention that the flu vaccine could cause an epileptic disorder like EPC. *Id.* at 262-63 ("I made my opinion based on I can't come up with a—anything better, and I can come up with a theory based on molecular mimicry to explain it"). He also acknowledged that the "widespread" existence of sequential homology between different self tissue structures and foreign antigens undercut the causal potential of vaccines to instigate autoimmune illness (and the immune system was equipped to effectively deal with the vast majority of resulting cross-reactive potential), but added that the presence of "other genetic and environmental factors" were what made the homology dangerous, and that molecular mimicry overall remained "key mechanism" in explaining the loss of immune tolerance in some circumstances. Steinman Second Rep. at 4-5.

Another stumbling block to Dr. Steinman's theory was the fact that the neuronal receptors that Dr. Steinman deemed homologous with some of the flu vaccine's antigenic components are *not* located solely in the brain. Tr. at 176. But the "antibody-mediated CNS degeneration" described by Dr. Steinman would involve a directed attack against the purportedly-homologous receptors. Ex. 15 at 21; Tr. at 236. If so, why did D.C. experience *focal* rather than generalized seizures, arising from cross-reactions occurring elsewhere in the body or even brain? Dr. Steinman defended his view by asserting that medical science could not provide an answer to that. *Id.* He

[9] Basic Local Alignment Search Tool ("BLAST") is a medical/scientific internet resource that assists researchers in finding regions of similarity between biological sequences of amino acids. The program compares nucleotide or protein sequences to sequence databases and calculates the statistical significance. BLAST, U.S. National Library of Medicine, https://blast.ncbi.nlm.nih.gov/Blast.cgi (last visited Nov. 19, 2020).

[10] NMDA stands for N-Methyl-D-Asperate. *Dorland's* at 1260.

[11] GABA stands for Gamma-aminobutyric acid. *Dorland's* at 745.

added that a likely genetic susceptibility to D.C.'s condition may also have played a role. *Id.* at 225-26.

In addition, Dr. Steinman's theory was further complicated by the immunologic character of autoimmune cross-reactions—which generally involve autoantibodies driving the disease process. The timing and nature of the vaccine reaction D.C. was alleged to have experienced most likely involved the adaptive arm of the immune response, since her initial symptoms (eye-fluttering) manifested two to three weeks post-vaccination (and thus could not have been the product of the immediate, innate response). Steinman First Rep. at 9. As Dr. Steinman explained, the adaptive immune response is driven by a combination of T cells (which often, although not exclusively, play a direct role in attacking invading pathogens) and B cells (which cause the manufacture of antibodies). Ex. 15 at 9; Tr. at 237. And his theory proposed that autoantibodies could have been stimulated by antigenic components of the flu vaccine. And yet—antibody tests D.C. received in the fall of 2014 were *negative* for any detectable antibodies to many proteins associated with autoimmune seizures. Tr. at 238 ((citing Ex. 5 at 234-36); Steinman First Rep. at 8; M. Toledano & S. Pittock, *Autoimmune Epilepsy*, 35 Semin Neurology 245, 245-47 (2015) filed as Ex. A Tab 2 on Oct. 17, 2017 (ECF No.20-3). Thus, the record did not establish that the antibodies likely to be involved in an autoimmune pathologic process were present.

Dr. Steinman responded by maintaining that even in the absence of detectable antibodies to many proteins associated with autoimmune seizures, T cell response is capable of inflicting considerable damage, deeming it the likely basis for D.C.'s epilepsy. Tr. at 237-38; Steinman First Rep. at 21 ("[s]uch antibodies are far less frequent than T cell responses in the pathogenesis of these autoimmune mediated epileptic conditions"). Indeed, he cited literature in support of the conclusion that despite the fact that certain autoantibodies were very "specific" to the neuronal targets of attack, their role in directly propagating autoimmune epilepsies (or larger syndromes like Rasmussen's manifesting as EPC) was not clear. Steinman First Rep. at 21; Varadkar at 5. Dr. Steinman thus concluded that "T cells are considered more likely the culprits in the pathogenesis of . . .. other immune mediated epilepsies." Steinman First Rep. at 20; *Id.* at 2.

But in so arguing, Dr. Steinman simultaneously attempted to play down the extent to which he relied solely on T cells as the likely immune system mediator of disease in this case. In particular, he pushed back against the assertions of Respondent's expert (Dr. Christine McCusker) that his causation theory centered around a specific kind of T cell (CD8+ cytotoxic cells) as attacking the purportedly-homologous neuronal receptors—even though those receptors were not "implicated" in a T cell-driven processes. Steinman Third Rep. at 3. In reaction, Dr. Steinman clarified that invariably autoimmune processes still involve T cells. *Id.* ("B cell responses require T cell help"). In particular, a *different* class of T cells - CD4+ "helper" T cells - assist B cells in the process of manufacturing antibodies. Steinman Third Rep. at 3. Thus, T cells do likely play a role in autoimmune epilepsy. *Id.* In addition, all such T cells have "cytotoxic capabilities," and that in fact Rasmussen's involves both (although as already noted Dr. Steinman had conceded D.C. did not likely have Rasmussen's). Tr. at 226-29.

Moving on to the medical history, Dr. Steinman endeavored to show how D.C.'s disease course was consistent with his causation theory. Since this was the first time D.C. had received the flu vaccine, it was highly unlikely she was experiencing a recall response in the hours immediately following vaccination. Moreover, although Dr. Steinman allowed for the possibility that she had experienced a febrile seizure in reaction, he did not connect that initial reaction to D.C.'s ultimate EPC diagnosis Tr. at 211-12, 213. In fact, because his theory for how the vaccine caused EPC relied on molecular mimicry (a process requiring an adaptive immune response), the absence of a possible recall response (in which a second exposure would prompt a more rapid reaction) meant that D.C.'s injury could *not* have begun with the febrile seizure. *Id.* at 213. Thereafter, however, the disease process began, and Dr. Steinman felt it unmistakable that D.C.'s twitches observed by her family were its start, evolving later to the outright seizures. *Id.* at 174. The subsequent chronicity of D.C.'s condition could be from "nests of T and B cells that take up residence in the brain and then periodically get triggered," based on his experience with other neuroinflammatory diseases. *Id.* at 270.

Dr. Steinman also deemed the ameliorative effect of IVIG therapy, which is known to be efficacious in the treatment of autoimmune conditions, as supporting his causation opinion. Tr. at 215.[12] And although D.C.'s testing for evidence of autoimmune etiologies at Mayo Clinic produced negative results, Dr. Steinman opined that the testing was not all-inclusive, and that some of the assays tested are "fragile," meaning that a negative response did not necessarily rule out an autoimmune epilepsy. *Id.* at 177-78. Treaters otherwise were unable to identify any other explanatory cause, like a genetic etiology, making D.C.'s responsiveness to the first-line immune therapies that are given for autoimmune epilepsy (namely corticosteroids and IVIG) "the best evidence we had." *Id.* at 178. On cross-examination, however, Dr. Steinman agreed that record evidence showed that the utility of IVIG treatment is not always proof of autoimmunity, since it can indirectly help treatment of epilepsy given its inflammatory mechanisms. *Id.* at 240.

The timing of D.C.'s onset, Dr. Steinman maintained, was consistent with his theory. Tr. at 168-69, 229-30. He opined that the eye twitching episodes observed in February 2014 constituted the first concrete manifestation of EPC. *Id.* at 171. Until that point, her condition was subclinical. Thereafter, consistent with how EPC progresses over time, D.C.'s symptoms progressed from eye fluttering into facial twitches, which in turn eventually progressed to hand and shoulder shaking in May 2014. *Id.* at 174. By this time D.C. had developed a "persistent

[12] Dr. Steinman strongly disagreed with the suggestion by Respondent's other expert, Dr. Jenny Linnoila, that conclusions regarding the efficacy of IVIG should depend on formal confirmation of the treatment's utility via clinical or structured immune therapy trials. Tr. at 216-17. He argued instead that it would be unethical to put such limits on treatment simply for the purpose of evaluating diagnostic relevance. Tr. 215-16. The topic was extensively addressed in some of Dr. Steinman's supplemental reports as well as those prepared by Dr. Linnoila. *See, e.g.*, Steinman Second Rep. at 1-2; Steinman Third Rep. at 1-3; Linnoila First Rep. at 6-7; Linnoila Second Rep.at 3-4; Linnoila Third Rep. at 1-5. This dispute between the experts did not, however, appreciably assisted my determination of this case—and there were ample independent bases for finding Dr. Steinman's causation theory wanting.

memory response" to the vaccine, making an on-going cross reaction driven by the vaccine likely. *Id.* at 214.

Dr. Steinman offered some items of independent literature to support his timeframe arguments (which effectively posited that the January 22nd vaccination did not cause a manifestation of EPC- related symptoms before some unspecified time in February 2014—ten to 21 days post-vaccination). In particular, he referenced articles supporting the medical acceptability of a ten-day post-immunization onset of encephalomyelitis. First Steinman Rep. at 22; L. Bennetto & N. Scolding, *Inflammatory/Post-Infectious Encephalomyelitis*, 75 J. Neurol. Neurosurg. Psychiatry i22-i28 (2004), filed as Ex. 32, Ref. 17 on Apr. 12, 2017 (ECF No. 12-9) ("Bennetto & Scolding"); Tr. at 218-19. Bennetto & Scolding, however, specifically discusses the post-vaccination timeframe for acute demyelinating encephalomyelitis ("ADEM")—a typically-monophasic neurologic injury distinguishable from EPC. Benneto & Scolding at i22. Dr. Steinman nevertheless deemed such evidence the "best fit I could find," given the lack of literature specific to post-vaccination EPC onset. Tr. at 257, 262.

