In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: July 31, 2025

MICHELLE CARROLL, on behalf of J.W., a minor child,	*	PUBLISHED
Petitioner,	*	No. 19-1125V
v.	*	Special Master Nora Beth Dorsey
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Entitlement; Diphtheria-Tetanus-Acellular-Pertussis ("DTaP") Vaccine; Epilepsy; Seizures; Encephalopathy.
Respondent.	*	

Jessica Wallace, Siri & Glimstad, LLP, Aventura, FL, for Petitioner.
Ryan Daniel Pyles, U.S. Department of Justice, Washington, DC, for Respondent.

DECISION[1]

I. INTRODUCTION

On August 2, 2019, Michelle Carroll ("Petitioner"), on behalf of J.W., a minor child, filed a petition under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42 U.S.C. § 300aa-10 et seq. (2018).[2] Petitioner alleges J.W. suffered "encephalopathy with residual seizure disorder and global developmental delay" as a result of

[1] Because this Decision contains a reasoned explanation for the action in this case, the undersigned is required to post it on the United States Court of Federal Claims' website and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the Decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material from public access.

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 to -34 (2018) ("Vaccine Act" or "the Act"). All citations in this Decision to individual sections of the Vaccine Act are to 42 U.S.C.A. § 300aa.

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the administration of pneumococcal conjugate, haemophilus b conjugate ("Hib-PRP-T"), inactivated polio ("IPV"), diphtheria, tetanus, acellular pertussis ("DTaP"), and rotavirus vaccinations on August 3, 2016 and DTaP/Hib/IPV, pneumococcal conjugate, and rotavirus vaccinations on October 11, 2016. Petition at Preamble (ECF No. 1). Respondent argued against compensation, stating that "this case is not appropriate for compensation under the terms of the Act." Respondent's Report ("Resp. Rept."), filed Mar. 17, 2020, at 1 (ECF No. 19).

After carefully analyzing and weighing the evidence presented in this case in accordance with the applicable legal standards,[3] the undersigned finds that Petitioner has failed to provide preponderant evidence that J.W.'s vaccinations caused the alleged injuries. Thus, Petitioner has failed to satisfy her burden of proof under Althen v. Secretary of Health & Human Services, 418 F.3d 1274, 1280 (Fed. Cir. 2005). Accordingly, entitlement must be denied.

II. ISSUES IN DISPUTE

The parties agree that J.W.'s "correct diagnosis is epileptic encephalopathy." Joint Prehearing Submission ("Joint Submission"), filed July 10, 2024, at 3 (ECF No. 161). They also agree that Petitioner has not alleged an "injury covered by the Vaccine Injury Table, 42 C.F.R. § 100.3." Id. at 3.

The parties dispute the onset of J.W.'s condition. Joint Submission at 2. The parties also do not "necessarily agree with the conclusions reached by medical personnel." Id. Specifically, Respondent disputes any conclusion that "J.W.'s condition is vaccine related" based upon opinions of J.W.'s treating physicians, whereas Petitioner disputes that such conclusions suggest "a lack of causal relationship." Id. at 2-3.

Further, all three Althen prongs are in dispute. Joint Submission at 3. Thus, the parties disagree whether there is preponderant evidence that the vaccinations administered to J.W. on August 3, 2016 and October 11, 2016 can cause epileptic encephalopathy or did so in this case. They also request a factual determination as to the onset of J.W.'s condition. Id.

III. BACKGROUND

A. Procedural History

On August 2, 2019, Petitioner filed a petition accompanied by medical records, immunizations records, and affidavits. Petition; Petitioner's Exhibits ("Pet. Exs.") 1-13.

[3] Although this Decision does not discuss all of the medical literature in detail, the undersigned reviewed and considered all of the medical records and all of the medical literature submitted in this matter. See Moriarty v. Sec'y of Health & Hum. Servs., 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though [s]he does not explicitly reference such evidence in h[er] decision."); Simanski v. Sec'y of Health & Hum. Servs., 115 Fed. Cl. 407, 436 (2014) ("[A] Special Master is 'not required to discuss every piece of evidence or testimony in her decision.'"), aff'd, 601 F. App'x 982 (Fed. Cir. 2015).

Petitioner filed additional medical records between October 2019 and June 2020. Pet. Exs. 14-23. On March 13, 2020, the case was reassigned to the undersigned. Notice of Reassignment dated Mar. 13, 2020 (ECF No. 17). Respondent subsequently filed his Rule 4(c) report arguing against compensation. Resp. Rept. at 1.

On July 23, 2020, Petitioner filed an expert report from Dr. Yuval Shafrir. Pet. Ex. 24. On November 11, 2020, Respondent filed an expert report from Dr. Christine McCusker followed by an expert report from Dr. Shlomo Shinnar on April 1, 2021. Resp. Exs. A, C.

The undersigned held a Rule 5 conference on May 25, 2021. Order dated May 25, 2021 (ECF No. 56). However, she was unable to provide her preliminary findings as updated medical and genetic records were needed. Id. at 1-2. After the requested medical records were filed, the parties could file supplemental expert reports if desired. Id. at 2.

Petitioner filed the requested medical records on August 25, 2021. Pet. Exs. 26-33. On April 29 and June 7, 2022, Petitioner filed an expert report from Dr. Omid Akbari and a supplemental report from Dr. Shafrir. Pet. Exs. 34, 36. On August 29 and September 6, 2022, Respondent filed a supplemental expert report from Dr. McCusker and an expert report from Dr. Eric Marsh. Resp. Exs. E-F.

