CORRECTED

In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 16-887V

* *

ALEX and TESS BECHEL, *parents of* G.J.B., *a minor*,

Petitioners,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

* *

Chief Special Master Corcoran

Dated: May 22, 2023

Isaiah Kalinowski, Bosson Legal Group, Fairfax, VA, for Petitioners.

Colleen Clemons Hartley, U.S. Dep't of Justice, Washington, DC, for Respondent.

ENTITLEMENT DECISION[1]

On July 26, 2016, Alex and Tess Bechel filed a petition as parents of G.J.B., seeking compensation under the National Vaccine Injury Compensation Program (the "Vaccine Program").[2] Petitioners allege that G.J.B. experienced encephalopathy, epilepsy, seizures, delirium, confusion, altered mental state, and other injuries due to the administration of several childhood vaccines on July 29, 2013. Petition (ECF No. 1) at 1–2.

The case was transferred to me in January 2021, and it had been set for an entitlement hearing to be held in February 2022. After Petitioners' initial counsel withdrew, however, it was

[1] Under Vaccine Rule 18(b), each party has fourteen days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the whole Decision will be available to the public in its present 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) ("Vaccine Act" or "the Act"). Individual section references hereafter will be to § 300aa of the Act (but will omit that statutory prefix).

determined by the parties that the case should instead be resolved on the papers. *See* Order, dated February 11, 2022 (ECF No. 68). Both parties have now filed briefs in support of their respective positions. Petitioners' Motion, dated May 31, 2022 (ECF No. 74-1) ("Mot."); Respondent's Opposition, dated August 25, 2022 (ECF No. 80) ("Opp."); Reply, dated September 16, 2022 (ECF No. 84) ("Reply").

For the reasons discussed in greater detail below, I hereby deny entitlement.

I. Factual Background

Birth and Early Care

G.J.B. was born full-term on May 13, 2009. Ex. 2 at 8. His Apgar scores were 8 and 9 at one and five minutes, respectively, and his newborn screen was normal. *Id.* at 8, 18. In his early life, he received pediatric care from Lexington Clinic, and Pediatric and Adolescent Associates, where he presented for both well and sick visits. Ex. 14 at 13–77; Ex. 3 at 1–41.

The record establishes a few pre-vaccination instances of health issues bearing on the claim. For example, at G.J.B.'s 18-month well visit on January 27, 2011, Ms. Bechel reported that G.J.B. had complained of "light" hurting his eyes for the prior three to four days, and that more generally he had displayed "some odd tendencies." Ex. 3 at 16–18. Ms. Bechel also stated to treaters her suspicion that her husband "may have [redacted] *Id.* At G.J.B.'s three-year-old well visit in 2012, Ms. Bechel's primary concern was G.J.B.'s speech, and she asked whether he could obtain entry into a "headstart program" to address this matter. *Id.* at 34–36. Later that same year (in October 2012), Petitioners had G.J.B. undergo a speech/language evaluation, and it was determined as a result that he likely had a delay in articulation, with speech therapy recommended. Ex. 16 at 2–3.

Relevant Vaccinations and Alleged Reaction

On July 29, 2013, G.J.B. was taken to his pediatrician at Pediatric and Adolescent Associates for his four-year-old well visit. Ex. 1 at 1–8; Ex. 3 at 43–47. It was again noted that Mr. Bechel might have [redacted], and that G.J.B. was enrolled at the time in speech therapy. *Id.* His physical examination was largely normal, and he was described in the record as alert, interactive, and appropriate for age. Ex. 1 at 4–5; Ex. 3 at 46–47. He received the following

[redacted]

vaccines: Kinrix (containing DTaP and IPV),[4] measles, mumps and rubella ("MMR"), and varicella ("VAR"). Ex. 1 at 5; Ex. 3 at 47.

There is no contemporaneous record evidence of any reaction to these vaccines. However, Ms. Bechel's witness statement maintains that the next day (July 30th), she "noticed his legs were a little red and swollen around the site of injection," and that he began "complaining of a headache that evening and continued to complain over the next few days off and on." Ex. 8 at ¶ 2. G.J.B.'s grandmother, Kay Bechel, has also averred that on Wednesday, July 31, 2013 (two days post-vaccination), G.J.B. developed "severe swelling in both of his thighs and a headache." Ex. 10 at ¶ 2.

Five days later, on Saturday, August 3, 2013, Ms. Bechel contacted Central Baptist Hospital for an assessment of G.J.B.'s condition. Ex. 5 at 1. She reported that G.J.B. could not remember some words, and did not know his name when asked. *Id*. The "onset/duration" was noted as "today." *Id*. The record of this communication also indicates that G.J.B. received his four-year vaccinations on the previous Monday, and that he "had speech problems in the past with stuttering." *Id*. The record identifies no other physical issues at the time or newly-observed symptoms, however, and reports G.J.B. to have been afebrile. *Id*. The nurse advised Ms. Bechel to seek emergency treatment "immediately," although the Petitioners did not do so. *Id*.

The day after (August 4th), a nurse with Pediatric and Adolescent Associates followed-up with Ms. Bechel. Ex. 3 at 48. Ms. Bechel confirmed that she had not yet taken G.J.B. to the emergency room, and that he was still stuttering and getting frustrated. *Id*. The record memorializes the note that "mom thinks this is all related to the 4 yr vaccines he got a few days ago." *Id*. Ms. Bechel also apparently reported at this time that G.J.B. did not have a history of this in the past, and did not have any other injury or illness. *Id*. Ms. Bechel was advised to monitor his condition, and bring him in the next day if concerns continued. *Id.*

On August 5, 2013, G.J.B.'s grandmother, Kay Bechel (who is apparently a registered electroencephalographic technologist), completed an EEG of G.J.B. at her home. Ex. 20 at 1–23; Ex. 10 at ¶ 4. While the notes are handwritten on the documentation filed, Kay Bechel has averred that the study results appeared "abnormal" to her, and she therefore recommended that G.J.B. be taken to his physician and a pediatric neurologist for a full work-up. Ex. 10 at ¶ 5. Ms. Bechel did so the next day. Ex. 3 at 50–52.

At this pediatric visit, Ms. Bechel reported G.J.B.'s recent vaccinations, and that he had complained of a headache after getting them. *Id.* Then, on August 3, 2013, he woke up "stuttering really bad" with a "blank look on his face"—a completely novel behavior, followed by off-and-on stuttering, and an instance where he forgot his name. *Id.* She admitted that G.J.B. had manifested

[4] "DTaP" is the acronym for diphtheria-tetanus-acellular pertussis vaccine, and "IPV" is the acronym for polio vaccine.

some issues with speech before, and was enrolled in a Head Start Program, but noted that he did not previously stutter. *Id.* The pediatrician observed G.J.B. stutter several times during the visit, although when examined he was alert and oriented with no focal deficits. *Id.* The pediatrician diagnosed G.J.B. with "stuttering" and referred him to Cincinnati Children's Hospital for a neurology consultation with Marissa Vawter, M.D. *Id.*

Post-Vaccination Evaluations and Epilepsy Diagnosis

On August 7, 2013, Petitioners took G.J.B. to St. Joseph Hospital for evaluation. *See generally* Ex. 12. On admission, Ms. Bechel reported that G.J.B. had "started stuttering on Saturday 7-29-13," and that he was doing so "up to 30 times a day," and often appeared "blank" during the stuttering episodes. *Id.* at 49. G.J.B. underwent a one-day video EEG study at the hospital. *Id.* at 34–35. The study yielded abnormal results and displayed 16 events, consisting of stuttering of speech or repeating words, but with no other clinical change noted. *Id.* It specifically revealed epileptiform discharges, most prominently in the left occipital electrode, and suggested the possibility of multifocal/generalized epileptogenicity. *Id.*

G.J.B. was evaluated several days later by Dr. Vawter with the neurology service at Cincinnati Children's Hospital. Ex. 6 at 1–35. Ms. Bechel now provided a more detailed history of G.J.B.'s health since the July vaccinations. *Id.* at 2. In particular, she represented that after leg swelling G.J.B. began reporting headaches on July 30th, and then on August 3rd began displaying stuttering and an inability to remember his name, which was also evident at a birthday party he attended, causing him to be upset and frustrated. *Id.* Such issues continued, and then by August 5th he had an episode of "spinning" while brushing his teeth. *Id.* Thereafter, his behaviors progressed, the aforementioned home EEG was performed, and then by August 9, 2013, "when he stuttered, his eyes seemed to get larger in size." *Id.* A few days later, he appeared "hyperactive and out of control." *Id.* Ms. Bechel denied, however, any developmental regression or urinary incontinence with any of the spells. *Id.*

In providing this history, Ms. Bechel also informed Dr. Vawter that G.J.B. had a history of difficulties with enunciation shared in his family, plus a history of headaches, with Mr. Bechel previously experiencing migraine-like headaches. Ex. 6 at 3. On physical examination, G.J.B. was alert and his detailed neurological exam was normal. *Id.* at 4–5. Dr. Vawter opined that G.J.B. had experienced at least two clinical seizures in the past ten days, singling out "the episodes where he had abnormal verbal speech patterns and/or repetitions." *Id.* at 5. In the context of his abnormal EEG, Dr. Vawter documented that he met the criteria for epilepsy with "unknown etiology," but that medication could help stabilize and control his seizure activity. *Id.* To that end, Dr. Vawter prescribed Keppra and ordered a brain MRI for further evaluation. *Id.* The brain MRI was performed on August 19, 2013, Ex. 3 at 144–45. It revealed a hypoplasia left maxillary sinus, but was otherwise unremarkable. *Id.*

On August 20, 2013, Ms. Bechel contacted the pediatrician's office to inform them of G.J.B.'s epilepsy diagnosis. Ex. 3 at 53. She also noted that G.J.B. had been complaining of his right leg and right eye hurting, and that he often refused to walk. *Id*. However, when G.J.B. was seen in the office the next day, he displayed no obvious musculoskeletal abnormalities on physical examination. *Id*. at 54–55. At the end of August 2013, Kay Bechel submitted a VAERS report[5] on his behalf. Ex. 15 at 1; Ex. 10 ¶ 7. This report identified onset of G.J.B.'s symptoms (manifesting as stuttering, repetition, and confusion) as August 3, 2013 (five days after the vaccinations), although it also described his headaches as beginning sooner (July 31–August 2, 2013). *Id.* The diagnoses reported included seizures, epilepsy, and an abnormal EEG. *Id.*

Further Treatment and Evidence of Other Comorbidities

About three months later (on November 12, 2013), G.J.B. was taken back to Dr. Vawter. Ex. 6 at 74–111. At that time, Ms. Bechel reported that he had experienced no seizures or episodes of stuttering since the initial visit in August, although he was having difficulty with his Keppra, so alternative medications were discussed. *Id*. at 76, 79–80. G.J.B. saw Dr. Vawter again in February 2014, at which time Ms. Bechel reported that G.J.B. had experienced only one seizure since changing anti-seizure medications. *Id.* at 123–185. Concerns were now also expressed about the possibility of "developmental regression." *Id.* at 124.

In March 2014, G.J.B. was evaluated at Cincinnati Children's Rheumatology service for joint pains for which he had obtained some treatment in the immediate months before. Ex. 3 at 135–38. On physical examination, G.J.B. displayed increased flexibility, particularly in his ankles and knees, and laboratory testing was recommended to evaluate him for a possible underlying autoimmune condition or thyroid condition. *Id.* That same month he also underwent an ophthalmological evaluation which revealed hyperopia.[6] Ex. 13 at 2–3. By May, treaters noted that testing for autoimmune/rheumatologic conditions had produced normal results, and physical therapy ("PT") was recommended for G.J.B.'s joint pain. Ex. 3 at 139–40. Subsequent PT evaluations revealed both functional weakness and gross motor delays. Ex. 7 at 4–7.

By early June 2014, G.J.B. had to be admitted to Cincinnati Children's Hospital due to increasing headaches, but was promptly discharged the next day. Ex. 6 at 1205–09. The headaches

[5] The Vaccine Adverse Event Reporting System ("VAERS") is a national warning system designed to detect safety problems in U.S.-licensed vaccines. *See About VAERS*, VAERS, https://vaers.hhs.gov/about html (last visited May 19, 2023). It is managed by both the CDC and the FDA. VAERS monitors and analyzes reports of vaccine related injuries and side effects from both healthcare professionals and individuals. *See generally Carda v. Sec'y of Health & Hum. Servs.*, No. 14-191V, 2017 WL 6887368, at *6 (Fed. Cl. Spec. Mstr. Nov. 16, 2017).

[6] "Hyperopia" is defined as "an error of refraction in which rays of light entering the eye parallel to the optic axis are brought to a focus behind the retina, as a result of the eyeball being too short from front to back." *Hyperopia*, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=23917&searchterm=hyperopia (last visited May 22, 2023).

continued that month, however, and then in July G.J.B. was admitted to the University of Cincinnati epilepsy monitoring unit for video monitoring. *Id.* at 1354–58. A brain MRI performed at this time displayed a stable appearance of two tiny nonspecific areas of hyperintense signals, which was thought to be gliosis. *Id.* at 1355; Ex. 3 at 146.

In September of that same year, G.J.B. underwent an occupational therapy evaluation for fine motor delays. Ex. 7 at 1–3. Ms. Bechel informed treaters at this time that G.J.B. was no longer taking anti-seizure medications, but was pursuing treatment from a new neurologist for "eye flitting movements" and other abnormal behaviors. *Id*. By this time, G.J.B. was receiving physical therapy once per week for leg and hip pain as well as muscle strengthening, and his occupational therapy evaluation revealed fine motor deficits related to manual dexterity. Further epilepsy monitoring was obtained in October 2014, but although Ms. Bechel reported G.J.B. to be often waking at night unresponsive, and displaying other physical manifestations of seizure activity, a video EEG revealed no clinical evidence of seizure. Ex. 4 at 1–77. G.J.B. returned to his rheumatologist on December 15, 2014, and he was diagnosed with hypermobility and possibly "Ehlers-Danlos syndrome."[7] Ex. 3 at 141–42.