Dr. Steinman otherwise felt a ten-day onset was supported by basic immunology principles. Within five to seven days of receipt of a flu vaccine, the adaptive arm of the immune system would begin making IgG, a potent antibody. Tr. at 258. Since EPC would (at least mostly) be antibody-driven, it would take this long for initial symptoms to manifest—consistent with what occurred in D.C.'s case. Dr. Steinman later testified, however, that he could also support a one-day onset in cases where an individual had previously received the same vaccine, or (on the longer end) up to a four-month onset based on literature covering different vaccines. *Id.* at 258, 260. When asked what the maximum onset time period he would support was, Dr. Steinman said anything from 42 days to a year was possible. Tr. 246-48 (citing other kinds of immune-mediated diseases such as GBS or NMO).

Finally, Dr. Steinman called into question some proposed alternative causes for D.C.'s condition offered by Respondent's experts. For example, Dr. Jenny Linnoila (whose opinion is discussed in greater detail below) noted medical record evidence of left-side lobe cortical thickening as possibly explaining D.C.'s illness. Although Dr. Steinman did not dispute the record support for this observation, he did not find that it was pursued by D.C.'s treaters. Tr. at 231. He also stated that there was no genetic test results that could illuminate the cause of D.C.'s EPC. *Id.* at 232.[13]

[13] I also note that throughout his testimony, Dr. Steinman repeatedly tried to vouch for his own credibility—although doing so backfired. Thus, he purported not to be an advocate for Petitioners herein (Tr. at 163, 166), but instead a neutral professional whose north star was science, emphasizing that he did not always accept cases for claimants when he did not feel he could fairly offer an opinion to support a particular claim (*Id.* at 164). Yet Dr. Steinman admitted his ultimate utility as an expert was measured not by whether he had offered a reliable independent opinion, but rather whether he had crafted an opinion that might help Petitioner succeed. *See, e.g.*, *Id.* at 164 ("when I am seen [at hearing], I can make a theory and support a case"), 166-67 (his goal is to determine "whether I could make any type of theory that would connect the vaccine that petitioner actually received . . . and the injury we're talking about today").

3. *Joseph Sullivan, M.D.* – Dr. Sullivan, the neurologist who has treated D.C. at UCSF, offered testimony describing that process. Tr. at 184-208. Dr. Sullivan is currently a professor of neurology and pediatrics and Director of the Pediatric Epilepsy Center at the University of California San Francisco. Curriculum Vitae, filed as Ex. 65 on Jan. 22, 2021 (ECF No. 63-3) ("Sullivan CV"). He is board certified in clinical neurophysiology, neurology, epilepsy, and pediatrics. Sullivan CV at 1-2. In his professional career, Dr. Sullivan has diagnosed more than 1,000 pediatric patients with seizure disorders, including approximately ten patients with autoimmune epilepsy and three patients with Rasmussen's. Tr. at 186-87.

Dr. Sullivan first met D.C. after she had already had an extensive workup done at Boston's Children's Hospital in April 2015—which produced a diagnostic hypothesis of immune-mediated epilepsy. Tr. at 187. Dr. Sullivan testified that it was very clear to him that D.C. had EPC (where one part of the body has continuous motor activity). *Id.* at 188. Rasmussen's syndrome/encephalitis, or a possible underlying brain injury, were also possible diagnoses, along with some rare mitochondrial or metabolic diseases or focal cortical dysplasia. *Id.*

Dr. Sullivan began his evaluation of D.C. with a brain MRI and an immune workup, which was the starting point to look for radiologic manifestations of Rasmussen's or focal cortical dysplasias. Tr. 188-89. At this point in D.C.'s treatment, Dr. Sullivan favored a Rasmussen's or Rasmussen's-like diagnosis, given the focal nature of her seizure activity and one-sided weakness, although the propriety of a Rasmussen's diagnosis required consideration of the patient's evolution over time—and in particular to look for evidence of progressive atrophy on MRI. *Id.* at 189-190. But D.C. recovered from certain of these suggestive presenting elements, which meant her presentation was never more (in retrospect) than "Rasmussen's-like." Tr. at 190-91. In fact, Dr. Sullivan acknowledged, after six or seven years of treatment D.C.'s course could not be said to reflect the typical trajectory of a Rasmussen's patient. *Id.* at 195. A future MRI would help confirm an absence of Rasmussen's progression. *Id.* at 196-97.

Despite some suggestion from the record that D.C.'s illness may be best understood as EPC, Dr. Sullivan opined that no firm diagnosis yet existed to explain her condition. At best, it was likely some kind of "immune-mediated epilepsy" regardless of whether it is in fact Rasmussen's. Tr. at 201, 208. On cross-examination, Dr. Sullivan admitted D.C.'s case did not fit

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In past cases, Dr. Steinman has been criticized for stepping outside his role of medical expert to opine on the legal standards to be applied in Program cases. *See e.g., D.G. v. Sec'y of Health & Hum. Servs.*, No. 11-577V, 2019 WL 2511769, at *189 (Fed. Cl. Spec. Mstr. May 24, 2019); *Rolshoven v. Sec'y of Health & Hum. Servs.*, No. 14-439V, 2018 WL 1124737, at *10, 21 (Fed. Cl. Spec. Mstr. Jan. 11, 2018). Although he refrained from doing so in this case, his various asides herein amounted to a different kind of "unforced error" that greatly detracted from his credibility. For he seemed to admit that an expert's job is to "shill" for the claimant, without regard for the independence and adherence to scientific principles he maintained guided him in deciding whether to offer an opinion in the first place. Dr. Steinman would be well advised in future cases to stick to the facts, and to explain only why his causation theory is reliable based on his own expertise—not to make comments that suggest he is aware there is less to his opinion than meets the eye.

a Rasmussen's diagnosis, and that at bottom her EPC is "of unclear etiology" despite an "exhaustive immune workup." *Id.* at 203, 204; Ex. 46 at 1. This is consistent with the letter Dr. Sullivan prepared for Petitioners. *See generally* Ex. 47.

D.C.'s treatment was now focused on "understanding the correlation between her EPC and her EEG findings" in conjunction with how she was doing on a day-to-day, week-to-week basis to help guide potential interventions and slow down the progress of the disease. Tr. at 191. D.C. had already received steroids and IVIG, which would aid in slowing progression or perhaps even stop the disease, obviating the need for more severe interventions. *Id.* at 191-92. Dr. Sullivan was unable to say that D.C.'s condition would never get worse—which was possible with either Rasmussen's or EPC. *Id.* at 192-93. Dr. Sullivan also acknowledged that a positive IVIG response did not necessarily equate with an underlying immune cause, because "anti-inflammatory immunologic treatments" often are employed for individuals who do not respond to more usual therapies. *Id.* at 204-05. And while he could not say whether the flu vaccine was casual despite a temporal association, he recommended that D.C. not receive future vaccinations. *Id.* at 200, 206.

C. Respondent's Experts

1. *Christine McCusker, M.D., PhD.* – Dr. McCusker, a pediatric immunologist and microbiologist, testified on behalf of Respondent, and also submitted three written reports. *See generally* Tr. at 273-335; Report, dated Oct. 17, 2017, filed as Ex. C (ECF No. 21-1) ("McCusker First Rep."); Report, dated April 10, 2018, filed as Ex. F (ECF No. 32-3) ("McCusker Second Rep."); Report, dated Sept. 21, 2018, filed as Ex. H (ECF No. 37-5) ("McCusker Third Rep."). Dr. McCusker contested Petitioners' contention that the flu vaccine could cause EPC or did so to D.C.

Dr. McCusker obtained a Bachelor's degree in microbiology and immunology from the University of Toronto. McCusker First Rep. at 1; Dr. McCusker Curriculum Vitae, filed as Ex. D (ECF No. 26-7) ("McCusker CV) at 1. She holds a master of science degree in molecular biology from McMaster University, where she also completed three years of a PhD program in immunology before attending medical school and obtaining her MD. *Id.* Dr. McCusker completed her residency training in pediatrics at the Montreal Children's Hospital and a clinical fellowship in allergy and immunology at McGill University in Montreal, Quebec. McCusker CV at 1-2. Currently, she is an Associate Professor of Pediatrics at McGill University and Division Director of Pediatric Allergy, Immunology and Dermatology at the Montreal Children's Hospital. Tr. at 274; McCusker First Rep. at 1. Dr. McCusker is also a clinical scientist with a fundamental research lab affiliated with the Meakins-Christie Labs of McGill University where her research focus is on the regulation of the immune responses. McCusker First Rep. at 1. She holds peer reviewed external grants from both Canadian and U.S. granting agencies, and she regularly publishes in peer-reviewed journals. *Id.*

Dr. McCusker began by broadly contesting whether there was any reliable evidence linking the flu vaccine to autoimmune epilepsy. Tr. at 278, 289. She noted that some of the general

evidence offered by Dr. Steinman to link vaccines to autoimmune diseases involved *different* conditions, like immune thrombocytopenic purpura. McCusker Second Rep. at 4. But clinical epilepsy studies did not reveal an increased incidence in infants of EPC or other seizure disorders post-vaccination. *Id.* at 319; K. Kotloff et al., *Clinical and Immune Responses to Inactivated Influenza A(H1N1)pdm09 Vaccine in Children*, 33 Pediatric Infectious Disease J. 865, 869-70 (2014), filed as Ex. C, Tab 2 on Oct. 17, 2017 (ECF No. 21-3) ("Kotloff"). Indeed, Dr. McCusker deemed the version of flu vaccine administered to infants and toddlers "actually a very poor immunogen." Tr. at 292; McCusker First Rep. at 4. Studies like Kotloff have established that barely a fourth of children "seroconvert," or develop antibodies to the wild flu virus, after the first dose of vaccine, and therefore it was generally unlikely that autoimmune cross-reactions would occur after its receipt. Tr. at 292-93; McCusker First Rep. at 4; Kotloff at 870.