The parties requested another Rule 5 conference. Joint Status Rept., filed Sept. 8, 2022 (ECF No. 85). In preparation for the Rule 5 conference, the undersigned identified additional medical records that were needed. Order dated Oct. 31, 2022 (ECF No. 88); see also Order dated Jan. 18, 2023 (ECF No. 97) (identifying additional missing records). Additional records were filed between November and December 2022, and on January 19, 2023, Petitioner reported that no other additional medical records existed. Pet. Exs. 37-43; Pet. Status Rept., filed Jan. 19, 2023, at 1-2 (ECF No. 98). After a review of the complete medical records, the undersigned informed that parties that she was unable to provide her preliminary findings at the Rule 5 conference given the complexity of the medical issues. Order dated Jan. 20, 2023 (ECF No. 99).

On March 9, 2023, the undersigned held a status conference to address the possibility of additional experts and the ultimate method for resolving the case. Order dated Mar. 9, 2023, at 1 (ECF No. 102). She authorized Petitioner to obtain to obtain an expert report from a genetic specialist and deferred to Petitioner's request for an entitlement hearing. Id. An entitlement hearing was initially set for July 16 through July 18, 2024. Prehearing Order dated June 6, 2023, at 1 (ECF No. 109). It was later rescheduled for July 30 through August 1, 2024. Order dated May 17, 2024 (ECF No. 140).

Between October 2023 and March 2024, Petitioner filed additional medical records and genetic testing records. Pet. Exs. 44-45. On April 25, 2024, Petitioner filed an expert report from Dr. Dmitriy Niyazov, a genetic specialist. Pet. Ex. 46.

Throughout June 2024, Petitioner filed updated medical records, photographs, videos, and other supporting documentation. Pet. Exs. 47, 50-69. On July 29, 2024, one day before the entitlement hearing, Petitioner filed a motion for leave to file newly discovered video evidence. Pet. Motion for Leave to File Video Evidence, filed July 29, 2024, at 1 (ECF No. 164). The late

discovered video evidence was addressed at the entitlement hearing, and Petitioner's motion was granted after Respondent withdrew his objection. Order dated Aug. 1, 2024 (ECF No. 169); Transcript ("Tr.") 4-6; Pet. Exs. 70-71.

The entitlement hearing was held on July 30 and July 31, 2024. Tr. 4, 229. Petitioner, Dr. Niyazov, Dr. Shafrir, Dr. Akbari, Dr. Marsh, and Dr. McCusker provided testimony. Tr. 16-221, 229-450.

On September 19, 2024, the parties reported that they did not wish to submit post-hearing briefs. Joint Status Rept., filed Sept. 19, 2024 (ECF No. 180).

This matter is now ripe for adjudication.

B. Factual History

1. Summary of Medical Records[4]

J.W. was born on May 30, 2016. Pet. Ex. 2 at 10. His Apgar scores[5] were nine at one minute and nine at five minutes. Id. at 11. J.W.'s birth weight was 35.4 kg; his height was 20 inches, and his head circumference was 14 inches.[6] Id. at 50. While he had mild neonatal jaundice, there were no significant complications. Id. at 17, 20.

On June 2, 2016, three days after birth, J.W. was seen by his pediatrician for a newborn well visit. Pet. Ex. 4 at 8-10, 16. At the visit, his weight was 3.20 kg (in the 24th percentile); his height was 49.5 cm (in the 36th percentile); and his head circumference was 34.5 cm (in the 22nd percentile). Id. at 9. He received a hepatitis b ("Hep B") vaccine at this visit. Id. at 10.

A weight check visit on June 9, 2016 showed J.W. weighed 3.20 kg (in the 16th percentile); his height was 50.8 cm (in the 36th percentile); and his head circumference was 34.5 cm (in the 14th percentile). Pet. Ex. 4 at 14-15. On June 16, 2016, J.W. had another weight check visit. Id. at 12-13. His weight was 3.32 kg (in the 12th percentile); his height was 51.4 cm

[4] The medical record summary is largely taken from Respondent's Pre-Hearing Brief, which the undersigned finds fairly and accurately depicts the events described in the medical records. Resp. Prehearing Brief ("Resp. Br."), filed July 10, 2024, at 2-9 (ECF No. 158).

[5] Apgar scores measure a newborn's "respiratory effort, heart rate, color, tone, and reflex irritability" at one minute and five minutes after birth. Deborah Consolini, Initial Evaluation of the Normal Newborn, Merck Manual, https://www.merckmanuals.com/professional/pediatrics/care-of-newborns-and-infants/initial-evaluation-of-the-normal-newborn (last visited July 28, 2025). A score between 7 and 10 is considered normal. Id.

[6] The medical records did not provide the percentile for these measurements. Dr. Marsh opined that J.W.'s head circumference at birth was in the 44th percentile. Resp. Ex. F at 1. Further, subsequent medical records report height and head circumference in metric units rather than inches.

(in the 28th percentile); and his head circumference was 35.0 cm (in the 12th percentile). Id. at 13. The assessment noted his weight was "now on the right track." Id. On June 24, 2016, J.W. again saw his pediatrician for a newborn weight check. Id. at 11-12. J.W.'s weight was 3.57 kg (in the 14th percentile); his height was 51.4 cm (in the 16th percentile); and his head circumference was 35.0 cm (in the seventh percentile). Id. at 11. His pediatrician noted he was "currently within normal expectations." Id. at 12.

He was next seen on July 1, 2016, for a one-month well-infant visit. Pet. Ex. 4 at 6. His weight was 3.88 kg (in the 19th percentile); his height was 52.7 cm (in the 20th percentile); and his head circumference was 36.0 cm (in the 11th percentile). Id. Assessment was normal. Id. at 7. J.W. received his second Hep B vaccine at this visit. Id. at 9.