Treatment in 2015 and Beyond

On February 25, 2015, G.J.B. obtained an initial evaluation with Thomas Dye, M.D., at the Neurology Clinic at Cincinnati Children's Hospital (with Dr. Dye becoming his neurologic treater thereafter). Ex. 6 at 645–76. G.J.B. was then reported to be experiencing worsening memory problems over the last two months, although his neurological examination was normal, he appeared alert and responsive, and his speech and articulation were also normal. *Id.* at 646, 650. Dr. Dye assessed him with "generalized epilepsy," noting as well that it did not appear his seizure activity was as controlled as it could be. *Id.* at 650. Subsequent assessments of G.J.B. in the context of his schooling that year confirmed that he was largely functional and meeting his goals. Ex. 17 at 75 (November 2015 assessment).

In 2016, Dr. Dye deemed G.J.B.'s seizure activity to be well controlled, although Ms. Bechel noted that he had displayed some episodes in the wake of a fever, and anti-seizure medications were adjusted to lessen the likelihood of side effects. Ex. 6 at 811–24. Rheumatologic follow-ups also noted progress and improvement, despite some ongoing joint pain. Ex. 3 at 133–34. By 2017, neuropsychological evaluations were evaluating whether G.J.B. should be medicated for attention-deficit hyperactivity disorder and anxiety. Beyond that year he received educational and treatment plans designed in light of this as well as his diagnosed epilepsy and Ehlers-Danlos

[7] "Ehlers-Danlos syndrome" is defined as "a group of inherited disorders of connective tissue; formerly subdivided into ten numbered types, they have been reclassified into six descriptive types. Prominent manifestations include hyperextensible skin and joints, easy bruisability, and friability of tissues with bleeding and poor wound healing, with additional symptoms specific for individual types." *Ehlers-Danlos syndrome*, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=110561 (last visited May 22, 2023).

syndrome. Ex. 38 at 4, and Exs. 83–85. Throughout the period as reflected by medical records filed in this case, his seizures remained in good control. *See, e.g.*, Ex. 86 at 45, 71, 137, 198, 207, 280.

II. Parties' Expert Reports

A. Petitioners' Experts

1. *Marcel Kinsbourne, M.D.*

Dr. Kinsbourne, a pediatric neurologist by training, prepared three written reports for this matter. Report, dated Jan. 9, 2018, filed as Ex. 23 (ECF No. 25-1) ("First Kinsbourne Rep."); Report, dated Nov. 19, 2018, filed as Ex. 39 (ECF No. 32-1) ("Second Kinsbourne Rep."); Report, dated May 17, 2019, filed as Ex. 54 (ECF No. 38-1) ("Third Kinsbourne Rep.").

Dr. Kinsbourne received his medical degree from Oxford University in England, along with his Bachelor of Arts, and his Master of Arts. Curriculum Vitae, filed as Ex. 24 (ECF No. 25-1) ("Kinsbourne CV") at 1. He then received his M.D. from the State of North Carolina. *Id.* Thereafter, Dr. Kinsbourne did several years of different post-doctoral training in neurology, pediatrics, and chest diseases, and is a member of the American Board of Pediatrics and Royal College of Physicians. *Id.* at 1–2. Dr. Kinsbourne held several academic positions—he was previously a professor of psychology, professor of pediatrics, lecturer in neurology, adjunct professor of linguistics and cognitive science, adjunct professor of occupational therapy, director of the behavioral neurology department at the Eunice Kennedy Shriver Center, and other positions related to neurologic and cognitive studies. *Id.* at 2–3. In addition, he also held positions on several editorial boards, professional societies, and administrative assignments. *Id.* at 4–6. Dr. Kinsbourne has conducted research into pediatric disorder, developmental delays and factors, cerebral deficiencies, learning disabilities, therapies, and epilepsy. *Id.* at 6–39. Importantly, however, Dr. Kinsbourne has not treated patients, pediatric or otherwise, for almost thirty years.[8]

First Report

The initial part of Dr. Kinsbourne's first report reviewed G.J.B.'s medical history. *See generally* First Kinsbourne Rep. at 1–4. He emphasized the onset of G.J.B.'s stuttering on August 3, 2013, followed by related symptoms ("dysfluency," word pronunciation difficulty, etc.) over the coming days. *Id.* at 1–2. He also highlighted treater views that some of these early clinical manifestations had likely been caused by seizures, and that his symptoms plus subsequent test results met the criteria for epilepsy. *Id.* at 3. Dr. Kinsbourne concurred in the diagnosis of

[8] *See L.M. v. Sec'y of Health & Hum. Servs.*, No. 14-714V, 2019 WL 4072130 (Fed. Cl. Spec. Mstr. July 23, 2019) (discussing Dr. Kinsbourne's more recent practice experience).

epilepsy/seizure disorder, with some motor and processing delays attributable to it (or to the medications needed to control seizures), although he deemed G.J.B.'s Ehlers-Danlos syndrome to be unrelated. *Id.* at 3–4.

Dr. Kinsbourne also noted that G.J.B.'s speech-associated episodes were consistent with seizure activity. Indeed, medicinal control of the seizures led to an end of such speech issues. First Kinsbourne Rep. at 4. But the same medication regime could have secondarily sparked additional symptoms, such as anxiety or issues processing information. *Id.* at 5. Otherwise, seizure disorders (especially when experienced in infants) were reasonably understood to impact long-term cognitive development and function. *See, e.g.*, G. Holmes and Y. Ben-Ari, *The Neurobiology and Consequences of Epilepsy in the Developing Brain,* 49 Ped. Research 3:320 (2001), filed as Ex. 64 (ECF No. 42-4), at 324 (review article noting that "prolonged or recurrent seizure activity" can "irreversibly" impact an immature/pediatric brain, increasing greatly the risk of future seizure susceptibility and associated injury).

Next, Dr. Kinsbourne proposed how the vaccines G.J.B. had received could be causal of his seizure disorder. He highlighted the fact that nothing in G.J.B.'s pre-vaccination history suggested a propensity for epilepsy (while diminishing the significance of "some problems with [speech] articulation" that had unquestionably manifested earlier in G.J.B.'s life). First Kinsbourne Rep. at 4. He focused on the MMR vaccine, noting that the underlying wild measles virus (included in the vaccine, albeit in an attenuated form) was itself known to be "neuropathic," and could thus cause encephalopathy secondary to an infection, or even seizures themselves. *Id.* Government publications had noted more directly that the vaccine had a causal association with "residual seizure disorder." K. Stratton et al., *Adverse Events Associated with Childhood Vaccines Other than Pertussis and Rubella,* 271 JAMA 20:1602 (1994), filed as Ex. 68 (ECF No. 42-8) ("Stratton I").

Stratton I is somewhat less supportive of causation than alleged, however. It discussed findings of committees established by the Institute of Medicine (the "IOM") to evaluate potential adverse effects of various vaccines. Stratton I specifically noted (in a summarizing chart) that the evidence had been deemed "inadequate to accept or reject" any causal relationship between a seizure disorder and vaccines containing tetanus/diphtheria-tetanus or measles. Stratton I at 1604. Stratton I also differentiated between reliable evidence *rejecting* a vaccine association (which it noted would in many cases have "insufficient statistical power to detect extremely rare causes of an outcome") and evidence suggesting a connection, stressing that "[t]he absence of data favoring acceptance of a causal relation did not lead [the committees] to rejection of a causal relation because of the possibility that adverse reactions *might have occurred that have not been reported* or recognized." *Id.* at 1603–04 (emphasis added). In other words, Stratton I was conservative in its conclusions, and careful not to categorically rule out a vaccine-injury relationship merely because

there was little *affirmative* evidence of an association (although an equivocal finding of causality either way did *not* mean that evidence *favoring* causality was abundant or even present).

A number of other publications, in Dr. Kinsbourne's view, also confirmed the association between vaccination and seizures (with the majority of the literature he cited focused on vaccines containing a measles virus component). *See generally* Kinsbourne Rep. at 5; R. Alderslade et al., *The National Childhood Encephalopathy Study* (1981), filed as Ex. 62 (ECF No. 42-2) ("Alderslade") at 168 (UK study establishing that for children receiving measles vaccine from January 1977 to the end of 1978, the relative risk of a seizure within two weeks of vaccination was higher when compared to an unvaccinated control group); R. Weibel et al., *Acute Encephalopathy Followed by Permanent Brain Injury or Death Associated with Further Attenuated Measles Vaccines: A Review of Claims Submitted to the National Vaccine Injury Compensation Program*, 101 Pediatrics 3:383 (1998), filed as Ex. 70 (ECF No. 42-10) ("Weibel") at 386 (based on review of Vaccine Program claims through the date of publication, study identified 48 instances of acute encephalopathy, followed by chronic encephalopathy/permanent or death, occurring within 2 to 15 days of receipt of measles or MMR vaccine, with 32 of the 48 first experiencing "generalized or focal seizures"); P. Landrigan & J. Witte, *Neurologic Disorders Following Live Measles-Virus Vaccination,* 223 JAMA 13:1459 (1973), filed as Ex. 29 (ECF No. 25-7) ("Landrigan & Witte") (considering incidence of different neurologic disorders after receipt of measles virus-containing vaccines from 1963 to 1971, and observing instances of "prolonged or focal" seizures after vaccination).

These specific items of literature, however, are only supportive of Petitioners' claims in a broad sense (to the extent they report observations of temporally-associated post-vaccination seizure activity, but do not draw reliable conclusions about causality from them). Weibel, for example, relied on cases filed in the Vaccine Program more than 30 years ago for its sample, and does not disclose whether inclusion of instances in its sample was based on *proof* of the claim or simply the claim's allegations. Moreover, Weibel seems to have relied on the Table claim framework for an encephalopathy after a measles virus-containing vaccine—a specific kind of injury in which seizure can be a presenting symptom but which requires other proof of injury (and indeed, the authors looked for cases resulting in "chronic encephalopathy or death").[9] Weibel at 384. Although Weibel did perceive an association with the looked-for injury and the vaccine, it acknowledged that "the incidence of acute encephalopathy caused by measles vaccine in this cohort can reasonably be described as very low." *Id.* at 387.

Alderslade relied on a very small total sub-sample (13 vaccinated individuals versus 10 controls), and the filed portion of this item of literature (a single page from a larger publication

[9] In this case, Petitioner does not allege a Table encephalopathy, nor does the record establish the level of chronic injury that would be sufficient to meet its requirements. 42 C.F.R. § 100.3(b)(2). Indeed, seizures are *excluded* by the Table construction of the claim as a presenting symptom of encephalopathy, absent other/subsequent evidence of injury. 42 C.F.R. § 100.3(b)(2)(i)(D).

containing a chart which provides the data relied upon by Dr. Kisnbourne) provides no information about the nature or contours of the control group. Alderslade at 168. It also does not indicate if the seizures observed were febrile—a critical issue here, given that G.J.B. was afebrile. Petitioner only filed a one paragraph abstract from Landrigan & Witte—and that paragraph only states that the article's authors observed 84 total cases of post-vaccination neurologic disorders in a 30-day onset (out of approximately *50 million* vaccine doses in the relevant time period), with the majority (59) involving "clinical features of encephalitis or encephalopathy"—injuries not alleged herein. Landrigan & Witte at 1.

Some studies, Dr. Kinsbourne contended, actually linked onset of *afebrile* seizures to vaccination (especially important here, since the record does not establish that G.J.B. experienced a fever immediately before his initial, post-vaccination episodes). *See, e.g.*, N. LeSaux et al., *Decrease in Hospital Admissions for Febrile Seizures and Reports of Hypotonic-Hyporesponsive Episodes Presenting to Hospital Emergency Departments Since Switching to Acellular Pertussis Vaccine in Canada: A Report from IMPACT,* 112 Pediatrics 5:e348 (2003), filed as Ex. 65 (ECF No. 42-5) ("LeSaux"). Facially, LeSaux would not seem to be an item of literature supporting Petitioner's claim, since its ultimate conclusion was that *febrile* seizures after receipt of the then-recently adopted acellular pertussis vaccine had decreased in a cohort of 218 Canadian children who were vaccinated between 1995 and 2001, and who received the MMR or pertussis-containing vaccine. LeSaux at e348. However, Dr. Kinsbourne observed, LeSaux recorded 16 of 94 instances of post-MMR afebrile seizures—with seven occurring in children in the same age group as G.J.B., and seven experiencing "partial" seizures akin to what he had (although it is not evident from LeSaux that these groups are actually congruent). *Id.* at e350, e351; First Kinsbourne Rep. at 5.

LeSaux, however, says nothing about the *propensity* of the MMR vaccine to cause afebrile seizures, and it does not propose that the numbers Dr. Kinsbourne highlighted had scientific meaning from a causation standpoint. At most, it comments that for the studied group the risk of afebrile seizures after pertussis vaccine receipt *declined*, while the risk was the same for MMR. LeSaux at e352. LeSaux allowed for the possibility that the afebrile seizure instances might have involved undetected but transient or small temperature increases, or that children with a lower seizure threshold were more likely to experience an afebrile seizure—but speculated that this may have been attributable to the fact that "[a] higher proportion of children with afebrile seizures had had *previous* afebrile seizures" compared to controls. *Id.* (emphasis added). Thus, LeSaux does not robustly support a relationship between afebrile seizures and vaccination, even if its data reveal some instances of post-vaccination afebrile seizures.

Dr. Kinsbourne concluded his first report with the opinion that G.J.B.'s onset was consistent with a vaccine cause. First Kinsbourne Rep. at 4, 6. He deemed onset as occurring within five days of vaccination, based on the record and as supplemented with witness statements. *Id.* at 4. In his estimation, onset occurring within as long as two weeks post-vaccination was "well-

recognized" to be validly associated, although he did not identify specific literature or studies corroborating this contention. *Id.* And he emphasized the lack of alternative explanations for G.J.B.'s seizure activity. *Id.* at 4, 6.

Second Report

This three-page report largely responded to the contentions of Respondent's sole neurologic expert, Dr. Shlomo Shinnar. Dr. Kinsbourne agreed that treaters had not accepted a causal relationship between the vaccines and G.J.B.'s epilepsy, maintaining it was a mischaracterization to suggest he had contended otherwise. Second Kinsbourne Rep. at 1. He denied the significance of treaters deeming the epilepsy as "of unknown cause," however, noting that evidence presented and/or highlighted in this case could still support vaccine causation. *Id.* at 2. And he allowed that while individuals with Ehlers-Danlos syndrome might be susceptible to epilepsy, the absence of evidence in this case that G.J.B. possessed any "comorbid structural neurological abnormalities" undermined the possibility that this was explanatory herein (although as noted below even Dr. Shinnar ultimately discounted Ehlers-Danlos syndrome as causal). *Id.* at 3.