In particular, the flu vaccine "poorly activate[s] CD8+ve T cells"—despite Dr. Steinman's heavy reliance on that particular immune cell as driving the pathologic process in question. McCusker First Rep. at 4; A. Altenburg et al., *Virus-specific T Cells as Correlate of (Cross-) Protective Immunity Against Influenza*, 33 Vaccine 500 (2015), filed as Ex. C, Tab 1 on Oct. 17, 2017 (ECF No. 21-2); N. La Gruta & S. Turner, *T Cell Mediated Immunity to Influenza: Mechanisms of Viral Control*, 35 Trends in Immunology 396, 401 (2014) filed as Ex. C, Tab 3 on Oct. 17, 2017 (ECF No. 21-4). By contrast, a variety of wild viral/bacterial infections were known to produce robust responses in the relevant demographic age group, including the kind of T cells invoked in Dr. Steinman's theory (although Dr. McCusker admitted there was no objective proof in this case that D.C. possessed a prior infection that could stand as a potential alternative cause for her EPC). Tr. at 333-34; McCusker First Rep. at 4.

Next, Dr. McCusker reviewed a number of aspects of Dr. Steinman's opinion that she felt were inadequate or unreliably supported. First, she took general issue with his embrace of a homologous cross-reaction as a pathogenic explanation for how the flu vaccine could initiate an autoimmune-driven epilepsy disorder. Dr. McCusker accepted Dr. Steinman's logic in looking for homology between brain receptors likely associated with focal seizures (although there were potentially "hundreds" in the brain that could be relevant) and the flu vaccine's components. Tr. at 318. She noted, however, that sequential homology could easily be demonstrated throughout the human body. *Id.* at 279 ("you can actually find homologies to so many other brain proteins that are not found in the brain").

Indeed, Dr. McCusker noted that she had been able (via her own "in silica"[14] research comparable to what Dr. Steinman performed for this case) to identify homology between the human brain receptor targets identified by Dr. Steinman and *other* infectious wild viruses common to children, like rhinovirus or cytomegalovirus ("CMV"), but not otherwise associated with EPC

[14] Dr. Steinman in a prior case coined this phrase to encapsulate the computer database-search "research" he often performs to identify homology between a given vaccine and alleged injury. *See e.g., Blackburn v. Sec'y of Health & Hum. Servs.*, No. 10-410V, 2015 WL 425935, at *10 (Fed. Cl. Spec. Mstr. Jan. 9, 2015).

or seizure disorders. McCusker First Rep. at 5-9; Tr. at 287-88. She identified six amino acid homology (out of a series of nine) for CMV, and six of twelve for the rhinovirus. McCusker First Rep. at 6. She observed similar sequential homology when comparing wild flu virus sequences with some cell surface receptors very common to immune system cells. *Id.* at 7-9. Because of the "ubiquitous distribution" of these receptor proteins, an autoimmune attack on them "would likely result in massive tissue destruction"—and yet there was no known autoimmune association known between them and the wild flu virus. *Id.* at 9.

Dr. McCusker also deemed it illogical to assume that a cross-reaction instigated by vaccination would *only* occur in the brain, since vaccines are administered peripherally (and hence would be more likely to cause cross-reactions with homologous tissues closer to the situs of administration). Tr. 286-87, 310, 318. Thus, mere demonstration of homology does not automatically mean autoimmune cross-reactivity is more likely—since if that were the case "none of us would survive our first viral infection," when in fact autoimmune-driven diseases are uncommon. *Id.* at 279-80. The immune system is, Dr. McCusker explained, actually prepared to resist cross-reaction, even in presence of autoantibodies. *Id.* at 281, 283-84. Possession of disease-associated antibodies also is no guaranty of a pathologic response, since there are many instances where individuals test positive for antibodies associated with disease or other damaging processes (like allergies) but do not become ill. *Id.* at 290; McCusker First Rep. at 10. Rather, for a disease process to arise, a "next step" is required. Tr. at 280.

Second, Dr. McCusker attacked other aspects of Dr. Steinman's theory relating to the proposed homology-driven autoimmune process leading to EPC. Tr. at 284. She agreed that certain brain neuronal receptors (NMDA-R and GABA) identified by Dr. Steinman were known to be associated with specific autoantibodies. McCusker Second Rep. at 2. But "neither of these receptors have been implicated in T cell-mediated diseases"—which Dr. Steinman plainly identified as the pathologic engine in this case. *Id.* at 3. In fact, D.C. had never been diagnosed with any of the diseases specifically associated with these neuronal receptors, like NMDA-R encephalitis. *Id.* at 2. And a 2013 study only found (in a 564-patient cohort) that less than two percent of patients with new-onset epilepsy even possessed the NMDA-R antibodies, and therefore their presence did not predict course or outcome—and could in fact be "an epiphenomena of refractory seizures" rather than causal of them. *Id.*; T. Brenner et al., *Prevalence of Neurologic Autoantibodies in Cohorts of Patients with New and Established Epilepsy*, 54 Epilepsia 1028 (2013), filed as Ex. F Tab 2 on Apr. 10, 2018 (ECF. No. 32-5).

Dr. McCusker relatedly pointed out that the record did not establish that D.C. possessed the autoantibodies specific to these two receptors focused upon in Dr. Steinman's homology BLAST searches. Tr. at 299-300. Although Dr. Steinman had proposed that the level of required autoantibodies could be impacted by some of the treatments D.C. was receiving (like IVIG or steroids), thus reducing what testing could reveal, Dr. McCusker insisted they would not be rendered wholly undetectable, so a test result that D.C. was *negative* for them, as here, was

trustworthy. *Id.* at 300-01. And she also took issue with the animal model[15] relied upon by Dr. Steinman to show how autoimmune cross-reactive diseases progress, arguing that (a) it relies on adjuvant-driven overstimulation, and hence does not provide a particularly apt comparable for the functioning of a child's immune response, and (b) it has more relevance to antibody-driven disease processes (which, as noted below, are inconsistent with Dr. Steinman's view of how an EPC or a similar autoimmune epilepsy would occur, i.e. via T cells). *Id.* at 291-92, 298.

Dr. McCusker spent a considerable amount of time addressing Dr. Steinman's theory regarding the role T cells would play in EPC or some other kind of autoimmune epilepsy, and whether the flu vaccine in particular could have any impact on such a process. Tr. at 281. She expressed considerable doubt about the latter, noting that any T cells activated by vaccination would not persist for a long period of time, and would have to "find their target" in the brain (a far less accessible location than peripheral myelin, which Dr. Steinman's EAE models focused on) to cause injury. *Id.* at 309-10. She also stressed that mimicry-driven T cell activation would require evidence about how the vaccine's antigen mimics would "present" to the self tissues, such that they could prompt cross-reactivity. McCusker First Rep. at 5; McCusker Second Rep. at 3. A T cell could not cross-react with a brain receptor, even given some degree of sequential homology, unless it "recognized" it. Tr. at 296. But Dr. McCusker denied that Dr. Steinman had provided any evidence that the antigenically-similar segments he had identified via online research could do this.[16] *Id.* ("you have to say, would a T cell see this? Because if a T cell won't see it, it's irrelevant that there is homology"). Since Dr. Steinman's causation theory "stopped" after it demonstrated potential homology, it did not go far enough in showing that the flu vaccine could promote production of the pathogenic T cells that would drive EPC. McCusker First Rep. at 10.

The body's immunologic "checks and balances" made it even less likely vaccination could produce pathologic T cells, since the processes[17] by which T cells become "highly educated" (meaning in this case able to recognize and cross-react with brain receptors homologous to flu antigens) usually results in deletion of the vast majority of potentially pathologic versions. Tr. at 297, 298, 281-82, 321; McCusker First Rep. at 10; M. Anderson, *The Cellular Mechanism of Aire Control of T Cell Tolerances*, 23 Immunity 227, 237 (2005), filed as Ex. C Tab 10 on Oct. 19, 2017 (ECF No. 26-1); C. Benoist & D. Mathis, *Autoimmunity Provoked by Infection: How Good is the Case for T Cell Epitope Mimicry?*, 2 Nature Immunology, 797, 800 (2001), filed as Ex. C

[15] Dr. Steinman relied on a model termed "experimental autoimmune encephalomyelitis ("EAE")." *Dorland's* at 580; Steinman First Rep. at 11-13.

[16] In fact, Dr. McCusker noted, one article filed by Petitioners and relied upon by Dr. Steinman actually suggested that the kinds of autoreactive T cells that could purportedly contribute to a specific central nervous system demyelinating injury, multiple sclerosis, were *also* present in individuals without the disease, undercutting the theory of their centrality to pathogenesis. McCusker Second Rep. at 4; K. Ota et al., *T-cell Recognition of an Immunodominant Myelin Basic Protein Epitope in Multiple Sclerosis*, 346 Nature, 183 (1990) filed as Ex. 38 Supp. Ref. 1 on Jan. 4, 2018 (ECF No. 28-4).

[17] As Dr. McCusker explained, naïve T cells migrate from the bone marrow to the thymus, where they "undergo education," and thus autoimmune T cells are mostly deleted. Tr. at 281.