He was seen on August 3, 2016, for a two-month well-infant visit. Pet. Ex. 4 at 4. His weight was 5.30 kg (in the 46th percentile); his height was 57.1 cm (in the 29th percentile); and his head circumference was 38.0 cm (in the 10th percentile). Id. Assessment was normal. Id. at 5. J.W. received pneumococcal conjugate, Hib-PRP-T, IPV, DTaP, and rotavirus vaccinations at this visit. Id.

On September 16, 2016, J.W. was seen by a different pediatrician as a new patient with a report of "chest congestion since birth" (noting that he sometimes seemed like he was wheezing) and "[three] days of projectile vomiting," with the note that "mom switched to Nutramigen on [September 15] and not vomiting since." Pet. Ex. 6 at 16. The patient history noted formula was introduced into J.W.'s diet around two months of age, and afterwards he had issues with spitting up and was diagnosed with reflux. Id. He had been spitting up more over the previous three days in "more projectile" fashion. Id. His formula had been switched to Nutramigen the previous day. Id. Assessment was "[s]pitting up infant" and "[n]asal congestion." Id. at 17. The examination was unremarkable. Id.

J.W. was seen again on September 22, 2016 for "left eye periorbital redness and possible pain," first noted on that date, and weight loss of two ounces since September 16, 2016. Pet. Ex. 6 at 14. At the time of the visit, the eye redness had significantly decreased. Id. J.W. had no fever or irritability. Id. He took bottles well with no vomiting or spitting up since starting Nutramigen. Id. Physical examination revealed "[l]eft eye slight redness and swelling around eye." Id. The plan was observation. Id. at 15.

On October 4, 2016, J.W. was seen for his four-month well-infant check. Pet. Ex. 6 at 11. He had cough and cold symptoms, so his parents held off on vaccinations. Id. His weight was 6.585 kg (in the 26th percentile); his height was 65 cm (in the 65th percentile); and his head circumference was 40.6 cm (in the 17th percentile). Id. at 13. Examination was normal except for mild congestion, and he was diagnosed with an upper respiratory tract infection ("URI"). Id. at 12-13.

J.W. returned on October 11, 2016 for his four-month vaccinations. Pet. Ex. 6 at 10-11. He was administered his second DTaP/Hib/IPV, second pneumococcal conjugate, and second rotavirus vaccinations. Id. at 11.

He returned October 21, 2016 for cough, congestion, and an intermittent, low-grade fever (maximum fever temperature was 99.5 degrees), all "since well visit [on October 4]," as well as a decreased appetite and vomiting (characterized as spitting up). Pet. Ex. 6 at 9. He was "[s]till pleasant and happy." Id. The examination was normal except for nasal congestion, and impression was viral URI with cough. Id. at 9-10. The pediatrician noted, "Reassured parents that he's well appearing and illness is likely [due to a] subsequent viral illness [and] not one continuously long illness." Id. at 10.

On November 8, 2016, J.W. was taken to the Children's Hospital of Philadelphia ("CHOP") for possible seizures with the following history in his neurology admission note:

> Beginning in mid-October, [his parents] noticed occasional twitching of his left leg. At the time, he was sick with a URI. He had nasal congestion, a dry cough, and possible fevers ([maximum temperature] measured as 100.3). He had also received his [four] month vaccinations [one] week prior to the beginning of these episodes. Parents report that they noticed [J.W.'s] leg fluttering once every other day and were not concerned. It appeared as a "muscle twitch." It only lasted for a matter of seconds and he had no associated symptoms. This left leg shaking progressed to his bilateral legs in the past week. Again, his legs were briefly shaking, which parents describe as "muscle twitches," every other day. The events lasted just a few seconds. He had no associated symptoms.
>
> This morning, [J.W.] woke from sleep around 7am. [Petitioner] moved him from his crib to his changing table. Just after setting him down on his back, he began to have rhythmic "shaking" movements of both legs. The "shaking" was coordinated and seemed to be limited in his legs. During this time, his eyes were open and deviated to the right. Additionally, he had a spurt of fast "blinking" with his right eyelid. Dad briefly tried to suppress the movement but could not. He was not responsive to his parents during this time. . . . The event lasted between [two to three] minutes and spontaneously resolved. Immediately after resolution, parents report that [J.W.] returned to his baseline, smiling, babbling and interacting with parents. He did not have any residual weakness or lethargy. Given this concerning episode, parents decided to bring [J.W.] to the CHOP [emergency department ("ED")]. [J.W.] was asleep in [Petitioner's] arms while checking in to the ED, and shortly after checking into the ED, [J.W.] woke from sleep and had a similar episode to the one previously described. Again there was rhythmic shaking of his lower extremities, he was focusing his eyes to the right, and the episodes lasted about [two] minutes and 30 seconds. Finally, he had a third episode in the ED. Again, the episode was described as the same as above and lasted between [two] and [three] minutes. He was not given any rescue medications in the ED.

Pet. Ex. 8 at 10.[7]

J.W. was admitted to CHOP. Pet. Ex. 8 at 10. He was found to have leukocytosis.[8] Id. On November 10, 2016, J.W. was discharged. Id. at 19. A video electroencephalogram ("EEG") showed "focal seizure activity from the midline central region during [a] clinical event, as well as four additional subclinical seizures with the same focal onset and electrographic pattern." Id. Brain magnetitic resonance imaging ("MRI") "was largely normal with no evidence of a seizure focus." Id. Neurologist France Fung, M.D., diagnosed J.W. with epilepsy. Id. at 21.

On December 16, 2016, in follow-up with his neurologist, Dr. Fung, it was noted that J.W.'s leg-jerking episodes first began two weeks prior to his hospitalization (October 25). Pet. Ex. 8 at 52. His "electroclinical seizures were reflex seizures, often triggered by diaper changes/anal wipe." Id. Those triggered seizures stopped on November 18, 2016, while J.W. was on an anti-epileptic titration, but his parents were concerned over the development of "repetitive right arm slapping/tapping movements" and episodes including J.W. "'throwing himself back' in an arching motion." Id. at 53. His hands were often fisted, and he would use his right hand to assist left-hand movements. Id. His development was "mostly age appropriate, although he [was] not sitting unsupported or rolling in both directions yet." Id. at 57.