Dr. Kinsbourne spent more time in his second report bulwarking his prior (albeit less-discussed) contentions that even *afebrile* seizures could be vaccine-caused (although to some extent he deferred to Petitioner's immunologic expert, Dr. Vera Byers, for opinions on that subject). Second Kinsbourne Rep. at 1–2. He referenced Weibel, for example, which found that five vaccinated children included in the study who had experienced encephalopathy had also been afebrile, versus 43 who had experienced a pre-encephalopathy fever. Weibel at 385. Again, however, Dr. Kinsbourne has mined a facially-supportive point from data contained in an article that actually says little (if anything) about the greater issue. Thus (and putting aside the fact that he *infers* the five subjects in question experienced afebrile seizures, despite no affirmative statement to that effect by Weibel's authors), the sample total was quite small—*48* vaccinated patients—with the majority experiencing a fever. *Id.* at 385–86. Weibel otherwise has nothing to say about post-vaccination risk of afebrile seizures, and focused on a different injury.

Another study, Dr. Kinsbourne maintained, also observed a small but significant number of afebrile seizure events post-vaccination. N. Verbeek et al., *Etiologies for Seizures Around the Time of Vaccination,* 134 Pediatrics 4:658 (2014), filed as Ex. 72 (ECF No. 42-12) ("Verbeek"). Verbeek's authors considered data from medical reports (from 1997 to the end of 2006) made to a Dutch public health entity, beginning its analysis with a cohort of 1,269 children who appeared to have experienced epileptic seizures within two years of life, then narrowing the sample to 990 children who had experienced a seizure within either 24 hours of receipt of DTaP vaccine or 5–20 days after the MMR. Verbeek at 659–60. Thus, Verbeek was deriving its conclusions based solely on reports involving a temporal association with vaccination. From this group, moreover, only 26

children ultimately were found to have a vaccine-related temporal onset—and more data could only be obtained through follow-up with the patients of 23 of these subjects, meaning the relevant group ended up being quite small (especially in comparison to the sample totals Verbeek's authors began with). *Id.* at 660.

In addition, out of these 23 patients, Verbeek observed that three subjects with assumed preexisting encephalopathy of some kind had experienced afebrile seizures, and that (as Dr. Kinsbourne noted) it was more common for children who did not go on to develop epilepsy to experience a higher temperature in the fever range than for those who did develop epilepsy. Second Kinsbourne Rep. at 1; Verbeek at 661, 663. But Verbeek's authors did not conclude that vaccination was the likely *cause* of an epileptic disease/seizure disorder. Rather, Verbeek speculated that "vaccination-related epilepsy" might *unmask* an existing genetic predisposition (perhaps because subjects who experienced seizure after vaccination were simply likely to be more sensitive to a smaller temperature change occasioned by vaccination). This said more about the children in question than the effect of vaccination—as Verbeek's authors allowed. Verbeek at 663 ("the large variability in electroclinical syndromes and corresponding cognitive outcomes in our study support the hypothesis that predisposing factors in the child, *and not the vaccination*, cause the observed neurologic deterioration") (emphasis added), 665.

Dr. Kinsbourne further emphasized that even though an IOM Report cited by Dr. Shinnar (from 2012—and hence generated nearly 20 years after the data discussed in Stratton I) did not accept that sufficient evidence had been presented to associate the MMR vaccine with afebrile seizures, the IOM had "elected to pitch the threshold for conceding causation at an extravagantly high level"—in other words, requiring certainty (when in the Vaccine Program the evidentiary test is lower). Second Kinsbourne Rep. at 2; *Adverse Effects of Vaccines: Evidence and Causality* 133–37 (K. Stratton et al., eds., 2011), filed as Ex. A Tab 6 (ECF No. 28-7) ("Stratton II").

Stratton II expressed a "high degree of confidence" in the findings of seven reliable epidemiologic studies that the MMR vaccine was likely associated with febrile seizures, but (based on only two large, controlled studies) placed "limited confidence" in the evidence suggesting an MMR/*afebrile* seizures association. Stratton II at 133–34. At most, it deemed available mechanistic evidence (ten items of literature in which afebrile seizures were reported after the MMR vaccine's administration, or receipt of its individual antigenic components (i.e., measles vaccine alone) of the vaccine as causal of afebrile seizures to be "lacking," since most studies simply observed temporal associations, often too short to be meaningful. *Id.* at 134–37. Thus, while Stratton II does not fully rebut Petitioner's theory (at least in its consideration of what then-available epidemiologic evidence showed), it does not reflect the demand for certainty for which Dr. Kinsbourne criticized it.

Third Report

Dr. Kinsbourne's final written report (succinct like the second) contained another round of responses to Dr. Shinnar's rebuttal contentions. First, he disputed the significance of the fact that G.J.B.'s treaters had deemed his seizure disorder to be idiopathic in origin (as opposed to vaccine-caused), asserting that this did not preclude vaccine causation. Third Kinsbourne Rep. at 1. Second, he took issue with Dr. Shinnar's characterization of Stratton II to be "authoritative," noting that the standards it set for accepting the possibility of vaccines being causal were so high that they bordered on requiring certainty, and that other Program decisions had observed this to be so. *Id.* at 1–2. And Dr. Kinsbourne re-emphasized as relevant the lack of evidence of an alternative explanation for G.J.B.'s illness, disagreeing with Dr. Shinnar's contention that this could not stand as indirect proof of causation; rather, Dr. Kinsbourne maintained, it was "normal procedure" in Vaccine Program cases to highlight when there was no competing explanation for an injury other than a vaccine. *Id.* at 4.

The majority of Dr. Kinsbourne's third report addressed the more centrally-substantive issue of whether vaccines are likely to trigger *afebrile* seizures. Third Kinsbourne Rep. at 2–3. Dr. Kinsbourne noted at the outset that the association between febrile seizures and vaccination was the product of "two independent effects"—the generation of fever due to vaccine-induced upregulation of certain proinflammatory cytokines, versus seizure propagation/mediation involving cytokines generally. *Id.* at 2. These two processes did not always occur simultaneously—and it was even possible that a fever could follow a seizure. *Id.;* C. Waruiru and R. Appleton, *Febrile Seizures: An Update*, 89 Arch. Dis. Child 751 (2004), filed as Ex. 84 (ECF No. 42-43) ("Waruiru").

Waruiru, however (a review article), is not supportive of Dr. Kinsbourne's attempt to de-link (or at least attenuate the relationship between) fever from seizures. Waruiru's focus was the *characteristics* of febrile seizures, and contains little discussion or evidence directly contrasting them to afebrile seizures. Waruiru does allow that the timing of febrile seizures may vary (with some occurring "early in the illness and may be the presenting feature"), and that the level of fever necessary for a febrile seizure is undetermined (with no clear findings in science at the time of the article's publication as to whether the *rate* of temperature increase is more or less important than the maximum temperature reached). Waruiru at 752. Thus, Waruiru does not find that *afebrile* seizures are no more than "early" febrile seizures (i.e., occurring before the fever fully manifests) triggered by the same pyrogenic or proinflammatory cytokines. At most, Waruiru comments that (based on some evidence that certain anti-fever medication does not prevent febrile seizures) "it may not be the fever itself that causes" the febrile seizure, but deems the "precise pathological or clinical significance" of cytokine theories for seizure pathogenesis to be "as yet unclear." *Id.*

Dr. Kinsbourne nevertheless maintained that an individual with a low seizure threshold might experience "[t]he temperature rise that attends the triggering of a seizure" in a subclinical or mild way, such that fever could be almost "overlooked." Third Kinsbourne Rep. at 2. As an example, Dr. Kinsbourne referenced Dravet syndrome,[10] a genetically-caused seizure disorder known to be triggered by vaccination, but where a "substantial minority" of individuals experience no fever. *Id.; see also* I. Scheffer, *Vaccination Triggers, Rather Than Causes, Seizures*, 15 Epilepsy Currents 6:335 (2015), filed as Ex. 81 (ECF No. 42-21) ("Scheffer") (noting that study of children with Dravet syndrome revealed they often experienced the initial seizure in the syndrome as afebrile but after vaccination, suggesting some role for the immune system in causing it, but adding that this triggering factor was not fully understood, and that it may simply be the product of the "first insult" for a child otherwise genetically predisposed to a seizure disorder). Dr. Kinsbourne's argument, however, depended on a finding that G.J.B. already possessed a low seizure threshold, such that the trigger would be "the innate immune system's reaction" to the vaccine, rather than reaction to a vaccine-caused fever. Third Kinsbourne Rep. at 3.

Independent of these considerations, Dr. Kinsbourne maintained, there were other factors supporting afebrile seizures as vaccine-associated. For example, he represented that it was understood that a number of infections could likely provoke afebrile seizures. W. Lee and H. Ong, *Afebrile Seizures Associated with Minor Infections: Comparison with Febrile Seizures and Unprovoked Seizures,* 31 Pediatric Neurology 3: 157 (2004), filed as Ex. 74 (ECF No. 42-14) ("Lee and Ong"). Lee and Ong is a retrospective cohort study that considered the medical histories of Singaporean children who had been hospitalized after initial seizures, focusing on over a thousand who had experienced a febrile seizure, 286 with "provoked" seizures—which the authors defined to be seizures occurring in the context of an infection (evidenced by illness symptoms, like cough) not typically affecting the brain, and not involving a fever at the time of seizure—and 125 with afebrile unprovoked seizures. Lee and Ong at 157–58. Lee and Ong ultimately concluded that the groups with provoked and febrile seizures likely shared an "age-related seizure susceptibility," with the latter simply possessing a higher seizure threshold than the former—and (somewhat contrary to Dr. Kinsbourne's suggestion) that a viral infection itself was not necessarily the triggering factor (since existence of virus was not found to be associated with more severe illness). *Id.* at 163.

[10] "Dravet syndrome" is defined as "an intractable developmental and epileptic encephalopathy that begins in infancy and proceeds with accumulating morbidity that significantly impacts individuals throughout their lifetime. Dravet syndrome is a rare disease, with an estimated incidence rate of 1:15,700, with the majority of patients carrying a mutation in the sodium channel gene SCN1A." *See What is Dravet syndrome?*, Dravet Syndrome Foundation, https://dravetfoundation.org/what-is-dravet-syndrome/ (last visited May 19, 2023). Program cases have noted that confirmation a child has the genetic basis for Dravet syndrome means even an unquestionably vaccine-caused febrile seizure cannot be deemed the cause of the subsequent seizure disorder, and have thus denied entitlement. *Oliver v. Sec'y of Health & Hum. Servs.*, No. 10-394V, 2017 WL 747846 (Fed. Cl. Feb. 1, 2017), *mot. for review den'd*, 133 Fed. Cl. 341 (2017), *aff'd*, 900 F.3d 1357 (Fed. Cir. 2018).

Another study, Dr. Kinsbourne maintained, observed an association with influenza, adenovirus, rotovirus, or RSV infections and afebrile seizures. B. Chung and V. Wong, *Relationship Between Five Common Viruses and Febrile Seizure in Children,* 92 Arch. Dis. Child 589 (2007), filed as Ex. 78 (ECF No. 42-18) ("Chung and Wong"). But Chung and Wong (conducting another retrospective study) focused on something different: whether specific viral infections (which could trigger febrile seizures) were *themselves* most key to sparking seizure—and also whether some were more likely causal than others. Chung and Wong at 589. They concluded that although the relevant data set revealed influenza infections to be most commonly associated with *febrile* seizures, "the type of viral infection was not found to be associated with subsequent recurrence," and that the more important risk factors for seizure disorders after an initial seizure (even one unquestionably virus-provoked) were "[y]oung age at onset, complex features and family history" of febrile seizure—with "individual susceptibility" the dominant explanatory factor. *Id.* at 591. While the authors admitted secondarily to the existence of "evidence" that certain viral infections, like gastrointestinal viruses, could be associated with afebrile seizures, and that the subject warranted further consideration, they did not formally propose the association for which Dr. Kinsbourne cited the paper.

Dr. Kinsbourne later admitted in his third report that the capacity of vaccination to trigger afebrile seizures remained "rarely studied." Third Kinsbourne Rep. at 3. But he maintained that at least one study had (based on review of passive surveillance data) observed that *any* kind of seizure was more likely on the first day after receipt of the DTaP vaccine. S. von Spiczak et al., *A Retrospective Population-Based Study on Seizures Related to Childhood Vaccination,* 52 Epilepsia 8:1506 (2011), filed as Ex. 82 (ECF No. 42-22) ("Spiczak"). The article considered 328 cases of "suspected vaccination-related seizures," based on a German database of reported post-vaccination adverse events, with follow-up inquiries directed at the patients and treaters involved to assess post-initial seizure outcomes. Spiczak at 1506–07. The majority of the sample subjects had experienced febrile seizures, however (with recipients of the MMR vaccine most likely to experience a febrile seizure); less than 20 percent of the sample experienced a single afebrile seizure. *Id.* at 1509. Spiczak was also not specific to DTaP or any other vaccine,[11] does not include any findings identifying which vaccines are most likely to cause different types of seizures, and in fact expressly disclaimed that it had shed light on relative risk or association between vaccines and seizure outcomes. *Id.* at 1507–08, 1511 (because Spiczak's authors relied on passive surveillance reporting, "we are . . . unable to generate incidences or relative risks of certain epilepsy syndromes in relationship to vaccination").

[11] At most, Spiczak references some supplemental tables that provide the kind of vaccine-specific evidence Dr. Kinsbourne references with respect to DTaP. Spiczak at 1508. But none of those supplemental tables have been filed with the version of Spiczak submitted in this case.

2. *Vera Byers, M.D., PhD.*

Dr. Byers (a medical doctor and immunologist with Immunology, Inc., a consulting company) offered two written reports for Petitioners. Report, dated October 12, 2018, filed as Ex. 42 (ECF No. 32-4) ("First Byers Rep."); Report, dated April 26, 2019, filed as Ex. 44 (ECF No. 37-1) ("Second Byers Rep.").