Tab 4 on Oct. 17, 2017 (ECF No. 21-5). And other immune cells would likely downregulate the overproduction of potentially harmful T cells as well. Tr. at 283. Dr. McCusker admitted, however, that (consistent with the fact that the causes of autoimmune diseases generally are not well-understood) in autoimmune disease processes *some* T cells likely did escape elimination in the body, and a genetic predisposition to autoimmunity might well play a role in allowing them to survive. *Id.* at 322-23.

Dr. McCusker noted a few other issues with Dr. Steinman's theory as it pertained to T cells and their role in propagating some form of autoimmune epilepsy. She agreed that T cells could be implicated in an immune response that was (as with the flu vaccine) primarily oriented toward inducing production of antibodies via B cells, although she distinguished the kinds of T cells involved: CD4+ "helper" T cells, which communicate with B cells and thus assist with antibody production. Tr. at 298-99. But these T cells are not equivalent to the cytotoxic CD8+ T cells allegedly involved in the autoimmune attack on brain receptors that Dr. Steinman's theory posited were central to the pathogenesis of autoimmune epilepsy[18]—and the latter kind of T cell is not understood to be activated by the flu vaccine in any event. *Id.* at 309; McCusker Third Rep. at 2. The two kinds of T cells are not even activated in the same way. McCusker Third Rep. at 2. Thus, another necessary link connecting the flu vaccine to the relevant disease process was missing.

Dr. McCusker also provided her view of incidents from D.C.'s medical history and what she believed they revealed about the flu vaccine's purported role in her EPC/autoimmune epilepsy. She expressed doubt, for example, that D.C. had in fact experienced a febrile seizure, noting that Petitioners had not deemed D.C. "hot" when she first appeared to seize at home, her alert mental status was not consistent with seizure, and initial treaters had not clearly defined D.C.'s reaction to constitute a febrile seizure either. Tr. at 325-26. Regardless, Dr. McCusker disputed that febrile seizures were triggers for epilepsy or other seizure disorders, maintaining that more recent medical research was starting to discredit the prior view of a relationship. *Id.* at 327; McCusker First Rep. at 11; N. Verbeek et al., *Etiologies for Seizures Around the Time of Vaccination*, 134 Pediatrics 658 (2014) filed as Ex. C Tab 15 on Oct 19, 2017 (ECF No.26-6). She also noted that the medical record ultimately did not later corroborate initial treater concerns that D.C. might have Rasmussen's syndrome. McCusker First Rep. at 10.

The efficacy of the IVIG treatments D.C. received, moreover, were not in Dr. McCusker's estimation corroboration of the autoimmune character of her epilepsy. McCusker First Rep. at 10. Dr. McCusker deemed IVIG treatments a "powerful anti-inflammatory" that certainly could be helpful to people experiencing seizures, but maybe more as "a response to chronic insult to the

[18] Dr. McCusker did not accept at face value Dr. Steinman's contention about the centrality of these CD8+ T cells to autoimmune diseases involving seizures, like Rasmussen's, noting that some of the literature cited for this proposition had found only a general increase in proliferation of a lymphocyte specific to a particular antibody-associated neuronal receptor—but that it was not confirmed these were T cells, let alone the CD8+ T cells identified as pathogenic by Dr. Steinman. McCusker Third Rep. at 2; Y. Takahashi et al., *Autoantibodies and Cell-mediated Autoimmunity to NMDA-type GluRε2 in Patients with Rasmussen's Encephalitis and Chronic Progressive Epilepsia Partialis Continua*, 46 Epilepsia 152, 157 (2005), filed as Ex. 45 Ref. 3 on July 6, 2018 (ECF No. 35-4).

central nervous system." Tr at 304; J. Geng et al., *Intravenous Immunoglobulins for Epilepsy*, 7 Cochrane Database of Systematic Revs. 1, 11-12 (2017) filed as Ex. C Tab 12 on Oct. 19, 2017 (ECF No. 26-3). As a result, although Dr. McCusker conceded that treaters may have reasonably in part deemed IVIG's efficacy as supporting an autoimmune etiology, she did not accept that the treatment's utility was strong evidence of this. *Id.* at 306-07.

Regarding the likely onset for D.C.'s EPC, Dr. McCusker observed a discrepancy between when the Petitioners claimed to have first noticed her eye twitching/blinking (February) and the onset supported by written medical records (which indicated the eye twitching was first observed in mid-May). Tr. at 277-78. Dr. McCusker concluded from this that the evidence best supported a later onset. *Id.* at 311. And although Dr. Steinman seemed to deem even a May onset as medically acceptable for causation purposes, Dr. McCusker disagreed, arguing that the slower adaptive immune response implicated by Dr. Steinman's theory would take far *less* time to occur (and thus certainly would not happen over a period of several months, based on her own preferred onset). *Id.* at 312-13.

Dr. McCusker admitted that a 10-14 day onset would be consistent at least with the time in which the flu vaccine would generate IgG antibodies via an adaptive immune process. Tr. at 320. But she challenged some of the literature Petitioners relied upon to support this timeframe. Benetto & Scolding, for example, was an older (16-17 years old) paper that not only involved a different disease (ADEM) but specifically stated that the incidence of post-vaccination ADEM was more common with vaccines manufactured from *neuronal* tissue, mentioning only the MMR vaccine in this regard. *Id.* at 314-15; Bennetto & Scolding at i24-i25. The flu vaccine was thus distinguishable.

Finally, Dr. McCusker questioned the overall timeframe in which the allegedly vaccine-initiated disease process had purportedly occurred. She expressed doubt that a process involving "asymptomatic progressive degeneration" (since other than the eye twitching, D.C. was not displaying progressive worsening in her clinical symptoms before May) could later manifest, more than three months post-vaccination, abruptly as chronic focal seizures, absent evidence of a brain tumor or some other obvious injury. Tr. at 313. D.C.'s disease process would not likely have proceeded in a stuttering, slowly-progressing fashion—especially since it was proposed in this case to be immune-mediated. *Id.* at 331 ("your immune system doesn't chip [away]" over weeks or months). At bottom, Dr. McCusker reasoned, Dr. Steinman's theory placed too much reliance on the flu vaccine's pre-onset administration, so that "what Dr. Steinman is describing is phenomenology, not causality." *Id.* at 334.

2. *Dr. Jenny Linnoila, M.D., PhD.* – Dr. Linnoila, a neurologist with a specialty in studying and treating autoimmune diseases, was Respondent's second expert, and she offered a number of written reports as well. *See generally* Tr. at 336-415; Report, dated October 13, 2017, filed as Ex. A (ECF No. 20-1) ("Linnoila First Rep."); Report, dated April 10, 2018,

filed as Ex. E (ECF No. 32-1) ("Linnoila Second Rep."); Report, dated September 13, 2018, filed as Ex. G (ECF No. 37-1) ("Linnoila Third Rep.").

Dr. Linniola received her bachelor's degree in computer science from the University of Chicago and studied biochemistry and pharmacology at the University of Cambridge. Dr. Linnoila Curriculum Vitae, filed as Ex. CV of Jenny Linnoila on Oct. 17, 2017 (ECF No. 20-9) ("Linnoila CV") at 1. She obtained a Ph.D. in molecular pharmacology along with a medical degree from the University of Pittsburgh. *Id.* Dr. Linnoila completed an internship in internal medicine at Alleghany General Hospital before completing a residency and research fellowship in neurology at Massachusetts General Hospital and a fellowship in autoimmune neurology at the Mayo Clinic. *Id.* She is currently a specialist in autoimmune neurology at Massachusetts General Hospital. Tr. 337. She spends approximately 75 percent of her time on laboratory research and 25 percent of her time in clinical practice seeing patients with autoimmune and paraneoplastic disorders of the central nervous system. Tr. 338. Dr. Linnoila has published many peer-reviewed articles, including on the topic of autoimmune encephalitis, and she is boarded in neurology but not pediatrics. Tr. at 343-44, 385; Linnoila First Rep. at 2. She also has experience in treating individuals like D.C., although much of it is derived from a prior clinical fellowship. *Id.* at 385-86; Linnoila First Rep. at 2. Thus, Dr. Linnoila reports to have seen many patients with autoimmune encephalopathies (which would include autoimmune epilepsy), and did on rare occasions see children diagnosed with EPC. Tr. at 339, 341. She acknowledged, however, that most of this overall experience was derived from her residency, and that she more commonly consulted on cases involving these kinds of illnesses. *Id.* at 341-42.

Dr. Linnoila began her testimony by defining some of the medical concepts and terms relevant to the case. She defined "encephalopathy" to mean brain inflammation—and in the case of autoimmune epilepsy, the inflammation would provoke seizures. Tr. at 340, 341. Because autoimmune epilepsy is thought to be a kind of autoimmune encephalitis, some experts believe treatment of the underlying inflammation could help reduce the resultant seizures. *Id.* at 340-41; Linnoila Second Rep. at 2. The seizures characteristic of autoimmune epilepsy often appear acutely and without warning, and can be severe and resistant to treatment. Tr. at 356-58; Linnoila First Rep. at 6. They can also be focal (meaning specific to a part of the brain) or multifocal, and vary in type. Linnoila First Rep. at 6. Although autoimmune epilepsy is often responsive to immunotherapy, its underlying etiology cannot often be identified even though its autoimmune pathogenic character is clear. Tr. at 358, 372-74.

Dr. Linnoila then turned to some of the specific diagnostic categories at issue. EPC is a focal process in the brain, and the seizures it produces can be "a nearly constant motor movement that can persist for minutes to hours to days, even months in some cases." Tr. at 349-50; *see also* 351; Linnoila First Rep. at 5. The underlying cause of EPC cannot always be determined, especially given its rarity, but it has been attributed to tumors, cortical malformation in the brain, genetic/metabolic disorders, autoimmune encephalitis, and Rasmussen's syndrome. Tr. at 351-52, 374-75. Dr. Linnoila defined Rasmussen's to be a progressive neuoinflammatory condition

impacting part of the brain (hence focal in nature), producing seizures on one side of the body plus brain atrophy. *Id.* at 352, 354-55; Linnoila First Rep. at 6. Rasmussen's disease process is poorly understood, but the condition itself is aggressive, difficult to control with treatment, and most common in children (although rare overall). Tr. at 355.