On January 25, 2017, J.W. was seen in neurology follow-up for epilepsy by Marissa DiGiovine, M.D. (attending). Pet. Ex. 8 at 78-83. He was continuing to make developmental gains. Id. at 79-80. Neurology examination showed J.W.'s tone was slightly decreased bilaterally in the lower extremities. Id. at 82. Dr. DiGiovine noted J.W.'s parents reported they "have also not been giving vaccines because they are convinced that vaccines played a role in [J.W.] developing seizures, and they have joined vaccine injury groups. His mom also reports she tested positive heterozygosity for [MTHFR] gene that she reports makes her sensitive to preservatives in the vaccines." Id. at 79. The neurologist noted they "also discussed that it is highly unlikely that his vaccines had any [e]ffect on [J.W.] developing seizures and [she] would strongly advise continuing vaccines to protect him against communicable diseases," specifically recommending the flu vaccine. Id. at 82-83.

At a physical therapy ("PT") evaluation on February 27, 2017, J.W. was observed to have low tone throughout (hypotonia) and developmental delays. Pet. Ex. 9 at 3-4. His gross motor

[7] The ED provider's history of present illness also included "[history] of intermittent twitching of left leg over past two weeks;" "[four days] ago had episode [with] both legs twitching very intermittently and lasting only seconds;" "This morning after waking from a nap with twitching of both legs and right eye deviating to right, lasting approximately 90 seconds, no color change. Mom taped on phone. . . . Once episode stopped resumed normal behavior with babbling." Pet. Ex. 14 at 7 (also noting "chronic upper airway congestion" over the previous two months).

[8] Leukocytosis is "a transient increase in the number of leukocytes in the blood . . . pathologically accompanying hemorrhage, fever, infection, or inflammation." Leukocytosis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=28055 (last visited July 15, 2025).

quotient, derived from standard scores of subtests evaluating gross motor development, was less than first percentile. Id. at 5-6. PT was recommended weekly for twelve months. Id. at 7.

On April 13, 2017, J.W. was taken to a holistic pediatrics practitioner, Linda Colon-Adames, M.D., in Coral Springs, Florida, with the following history given:

> Seizure - Onset: 04/13/2017[9] - Began at [two] month[s] with twitches on leg where vaccine had been given. Twitches began at that same moment. Initially [Petitioner] had thought twitch had been because needle had been 'placed on nerve' but then twitches were seen on both legs then subsequently developed seizures. On meds.

Pet. Ex. 10 at 2. Dr. Colon-Adames provided Petitioner with a permanent medical exemption from vaccination for J.W., however, the medical reason for exemption is not reflected in the record. Id. at 140.

On April 14, 2017, J.W. was taken to the ED of Nemours/duPont Hospital for Children after Petitioner "notic[ed] that [J.W. was] having blank stares for the past few weeks." Pet. Ex. 6 at 24. When she called his neurologist the previous night, the neurologist requested an emergency EEG. Id. Petitioner reported that J.W. developed left leg twitching at two months, which "happened after [his two-] month vaccines." Id. She continued to report that "[a]t [four] months after [four-]month vaccines, [his] right leg started twitching too." Id. Petitioner wished to switch his neurology care to Nemours. Id. EEG showed "frequent sharp wave discharges arising independently in the right and left parietal-temporal regions" and "Periodic Lateralized Epileptiform Discharges, PLEDs, in the right temporal region." Pet. Ex. 9 at 89. No seizures were documented, but the pediatric neurologist Alana Salvucci, D.O., concluded, "The presence of independent sharp wave activity in the right and left parietal-temporal region suggests hyperexcitability and is indicative of an increased risk of partial and secondary generalized epileptic seizures which may arise from these regions." Id. at 90. The plan was to transition his epilepsy medication from Trileptal to Keppra. Pet. Ex. 6 at 27.

On May 2, 2017, J.W. was seen in the Nemours ED for increased seizure frequency, having had three absence seizures that day. Pet. Ex. 9 at 95. He was evaluated by pediatric neurologist Molly Deak, M.D. Id. at 99. His Keppra level was found to have been subtherapeutic, and he was discharged to follow up with neurology. Id. A May 11, 2017 overnight EEG showed occasional semi-rhythmic trains of sharp wave discharges, rare high amplitude discharges, and occasional spike and wave discharges in the left temporal and right frontal regions. Id. at 152. This suggested an increased risk of epileptic seizures arising from multiple origins. Id. at 153. J.W.'s last tonic clonic seizure had been in the fall, but he had been having staring episodes about once per week. Id. at 159.

J.W. was hospitalized from May 17-19, 2017, for increased seizure activity. Pet. Ex. 9 at 268, 277. On May 19, 2017, he had an occupational therapy evaluation, at which time it was

[9] This date appears to be an error, since it is the date of the visit and does not correspond with earlier histories given by J.W.'s parents.

noted that J.W. had inconsistent rolling, was unable to sit without support, did not finger feed, did not hold a bottle, and babbled. Id. at 224. The assessment documented, "[J.W.] demonstrated a weak core with poor head control and trunk stability for functional play positions. He also showed limited fine motor skills development." Id. at 226.