Dr. Byers did not offer a CV in this case, but she has repeatedly testified in Program cases, so her credentials are generally understood among the special masters. Dr. Byers received her bachelor's degree, master's degree in microbiology, and Ph.D. in immunology from the University of California, Los Angeles. *See L.M. v. Sec'y of Health & Hum. Servs.*, No. 14-714V, 2019 WL 4072130, at *10 (Fed. Cl. Spec. Mstr. July 23, 2019). She completed two post-doctoral fellowships before pursuing her medical degree—one in protein chemistry at Abbott Labs in Chicago, Illinois, and another in clinical and tumor immunology at the University of California, San Francisco ("UCSF"). *Id.* Thereafter, Dr. Byers received her medical degree and completed a three-year residency at UCSF. *Id.* She has frequently served as an expert witness in lawsuits over the past fifteen years, including Vaccine Program cases. *Id.* Throughout her career, Dr. Byers maintained several positions as an allergist and immunologist performing research and clinical trials in a variety of different areas. *Id.* Despite an extensive list of publications, Dr. Byers has not published on the causes of seizures, nor on cytokine responses to vaccinations. *Id.*

First Report

Dr. Byers's initial report was based on her own review of the medical record plus the initial reports offered by Drs. Kinsbourne and Shinnar. First Byers Rep. at 1–2. She began by noting how common febrile seizures are in children, and that science has linked fever with seizures due to the production of pro-inflammatory cytokines. *Id.* at 2. However, she opined that the processes involved in fever and seizures were "independent of each other," such that cytokines might be capable of causing seizures independent of fever. *Id.* One cytokine in particular, IL-1β, could reduce seizure thresholds even if it could also cause fever, suggesting it might play such a dual role. A. Mazarati, *Cytokines: A Link Between Fever and Seizures,* 5 Epilepsy Currents 5:169 (2005), filed as Ex. 73 (ECF No. 42-13) ("Mazarati") (noting the scientific possibility that because afebrile seizures appeared to encourage production of IL-1β, the cytokine might also itself contribute to the exacerbation of seizures). Mazarati, however, is only a commentary on an item of literature Petitioner *did not* file, and it notes that the role this cytokine plays in infection-associated seizures has not been fully assessed.[12] Mazarati does not otherwise establish that the

[12] Mazarati includes a diagram that Dr. Byers reproduced in her first report. *Compare* Mazarati at 170 *with* First Byers Rep. at 2. Dr. Byers erroneously referred to Mazarati *as* "Dube" (the article it discusses)—an article Petitioners did not file—although she cited to it the source of this diagram. Petitioners' exhibit filings repeated this error—thereby causing confusion on Dr. MacGinnitie's part, when he accessed the underlying article independently but was unable to find the diagram therein. *See* Report, date January 29, 2019, filed as Ex. C (ECF No. 33-1), at 5–6.

IL-1β cytokine equally responds to pyrogenic signals from viruses (resulting in fever) in the same way as it might independently *contribute* to a seizure, and in the absence of an external infection.

Dr. Byers maintained that afebrile seizures were distinguishable from febrile, both in terms of triggers and features. First Byers Rep. at 2–3. Some studies, for example, observed that certain kinds of infections had a "better prognosis" after an afebrile seizure than other kinds of infection-associated afebrile seizures (or seizures unprovoked by any infection). *Id*. at 3; T. Zhang et al., *Are Afebrile Seizures Associated with Minor Infections a Single Seizure Category? A Hospital-Based Prospective Cohort Study on Outcomes of First Afebrile Seizure in Early Childhood,* 55 Epilepsia 7:1001 (2014), filed as Ex. 53 (ECF No. 37-10) ("Zhang"). Zhang, however, is narrowly focused on a general association observed from the data its authors obtained, does not comment on the differing roles cytokines might play in febrile vs. afebrile seizure contexts, and also notes that in cases where the afebrile but infection-associated seizure was accompanied by acute symptoms, the afebrile seizure was "in all probability an entity in the same category with febrile seizures of acute symptomatic seizures"—meaning the ultimate outcome was essentially the same (in comparison to fully-unprovoked seizures). Zhang at 53.

The cytokine profiles for individuals suffering from the two different kinds of seizures were also distinguishable, Dr. Byers argued. First Byers Rep. at 3. In fact, Dr. Byers suggested that patients with febrile seizures likely possessed elevated levels of types of cytokines that were "potent anti-epileptogenic agents" (thus perhaps explaining why febrile seizures did not invariably lead to seizure disorders), although Dr. Byers did not so directly opine, and the "recent study" she specifically referenced for this point was never filed. *Id.* Indeed, Dr. Byers referenced two other items of literature that she reported showed different kinds of cytokine levels in febrile seizure patients that she represented were relevant to her contentions, but both were unfiled. *Id.*

Given the foregoing, Dr. Byers opined that the core difference between afebrile and febrile seizures was merely cytokine profiles—and so (presumably) since IL-1β could always be upregulated by vaccination, the absence of fever did not mean the vaccine was less likely causal. First Beyers Rep. at 3. Dr. Byers did not, however, explain how vaccination would cause the production of this cytokine at levels sufficient to precipitate seizure, and *then* lead to a seizure-oriented illness, without also causing fever.

Second Report

Dr. Byers's second report was as brief as the first, although she expanded her focus to include responses to the opinions offered by Respondent's immunologic expert, Dr. Andrew MacGinnitie. She reemphasized her contention that "cytokines cause fevers and the seizures independently," citing again an item of literature never filed in this case in support. Second Byers Rep. at 1. In effect, the cytokines produced in reaction to vaccination would have the same effect

as a mild infection—and thus a vaccine-induced afebrile seizure was comparable to a "provoked" seizure caused by an infection (relying on the seizure classifications proposed in Lee & Ong). *Id.* at 2. In addition, the fact that G.J.B. likely had experienced the presence of pro-inflammatory cytokines sufficient to provoke seizures was evidenced by the leg swelling and headaches that he had undergone after vaccination, as reported by his family members. *Id.* Thus, to the extent Respondent's experts questioned whether febrile and afebrile seizures could have comparable etiologies, they displayed their ignorance of "the current neuro/science" on the topic. *Id.* at 1, 3 (deeming Respondent's expert's analyses "out of date").

In further support of her opinion on this subject, Dr. Byers identified a study observing that a *different* cytokine from what she had previously identified, tumor necrosis factor alpha ("TNF-alpha"), was present in the serum of patients with afebrile seizures, but at levels compatible to those patients who had experienced fever but no seizures.[13] J. Ha et al., *Interleukin-4 and Tumor Necrosis Factor-Alpha Levels in Children with Febrile Seizures,* 58 Seizure 156 (2018), filed as Ex. 47 (ECF No. 37-4) ("Ha").

Ha sought to delve into the pathophysiology of febrile seizures (and in particular the role cytokines play in causing them). To do so, its authors compared blood serum measurements obtained from 50 subjects who had experienced febrile seizures against a control group of 39—but also considered 13 afebrile subjects independently, "to exclude the effects of fever on cytokine levels." Ha at 157. Although Dr. Byers's characterization of the specific TNF-alpha cytokine level findings in Ha is accurate, the detected levels of that cytokine were highest in the febrile seizure group with a history of *past* febrile seizures, and slightly lower than the primary febrile seizure group subjects—suggesting the cytokine's levels might be attributable to seizure activity itself. *Id.* at 158–160. The levels of a different cytokine were lowest of all in the afebrile group, and both measured cytokines were lower in the afebrile group compared to febrile subjects. *Id* at 159. Thus, all things being equal, the afebrile groups possessed lower levels of any putatively seizure-causing cytokines (making it difficult to conclude from such findings that the mere *presence* of these cytokines induced seizure). More importantly, although Ha's authors deemed "convincing" the argument that (assuming "[c]ells from children who are prone to seizures may produce more pro-inflammatory cytokines" that in turn induce seizures) cytokine levels might relate to seizure incidence, they only so opined with respect to *febrile* seizures, offering no opinion on the role these cytokines would play in the absence of fever. *Id.* at 159.

[13] By contrast, Dr. Byers noted that another item of literature revealed low levels of TNF-alpha cytokines in individuals with afebrile seizures—although in her estimation, the fact that individuals who had experienced afebrile status epilepticus had high levels of these cytokines, and others, supported her broader contention that the cytokines could cause seizure regardless of fever. Second Byers Rep. at 3. However, the item she referenced for this point was (like several others) never filed.

Dr. Byers referenced several additional studies specific to vaccines. One, she purported, considered a small subset of children who had experienced afebrile seizures within 30 days of receipt of the DTP (a whole-cell pertussis formulation not at issue in this case) and MMR vaccine. Second Byers Rep. at 2; W. Barlow et al., *Risk of Seizures Following DTP and MMR Vaccines,* 15 Pediatric Neurology Briefs 9:65 (J. Millichap, ed.) (2001), filed as Ex. 50 (ECF No. 37-7) ("Millichap"). The item filed, however, is merely the underlying article's abstract. And the cited article reported far fewer afebrile seizures in comparison to febrile (74 febrile after vaccination versus 13 afebrile, with only three after the MMR vaccine). Millichap at 65. Dr. Byers also referenced Lee and Ong as establishing instances in which afebrile "provoked" seizures occurred—ostensibly because this showed that a mild infection (which Dr. Byers seemed to equate to the effect of vaccination) could cause seizure despite the absence of fever. Second Byers Rep. at 2; Lee and Ong at 157, 163.

Case reports were deemed by Dr. Byers supportive of the vaccine-seizure association she proposed. In one, a child experienced nonfebrile seizures within one to two weeks after receipt of vaccines comparable to the MMR or varicella vaccines. I. Eckerle et al., *Nonfebrile Seizures After Mumps, Measles, Rubella, and Varicella-Zoster Virus Combination Vaccination with Detection of Measles Virus RNA in Serum, Throat, and Urine*, 20 Clin. And Vaccine Immun. 7:1094 (2013), filed as Ex. 46 (ECF No. 37-3) ("Eckerle"). The patient discussed in Eckerle was eleven, however, and even a year after the vaccine-associated seizure had not experienced any additional seizures or signs of epilepsy. Eckerle at 1094–95. Eckerle's authors referenced two additional incidents in Germany of nonfebrile seizures after receipt of the MMR vaccine, although they were identified from a search of a German vaccination adverse events database comparable to VAERS, and Eckerle affirmatively noted that the overall case report could not stand as evidence of a causal link between vaccination and afebrile seizures. *Id.* at 1095–96.

At bottom, Dr. Byers allowed that *febrile*-associated seizures were more common after vaccination, but she attributed this to the fact that fever "is one of the most common adverse events" of vaccination. Second Byers Rep. at 3. What was really determinative of seizure susceptibility was the child's age—and thus the absence of a febrile seizure simply revealed a high susceptibility to seizures per se, which could be triggered simply by sufficient provocation (here, the cytokine increase she deemed attributable to vaccines). *Id*. The latter possibility, she maintained, was established by several independent items of literature. *See, e.g.*, G. Li et al., *Cytokines and Epilepsy,* 20 Seizure 249 (2011), filed as Ex. 75 (ECF No. 42-15) ("Li"). Li sought to cast some light on the "complex relationship between epilepsy and the immune system" by providing an overview on the current knowledge" about the association, reviewing a large number of studies with respect to three different cytokines: IL-1β, IL-6, and TNF-alpha. Li at 249. Li's authors observed that IL-1β is involved in epilepsy's pathogenesis generally, and in mediating seizures specifically—but *not* that this cytokine is likely causal of all initial seizures (febrile or

afebrile), or that vaccines upregulate the cytokines in levels sufficient to be seizure-inducing.[14] *Id.* at 250–51.

B. Respondent's Experts

1. *Shlomo Shinnar, M.D.*

Dr. Shinnar is a pediatric neurologist with demonstrated specific expertise in treatment of epilepsy, and he prepared three written reports for Respondent. Report, dated April 22, 2018, filed as Ex. A (ECF No. 28-1) ("First Shinnar Rep."); Report, dated March 6, 2019, filed as Ex. E (ECF No. 36-1) ("Second Shinnar Rep."); Report, dated Sept. 9, 2019, filed as Ex. G (ECF No. 47-1) ("Third Shinnar Rep.").

Dr. Shinnar received his undergraduate degree in physics from Columbia College in New York, NY in 1971, and his Ph.D. and medical degree from Albert Einstein College of Medicine in Bronx, NY in 1977 and 1978. Curriculum Vitae, filed as Ex. B on Apr. 27, 2018 (ECF No. 28-13) ("Shinnar CV") at 1. He completed his training in 1983 and has practiced neurology since. Shinnar CV at 1. He became board certified by the American Board of Psychiatry and Neurology in Neurology with special competence in Child Neurology (1984) with an added Qualification in Epilepsy (2013) Shinnar CV at 2; Shinnar First Rep. at 1. Dr. Shinnar is also board certified in Pediatrics (1984). *Id.* Currently, he is Professor of Neurology, Pediatrics, and Epidemiology and Population Health at Albert Einstein College of Medicine. CV at 2; Shinnar First Rep. at 1. Dr. Shinnar is also the Hyman Climenko Professor of Neuroscience Research and the Director of the Comprehensive Epilepsy Management Center at Montefiore Medical Center and the Albert Einstein College of Medicine. *Id.* He has treated and supervised thousands of children with seizure disorders, and has conducted research primarily focused on childhood seizures. *Id.* In addition, Dr. Shinnar has published numerous papers and reviewed articles and chapters, a majority of which relate to seizure disorders. *Id.*

First Report

Like Dr. Kinsbourne, Dr. Shinnar provided his own overview of G.J.B.'s medical history. *See generally* First Shinnar Rep. at 3–5. He noted (and perhaps gave a bit more emphasis to) the pre-vaccination evidence of G.J.B.'s "speech deficit," along with other more circumstantial evidence about family neurologic issues. *Id.* at 3–4. Dr. Shinnar also acknowledged record

[14] At most, Li mentioned that seizures induced by the now-discontinued whole cell pertussis vaccine could be reduced if IL-1β were inhibited, confirming that this cytokine is significant in contributing to *febrile* seizures (especially when another antigen is likely the primary instigator). Li at 250. But the fact that this cytokine, or others, *mediates* seizure activity cannot be equated with being *causal* by itself.

evidence of a five-day, post-vaccination incident of stuttering, although he maintained that subsequent EEG testing suggested that this episode was nonepileptic in character. *Id.* at 4.