D.C., Dr. Linnoila opined, most likely suffered from EPC (an opinion largely consistent with D.C.'s treaters' views). Tr. at 348; Linnoila First Rep. at 5. D.C. likely did not have Rasmussen's, despite the fact that many treaters (including Dr. Sullivan) had included it in their diagnostic differentials), and in so concluding Dr. Linnoila pointed to D.C.'s overall medical history, which did not reveal brain tissue loss/atrophy or other associated progressive neurologic decline usually seen in Rasmussen's. Tr. at 355-56; Linnoila First Rep. at 6, 8. She also agreed with Dr. Steinman that D.C.'s immediate vaccine reaction, however classified, was not related to D.C.'s later EPC course—although unlike Dr. Steinman, Dr. Linnoila questioned if D.C. had even experienced a febrile seizure, given that D.C.'s observed shaking despite no clear loss or lack of consciousness was not consistent with a febrile seizure. Tr. at 351, 368-71.

Dr. Linnoila did not completely embrace the conclusion that D.C.'s EPC was most likely autoimmune in nature. Rather, she opined that no explanatory cause for D.C.'s EPC could be identified, with autoimmune epilepsy only one of several plausible/possible explanations. Tr. at 367-68, 371, 375, 391-92; Linnoila First Rep. at 7; Linnoila Second Rep. at 3.[19] Dr. Linnoila found particularly compelling the fact that testing had not revealed that D.C. possessed any of the specific autoantibodies thought to be associated with autoimmune epilepsy. Tr. at 366-67, 397. She admitted that such autoantibodies could not always be found even in cases with "features of autoimmune epilepsy," but maintained that more often than not they would be present if in fact the epilepsy arose from an autoimmune process. Linnoila First Rep. at 6; Tr. at 411-13. But, she admitted, this did partially explain why it was difficult to be definitive in confirming an autoimmune epilepsy diagnosis. Tr. at 413-14.

The evidence of a successful response to IVIG was also not, in Dr. Linnoila's view, proof of the autoimmune character of D.C.'s epilepsy. She admitted that autoimmune neurologic illnesses and disorders are often highly responsive to immunotherapies. Linnoila First Rep. at 6. She also did not dispute that pre-IVIG, D.C.'s seizures were not responsive to treatment, and that fact plus the prior, more severe nature of her course reasonably suggested a possible autoimmune etiology given IVIG's effectiveness.[20] Tr. at 365, 395. But seizures are "highly irritating to the

[19] Dr. Linnoila noted, for example, evidence in the medical record suggesting that an MRI had revealed a potential left parietal lobe malformation—consistent with the fact that D.C.'s EEG abnormalities occurred in her left brain. Tr. at 352-53; Ex. 5 at 295; Linnoila First Rep. at 5. Such a brain malformation was a potential alternative explanation for D.C.'s illness.

[20] In fact, Dr. Linnoila observed that the record showed that IVIG had *not* been persistently effective. Thus, D.C. had experienced seizure relapses in December 2014 (and even later in February 2015), even in the midst of receipt of IVIG. Tr. at 415. I note, however, that the record does support the conclusion that the seizures returned in periods in which D.C. was not actively receiving an IVIG course. Ex. 5 at 182, 208, 219-20.

brain," exciting the immune system while encouraging additional inflammation (on top of what already may have occurred), and hence IVIG might simply be effective in treating the inflammation that is *secondary* to the initial cause of a seizure. *Id.* at 366. In addition, Dr. Linnoila noted that proof of IVIG's effectiveness is not a diagnostic criteria for autoimmune epilepsy. *Id.* at 396; Linnoila First Rep. at 6-7; F. Graus et al., *A Clinical Approach to Diagnosis of Autoimmune Encephalitis*, 15 Lancet J. 391 (2016) filed as Ex. E Tab 1 (ECF No. 32-2). And IVIG is also not specifically associated with the treatment of Rasmussen's, a rare condition that does not yet even have an agreed-upon treatment. *Id.* at 406-09.

In discussing the above, Dr. Linnoila directly questioned whether the clinical manner in which IVIG had been administered to D.C. allowed any reliable conclusions about its efficacy in the first place. Tr. at 358, 398-404. She felt only a "structural immunotherapy trial," in which treatment was subject to scientific controls, could shed light on whether the ameliorative nature of the treatment was evidence of its underlying autoimmune character. *Id.* at 358-62, 414. But this had not been done in D.C.'s case. *Id.* at 362-65.[21]

Moving to the causation questions central to Petitioners' claim, Dr. Linnoila contested that the flu vaccine could cause EPC or an autoimmune epilepsy. Tr. at 375. In so proposing, however, she relied greatly on the fact that she was unaware of support for this contention in the medical or scientific community. *Id.* at 372; First Linnoila Rep. at 8-9; *See* Institute of Medicine, *Adverse Effects of Vaccines: Evidence and Causality* 333 (National Academy of Sciences) (2012), filed as Ex. 33, Ref. 18 on April 12, 2017 (ECF No. 12-10). She did observe (in the context of opining that D.C. did not likely suffer from Rasmussen's syndrome) that MRI imaging for D.C.'s brain, conducted between August 2014 and February 2015, showed stability, and this "argued against a T-cell mediated process" as alleged by Dr. Steinman, since brain atrophy is usually a product of such T-cell attack. Linnoila First Rep. at 8.

Dr. Linnoila also contended that D.C.'s symptoms associated with her later diagnoses likely did not begin before April or May of 2014, asserting that the Caredios's recollection of D.C. dropping food from her hand around this time sounded like how EPC might initially manifest. Tr. at 350-51. But this timeframe from vaccination to first onset was in her view too long to acceptably link the flu vaccine to D.C.'s injury. *Id.* at 375-76. Dr. Linnoila did not accept that D.C.'s onset could have begun earlier, manifesting as the eye twitching the Petitioners and other witnesses testified to observing closer in time to vaccination. Those observed incidents, she proposed, could

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[21] As noted above, Dr. Steinman took specific issue with this point, and he and Dr. Linnoila ended up devoting much space in their written reports to address it. *See, e.g.*, Linnoila Second Rep. at 3-4; Linnoila Third Rep. at 1-5. Ultimately, however, my resolution of this claim does not turn on whether IVIG's effectiveness "proved" the autoimmune character of D.C.'s epilepsy, or whether it lacked the scientific rigor and controls required to reach that conclusion. Preponderant evidence overall slightly *better* supports the conclusion that the ameliorative impact of IVIG on D.C. reasonably suggested an autoimmune pathology—although *this does not mean* the flu vaccine was causal simply because D.C.'s epilepsy likely was autoimmune in nature.

simply have been evidence of anxiety, like tics, and she found it significant that Petitioners never reported them to D.C.'s pediatricians (despite seeking treatment for other issues). Tr. at 347-48, 379.[22] Such behaviors were also distinguishable from D.C.'s later, more obvious signs of EPC, which Dr. Linnoila deemed a "different phenomenon." *Id.* at 349, 350. D.C.'s course progression, which showed a persistence of eye twitching or blinking even after her more troubling seizures and associated involuntary motor movements had ceased, further convinced Dr. Linnoila that the initial eye twitching was not EPC-related. *Id.* at 376-77, 378.

III. Procedural History

After the case's initiation in January 2017, Petitioners filed medical records supporting the claim as well as Dr. Steinman's first report, with the Statement of Completion filed in August 2017. ECF No. 17. Respondent's Rule 4(c) Report, plus the initial reports of Drs. McCusker and Linnoila, were all filed in October of that same year. Expert discovery was completed by September 2018, and then the case was delayed for several months while it awaited scheduling for a hearing. After the matter was transferred to me in July of 2000, I held a status conference with the parties and subsequently set the matter for a hearing, to be held January 28-29, 2021. ECF No. 46. The trial occurred as scheduled, and the matter is now ripe for resolution.

IV. Applicable Legal Standards

A. *Petitioner's Overall Burden in Vaccine Program Cases*

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[23] In this case, Petitioners do not assert a Table claim.

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[22] One issue raised in connection with Winter 2014 pediatric visits—particularly to see Dr. Deldin—was the poor legibility of his notes or their cursory nature, and whether therefore it was possible that the Petitioners *had* raised concerns about the eye twitching sooner than other records suggested. *See, e.g.*, Tr. at 379-83. Petitioners' counsel also asked Dr. Linnoila many questions about the precise nature of the eye twitch, in an effort to gauge its severity or relationship to D.C.'s later seizures. *Id.* at 386-89. I do not find that either line of inquiry was particularly significant in swaying me one way or another in deciding the claim, however. The record sufficiently supports Petitioners' onset contention, and that onset manifested with the eye twitching, without having to evaluate whether handwriting illegibility for the relevant pediatric records explains the failure to mention D.C.'s initial EPC-related manifestations in those same records.

[23] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Hum. 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 & Hum. Servs.*, 59 Fed. Cl. 121,

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

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005): "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury."

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. 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. Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus the 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." *Andreu,* 569 F.3d at 1380.