By October 15, 2018, J.W. saw medical geneticist Julie Kaplan, M.D., at Nemours. Pet. Ex. 19 at 5. The impression was in part,

> [J.W.] is a [two] year [four] month old boy with global developmental delay, seizures, hypotonia, and microcephaly. Whole exome sequencing [] showed a [variant of uncertain significance] in MTOR and a [variant of uncertain significance] in MT-CYB. We discussed with parents that, because these are variants of uncertain significance, we cannot say for certain if these mutations are causing his issues. Please see genetic counseling note by Kelly Kemak for full details of discussion.[10]

Id. at 11.

On November 23, 2018, J.W.'s neurologist, Dr. Salvucci, referred J.W. for an evaluation at Kennedy Krieger Institute, noting the following:

> [J.W.] has intractable epileptic encephalopathy, developmental delay[,] and hypotonia. [J.W.] experiences weekly seizures that can last [seven] minutes or longer and are typically associated with oxygen desaturations down to the 70's requiring administration of oxygen. [J.W.] has been on the following antiepileptic medications in the past: Onfi, Keppra, Trileptal[,] and Vimpat [on] which he had no improvement in his seizures. [J.W.] is currently on a Modified Atkins Diet and CBD oil. During seizures [Petitioner] gives [J.W.] CBD oil as an abortive medication. He responds to abortive CBD administration and [Petitioner] has a video where he is seizing and is given the medication through a syringe and the seizure abates. [J.W.] has undergone multiple diagnostic tests at our facility including an MRI, extensive laboratory tests, EEG's[,] and a whole exome sequencing. His whole exome sequencing did show a mitochondrial variant of unknown clinical significance in the MTCYB, which has not been reported as a pathogenic variant or benign variant. In addition, there was, on the whole exome, a MTOR related gene of autosomal dominant of unclear clinical significance.[11]

Pet. Ex. 12 at 1. On December 3, 2018, J.W. had an "[e]ssentially unremarkable non-contrast brain MRI." Pet. Ex. 11 at 36. As of December 24, 2018, Dr. Salvucci's impression included the following:

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[10] For the report from genetic counselor Kelly Kemak, MS, LCGC, see Pet. Ex. 19 at 12-14.

[11] See Pet. Ex. 11 at 3-4 (genetics testing report discussing mTOR gene). Later genetic testing determined that the mTOR gene variant was "likely benign." Pet. Ex. 44 at 4.

> [J.W.] is a [two]-year-old male [] with an epileptic encephalopathy of unknown etiology[] [and] he has had whole exome, as well as mitochondrial panel, which showed a variant of unknown clinical significance. He also has had recent spinal tap showing a low tetrahydrobiopterin. He does not fit the classical clinical picture, given that he does not have a clear movement disorder. I would like him to be seen by the Metabolic Clinic at CHOP to further gain insight into the interpretation of these results. . . . We did discuss today that [given] his unclear etiology, medical complexity would be best served with a neurologist specializing in Genetics and we will be happy to [follow up] on an as needed basis.

Pet. Ex. 12 at 129.[12]

The record overall supports that J.W. is profoundly globally developmentally delayed, consistent with Petitioner's affidavit. Pet. Ex. 1 at ¶¶ 70, 73-74; see, e.g., Pet. Ex. 31 at 177 (history provided during 2021 individual education program reevaluation).

Updated medical records reflect that a mitochondrial disorder is not suspected. See Pet. Exs. 44-45. Additionally, although genetic testing has been completed, no specific genetic abnormality has been identified relevant to J.W.'s epilepsy. Tr. 72-73; see also Pet. Ex. 44 at 4 (noting that mTOR was likely benign); Pet. Ex. 45.

2. Petitioner's Testimony and Affidavit[13]

Petitioner is the mother of the minor child, J.W. Tr. 16. She and her husband have two children, J.W. and an older daughter. Id. At the date of the hearing, J.W. was eight years old. Tr. 17.

Petitioner testified that with J.W. she had a healthy pregnancy with no complications. Tr. 17. When she was 32 weeks pregnant, she was in an elevator when it suddenly dropped "a few floors." Tr. 18. Her left leg "just gave out" and she sought care at a hospital, and was admitted for monitoring, but released the following day. Id.

J.W. was born on May 30, 2016. Tr. 18. There were no complications during labor and delivery. Id. J.W.'s APGAR scores were nine and nine. Id. He was a happy newborn, without any feeding issues, or behavioral symptoms. Tr. 19-21. He achieved his developmental

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[12] Lumbar puncture and cerebrospinal fluid ("CSF") testing were done as part of this evaluation. See generally Pet. Ex. 69. For autoimmune evaluation of the CSF, see Pet. Ex. 69 at 23-26. While no "informative autoantibodies were detected" in J.W.'s CSF results, the interpretive note stated that "a negative result does not exclude autoimmune encephalopathy" or other causes. Id. at 23.

[13] Petitioner testified at the entitlement hearing and submitted one affidavit. Tr. 16-67; Pet. Ex. 1. In her affidavit, Petitioner described J.W.'s clinical course after his diagnosis of epilepsy. See Pet. Ex. 1 at ¶¶ 25-74. As these events are documented in J.W.'s medical records, and discussed by the experts, Petitioner's account of them is not summarized herein.

milestones. Id. J.W. did not have any reaction to his first or second Hep B vaccinations. Tr. 21-22. On August 3, 2016, at his two-month visit, J.W. received his two-month vaccines. Tr. 22. These included pneumococcal conjugate, Hib-PRP-T, IPV, DTaP, and rotavirus. Tr. 26. He was doing great and achieving his age-appropriate milestones. Tr. 22. Physical examination showed that J.W. had "normal tone and symmetry of movement." Tr. 24. There were no abnormal findings. Tr. 25.