Dr. Shinnar agreed with G.J.B.'s epilepsy diagnosis. First Shinnar Rep. at 5. He also proposed, however, that G.J.B. likely possessed certain risk factors for epilepsy, such as his preexisting speech issues and his Ehlers-Danlos syndrome,[15] which literature that he filed associates with epilepsy. *Id;* A. Verrotti et al., *Ehlers-Danlos Syndrome: A Cause of Epilepsy and Periventricular Heterotopia,* 23 Seizure 819 (2014), filed as Ex. A Tab 1 (ECF No. 28-2). But Dr. Shinnar ultimately felt a diagnosis with an "unknown cause" explanation (meaning idiopathic) best captured G.J.B.'s presentation overall—especially since his secondary speech issues later resolved, while brain imaging had produced normal results. First Shinnar Rep. at 5. In Dr. Shinnar's experience, most cases of epilepsy lacked an identifying cause (thus reducing for him the persuasive value of the fact that in this particular case, only vaccination had been specifically identified as potentially explanatory). *Id.; Epilepsy Across the Spectrum: Promoting Health & Understanding* (M. England et al., eds.) (2012), filed as Ex. A Tab 2 (ECF No, 28-3) ("England").[16]

Dr. Shinnar attempted to rebut Dr. Kinsbourne's contentions that epilepsy could be caused by the MMR vaccine. First, he observed that any such association was specific to the context of *febrile* seizures. First Shinnar Rep. at 5 (*citing* Stratton II). But G.J.B. had not experienced a febrile seizure. Stratton II actually was noncommittal as to whether a relationship existed between afebrile seizures and the vaccine, and other items Dr. Kinsbourne offered were either now greatly outdated or lacked reliable methodologic controls. *See, e.g.*, First Shinnar Rep. at 5 (referencing Weibel as "without controls or a denominator"). And although Dr. Kinsbourne's first report focused almost wholly on the MMR vaccine, Dr. Shinnar also referenced literature disputing a reliable association between the DTaP vaccine (which G.J.B. had also received) and seizures. First Shinnar Rep. at 5 (*citing* W. Huang et al., *Lack of Association Between Acellular Pertussis Vaccine and Seizures in Early Childhood,* 126 Pediatrics 263 (2010), filed as Ex. A Tab 7 (ECF No. 28-8)) ("Huang").

Huang's authors conducted a retrospective observational study relying on Vaccine Safety Datalink data of over 430,000 children (aged six weeks to 23 months) who received the DTaP vaccine between 1997 and 2006, looking for instances in which individuals within the cohort also had been deemed (according to uniform diagnostic classifications applicable to all relevant patients in the sample) to have experienced a seizure. Huang at 264. No increased risk of seizure was

[15] Later in this first report, however, Dr. Shinnar more forthrightly opined that Ehlers-Danlos syndrome did not in this case likely explain G.J.B.'s epilepsy, since Petitioner's imaging results had not revealed issues with his brain. First Shinnar Rep. at 6.

[16] Respondent opted to file the *entirety* of England's text—569 pages—rather than simply those portions relevant to Dr. Shinnar's argument. That sort of conduct is wasteful, and also prevents me from identifying what in England would specifically support this aspect of Dr. Shinnar's report.

observed within zero to three days of vaccination—especially notable in light of prior findings of a higher risk for the acellular form of pertussis contained in DPT. *Id.* at 268. Huang did not distinguish between risks for febrile versus afebrile seizures (or even identify the distinction in parsing the data), but did note that although both the DPT vaccine and MMR had been associated in the past with febrile seizures, the same association had not been observed for afebrile seizures. *Id.* at 263–64, 267.

Dr. Shinnar took less issue with Dr. Kinsbourne's contentions about the secondary relationship between epilepsy and subsequent cognitive difficulties. First Shinnar Rep. at 5. However, he proposed that these kinds of additional symptoms/clinical presentations might well be better understood to be *baseline* conditions often observed in advance of a seizure disorder diagnosis, and thus could *themselves* be seen as causal of the epilepsy itself. *Id;* P. Fastenau et al., *Neuropsychological Status at Seizure Onset in Children,* 73 Neurology 526 (2009), filed as Ex. A Tab 8 (ECF No. 28-9) ("Fastenau"). Fastenau involved a prospective study comparing a cohort of 282 children who had experienced a seizure versus 147 healthy siblings. Fastenau at 5262–67. The possession of additional risk factors (including whether the seizure disorder's etiology was associated with a presumed prior condition) greatly increased the likelihood that a child experiencing seizures would go on to develop more significant neuropsychological impairment. *Id.* at 528–29, 532. Dr. Shinnar also denied that the temporal association in this case between Petitioner's first manifestation of symptoms and earlier vaccination was meaningful—in particular because the seizures were afebrile (given that it was known only that vaccines can trigger *febrile* seizures). First Shinnar Rep. at 5.

Second Report

Dr. Shinnar's next report responded to Dr. Byers's first report, as well as criticisms leveled against him by Dr. Kinsbourne. Second Shinnar Rep. at 2. He reiterated the medical history timeline before providing additional opinions. *Id.* at 2–4. In particular, Dr. Shinnar emphasized the fact that G.J.B.'s treaters had not affirmatively embraced vaccination as causal, but instead only deemed his epilepsy/seizure disorder "of unknown cause"—rejecting Dr. Kinsbourne's contention that this left room for vaccination as causal (since presumably the treaters would have said so if they believed vaccination had played a role). *Id.* at 4; Ex. 6 at 79. He also noted that the definition he employed for "unknown cause" was derived from the International League Against Epilepsy, and thus did not reflect a permissive or open-ended framework that left room for vaccination as causal. *Guidelines for Epidemiologic Studies on Epilepsy*, 34 Epilepsia 4:592 (Commission on Epidemiology and Prognosis, Int'l League Against Epilepsy, eds.) (1993), filed as Ex. A Tab E (ECF No. 36-1), at 593–94.

Dr. Shinnar stressed that the record showed G.J.B. possessed some deficiencies pre-vaccination, and which likely had some association to his subsequent epilepsy. Studies had

recognized that such symptoms (along with the reported family history of problems) were often present in individuals when seizures first manifest—and thus underscored why in this case G.J.B.'s seizure disorder was best deemed the product of an unknown etiology. Second Shinnar Rep. at 4, referencing Fastenau; *see also* D. Masur et al., *Pretreatment Cognitive Deficits and Treatment Effects on Attention in Childhood Absence Epilepsy,* 81 Neurology 1572 (2013), filed as Ex. A Tab 9 (ECF No. 28-10 ("Masur"). Masur conducted a double-blind, randomized clinical study of 446 children recently diagnosed with a previously-untreated form of epilepsy often deemed benign, finding that secondary symptoms are not only associated with it but (a) can be present when seizures begin, and (b) can persist even after seizures are medically controlled. Masur at 1573, 1577–79.

Dr. Shinnar then reacted to Dr. Kinsbourne's comments. *See generally* Second Shinnar Rep. at 4–5. He maintained that the evidence G.J.B.'s seizures had been afebrile undermined a vaccine association, given existing medical/scientific understanding. The IOM's conclusions contained in Stratton II, he contended, had reliability and probative value at least because they were based on the review of then-existing literature on the lack of association between the MMR vaccine and afebrile seizures. *Id.* at 4; Stratton II at 134. By contrast, Dr. Shinnar deemed Verbeek of limited persuasive value—for Verbeek had identified only *three* out of 990 children who experienced post-MMR vaccine afebrile seizures, with two having possessed a family history of afebrile seizure. Verbeek at 661. Verbeek also involved children far younger than G.J.B., further eliminating the weight its otherwise-limited findings should be given. Second Shinnar Rep. at 4.

Dr. Shinnar concluded the report with his reactions to Dr. Byers's report. Second Shinnar Rep. at 5–6. He deemed her opinion "confusing at best," observing the circular nature of her statement that since febrile seizures were common, physicians likely assumed all seizures were febrile—especially since (as was definitely established by the medical record herein) G.J.B.'s seizures unquestionably were *not* febrile. *Id.* at 5. And he disagreed with her specific point that any kind of seizure (febrile or afebrile) would have the same general cytokine-associated mechanism, noting that the item she cited for this proposition[17] did not actually support the contention, but instead (as evidenced by its title) was specific only to the association between IL-1β and febrile seizures. *Id.*

As support for his argument that febrile and afebrile seizures did not likely share a common immunologic mechanism, Dr. Shinnar offered a textbook chapter he had authored. S. Shinnar, *Febrile Seizures*, in Swaiman's Pediatric Neurology, Vol. 1 (5th ed. 2012), at 790–97, filed as Ex. 3 Tab 1 (ECF No. 36-2) ("Shinnar"). Shinnar specifically states that most febrile seizures occur after manifestation of fever, are thought more associated with peak temperature than rate of rise of

[17] Dr. Shinnar's comments on this subject were directed at "Dube," an article Petitioner did not actually file, as previously discussed. But it appears Dr. Shinnar was familiar with its content, and therefore was able to comment upon it. Second Shinnar Rep. at 5 (terming it "an elegant paper which I am very familiar with"). Dr. MacGinnitie, however, did offer this article in connection with his report, and I address it below.

temperature, and are more associated with some kinds of infectious processes than others (although their ultimate pathophysiology is unknown). Shinnar at 791–92. In addition, Shinnar observes that although febrile seizures do not always lead to development of epilepsy, certain risk factors (neurodevelopmental abnormalities, family history, or the complexity and temporal proximity of fever to seizure) are so associated if combined with febrile seizure occurrence. *Id.* at 794. The only relevant comment herein about *afebrile* seizures, however, is the fact that children with neurologic abnormalities and who have experienced febrile seizures are more likely to experience afebrile seizures later. *Id.* at 790.

Third Report

The final written report authored by Dr. Shinnar reacted to the additional supplemental reports from Drs. Kinsbourne and Byers. Regarding Dr. Kinsbourne, Dr. Shinnar again repeated his contention that the record best supported an idiopathic/unexplained cause for G.J.B.'s epilepsy, noting that in his experience, epileptologists assumed "unknown" to mean of unidentified genetic origin. Third Shinnar Rep. at 6. He further noted that Scheffer had in fact discussed a body temperature reflective of fever in discussion of seizure etiology, adding that IL-1β unquestionably was the "chief human cytokine involved in triggering fever," and that even when fever occurs *after* seizure manifestation, it still occurs. *Id.;* Scheffer at 336 (observing that "[t]he immune basis is not understood" for why a vaccine might arguably trigger seizure in a susceptible child). Otherwise, literature (like Stratton II) only reliably observed an association between vaccines like the MMR and *febrile* seizures—and again, G.J.B. had not experienced a post-vaccination *febrile* seizure. Third Shinnar Rep. at 6.

Dr. Shinnar also criticized Dr. Byers's supplemental arguments. Third Shinnar Rep. at 6–7. He again maintained that literature she had referenced did *not* establish that seizures, febrile or not, all involve IL-1β. *Id.* at 6. And he sought to refute Dr. Byers's contention that he was not up to date on the latest science on the cause of afebrile seizures, noting that his regular work includes large government grants to study children who suffer from prolonged febrile seizures, and that he had published many other articles specific to that issue as well as the role cytokines play in seizures. Third Shinnar Rep. at 6–7.

In addition, Dr. Shinnar reacted to some other items of literature referenced by Dr. Byers. Lee and Ong, for example, not only was a retrospective historical analysis of outcomes (instead of a case-controlled study) but dealt only with "new onset seizures," and said nothing about vaccine association. Third Shinnar Rep. at 7; Lee & Ong at 157, 159. He deemed Lee & Ong to adopt a "controversial" classification for seizure etiologies, moreover, and noted that Dr. Byers's embrace of this classification system underscored the lack of generally-sufficient on-point literature filed in this matter specific to the alleged vaccine-afebrile seizure connection. Third Shinnar Rep. at 7. Ha, Dr. Shinnar maintained, only observed the *existence* of higher TNF-alpha cytokine levels in

children with seizure disorders, and did not establish causality; indeed, Dr. Shinnar noted, it was equally likely *the seizures themselves were the cause* of the expression of these cytokines rather than vice-versa. Ha at 159; Third Shinnar Rep. at 7.

2. *Andrew MacGinnitie, M.D., PhD.*

Dr. MacGinnitie served as Respondent's immunologic expert, and prepared two written reports opining against vaccine causation of G.J.B.'s afebrile seizures. Report, dated January 29, 2019, filed as Ex. C (ECF No. 33-1) ("First MacGinnitie Rep."); Report, dated July 29, 2019, filed as Ex. F (ECF No. 44-1) ("Second MacGinnitie Rep.").

Dr. MacGinnitie is an attending physician and the Clinical Director for the Division of Immunology at Boston Children's Hospital in Boston, Massachusetts. Curriculum Vitae, filed as Ex. D on Feb. 12, 2019 (ECF No. 34-6) ("MacGinnitie CV"), at 1–2. He is also an Associate Professor of Pediatrics at Harvard Medical School. MacGinnitie CV at 1. Dr. MacGinnitie received his undergraduate degree from Yale University, followed by both a medical degree and Ph.D. from the University of Chicago. *Id.* Thereafter, he completed his residency, followed by a fellowship in allergy and immunology at Boston Children's. *Id*. He is board certified in pediatrics and allergy and immunology, and has been in practice as an allergist/immunologist since 2004. *Id*. at 9. Further, he has not only seen patients with various immunologic diseases, including reactions to vaccines, but has published several articles in the area. *Id.* at 11–14.

First Report

Dr. MacGinnitie's first report reacted to the initial opinions offered by Drs. Kinsbourne and Byers. He admitted that he had "struggled to follow a logical theory of how vaccination triggered seizures" as set forth in their reports, but had nevertheless attempted to comprehend their theories. First MacGinnitie Rep. at 3. He interpreted Dr. Kinsbourne's opinion to focus on the MMR vaccine's general capacity to cause seizure (as well as the secondary issues attributable to the overall epilepsy/seizure disorder and/or treatment of it), while he read Dr. Byers's report to be maintaining that any of the vaccines G.J.B. had received could cause fever but also could lower the seizure threshold, and thus cause seizures even in the absence of fever. *Id.* In either case, Dr. MacGinnitie opined, the theories presented were weak and/or unreliable (although he deferred to Dr. Shinnar on diagnostic issues specific to pediatric seizure disorders). *Id.* And he echoed Dr. Shinnar's emphasis on treater views, which in this case did not support vaccine causation (and to the extent vaccination was even mentioned, did so in history sections of records in which G.J.B.'s family recounted their version of his experiences). *Id.* at 7.