However, the Federal Circuit has *repeatedly* stated that the "can cause" prong requires a preponderant evidentiary showing. *See Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1360 (Fed. Cir. 2019) ("[w]e have consistently rejected theories that the vaccine only "likely caused" the injury and reiterated that a "plausible" or "possible" causal theory does not satisfy the

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

standard"); *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1350 (Fed. Cir. 2010); *see also Moberly,* 592 F.3d at 1322 (discussing generally preponderance and the nature of showing a claimant must meet in Program cases). This is consistent with the petitioner's ultimate burden to establish his overall claim by preponderant evidence. *W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted). If the causation-in-fact evidentiary standard requires a preponderant showing, it makes no sense to conclude that standard is relaxed for any of the individual prongs making up the showing.

Petitioners may offer a variety of individual items of evidence pertaining to the first *Althen* prong, without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or even a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). The individual items of proof offered for the "can cause" prong must *each* reflect or arise from "reputable" or "sound and reliable" medical science. *Boatmon,* 941 F.3d at 1359-60.

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 & Hum. 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 & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

Medical records and statements of a treating physician, however, 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 & Hum. 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 be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Hum. 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); *Veryzer v. Sec'y of Dept. of Health & Hum. 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. Appx. 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." *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must align 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 & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 F. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for rev. denied* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Legal Standards 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 & Hum. Servs.*, 3 F.3d 415, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

Medical records that are created contemporaneously with the events they describe are presumed to be accurate and "complete" (i.e., presenting all relevant information on a patient's health problems). *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Hum. Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd sub nom. Rickett v. Sec'y of Health & Hum. Servs.*, 468 F. Appx. 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 & Hum. Servs.*, No. 11-685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Hum. Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie*, 2005 WL 6117475, at *20. 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*, 23 Cl. Ct. at 733 (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.")).

There are, however, 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 & Hum. 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 & Hum. 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 & Hum. 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. *Lalonde v. Sec'y of Health & Hum. Servs.*, 110 Fed. Cl. 184, 203-04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the

result of a rational determination. *Burns*, 3 F.3d at 417.

C. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Hum. 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 & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. 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 may be used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. 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. 136, 146 (1997)); *see also Isaac v. Sec'y of Health & Hum. Servs*., No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for rev. denied*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. Appx. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of

competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

Expert opinions based on unsupported facts may be given relatively little weight. *See Dobrydnev v. Sec'y of Health & Hum. Servs.*, 556 F. Appx. 976, 992–93 (Fed. Cir. 2014) ("[a] doctor's conclusion is only as good as the facts upon which it is based") (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")). Expert opinions that fail to address or are at odds with contemporaneous medical records may therefore be less persuasive than those which correspond to such records. *See Gerami v. Sec'y of Health & Hum. Servs.*, No. 12-442V, 2013 WL 5998109, at *4 (Fed. Cl. Spec. Mstr. Oct. 11, 2013), *aff'd*, 127 Fed. Cl. 299 (2014).

D. *Consideration of Medical Literature*

Both parties filed numerous items of medical and scientific literature in this case, but not every filed item factors into the outcome of this Decision. While I have reviewed all the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioners' case—just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Hum. 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); *see also Paterek v. Sec'y of Health & Hum. Servs.,* 527 F. Appx. 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

ANALYSIS

I. Threshold Issues Relevant to Diagnosis

A. *D.C. Likely Experienced EPC*

In many cases, application of the *Althen* causation test is appropriately dependent on first deciding if a petitioner's claimed injury has preponderant support. *Broekelschen*, 618 F.3d at 1349. Indeed, sometimes consideration of the *Althen* prongs is entirely unnecessary once it is determined

that the asserted injury cannot be proven, since a claimant's causal theory may completely rely on such a finding. *Lombardi v. Sec'y of Health & Hum. Servs.*, 656 F.3d 1343, 1353 (Fed. Cir. 2011).

This is not such a case. Petitioners' testifying treaters largely agreed that D.C. suffered from *some* form of epilepsy, likely EPC, and I find their views to be wholly consistent with the medical record. Accordingly, I will analyze Petitioners' claim based on the determination that her injury was consistent with EPC.

In addition, I find there is record support, bulwarked by the testimony of treating physicians Drs. Van Haren and Sullivan, that D.C.'s epilepsy/seizures were more likely than not autoimmune in pathogenesis. This conclusion was reached by a large number of independent treaters who saw D.C. at different times (from Dr. Van Haren in the fall of 2014 to doctors at Boston Children's Hospital in the spring of 2015). Some treaters may have rooted their conclusions in part on a mistaken connection between D.C.'s febrile seizure and her EPC (a connection Petitioners' primary testifying expert, Dr. Steinman, expressly disavowed), but their views overall merit evidentiary weight. Respondent also reasonably observed that D.C. never tested positive for any specific autoantibodies associated with an autoimmune form of epilepsy, but that datapoint does not preclude a finding that her disease process was immune-driven.

The proposed autoimmune character of D.C.'s injury gains some corroborative support from the fact that IVIG treatment was successful. Respondent reasonably pointed out a number of deficiencies with this contention, noting that such treatment is not a diagnostic criteria for autoimmune epilepsy/EPC, as well as the fact that IVIG can be beneficial simply because it can reduce inflammation independently associated with epileptic seizures. But treaters directly responsible for D.C.'s care deemed the efficacy of this treatment as significant in identifying the underlying disease process's pathologic nature, and again it is appropriate to give their conclusions some deference.

The record in this case does *not,* however, support the conclusion that D.C. had or has Rasmussen's syndrome. D.C.'s overall progression and presentation is simply not consistent with that illness—which is unquestionably even more severe. Varadkar at 2-3. At best, treaters included it in diagnostic differentials because of D.C.'s focal seizure presentation—but the evidence over the total course of her treatment never confirmed it. And although both of D.C.'s testifying treaters (as well as Dr. Steinman) defended consideration of Rasmussen's, *none* affirmatively testified that in fact this best characterized D.C.'s disease. *See, e.g.*, Tr. at 226-29; Ex. 47. The diagnosis is not ultimately embraced in the medical record otherwise. This determination does not prevent a favorable entitlement finding, but it does mean that the comparison of D.C.'s course to Rasmussen's, or analogies made between it and the causation theory proposed, are ultimately unhelpful in evaluating whether Petitioner has carried her burden of proof.

B. *Program Treatment of Autoimmune Epilepsy Cases*[24]

Vaccine Program petitioners have successfully established that different vaccines can cause an autoimmune injury featuring or characterized by epileptic seizures. *See, e.g.*, *Agarwal v. Sec'y of Health & Hum. Servs.*, No. 16-191V, 2020 WL 5651683 (Fed. Cl. Spec. Mstr. Aug. 31, 2020) (child developed autoimmune limbic encephalitis (ALE) with intractable seizures after receiving Tdap and meningococcal vaccines); *McCulloch v. Sec'y of Health & Hum. Servs.*, No. 09-293V, 2015 WL 3640610 (Fed. Cl. Spec. Mstr. May 22, 2015) (human papillomavirus vaccine caused minor child to develop encephalitis, intractable epilepsy, and subsequent developmental delays). I note, however, that hardly any of these cases involve causation theories implicating the flu vaccine alone—and those that do are often readily distinguishable. *See, e.g.*, *Raybuck v. Sec'y of Health & Hum. Servs.,* No. 06-846V, 2010 WL 4860778 (Fed. Cl. Spec. Mstr. Nov. 9, 2010) (flu vaccine found to cause rash in child with preexisting seizure disorder; rash led to discontinuation of anti-convulsant medication, prompting exacerbation of child's pre-existing epilepsy).

In addition, there is a significant factual element of this case separating it from many other cases (even involving the flu vaccine) in which damages have been awarded for epilepsy/seizures. Often, a petitioner can show that an injured child experienced a vaccine-induced fever, which then triggered a *febrile seizure*—thereby instigating an autoimmune form of epilepsy. *See, e.g.*, *Ginn v. Sec'y of Health & Hum. Servs.*, No. 16-1466V, 2021 WL 1558342 (Fed. Cl. Spec. Mstr. Mar. 26, 2021) (five vaccines, including the flu vaccine, triggered a febrile seizure in four year-old that contributed/led to development of epilepsy); *Tembenis v. Sec'y of Health & Hum. Servs.,* No. 03-2820V, 2010 WL 5164324, at *15-16 (Fed. Cl. Spec. Mstr. Nov. 29, 2010) (febrile seizure attributable to DTaP vaccine caused epilepsy and death). In such cases, the vaccine's causal contribution to subsequent disease flows directly from the impact of vaccination on a child's innate/immediate immune response.

But in this case, Dr. Steinman—Petitioners' primary causation expert—readily conceded that D.C.'s immediately post-vaccination febrile seizure had *no* relationship to her subsequent development of EPC, even if it had been directly caused by the flu vaccine (as he seemed to accept). Tr. at 211. Indeed, he admitted at hearing that his proposed causation theory (that a

[24] In reaching a decision in this case, I have considered other decisions issued by special masters (including my own) involving similar injuries, vaccines, or circumstances. There is no error in doing so. Although only Federal Circuit decisions *control* the outcome herein (*Boatmon,* 941 F.3d at 1358-59; *Hanlon v. Sec'y of Health & Hum. Servs.*, 40 Fed. Cl. 625, 630 (1998)), special masters reasonably draw upon their experience in resolving Vaccine Act claims. *Doe v. Sec'y of Health & Hum. Servs.,* 76 Fed. Cl. 328, 338-39 (2007) ("[o]ne reason that proceedings are more expeditious in the hands of special masters is that the special masters have the *expertise and experience to know the type of information that is most probative of a claim*") (emphasis added). They would therefore be remiss in ignoring prior cases presenting similar theories or factual circumstances, along with the reasoning employed in reaching such decisions.

molecular mimicry-driven cross-reaction instigated by the flu vaccine produced D.C.'s EPC) *could not occur* in such a short timeframe. Tr. at 213.