The evening after his two-month vaccinations, J.W. was fussy, irritable, had a low-grade fever, and "was arching himself back, and he just wasn't himself." Tr. 26. He had redness and a little swelling around the vaccination injection site. Id. Most of the symptoms went away in a few days, but J.W. continued to have low-grade fevers (between 99.9 and 100.3 degrees) and arching of his back. Tr. 27, 31. Also, within a few days, J.W.'s parents noticed that his "left leg would [] flare out and do . . . [an] up and down motion movement." Tr. 27.

At the hearing, Petitioner showed a video she took on August 20, 2016. Tr. 28; Pet. Ex. 71; see also Pet. Ex. 70. The video showed very subtle jerking of J.W.'s left leg. Tr. 29-30. Petitioner testified that this leg jerking began two to three days after his two-month vaccinations. Tr. 32. It occurred most often during his diaper change or when he was falling asleep or waking from a nap. Tr. 32, 34. Petitioner though it was a response to the vaccine given in his leg, thinking it "hit a nerve," and causing pain during J.W.'s diaper changes. Tr. 32-33. The movements did not concern Petitioner because J.W. looked fine, and she thought the person who administered the vaccines "pushed too hard and possibly hit a nerve." Tr. 33.

On September 16, 2016, Petitioner took J.W. to CHOP Care Network, a different pediatric practice, to establish care. Tr. 35. J.W. was having congestion, vomiting, and reflux. Tr. 36. Petitioner expressed her concern about J.W.'s leg jerking to the nurse and was told it was normal baby behavior. Id. At the hearing, Petitioner was questioned about the records from this visit, because the records do not reference J.W.'s leg jerking. Tr. 37-41. There is, however, a reference to pain. Tr. 38 (citing Pet. Ex. 6 at 16). Petitioner explained that she thought J.W. had pain in his left leg. Id. The record also references reflux issues and nasal congestion. Tr. 38-39. Four-month vaccines were offered at this visit, but Petitioner deferred these vaccines since J.W. was not feeling well at that visit. Tr. 39-40.

At J.W.'s four-month well-child visit on October 4, 2016, Petitioner again brought up the leg jerking issue and was told it was normal. Tr. 42. J.W.'s physical examination was documented as normal. Tr. 42-43 (citing Pet. Ex. 6 at 12-13). The pediatrician said he was reaching age-appropriate milestones and there were no concerns with his development. Tr. 43.

J.W. was taken back to the pediatrician by Petitioner on October 11, 2016 because he was continuing to have "back-to-back respiratory infections." Tr. 44. He received his four-month vaccines this visit, including DTaP/Hib/IPV, pneumococcal conjugate, and rotavirus. Id. After receiving these vaccinations, J.W. was fussy, irritable, had redness and swelling at the vaccine injection site, low-grade fevers, screaming, and arching his back. Tr. 45. Within a few days, he began having up and down movements of both legs. Id. Sometime after the vaccinations on October 11 but before November 4, Petitioner took a video of J.W. during a diaper change, showing the up and down movement in both legs. Tr. 48-49 (citing Pet. Ex. 65). Petitioner

confirmed that the bilateral leg jerking referenced in her affidavit began in mid-October, as depicted in the video. Tr. 50; see also Pet. Ex. 1 at ¶ 27.

Due to her concern about J.W.'s bilateral leg jerking movements, Petitioner made an appointment for October 21, 2016. Tr. 50-51. The note from that visit stated that J.W. had an intermittent low-grade fever since October 4. Tr. 52 (citing Pet. Ex. 6 at 9-10). The record also referenced pain, but did not state that J.W. had bilateral leg jerking. Tr. 52-53 (citing Pet. Ex. 6 at 9-10). Petitioner testified that she does not know why this complaint was not documented. Tr. 53. Petitioner also recalls that towards the end of October, after the visit to the pediatrician on October 21, J.W. was "very sick and his pupils were very dilated." Id.

In the early morning of November 8, 2016, Petitioner went to change J.W.'s diaper and found him in a "full-blown seizure" with shaking of his arms, legs, and body. Tr. 54. His "eye was [] rapidly going up and down." Id. Petitioner took a video of J.W.'s seizure. Tr. 55 (citing Pet. Ex. 66). She took J.W. to the ED at CHOP and on arrival J.W. was seizing. Tr. 56. Many diagnostic tests were done and J.W. was given a diagnosis of epilepsy. Id. Since then, his seizures have not resolved. Id. There were days he had up to about a hundred very short seizures and other times that he had "longer, very bad seizures" lasting up to 20 minutes. Tr. 57.

J.W.'s current diagnosis is intractable epilepsy, developmental delay, and hypotonia. Tr. 58. He has been given many different medications, but none have helped. Id. The cause of J.W.'s seizure disorder was thought to be genetic, but "that was ruled out." Tr. 59. J.W. is unable to talk, or walk, or chew his food. Tr. 60. His seizures are typically short and he may have one to two a day, while waking or falling asleep. Tr. 59. Therapists provide care to him daily. Tr. 59-60.

On cross-examination, Petitioner was asked about her affidavit. Tr. 61-65; see Pet. Ex. 1. In the affidavit, she did not mention that after J.W.'s two-month vaccinations he had a high pitched scream, which she testified about at the hearing. Tr. 62-63; Pet. Ex. 1 at ¶ 15. When asked why she did not include that fact in her affidavit, Petitioner explained that she did not realize she left it out of her affidavit. Tr. 62-63.

Petitioner also explained that she did not call the physician after J.W.'s two-month vaccinations because at the time, it did not seem like an emergency, and according to the paperwork they received, the post-vaccination symptoms seemed common. Tr. 63. They were told that if J.W. had a high fever, that would be concerning. Id. Regarding the arching of his back, Petitioner testified that while J.W. still does this occasionally, it mostly cleared up. Tr. 64.

As for the failure of the records to note J.W.'s leg jerking, Petitioner testified that she did not "know why they [the health care providers] didn't record it." Tr. 65. She added that there were "several things that were misreported in the records." Id.