One point raised by Dr. Shinnar, but emphasized by Dr. MacGinnitie, was that most accepted medical science associated inflammatory cytokines only with *febrile* seizures—but those

same cytokines had not been shown to be causal of afebrile seizures, let alone increased due to vaccination in sufficient amounts to be harmful. First MacGinnitie Rep. at 4–6. Dr. Byers's initial report had only referenced only a few articles dealing with afebrile seizures, and they were either specific to infections or did not offer any discussion of what the necessary cytokine levels would be to produce seizure. *See, e.g.*, Zhang at 1002, 1005; Lee at 162–63.

Indeed, one article (which Dr. Byers cited to but did not file—although Respondent offered it later) specifically showed that cytokine levels were *not* increased in afebrile seizure patients, for any of the cytokines Dr. Byers had proposed as potentially causal. First MacGinnitie Rep. at 4–5; J. Choi et al., *Increased Levels of HMGB1 and Pro-Inflammatory Cytokines in Children with Febrile Seizures,* 8 J. Neuroinflamm. 135, filed as Ex. C Tab 5 (ECF No. 33-6) ("Choi"). In Choi, blood sera of 41 Korean children who had experienced febrile seizures were tested for cytokines, against a comparably-sized group of children with a non-seizure febrile illness—as well as different groups who had experienced afebrile seizures (or neither). Choi at 135. Choi's authors discovered that levels of the tested-for cytokines (including IL-1β and TNF-alpha) were routinely higher in the febrile group, and not elevated in the afebrile controls. Choi at 139–40, 142 (noting that "[t]he causative role of cytokine in epileptogenesis remains to be elucidated," but stressing that overall pro-inflammatory cytokine levels were higher in febrile seizure patients).

Next, Dr. MacGinnitie amplified Dr. Shinnar's contention that increased levels of cytokines in individuals suffering from seizures could be the *result* of seizure activity rather than the cause. First MacGinnitie Rep. at 4. Cytokines, he pointed out, were understood to be "secreted proteins that act as signaling molecules between cells," and thus, they not only could proactively impact seizure activity but could also be produced in the aftermath of seizure harm to the brain or central nervous system. *Id;* Li at 250–52. For causation to be established herein, however, it needed to be shown that vaccination was likely to instigate the increased production of these cytokines—and (more importantly) at levels sufficiently high to be pathogenic.

Dr. MacGinnitie granted that animal studies existed that supported the contention that inflammatory cytokines like IL-1β could lower the seizure threshold, but other evidence showing heightened cytokine levels post-seizure did not establish a causation association (although he acknowledged that measurement of cytokine levels in humans could only reliably be performed post-seizure in the first place, making it very difficult to measure causation in any event). Otherwise, higher levels of IL-1β (for example) found in "patients with intractable epilepsy and afebrile status epilepticus" were more likely attributable to cytokines released *due* to seizure activity—a "well-recognized phenomenon" in Dr. MacGinnitie's view. First MacGinnitie Rep. at 5; Li at 249–50 (seizures enhance expression of IL-1β, although some studies revealed no significant differences between IL-1β levels pre or post tonic-clonic seizures, and it otherwise is difficult to use human blood serum testing to assess how the cytokine functions in human epilepsy pathogenesis).

Dr. MacGinnitie also discussed the possibility of vaccines generally (and the MMR vaccine specifically) to produce seizure. Of the many kinds of "immune challenge" individuals confront on a daily basis, the risk posed by vaccines was far outweighed by wild infections. First MacGinnitie Rep. at 6. Even though immune dysfunction and/or autoimmunity were potential mediators for various illnesses, such processes would not simply appear in the wake of vaccination. Overall, he deemed vaccination "a mild immune stimulus," unlikely as a general matter to provoke injury. *Id.* at 7.

The MMR vaccine in particular, Dr. MacGinnitie noted further, was only associated with an elevated risk for *febrile* seizures (and Dr. Kinsbourne could only reference case reports to support any other kind of association). First MacGinnitie Rep. at 6. N. Klein et al., *Measles-Containing Vaccines and Febrile Seizures in Children Age 4 to 6 Years,* 129 Pediatrics 809, filed as Ex. C Tab 9 (ECF No. 33-10) ("Klein"). Klein (which Dr. MacGinnitie deemed "a detailed epidemiologic study") considered Vaccine Safety Datalink evidence of seizures in a sample of more than 60,000 children who had received the MMR vaccine or one containing its components, and found no elevated risk of seizure within six weeks of vaccination. Klein at 812. At worst, there was some increased risk of *febrile* seizure for infants 12-18 months old, but only after the first dose (and that group did not apply to G.J.B., who was four years old at the time of the relevant vaccinations). First MacGinnitie Rep. at 6; Klein at 813.

As an aside, Dr. MacGinnitie noted that the illustration contained in Dr. Byers's first report, which she had included to show how "cytokines can cause seizure independent of fever," came from Mazarati—not the article to which it referred. First MacGinnitie Rep. at 5–6. But Dr. MacGinnitie offered the underlying article. *See* C. Dubé et al., *Interleukin-1β Contributes to the Generation of Experimental Febrile Seizures,* 57 Ann. Neurol. 152 (2005), filed as Ex. C Tab 4 (ECF No. 33-5) ("Dubé"). In Dubé, researchers employed an animal model to evaluate what role IL-1β likely played in causing or contributing to febrile seizures. Dubé at 152. In particular, Dubé's authors were interested in evaluating whether this cytokine might not only (because of its proinflammatory and pyrogenic character) cause fevers that lead to seizures indirectly, but also whether the cytokine could be shown or observed to play a more direct role in seizure pathogenesis. It is known that in the context of a fever, brain microglia (central nervous system immune cells)[18] release IL-1β, which can bind to certain receptors in portions of the brain and lead to "enhanced neuronal excitability and decreased seizure threshold." *Id.* Hence, there is some potential for the cytokine to contribute or cause seizure activity that might occur outside, or independent to, the context of a fever.

[18] "Microglia" is defined as "the small, nonneural, interstitial cells of mesodermal origin that form part of the supporting structure of the central nervous system. They are of various forms and may have slender branched processes. They are migratory and act as phagocytes to waste products of nerve tissue. *Microglia*, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=31308 (last visited May 22, 2023).

Dubé's authors worked with mice specifically engineered to be deficient in the receptor pertaining to IL-1β, and then used an experimental method to cause increased core and brain temperatures in the mice comparable to what would be experienced in a fever, thereafter, inducing seizures. Dubé at 152–53. They also directly administered IL-1β into some of the mice, at different temporal stages of this process. They concluded that the cytokine was implicated "among the mechanisms by which fever provokes seizure in the developing brain," likely by contributing to "the hyperexcitability and seizures" occurring after fever. *Id.* at 154–55. Importantly, however, seizures could only be directly induced in the mice subjects by administration of "high doses" of IL-1β; Dubé did not comment on whether vaccines (or infections) cause the body to produce the cytokine in levels sufficient to provoke afebrile seizure in humans. *Id.* at 154.

Second Report

The final written report prepared by Dr. MacGinnitie (like his earlier report) responded to Drs. Kinsbourne's and Byers's comments, with more emphasis on Dr. Byers's criticisms. He began by arguing that Dr. Byers had misconstrued several items of her own literature. Millichap, for example, actually referenced an entirely different (but also not filed) article involving a large-scale epidemiologic study which itself found *no* DTP (the whole-cell form of the DTaP vaccine no longer administered) or MMR association with *afebrile* seizures—and therefore supported Respondent's position. Second MacGinnitie Rep. at 1–2; W. Barlow et al., *The Risk of Seizures After Receipt of Whole-Cell Pertussis or Measles, Mumps, and Rubella Vaccine,* 345 N. Engl. J. Med. 9:656 (2001), filed as Ex. F Tab 1 (ECF No. 44-2) ("Barlow"), at 660 (finding "significantly elevated risks of febrile seizure" the day of DPT vaccine receipt, or 8-14 days after the MMR vaccine, but no such risk for afebrile seizures "*at any time after vaccination*") (emphasis added). Barlow, a retrospective cohort study, looked at a total sample of over 675,000 children (seven years old or less) enrolled in four health care maintenance organizations who had received the DPT (again, the since-discontinued form of DTaP vaccine) and MMR vaccines—more than 477,000 doses. Barlow at 657, 660. It also characterized the observed enhanced risk of the MMR vaccine to result in febrile seizures as only "transient." *Id.* at 660. Another item, Eckerle, was a single-patient case report involving the first dose of MMR vaccine, and did not, in Dr. MacGinnitie's opinion, constitute a reliable view on causation. Eckerle at 1094–95.

Lee and Ong, Dr. MacGinnitie noted, was similarly unhelpful to Petitioners' claim. Second MacGinnitie Rep. at 2. While this article focused on associations with "provoked" afebrile seizures, the seizures G.J.B. had experienced could not be deemed provoked (especially since there is no evidence he was at the time suffering from an infection). Rather, based on the taxonomy Lee and Ong proposed (febrile, provoked, and true afebrile seizures), G.J.B.'s age (over four years old at the time) made his experience more consistent with their description of *afebrile* seizures—including the fact that (as the article reported) afebrile seizures were generally more likely to lead

to *additional* afebrile seizures, as was the case with G.J.B. Lee and Ong at 162–63. And Ha's comparisons of TNF-alpha cytokine levels in different patient groups did not also involve a control group—nor had Ha's authors collected blood samples soon enough after seizure activity to deem the cytokines likely causal (as opposed to being a byproduct of the seizure activity). Ha at 160–61.

Dr. MacGinnitie concluded by emphasizing the fact that epidemiologic evidence underscored only a heightened risk of febrile seizures when a child was younger than 18 months old, and primarily after the receipt of the first dose of vaccine. Second MacGinnitie Rep. at 2–3. Evidence like Barlow, by contrast, reliably highlighted the lack of an association between vaccines like the MMR and afebrile seizures. Barlow at 658.

III. Parties' Arguments

A. *Petitioners*

Petitioners contend they have met all the prongs for establishing causation in fact under *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005). First, they maintain that they have offered reliable preponderant proof that the MMR and DTaP vaccines can trigger afebrile seizures. Mot. at 10–13. Lee & Ong, for example, observed some afebrile post-infection seizures as a possible middle category (between febrile seizures and seizure disorders due to some preexisting genetic condition). *Id.* at 10–12; *see also* Chung & Wong at 592. Petitioners also highlighted the case report and epidemiologic evidence in favor of their theory. Mot. at 14–18. Some studies they offered had connected the MMR vaccine specifically with adverse events. Weibel at 383–86 (noting association between the MMR vaccine and encephalopathy, and also observing some instances where onset involved seizure (p. 386 Table 1). And the IOM itself only determined that it could not "conclusively" associate the MMR vaccine with seizures—not that the association lacked any evidentiary basis at all. Mot. at 19–21.

In addition, Petitioners attempted to distinguish Verbeek, arguing that its authors had not persuasively rebutted the possibility of vaccines as triggering afebrile seizures in a large proportion of studied children, and otherwise assumed without evidence that a genetic cause was always more likely in such cases. Mot. at 21–23; Verbeek at 663–64. Verbeek also, in their reading, provided a post-vaccination timeframe consistent with this case. Mot. at 21–22; Verbeek at 660. And its determination was not inconsistent with the possibility of vaccines occasionally triggering seizures in the absence of fever, as other items of literature allowed. Scheffer at 336. The term "trigger," Petitioners maintained, had to be distinguished from "cause"—with the former more consistent with the legal exercise being conducted herein than the latter. S*ome* individual susceptibility would always be at issue when a vaccination sparked a seizure (even if the susceptibility did not rise to a level of "genetic determinism"). Mot. at 25. And several other studies offered by Petitioner's

experts were consistent with the MMR vaccine's capacity to cause seizures. *Id.* at 26–28 (discussing Spiczak, Chung and Wong).

Petitioners further amplified their explanation of the role cytokines would play in triggering post-vaccination afebrile seizures. Mot. at 28–32. Dr. Byers, they maintained, had offered a theory supported by reliable articles (Li, Ha) that cytokines like IL-1β were well understood to play a role in causing seizures leading to epilepsy, and that the pyrogenic (fever-causing) capacity of such cytokines was independent from their seizure-provoking capability. *Id.* at 29–30. To the extent the theory had limitations or omissions of support (in particular, whether vaccination upregulated these cytokines *sufficiently* to trigger a seizure—let alone how—and/or whether the absence of the effects of fever first had anything to do with the likelihood of seizure), Petitioners noted that the preponderant standard applied to Vaccine Act claims did not require certainty, and that not enough was known about the immune response in any event to require such evidence. *Id.* at 31. It was enough, they maintained, that cytokines were involved in inflammatory responses and/or lowering of the seizure threshold. *Id.* at 32.

With respect to the "did cause" prong, Petitioners argued that literature they had offered supported the conclusion that under a "complex systems" conception of seizure disorders like epilepsy, a first seizure episode was likely to provoke more similar instances later, even if the inciting event was self-limiting—in effect, that "seizures beget seizures." Mot. at 33–34; T. Sutula, *Mechanisms of Epilepsy Progression: Current Theories and Perspectives From Neuroplasticity in Adulthood and Development,* 70 Epilepsy Research 161 (2004), filed as Ex. 69 (ECF No. 42-9), at 164–65 (review article discussing brain harm occurring in wake of seizures, and interrelationship between the same). The injury to the brain from the first event would be explanatory for the subsequent course, and thus the vaccine(s) precipitating the first event were responsible for what followed. There was also no reasonable alternative explanation for G.J.B.'s seizures, and no evidence ("aside from some deficits in speech development," which Petitioners offer no explanation for) of any pre-onset issues. Mot. at 35–36. And G.J.B.'s five-day post-vaccination first episode was consistent with vaccine cause, although Petitioners admitted there was no cytokine testing that would directly confirm the theory working in real time, *Id.* at 36.

Petitioners also filed a reply—clocking in at 24 pages in length, and thus nearly as long as Respondent's opposition brief. In it, Petitioners took great umbrage at the criticisms lodged by Respondent against Drs. Kinsbourne and Byers, but based on prior cases regarding their qualifications or adequacy of expert opinions, maintaining that such attacks disregarded the persuasiveness and validity of the opinions as offered herein. Reply at 2–5. Further, Petitioners maintained that mere "plausibility" is the evidentiary standard applicable to the *Althen* prong one showing, attempting to tease out support for that view from prior Federal Circuit decisions, and distinguishing that evidentiary burden from the broader, clearly-preponderant standard applicable

to a claimant's *overall* burden of proof. *Id.* at 5–9. Petitioners similarly defended the use of case reports to support causation. *Id.* at 9–11.