Thus, the question posed by this case is whether the flu vaccine could precipitate a disease process beginning approximately 10 to 14 days post-vaccination—not the same day as vaccination—and manifesting as eye twitching, but then evolving into outright focal, but afebrile, seizures one to three months later. While there are some cases in which afebrile seizures have been linked to vaccination, they have mostly involved vaccines containing components (like pertussis toxin) thought to be seizure-provoking.[25] Cases involving afebrile seizures have been less successful. *See, e.g.*, *K.L. v. Sec'y of Health & Hum. Servs.*, 134 Fed. Cl. 579, 587 (2017) (affirming special master's determination that vaccine did not trigger afebrile seizure resulting in epilepsy); *Dodd v. Sec'y of Health & Hum. Servs.*, 114 Fed. Cl. 43, 55–57 (2013) (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).

II. Petitioners Have not Carried Their Burden of Proof

A. *Althen Prong One*

Dr. Steinman was the primary expert proposing the flu vaccine could cause EPC, as Drs. Sullivan and Van Haren disclaimed offering such an opinion. He reasoned as follows: (a) vaccines impact the immune system, (b) EPC can be an autoimmune condition, (c) vaccines can cause autoimmune diseases, (d) autoimmune processes can occur via the mechanism of molecular mimicry, and (e) homology (necessary to spark an autoimmune cross-reaction based on molecular mimicry) can be demonstrated between components of the flu vaccine and putative neuronal receptors in the brain reflective of the target of an autoimmune cross-reaction sufficient to initiate seizure activity. And he analogized the autoimmune process relevant herein to comparable autoimmune diseases involving intractable seizures, like Rasmussen's, in which the immune-mediated attack focuses on neuronal brain receptors (although my determination that the record does not establish that D.C. had Rasmussen's limits greatly the value of such analogies).

While certain components of this casual theory *do* have reputable and reliable scientific/medical support, they do not add up to a causation theory that is more than speculative, as many links necessary for the conclusion that the flu vaccine could cause EPC are missing.

The core deficiency of Dr. Steinman's opinion is the degree to which he relied almost wholly (by his own admission) on sequential homology to carry the day. He offered no evidence otherwise linking the flu vaccine to EPC—and Dr. McCusker cited to reliable epilepsy studies, like Kotloff, that cast doubt on any such vaccine association. Moreover, and unlike many Vaccine

[25] *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 vaccine); *Almeida v. Sec'y of Health & Hum. 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 of the day she received a DPT vaccine).

Act cases, Dr. Steinman did not endeavor to identify case reports suggestive of a vaccine-EPC association—and while case reports are not viewed in the Vaccine Program as particularly probative of causation, as a class of evidence they still possess *some* limited value. *Campbell v. Sec'y of Health & Hum. Servs.*, 97 Fed. Cl. 650, 668 (Fed. Cl. 2011) (case reports "do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value"); *Cf. Contreras v. Sec'y of Health & Hum. Servs.*, 107 Fed. Cl. 280, 304 (2012) (finding that a special master's decision to award case reports zero weight was contrary to authority).

Dr. Steinman therefore had to look elsewhere to substantiate his opinion, and did so by focusing on molecular mimicry. He *was* able to show amino acid homology between the flu vaccine's antigenic components and putative antigenic targets in the brain where an autoimmune form of epilepsy *might* occur (although this part of his argument lost some resonance to the degree to which it invoked Rasmussen's—a disease the record does not suggest D.C. had). Moreover, molecular mimicry is unquestionably a reliable scientific theory for how autoimmune diseases can pathologically progress. *Chinea v. Sec'y of Health & Hum. Servs.*, No. 15-095V, 2019 WL 1873322, at *15 (Fed. Cl. Spec. Mstr. Mar. 15, 2019). But I have repeatedly noted that *demonstration of homology alone is not enough to establish a preponderant causation theory. Schultz v. Sec'y of Health & Hum. Servs.*, No. 16-539V, 2020 WL 1039161, at *22 n.24 (Fed. Cl. Spec. Mstr. Jan. 24, 2020) ("[m]ere demonstration of theoretical homology alone, based on computer-driven searches involving databases of amino acid sequences, does not carry the day").

The reasons that invocation of molecular mimicry (and a showing of homology as part of it) is insufficient to meet the "can cause" prong are many. As Dr. McCusker noted in rebutting Dr. Steinman's opinion, homology is common in nature, and frequently exists without resulting in autoimmune injury, since the immune system usually is able to prevent an autoimmune cross-reaction, or delete the immune cells that would likely specifically target self structures and proteins. She was also able to demonstrate, via the same kind of BLAST search performed by Dr. Steinman, that homology *also* exists between the neuronal receptors Dr. Steinman identified and other wild viruses common in children, but not considered associated with autoimmune forms of epilepsy. McCusker First Rep. at 5-9. Homology does not inexorably lead to disease.

As a result, to establish that a vaccine could prompt harm arising from a potential autoimmune cross-reaction that would occur due to homology, more is needed.[26] Here, that "more"

[26] The rarity of vaccine injury, oft referenced by petitioners in justifying the causation showing they attempt to make, does not excuse petitioners from their preponderant burden. It is well understood in the Program that entitlement determinations are made in a field "bereft" of direct evidence, and that the fact that vaccine injuries do not occur commonly does not mean they *cannot* occur (or cannot be proven with indirect evidence). *Althen,* 418 F.3d at 1280; *Capizzano,* 440 F.3d at 1324 ("[I]n a field bereft of complete and direct proof of how vaccines affect the human body," a *paucity of medical literature* supporting a particular theory of causation cannot serve as a bar to recovery" (emphasis added)); *see also Daubert,* 509 U.S. at 593 ("[I]n some instances well-grounded but innovative theories will not have been published.... Some propositions, moreover, are too particular, too new, or of too limited interest to be published"). Indeed, the Program arises from the bedrock assumption that vaccines generally *are* safe—and that the public benefit of vaccination is served by a compensation system in which those rare individuals who are injured, and can prove the same, have redress.

is absent—for the additional evidence filed in this case did not preponderantly support causation, and Dr. Steinman could not fill in these holes by citing to his own direct experience, either in researching the adverse effects of the flu vaccine or studying autoimmune forms of epilepsy.

Instead, Dr. Steinman's argument borrowed neuronal receptors associated with *other* autoimmune central nervous system injuries to propose how an autoimmune epilepsy would unfold. He in fact used these receptors to establish homology with the flu vaccine antigens. But those receptors are not typically implicated in T cell-mediated diseases, which Dr. Steinman unquestionably maintained was likely the character of D.C.'s epilepsy. McCusker Second Rep. at 2-3. Indeed, D.C. did not even test positive for the autoantibodies associated with NMDA-R autoimmune illness. And Dr. Steinman's opinion ignored Dr. McCusker's point that a peripherally-administered vaccine could not be assumed to "beeline" for specific locations in the brain, especially since the vaccine's antigens would have other comparably-homologous neuronal targets, in the brain as well as elsewhere in the body.

Dr. Steinman's theory could have been supported with any number of different evidentiary items. He was certainly not required to marshal direct proof, or some specific type of evidence. But he could rest his opinion on speculation that an autoimmune disease process could flow from the *theoretic possibility* of an autoimmune cross-reaction. That is all demonstrating homology accomplishes—and it does not constitute a preponderant showing. Were it otherwise, then 99 percent of non-Table claimants could establish the "can cause" *Althen* prong, in *any* case involving an autoimmune disease, as long as they proved sequential homology via the testimony of a suitably-credentialed medical or scientific expert, and then demonstrated a temporal association between vaccine and injury. This would effectively relieve petitioners of their actual burden in non-Table cases, rendering the standard for assessing the "can cause" prong a simple factual determination, rather than a weighing process that takes into account the medical and scientific reliability of the individual components offered to support the theory in question.[27]

In addition to the above, Dr. Steinman's theory faltered in other important regards. He opined that the disease process at issue was primarily propagated by cytotoxic T cells—making its pathogenesis distinguishable from illnesses in which a cross-reactive autoimmune attack due to

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Thus, the fact that cross-reactivity is not common (due perhaps to the general reasons invoked by Dr. McCusker) does not end the analysis and result in dismissal. *But claimants must still meet their preponderant burden*—and in off-Table cases, that burden is not insignificant. *Hodges v. Secretary of Health & Hum. Servs*., 9 F.3d 958, 961 (Fed.Cir.1993) (while "the [Vaccine Act] does the heavy lifting" when a claimant seeks to establish a Table injury, in the causation-in-fact context "the heavy lifting must be done by the petitioner, and it is heavy indeed").

[27] Suggestions that this is in fact the proper standard to be applied in non-Table cases—based on the view that it is unfair to Vaccine Act claimants to have to address the scientific limits of their causation theories, given how little is known about how vaccines can injure individuals—have been succinctly criticized. *See e.g., Boatmon*, 941 F.3d at 1363 ("[a]n unverified assertion of fact [regarding a causation theory] is not common sense; it is a non-cognizable argument. A statement of law without basis in statute or precedent is not sound reason") (*Wallach, J*., concurrence).

molecular mimicry is mostly attributable to antibodies manufactured by *B cells. See, e.g.*, Nibber. But as Dr. McCusker observed, a T cell-driven attack on self requires more than just a showing of initial sequential homology. Instead, it must be demonstrated that the cross-reacting T cells would *recognize* the self structure before concluding they could attack it. McCusker First Rep. at 5; McCusker Second Rep. at 3; Tr. at 296.