3. Declaration of Cynthia Carroll[14]

Ms. Carroll is the maternal grandmother of J.W. Pet. Ex. 68 at ¶ 1. She has been involved in J.W's life since his birth. Id. at ¶ 2. She lives near J.W., visits him often, and is "familiar with J.W.'s behaviors and routines." Id. at ¶¶ 3-4. Her declaration addressed the onset of J.W.'s leg jerking.

While Ms. Carroll couldn't recall the exact date that she first witnessed J.W.'s leg jerking, she averred the leg jerking occurred after J.W. received his two-month vaccines. Pet. Ex. 68 at ¶ 5. Ms. Carroll recalled that Petitioner "called her in a panic and asked her to come over right away" and she recalled J.W's "left leg jerking because it was an unusual movement" that Ms. Carroll "had never seen before in any child." Id. at ¶¶ 5-6. In early November 2016, Ms. Carroll was watching J.W. while his parents and sister were away. Id. at ¶ 7. She observed that "the left leg jerking was now in both of his legs" with the episodes "becoming more intense" and occurring "much more frequently than when it was just the left leg that was affected." Id. at ¶ 8.

C. Expert Reports[15]

1. Petitioner's Expert, Yuval Shafrir, M.D.[16]

a. Background and Qualifications

Dr. Shafrir currently practices, *locum tenens*, as a pediatric neurologist. Tr. 91. He is board-certified in neurology with a specialty in pediatric neurology and clinical neurophysiology. Tr. 89; Pet. Ex. 72 at 1. He received his M.D. from Tel Aviv University Sackler School of Medicine in Israel and conducted his pediatric residency rotations in Israel. Tr. 89; Pet. Ex. 72 at 1. After moving to the United States, he completed a pediatric residency at Cornell University Medical College. Pet. Ex. 72 at 1. Afterwards, Dr. Shafrir completed a fellowship in pediatric neurology at Washington University Medical Center in St. Louis and a second fellowship in pediatric neurophysiology and epileptology at Miami Children's Hospital in Florida. Id. In

[14] Ms. Carroll submitted one declaration. Pet. Ex. 68.

[15] For the sake of brevity, the undersigned does not summarize all the experts' opinions but only those relevant to the material issues. Where a parties' expert's opinions are duplicative or repetitive with another expert, the duplicative opinions are not summarized. Additionally, the expert report of Dr. Shlomo Shinnar is not discussed, since he was withdrawn as pediatric neurology expert by Respondent. See Resp. Motion for Extension of Time to File Expert Reports, filed June 28, 2022, at 1 (ECF No. 75) ("Dr. Shinnar has become unavailable to [R]espondent. This is not based on case specific analysis and applies to all cases in which Dr. Shinnar may have given testimony."). The undersigned has, however, reviewed his expert report. Even if Dr. Shinnar's report had been discussed and considered, the outcome would be the same.

[16] Dr. Shafrir testified at the entitlement hearing and submitted two reports. Tr. 88-180, 428-450. Pet. Exs. 24, 36.

addition to his active private practice in pediatric neurology, Dr. Shafrir previously served as an assistant Professor in neurology and pediatrics at multiple academic and medical institutions, most recently, Penn State College of Medicine. Id. at 6-7. He has published more than 20 peer-reviewed articles and abstracts on topics of such as gene mutations in epilepsy, EEG findings, and Dravet syndrome. Id. at 8-9; Tr. 90-91. Dr. Shafrir was offered and admitted as an expert in pediatric neurology and epileptology without objection. Tr. 92-95.

b. Opinions

Dr. Shafrir opined that J.W. has "a severe form of progressing epileptic encephalopathy." Tr. 97; Pet. Ex. 24 at 61. The causes of this form of encephalopathy can be genetic, brain malformation, insult during pregnancy (i.e., inflammatory infection), postnatal infections (i.e., herpes simplex virus infection), and immunological conditions (i.e., infantile spasms associated with antineuronal antibodies). Tr. 97-98. He testified that vaccines can also cause encephalopathy. Tr. 98.

J.W.'s illness was further described by Dr. Shafrir as a progressive illness, demonstrated by his EEG and development regression over the first three years of his life. Tr. 98-99. Relative to J.W.'s seizures, Dr. Shafrir defined seizures as behavioral changes which typically have a "correlated change in the EEG." Tr. 99. Behavioral changes seen in seizures can range from a "little twitching of one limb or the eye [] to a full-blown status epilepticus" characterized by continuous shaking that can be difficult to stop. Tr. 99-100.

During the hearing, Dr. Shafrir reviewed the video of J.W. taken August 20, 2016, showing what Petitioner described in her affidavit and testimony as leg jerking. Tr. 100 (reviewing Pet. Ex. 71). Dr. Shafrir testified that "in isolation" this was possibly a seizure, but no one could say that it was "necessarily a seizure." Tr. 100-01.

However, a later "second video"[17] and "most importantly . . . the video EEG from [CHOP]" show a "very unusual seizure." Tr. 101. The EEG provides evidence that clearly shows a seizure.[18] Id. In the second video, the "movement of the legs are clearly jerky, with the rapid phase followed by [the] slower phase." Id. Dr. Shafrir described this as an "unusual seizure" because it was isolated to one leg and the child was able to maintain consciousness during the seizure, characteristic of a "simple partial seizure." Tr. 101-02, 170. Dr. Shafrir opined that "after the onset of this seizure," J.W. had arrested development, hypotonia, and declining head growth. Tr. 103. According to Dr. Shafrir, these changes heralded the onset of J.W.'s epileptic encephalopathy and occurred after the second set of vaccinations. Tr. 103-04.