Regarding specifics relevant to the opinions offered in the case, Petitioners reiterated their contentions that they had met their burden. They attempted to rebut Dr. Shinnar's contentions that G.J.B.'s seizure disorder was consistent with what many children experience, disputing specifically that Stratton II suggested afebrile seizures were less credibly associated with vaccination than febrile, and maintaining that Dr. Shinnar had not even confronted Dr. Kinsbourne's theory. Reply at 12–18. Dr. MacGinnitie received comparable treatment. The Petitioners acknowledged that he had directly addressed their theory, but contended that he had mistakenly differentiated between afebrile and febrile seizures, without noting that the one cytokine was common to both. *Id.* at 18–20. Petitioners also argued that alleged epidemiologic studies that did not find a link between certain vaccines (MMR and DTaP) and afebrile seizures were unreliable or unable to detect rare events, even if they involved large samples of patients/subjects. *Id.* at 20–21.

B. Respondent

Respondent argues Petitioners have not met their burden of proof. Opp. at 22–27. First, he maintains that it cannot be shown that any of the vaccines received by G.J.B. in July 2013 can cause afebrile seizures. Opp. at 22–24. Respondent's experts demonstrated not only that there was a dearth of recent reliable literature supporting any broader association between certain vaccines (particularly the MMR or DTaP) and afebrile seizures, but more specifically that Dr. Byers's proposed mechanism (pro-inflammatory cytokines upregulated in response to the vaccines causing afebrile seizures) lacked substantiation. *Id.* at 22–23. Rather cytokines like IL-1β had only been shown to be associated with *febrile* seizures (and even in that context, only for a younger cohort that would not include G.J.B., since he was four when his first post-vaccination seizure manifested). Choi at 139–40, 142. Otherwise, Respondent noted that reliable epidemiologic studies, like Barlow, were unsupportive of a vaccine/afebrile seizure link, and Petitioner's reliance on case reports was misplaced since they were not probative of causation.

Second, Respondent contended that the "did cause" prong is not met. Opp. at 24–25. He observed that none of G.J.B.'s treaters had directly opined his vaccines were associated with his seizures; rather, records only referenced the prior *fact* of vaccination, but without proposing any causal link. *Id.* at 24–25. Treaters had more often than not concluded they could not pinpoint a cause for G.J.B.'s seizures, and Dr. Shinnar had noted that this (as well as the onset of the seizures at age four) was common for epileptic patients. *Id.* G.J.B.'s family history also provided some alternative factors that might better contextualize his seizure disorder, suggesting a genetic origin as opposed to vaccination. *Id.* at 25.

Finally, Respondent denied that the timeframe for onset of seizures (which Respondent did not squarely identify, although he did in his fact recitation note that G.J.B.'s first occurrence of forgetting words had occurred within approximately five days from the date of vaccination) had been shown to be medically acceptable, linking this contention to his earlier argument that Petitioners did not show in the first place that the vaccines could cause afebrile seizures. Opp. at 26. Respondent also throughout this brief raised a number of objections to the qualifications and competency of Drs. Kinsbourne and Byers (objections that as noted above prompted a fervent reaction by Petitioners), maintaining that their lack of updated/recent treatment expertise, or tendency to offer unreliable and garbled opinions that far exceed their demonstrated fields of knowledge, had been raised as an issue in numerous prior special masters' decisions. *Id.* at 13–17.

IV. Procedural History

Because this case was initiated in the summer of 2016, it is now nearly seven years old, and was originally assigned to a different special master. The parties filed records and the expert reports discussed above through mid-2019, and at that point some efforts to settle the case were made, although they proved unsuccessful. The matter was reassigned to me in January 2021, and I set it down for trial to be held in February 2022. ECF No. 64. However, in November 2021 Petitioners' former counsel asked that the trial date be continued, since he intended to withdraw from the matter. ECF No. 65. I took the case off the trial calendar, but opted instead to have the parties brief entitlement and resolve the case via ruling on the record, given my concerns about the case's age (and attendant desire that it be resolved as expeditiously as possible). ECF No. 68. After present counsel appeared in the matter for Petitioners, the parties filed their respective briefs, and the matter is ripe for resolution.

V. Applicable Law

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

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & 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).[19]

[19] 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, 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).

In this case, Petitioner cannot assert a Table claim based on the contention that the DTaP with IPV, MMR, and Varicella vaccines can cause afebrile seizures.

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*, 418 F.3d at 1278: "(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.

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden

placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras*, 121 Fed. Cl. at 245 ("[p]lausibility . . . in many cases *may* be enough to satisfy *Althen* prong one" (emphasis in original)).

In discussing the evidentiary standard applicable to the first *Althen* prong, the Federal Circuit has consistently rejected the contention that it can be satisfied merely by establishing the proposed causal theory's scientific or medical *plausibility*. *See Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019); *see also LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) ("[h]owever, in the past we have made clear that simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof." (citing *Moberly*, 592 F.3d at 1322)); *see also Howard v. Sec'y of Health & Hum. Servs.*, No. 16-1592V, slip op., at *6 (Fed. Cl. Feb. 27, 2023) ("[t]he standard has been preponderance for nearly four decades"). Petitioners consistently have the ultimate burden of establishing their *overall* Vaccine Act claim with preponderant evidence. *W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted); *Tarsell v. United States*, 133 Fed. Cl. 782, 793 (2017) (noting that *Moberly* "addresses the petitioner's overall burden of proving causation-in-fact under the Vaccine Act" by a preponderance standard).

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 are 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 v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339,1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743

(quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 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 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 Petitioner's 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").

E. *Determining Matter on Record Rather Than at Hearing*

I have determined to resolve this case based on written submissions and evidentiary filings, including the numerous expert reports that have been submitted, rather than hold a trial, and the parties have not formally objected to this means of adjudication. My determination is consistent with the Vaccine Act and Rules, which not only contemplate but *encourage* special masters to

decide petitions (or components of a claim) on the papers where (in the exercise of their discretion) they conclude that such a means of adjudication will properly and fairly resolve the case. Section 12(d)(2)(D); Vaccine Rule 8(d). The Federal Circuit has affirmed this practice. *Kreizenbeck v. Sec'y of Health & Hum. Servs.*, 945 F.3d 1362, 1365–66 (Fed. Cir. 2020). It simply is not the case that every Vaccine Act claim need be resolved by hearing—even where the petitioner explicitly so requests.

ANALYSIS

I. Vaccine Program Treatment of Seizure Disorder/Epilepsy Claims

Vaccine Program petitioners have successfully established that different vaccines can cause autoimmune injuries 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). However, the specifics of such claims matter—and the nature of the seizure in question is important.

Some cases have established that particular vaccine components can cause seizures, but a more common path to a favorable entitlement finding involves demonstrating an *impact* of vaccination separate from the vaccine's specific antigenic contents. Petitioners are often successful by showing that the injured child experienced a vaccine-induced fever, which then triggered a *febrile seizure*—thereby instigating epilepsy or some other kind of seizure disorder. *See, e.g.*, *Weaver v. Sec'y of Health & Hum. Servs.*, 164 Fed. Cl. 608 (2023); *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, under the theoretical contention that one febrile seizure harms the brain sufficiently to trigger more—that "seizures beget seizures."

It cannot be credibly disputed in this case that certain vaccines can trigger febrile seizures, as a result of the vaccine's stimulation of the innate immune system (which includes upregulation of pro-inflammatory cytokines specifically associated with fever). *See* First Shinnar Rep. at 5. But a single febrile seizure attributable to vaccination does not *inevitably* lead to some form of epilepsy. Whether a first seizure connects to what follows depends broadly on the facts of the specific case.

See, e.g., *Caredio v. Sec'y of Health & Hum. Servs.*, No. 17-0079V, 2021 WL 4100294 (Fed. Cl. Spec. Mstr. July 30, 2021), *mot. for review den'd,* No. 17-79V 2021 WL 6058835 (Fed. Cl. Dec. 3, 2021) (dismissing case where infant's autoimmune epilepsy was argued to have been caused by a flu vaccine; petitioners' expert did not contend that an initial, vaccine-caused febrile seizure explained child's subsequent seizure disorder); *see also Weaver,* 164 Fed. Cl. at 616–18 (initial febrile seizure deemed more likely than not to have caused seizure disorder/epilepsy despite absent of brain damage close in time to first seizure); *Ginn*, 2021 WL 1558342 (vaccine-caused febrile seizure deemed causal of further seizure activity; medical record revealed that brain changes/damage had occurred after the first seizure).

Cases involving first-time, post-vaccination *afebrile* seizures, by contrast, 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). Here, the record clearly *does not establish* that G.J.B. experienced a febrile seizure. Thus, Petitioners' claim can make limited use of what is known about the association between febrile seizures and vaccines, and needed instead to establish a vaccine association with afebrile seizures.

II. Petitioners Have not Carried Their Burden of Proof

A. *Althen* Prong One

Petitioners have not established that any of the vaccines G.J.B. received (but in particular the MMR or DTaP) can cause afebrile seizures. Before discussing the evidence offered for this contention, however, it is important to address Petitioners' threshold argument that this prong (unlike the other two) is subject to a *plausibility* standard. *See, e.g.*, Reply at 5-9.

This conception of the legal burden is simply mistaken—as the Court of Federal Claims has recently (and repeatedly) emphasized. *See, e.g.*, *Howard,* No. 16-1592V, slip op.; *K.A. v. Sec'y of Health & Hum. Servs.,* 164 Fed. Cl. 98, 125–26 (2022) (affirming application of preponderance standard to first *Althen* prong), *appeal docketed,* No. 2023-1315 (Fed. Cir. Jan. 3, 2023). I myself have previously addressed at length the fallacious reasoning animating this contention. *See K.A. v. Sec'y of Health & Hum. Servs.,* No. 16-989V, slip. op., at 34–37 (Fed. Cl. Spec. Mstr. Apr. 18, 2022), *mot. for review den'd,* 164 Fed. Cl. 98 (2022), *appeal docketed,* No. 2023-1315 (Fed. Cir. Jan. 3, 2023). In short, the Federal Circuit has consistently stated that the relevant standard for the first prong is preponderance, even though Petitioners may *satisfy* that prong with a wide array of circumstantial evidence (and thus cannot be faulted for not affirmatively offering *any one particular kind* of evidence, such as a reliable epidemiologic study). The Program's lenient standards (which recognize that proving an injury's association to vaccination is difficult) are also

reflected in the lack of evidentiary admission rules. Claimants need not establish a vaccine can cause an injury to a certainty, but they *must* establish this is *more likely than not* the case—the same standard employed for the two other *Althen* prongs.

Moving on to the evidence offered by Petitioners, their experts' "can cause" theory possesses several deficiencies. This is not to say that each *individual* item of evidence offered was unreliable, unpersuasive, or worthy of no probative weight. Petitioners did, for example, reference reliable literature showing that the cytokine most associated with fever, IL-1β, likely plays some greater role in *mediating* seizures as well. *See, e.g.*, Dubé. Several articles noted some general association between the vaccines at issue and adverse events (even if they often tended to be dated, say nothing about the nature of the seizure, or involved a distinguishable injury entirely). *See* Weibel (encephalopathy), Stratton II, Spiczak. Other articles suggest that seizure susceptibility may simply reflect a lower seizure threshold—and in turn that this means that seizures can occur without also requiring the neurologic impact of fever (at least for certain individuals). *See* Lee and Ong. Some items were even specific to vaccines at issue (although evidence of post-vaccination afebrile seizures often had to be "mined" from larger data sets, and did not usually reflect the topline conclusions of an article's authors). *See, e.g.*, LeSaux at e352 (observing some post-MMR vaccine afebrile seizures in study otherwise concluding that *febrile* seizures were less likely after administration of vaccines containing acellular pertussis). The general gist of Petitioners' causation theory—that cytokines generated in association with vaccination, and that prompt fever, could theoretically cause afebrile seizures in a susceptible individual—had a baseline level of plausibility.

This, however, is not enough to prevail upon in a Program case, as noted above. In particular, the theory over-relies on how vaccines are generally understood to function. Vaccination (which stimulates an innate/immediate response that can lead to some transient symptoms often characterized as "malaise") is known to cause an upregulation of many pro-inflammatory cytokines, including IL-1β, which in turn can produce fever in the body (usually indirectly, since the cytokine need not travel into the brain to direct the hypothalamus to increase body temperature). Scheffer at 336. But linking the actual way vaccines work to even *reasoned* speculation about cytokine-seizure association does not amount to a successfully-established causal theory—without more evidence. I have specifically noted in other cases that relying on a vaccine's anticipated stimulation of cytokine production is not enough of a basis for causation if not also connected to preponderant evidence that this expected immune response can become aberrant in some manner. *See Zumwalt v. Sec'y of Health & Hum. Servs.*, No. 16-994V, 2019 WL 1953739 (Fed. Cl. Spec. Mstr. Mar. 21, 2019); *Inamdar v. Sec'y of Health & Hum. Servs.*, No. 15-1173V, 2019 WL 1160341 (Fed. Cl. Spec. Mstr. Feb. 8, 2019); *Dean v. Sec'y of Health & Hum. Servs.*, No. 13-808V, 2017 WL 2926605 (Fed. Cl. Spec. Mstr. June 9, 2017).

Rather, Petitioners needed to offer evidence of some form supporting the conclusion that vaccination can cause production of cytokines in sufficient amounts, and of the right "type," to cause afebrile seizures (which in turn would also require reliable proof that the cytokines alone can cause *afebrile* seizures in the first place). This did not occur—and the omissions and deficiencies in Petitioners' theory are large and small.