Such an evidentiary showing was not made—and Dr. Steinman's pointing out that *some* T cells always play a role in antibody production (and hence will be involved even in antibody-driven autoimmune processes) seemed only intended to muddy the waters rather than meet head-on this deficiency in his causation theory, since the kinds of T cells that help the manufacture of antibodies are distinguishable from those that Dr. Steinman posited were causal. Dr. Steinman similarly could not overcome Dr. McCusker's persuasive showing that the flu vaccine was not even likely to upregulate the type of T cells he deemed central to the relevant disease process. McCusker First Rep. at 4. And (as noted above), Dr. Steinman unpersuasively analogized the autoimmune process herein to distinguishable disease processes understood to be *B cell* driven, borrowing receptors for his homology experiment like NMDA that cross-react with antibodies primarily rather than T cells. Tr. at 284; McCusker Second Rep. at 2-3.

I also note that after listening to both sides' immunologic experts and reviewing the transcripts of their testimony, I gave far more weight to Dr. McCusker's statements and opinions than to those of Dr. Steinman. Her testimony not only covered overarching weaknesses in Petitioners' theory, but homed in on the individual elements of Dr. Steinman's theory, and the views she expressed arose from her specific expertise in pediatric immunology. She persuasively rebutted the points made in favor of causation. Dr. Steinman, by contrast, placed far too much emphasis on molecular mimicry and homology in constructing a causation theory, ineffectively shielding his theory from challenge either by invoking the limits of science to understand the processes at issue, admitting outright that his opinion could not be better bulwarked, or acknowledging that he had simply fashioned an opinion that fit the facts of the case.[28] Tr. at 262-63. Other special masters have observed Dr. Steinman's tendency when acting as a Program expert to "shoehorn molecular mimicry into every causation in fact case" in which he testifies. *See, e.g.*, *D.G. v. Sec'y of Health & Hum. Servs.*, No. 11-577V, 2019 WL 2511769, at *189 (Fed. Cl. Spec. Mstr. May 24, 2019). That tendency was fully on display here, undermining his overall credibility.

In reaching the determination that Petitioners' causation showing on the first *Althen* prong was inadequate, I am *not* requiring "scientific certainty," and hence raising the evidentiary bar. *Knudsen*, 35 F.3d at 549. I well understand and accept that preponderance as an evidentiary standard inherently does *not* require certainty. Indeed, the fact that a claimant's causal theory is found preponderant *does not mean* it is "scientifically certain" the vaccine can cause the relevant injury. Rather, it only signifies that the evidentiary weighing process performed by the special

[28] *See* footnote 13, above.

master (based on the collective probative value of several individual evidentiary items plus expert opinions) *in the relevant case* has resulted in a favorable determination.

Similarly, the opposite determination—that a causation theory has *not* been preponderantly established—is not predicated on a special master's unreasonable *requiring* of certainty. Petitioners may well offer several individual items of evidence (for example, molecular mimicry as a proposed autoimmunity mechanism) relevant to *Althen* prong one that are reliable or scientifically reputable. Yet the totality of evidence, when weighed against Respondent's showing, may *not* permit the special master to conclude causation is more likely than not.

Here, it is my determination, after weighing the evidence and expert testimony, that Dr. Steinman's causation theory over-relied on demonstrating sequence homology between components of the flu vaccine and certain neuronal receptors where focal seizures might occur, but without also proposing additional reliable evidence necessary to find that the flu vaccine could be associated with autoimmune epilepsy/EPC. Accordingly, I conclude that the preponderant "line" was not crossed.

B. *Althen Prong Two*

The facts of this case do not preponderantly support the conclusion that D.C.'s receipt of the flu vaccine was responsible for her EPC.

D.C. likely experienced a febrile seizure associated with her receipt of the flu vaccine that same day, despite the testimony of Respondent's experts that this diagnosis lacked some evidentiary support. And yet—because Dr. Steinman *disavowed* the febrile seizure as having any relationship to D.C.'s later-diagnosed EPC, the vaccine's causal relationship to a one-time febrile seizure has no bearing on entitlement in this case.

The medical record thereafter, however, does not suggest a relationship between vaccination and D.C.'s illness either. I accept the testimony of Petitioners and the other witnesses that D.C. began displaying eye fluttering in early February 2014, and that this fluttering was likely related to the EPC she was later diagnosed with, and thus the seizures that clinical evidence establishes she experienced in May that same year. Even though the medical record does not fully corroborate witness contentions about D.C.'s initial symptoms (and at best establishes symptoms onset *later* than alleged), it does not undermine them either—and relevant case law clearly permits Program claimants to establish these kinds of onset-related matters with individual sworn testimony, especially in the face of a silent or ambiguous record. *Kirby v. Sec'y of Health & Hum. Servs.*, 997 F3d. 1378, 1382-83 (Fed. Cir. 2021).

However, Petitioners' observations of initial outward manifestations of D.C.'s EPC do not establish that the flu vaccine harmed her. The record is far less supportive of such a contention. Thus, D.C. never tested positive for any autoantibodies that would be associated with an autoimmune form of epilepsy—and while this fact may not have prevented treaters from

confirming their ultimate diagnosis, it somewhat undercuts the conclusion that the flu vaccine caused it (although Dr. Steinman made reasonable points about how significant the presence of such autoantibodies would be—especially since he posited D.C.'s EPC was T cell-driven). In addition, treater support for the vaccine being causal is sparse, with no actual treaters opining "in real time" that the vaccine could have caused seizures that ultimately manifested months after vaccination. While admittedly Dr. Sullivan agreed that vaccination should be avoided for D.C. in August 2016, that treater advice seems more the product of caution on his part than a reliable determination that the vaccine was causal (as he admitted in his testimony). Ex. 10; Tr. at 200, 206.

A larger issue inconsistent with the determination that the flu vaccine caused D.C.'s EPC/autoimmune epilepsy is the course of her illness from vaccination to manifestation of acute seizures. Having accepted Petitioners' testimony plus Dr. Steinman's view of symptoms onset, I have found that D.C.'s February 2014 eye fluttering was likely the start of some otherwise-undetected neurologic process that later progressed into outright focal seizures. But how is this course reflective of a disease process instigated by vaccination? Petitioners can only point to the fact that vaccination occurred first—and it is well known that a temporal association does not prove causation. *Moberly*, 592 F.3d at 1323.

Dr. Steinman's theory said much about how T cells might instigate harm, and attempted unsuccessfully to link this immunologic process to vaccination. But he similarly was unsuccessful in explaining how a flu vaccine might initiate a neurologic process that would take several months before becoming acute. He did not establish that the T cells he maintains would be increased due to an autoimmune cross-reaction instigated by molecular mimicry would *first* cause eye twitching that would later change into focal seizures. Indeed, he never effectively responded to Dr. McCusker's contention that the flu vaccine would do a poor job of stimulating production of T cells in the first place.

C. *Althen Prong Three*

Because Petitioners' showing on the first two *Althen* prongs was unsuccessful, determining Petitioners' success in establishing the third prong is unnecessary. But although the timeframe prong was substantiated in part with reliable medical and scientific evidence, my reservations about the overall preponderant strength of evidence offered for it makes it difficult for me to conclude it was satisfied.

On the one hand, Petitioners marshaled preponderant evidentiary support for the conclusion that an autoimmune reaction to the flu vaccine, propagated by the adaptive arm of the immune system via the mechanism of molecular mimicry, could occur in a 10-20 day period. Here, this defines the approximate timeframe between D.C.'s January 2014 vaccination and onset of her

eye blinking/fluttering in early February.[29] Because that twitching was persuasively established to be likely associated with D.C.'s subsequent EPC/autoimmune epilepsy, the post-vaccination timeframe for onset was medically acceptable (assuming the inquiry focused *only* on that period).

On the other hand, Dr. Steinman did not persuasively establish that a vaccine-caused EPC would have a slowly progressive course *after* inception. Petitioners proposed autoimmune injury instigated by antigenic cross-reaction, but as Dr. McCusker noted, D.C.'s course (which features progression from eye fluttering to outright acute/focal seizures two to three months later) would reflect a "chipping away" process that is not consistent with how an immune-mediated injury (dependent on the chronic production of T cells necessary to cause neurologic injury) would typically advance. Tr. at 313, 331. Dr. Steinman for his part seemed only to gesture to the contrary, offering little reliable evidence to support the contention that the flu vaccine could initiate such a lagging, slightly progressive process that would later become acutely/clinically evident, other than to maintain that immune memory sparked by the January 2014 vaccination would eventually make the process chronic. Tr. at 214. At bottom, the fact that the vaccine was not demonstrated to likely be associated with EPC moots the need to decide this prong—but I acknowledge the question was much closer here than in resolving the first two prongs.

CONCLUSION

The Caredios have suffered heart-breaking setbacks in their care of D.C., and have unquestionably struggled in the process. For this, they have my deepest admiration—and it would have been personally a great pleasure to award them compensation. But I am bound to apply the law correctly, and in this case Petitioners have not met their evidentiary burden. I therefore must dismiss the claim.

In the absence of a motion for review filed pursuant to RCFC Appendix B, the clerk of the court **SHALL ENTER JUDGMENT** in accordance with the terms of this decision.[30]

IT IS SO ORDERED.

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

[29] The record does contain some evidence that might suggest a pre-vaccination onset. *See, e.g.*, Ex. 6 at 226–27, 244; Ex. 7 at 4-6 (records from May 29, 2014 neurologic evaluation); Ex. 12 at 12. However, this possibility was not fully fleshed-out at trial, nor did treaters ultimately propose or conclude that D.C.'s condition was so long in its development, and therefore I do not give weight to the point in evaluating the third *Althen* prong.

[30] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment if (jointly or separately) they file notices renouncing their right to seek review.