To start, the evidence associating a number of inciting triggers—including infection and vaccination—with *febrile* seizures is significant and robust. *See, e.g.*, Barlow; Stratton II; Waruiru; Klein. Certainly, the evidence in this case supports an association between the MMR vaccine and febrile seizures (albeit in young children only). Barlow at 657, 660. By contrast, little if any literature was offered in this case proposing causes of *afebrile* seizures (beyond some unspecified/presumed susceptibility), and/or whether the same pyrogenic cytokine responsible for febrile seizures could cause seizure without fever. At most, articles like Dubé have taken tentative steps in that direction, employing useful animal models (perhaps in part because existing studies testing cytokine levels in actual humans show almost no difference in these levels pre and post-seizure) with the goal of better understanding the role of IL-1β in seizure activity generally. But the articles filed in this case do not collectively support the conclusion that it is likely (even if still not certain) that proinflammatory, pyrogenic cytokines like IL-1β can cause afebrile seizures alone. Articles filed that addressed seizure susceptibility did not also discuss how or why vaccination would be seizure-causing in that context. Lee and Ong at 157–58 (stressing age-related susceptibility as most important factor); Chung and Wong.

Thus, not enough reliable evidence was offered in this case to conclude that cytokines like IL-1β are likely to cause afebrile seizures simply because some studies show they also play a role in mediating *existing* seizures, or simply by first causing fever. Indeed—some items filed by Respondent suggest the cytokines are produced secondarily, in *response* to seizure activity. *See, e.g.*, Li at 249–52. Other items even show patients who experienced febrile seizures generally display *higher* levels of the purportedly-causal cytokines, versus afebrile seizure-experiencing subjects, whose levels remain normal (somewhat undermining the contention that the cytokines themselves are causal). *See generally* Li; Choi; Ha. And literature discussing reactions to infection, like Lee and Ong or Zhang, cannot simply be applied to the context of vaccination, since the process of an active infection is inherently more damaging to the body, and involves a more mounted immune response.

More narrowly, insufficient evidence was offered associating the specific vaccines at issue with afebrile seizures. While some items of literature associate the MMR with *febrile* seizures, or the distinguishable DPT vaccine with same, or either with other kinds of injuries (in particular encephalopathy), the afebrile association remains unaddressed, or was deemed to have been confirmed by Petitioners' experts based on data they pulled from larger studies that either contradict a relationship overall, or where the numbers are too small to deserve significant weight.

See, e.g., Wariuru, Spiczak. In comparison, a large epidemiologic study, Barlow, rejected a relationship between the MMR vaccine and *afebrile* seizures. Barlow at 660. Many items offered for an association were weaker in their actual conclusions than allowed for by Petitioners' experts. *See, e.g.*, Stratton I, Spiczak. Others involve small samples, stale studies, or incompletely-filed documents that do not permit a full understanding of the scope of the purported findings. *See, e.g.*, Alderslade, Verbeek. Several reliable items affirmatively stated a vaccine-seizure relationship had not been scientifically demonstrated, regardless of form, and that individual susceptibility was a more likely etiologic explanation. *See, e.g.*, Huang at 263–64, 267; Verbeek at 665. In addition, it appears that even in the context of a febrile seizure/vaccine association, the timeframe of onset or the child's age is very important (*see* Lee and Ong, Klein, Barlow)—and here, although G.J.B. is alleged to have experienced seizures five days post-vaccination, his older age means studies specific to infants (e.g. 18 months or younger) have far more limited applicability.

The quality of evidence offered in the case, and its pertinence to the circumstances and theory at issue, also was relevant—with Respondent's submissions overall more recent and more specific to the question posed. Ignoring the number of items of literature that Petitioners' experts discussed but were not filed, or were only abstracts or incomplete summaries, or were dated, Petitioners over-relied on research pertaining to *febrile* seizures or other kind of injuries. They also offered studies that derived conclusions from VAERS-like databases that themselves observed only temporal associations between seizure onset and vaccines, or even older Program case information involving distinguishable injuries. *See,* e.g., Verbeek, Weibel. And they relied on case reports, like Eckerle, that involved facially distinguishable patients - and in any event case reports do not merit significant weight. *See e.g.*, *Pearson v. Sec'y of Health & Human Servs.*, No. 17-489V, 2019 WL 1150044, at *11 (Fed. Cl. Spec. Mstr. Feb. 7, 2019) (concluding that case reports receive only limited evidentiary weight); *Harris v. Sec'y of Health & Human Servs.*, No. 10-322V, 2014 WL 3159377, at *18 (Fed. Cl. Spec. Mstr. June 10, 2014) ("case reports are generally not a valuable form of evidence").

Overall, then, it was not preponderantly established that (a) pro-inflammatory cytokines associated with febrile seizures can also likely cause afebrile seizures, or (b) cytokines stimulated/produced by vaccination reach levels comparable to what is produced in reaction to a wild infection (or what levels would be necessary in the first place) sufficient to cause an afebrile seizure. It does not matter, for present purposes, if one seizure could lead to more, and/or that seizure activity is generally harmful to a child's developing brain. The linchpin of a Vaccine Act case is a showing that the vaccine could have kicked off the entire pathogenic process, and that has not been demonstrated.

In evaluating the strength and persuasiveness of Petitioners' expert opinions, I take some note of Respondent's impeachment attacks on the competence and/or reliability of Drs. Kinsbourne and Byers, as reflected in prior Vaccine Program matters, as well as Petitioners' sharp

reaction thereto. *See, e.g.*, Opp. at 13–16; Reply at 2–4. Petitioner is certainly correct that special masters should always endeavor to give due consideration to an expert opinion *as presented in an individual case*, rather than emphasize the expert's prior Program "history." The fact an expert has been criticized before does not automatically mean a subsequent opinion is inherently questionable. The newly-presented report may have its own evidentiary value, or be reliable in a way prior opinions were not, and it is unfair to a claimant to dismiss an opinion out of hand based on an expert's past conduct (as opposed to evidence the expert's base credentials are reasonably called into question).

At the same time, special masters draw on their experience when deciding new cases—especially where the ground has previously been "well plowed" with respect to a specific kind of claim. They also fairly may discern certain kinds of bad habits specific to a particular expert that get repeated over time (a particular danger in the Vaccine Program, since the pool of experts both sides utilize is limited). And they may notice that comments explicitly included in decisions, in the hope that an expert will take greater care in the future in how an opinion is presented, go unheeded by counsel,[20] who retain the same experts again and again, without any attempt to improve the expert's performance.

Here, Respondent has pointed out that Drs. Kinsbourne and Byers have repeatedly been criticized for (a) offering opinions well outside their overall-demonstrated expertise, and/or (b) providing confusing opinions that use complex medical/science ideas to obscure the lack of a well-substantiated theory. Opp. at 14–16. These kinds of expert acts can diminish the value of the opinion offered or weight it should receive, and I do not deem Respondent to have acted unethically or inappropriately in noting the experts' histories from past cases.

However, I can decide this matter without relying on Respondent's objections. Petitioners' experts simply did not offer sufficiently reliable opinions *in this case*—independent of their past conduct in other cases. Although both experts may have been a bit sloppy in presenting support for their arguments,[21] my determination herein turns on the fact that these expert opinions were less persuasive and reliably supported than what Drs. Shinnar and MacGinnitie offered. Dr. Shinnar was the most competent expert to opine on diagnostic questions pertaining to epilepsy, and Dr. MacGinnitie succinctly and effectively established why Dr. Byers's causation opinion (somewhat supplemented by Dr. Kinsbourne) was deficient. These were sufficient reasons for finding Respondent's efforts more persuasive.

[20] I recognize in this case that present counsel came into the matter well after the expert reports at issue were generated, and thus had nothing to do with the selection of either individual, or any decisions relating to the opinions they offer.

[21] In particular, Dr. Byers omitted the filing of several items of literature her reports discussed, or mistakenly referenced items (such as the chart from Dubé) that were not contained in, or different from, what was filed, while Dr. Kinsbourne filed some items that were merely abstracts, or omitted relevant sections from the literature filings that would have helped me better ascertain its reliability (*see, e.g.*, Alderslade, Landrigan & Witte).

Althen Prong Two

The record in this case establishes several instances in which Petitioners expressed their *personal view* to treaters that the vaccines G.J.B. received had caused his seizure activity. *See, e.g.*, Ex. 3 at 48. Neurologic treaters, however, did not endorse vaccine causality. Ex. 6 at 5. And I have not discerned from the record instances in which a contemporaneous treater speculated that vaccination had triggered G.J.B.'s seizures. This is therefore not a case in which a claimant can reference contemporaneous treater comments (no matter the foundation for their statements) that vaccination had been involved in disease pathogenesis as evidence the vaccine likely "did cause" G.J.B.'s seizures.

There is better record support (albeit derived more from witness statements than actual record evidence) for the conclusion that G.J.B. experienced some post-vaccination inflammation, followed by the stuttering and language activity that later treaters viewed as reflective of seizure activity. However, Petitioners' experts (although they posit a causation theory based on aberrant cytokine impact) did not establish that any initial vaccine malaise was caused by the same cytokine response (IL-1β in particular) that would usually cause fever as well, but did not here. This latter point deserves emphasis: *the record does not at all establish the vaccines produced in G.J.B. any fever—or that his seizures were febrile*. Thus, there is an evidentiary "disconnect" between the fact of some possible initial vaccine reaction and the proposed afebrile mechanism for how G.J.B.'s seizures would later occur, which makes it difficult to give the mere evidence (based on witness testimony, moreover) of an initial malaise reaction much weight.

Otherwise, I cannot identify in this record evidence that would suggest Petitioners' causation theory was occurring in "real time" as proposed by their experts. No test results[22] or other exam information corroborates Petitioners' theory. If (under the "logical sequence of cause and effect" characterization of the "did cause" prong) I found otherwise, I would be elevating the fact that G.J.B.'s seizures occurred temporally after vaccination into significant proof of causation—the essence of *post hoc ergo propter hoc* reasoning. *See Galindo v. Sec'y of Health & Human Servs.*, No. 16-203V, 2019 WL 2419552, at *20 (Fed. Cl. Spec. Mstr. May 14, 2019). Vaccine Program claimants do not prevail merely because their injury follows a vaccine.

There is also the medical record evidence that pre-seizures, G.J.B. had displayed some language issues that might have been associated with his post-vaccination presentation. I do not

[22] For example, there is no evidence in the record that the cytokines Petitioners' experts posit as potentially causal of afebrile seizures were at levels in G.J.B. high enough to produce seizure in him. Of course, in so noting I also accept that this kind of testing would rarely occur, and I am therefore not faulting Petitioners for being unable to marshal it. My point is only that other than the witness testimony about post-vaccination malaise, the record does not contain *any* independent evidence that the theory espoused was actually occurring—meaning that deeming the second prong satisfied would be the product of a legal analysis that elevated the temporal association of seizures to vaccination date over all else.

on the basis of this record deem this evidence to come close to preponderantly establishing an alternative explanation for his seizures, nor were Petitioners obligated to rebut these factors as more likely than not non-causal. At the same time, however, ample authority establishes that this kind of unhelpful evidence can be reasonably evaluated when assessing a claimant's success in establishing causation. *See Stone v. Sec'y of Health & Hum. Servs.*, 676 F.3d 1373, 1379 (Fed. Cir. 2012); *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1353 (Fed. Cir. 2008). And Dr. Shinnar persuasively explained in his reports why (from his perspective as a pediatric neurology expert) he found this evidence significant, allowing him to conclude that G.J.B.'s epilepsy was not vaccine-caused but instead reflective of an unknown/idiopathic cause.[23]

I acknowledge that G.J.B. did not manifest seizure activity *prior* to the vaccinations at issue. And I cannot on the basis of this record make a finding as to what the likely cause of his condition is. But Dr. Shinnar (the most competent expert on the subject of pediatric seizures) provided a compelling interpretation of G.J.B.'s history, concluding it likely that an idiopathic origin for G.J.B.'s seizures was the best understanding of the facts, and he rooted this opinion in persuasive evidence suggesting this is how most epilepsy experts would read the medical record in this case. First Shinnar Rep. at 5. Given the overall state of the science on the issue of afebrile seizures and their cause, this construction of the medical record warrants more weight than Petitioners' contentions.

Althen Prong Three

The record preponderantly establishes that G.J.B.'s post-vaccination episodes of language issues and stuttering were interpreted by initial neurologic treaters as likely the product of seizure activity. *See*, *e.g.*, Ex. 6 at 3–5. Petitioner has contended that these seizures manifested within about five days of vaccination, or by August 3, 2023, and there is record support for this conclusion. Ex. 5 at 1; Br. at 35–36. Based on the foregoing, and the fact that Respondent has not directly questioned the factual issues relating to onset, I find that this is the most likely timeframe in which G.J.B.'s seizure onset occurred.

Petitioners' experts argue that it would be medically acceptable, under their theory, for onset of a vaccine-induced form of epilepsy to occur within two weeks of vaccination (relying specifically on literature involving the MMR vaccine). *See, e.g.*, First Kinsbourne Rep. at 4–5. Some of the evidence offered for this opinion is insufficiently robust, or has a conclusory quality (such as Alderslade). However, the general concept that a vaccine's stimulation of the innate immune system—during which cytokines are activated—would occur in a shorter timeframe than the adaptive process (in which antibodies produced in reaction to vaccination are deemed central

[23] Petitioners also did not offer the theory that the vaccines significantly aggravated either a subclinical seizure disorder or these kinds of language-associated symptoms.

to a disease's pathogenesis) is reliable. Moreover, G.J.B.'s actual onset of five days is even *more* consistent with such a rapid innate response.

Accordingly, I find that Petitioner's *Althen* prong three showing is fully consistent with the theory advanced and the evidence offered in this case. Had I *also* found that the vaccines at issue could cause afebrile seizures in the manner proposed, it could have been determined that onset was medically acceptable. However, it is axiomatic that Program petitioners must satisfy *all three Althen prongs*—meaning that Petitioners' inability to meet the first two results in dismissal of the case regardless. The fact that the onset timeframe is consistent with the theory proposed, as here, does not render the underlying theory more likely or persuasive.[24]

CONCLUSION

While I have great sympathy for Petitioners' efforts in this case, I cannot find entitlement if the causation elements are not met. Accordingly, dismissal of this case is required. 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.[25]

IT IS SO ORDERED.

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

[24] The same principle adheres under the opposite circumstances. Claimants may well be able to establish that a particular vaccine "can cause" a specific injury, thereby satisfying the first *Althen* prong. But if the timeframe in which onset occurs is not medically acceptable – say, an onset *five years* post-vaccination for an acute nerve demyelinating illness—the case will fail, with the third prong showing gaining no "steam" from the success of the first.

[25] 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.