[17] Although Dr. Shafrir references a "second video" no exhibit number was provided, so it is not clear which video he was referencing.

[18] J.W. was admitted to CHOP on November 8, 2016. Pet. Ex. 8 at 19. Video EEG done during that admission captured "[one] clinical push button event[] . . . with 20 seconds of lower extremity circumduction. His video EEG showed focal seizure activity from the midline central region during his clinical event, as well as four additional subclinical seizures with the same focal onset and electrographic pattern." Id.

Dr. Shafrir made it clear that J.W. did not have febrile seizures. Tr. 177. With febrile seizures, there is "significant fever," and there is no indication in the record that J.W. had such a fever. Id.

i. Althen Prongs One and Two

Dr. Shafrir opined that the "DTaP vaccination can cause encephalopathy." Pet. Ex. 24 at 63. Dr. Shafrir opined that the whole cell pertussis vaccine, found in the diphtheria tetanus pertussis ("DTP") vaccines[19] can cause "an increased reaction, initially of the innate immune system with production of cytokines, that then affect that cytokine in the brain," followed by "reproduction of the cellular and then humoral arms of the adaptive immune system that cause[] a persistence of symptoms." Tr. 105. According to Dr. Shafrir, the NCES study[20] found that the DTP vaccination caused "significant neurological dysfunction." Id. (citing Pet. Ex. 24, Tab K). However, the NCES study did not study the acellular form of the pertussis vaccine found in DTaP vaccination.

In support of his position that the acellular form of the DTaP vaccine also causes seizures and encephalopathy, Dr. Shafrir cited a paper by Zieliński and Rosińska.[21] Tr. 105-06 (citing

[19] DTP vaccines contain whole cell pertussis vaccine combined with diphtheria and tetanus toxoids while DTaP vaccines contain acellular pertussis vaccines combined with diphtheria and tetanus toxoids. See, e.g., Resp. Ex. C, Tab 6 at 2 (Wan-Ting Huang et al., Lack of Association Between Acellular Pertussis Vaccine and Seizures in Early Childhood, 126 Pediatrics e265 (2010)). In 1997, the Advisory Committee on Immunization Practices recommended adoption of acellular pertussis vaccines. Id. DTaP vaccines (including DTaP component or combination vaccines) are the only pertussis vaccines currently licensed for children in the United States. Id.

[20] The National Encephalopathy Study ("NCES study") was a 1976 United Kingdom study set up as an independent scientific enquiry into severe acute neurological illnesses associated with whole cell pertussis vaccine. Pet. Ex. 24, Tab K at 10 (R. Alderslade et al., The National Childhood Encephalopathy Study: A Report on 1000 Cases of Serious Neurological Disorders in Infants and Young Children from the NCES Research Team, in Whooping Cough: Reports from the Committee on Safety of Medicines and the Joint Committee on Vaccination and Immunisation (Her Majesty's Stationary Office, 1981)). The researchers found a "statistically significant association between the onset of various neurological disorders [] and immunization with [DTP] vaccine within the previous [seven] days . . . . The association with DTP was greatest within the first 72 hours, and for cases of severe convulsions or encephalopathy." Id. at 40. The authors "emphasised that the estimates of risks are made *without* exclusion of cases in which there is evidence of another possible cause." Id.; see also Pet. Ex. 24, Tab L (DL Miller et al., Pertussis Immunisation and Serious Acute Neurological Illness in Children, 282 Brit. Med. J. 1595 (1981) (providing further details on the NCES study)).

[21] Andrzej Zieliński & Magdalena Rosińska, Comparison of Adverse Effects Following Immunization with Vaccine Containing Whole-Cell vs. Acellular Pertussis Components, 62 Epidemiologiczny 589 (2008).

Pet. Ex. 24, Tab N). The authors conducted a large scale study of the adverse effects after whole cell and acellular pertussis vaccinations from 2001 to 2005 in Poland. Pet. Ex. 24, Tab N at 1. The study compared 7,031,929 doses of whole cell pertussis with 1,334,143 doses of acellular pertussis. Id. at 4 tbl.II. Relative to afebrile seizures, 37 children who received the whole cell vaccine had a first episode of afebrile seizures compared to three in the acellular group. Id. Eleven children who received the whole cell vaccine had acute encephalopathy compared with two in the acellular group. Id. The authors noted that "[a]cute encephalopathy occurred very rarely in either group. It was reported only in two cases following acellular vaccine." Id. at 6. "Although [acute encephalopathy] follows injections with pertussis vaccine[,] it is so rarely reported[,] [and] its occurrence seems to require some other special predisposing factors, which should be carefully investigation in all cases of reported post-vaccination encephalopathy." Id. The authors concluded that while severe reactions are "very rare after either type . . . and even if they are more frequent after whole cell vaccines, the rates were not significant[ly]" different between the two groups. Id.

Next, Dr. Shafrir turned to a discussion of cytokines. Tr. 109. He cited an article by Talaat et al.[22] that showed the effect of the influenza vaccination on cytokines in healthy volunteers. Tr. 108-09 (citing Pet. Ex. 36, Tab 9). Dr. Shafrir explained that there was one "outlier" who had a cytokine reaction ten times greater than the other study participants. Tr. 109 (citing Pet. Ex. 36, Tab 9 at 6 fig.3). According to Dr. Shafrir, the outlier patient did not have an adverse reaction, but he did have fever and malaise, illustrating the "individual differences in reaction of the immune system." Tr. 109-10.

Relevant here, Dr. Shafrir opined that "the vaccine[23] caused an inflammatory reaction in the brain that produced initiation of a seizure, and then the seizure continued because of [an] ongoing autoimmune process, and that continued to cause seizures and encephalopathy." Tr. 104. Dr. Shafrir "presume[d]" that J.W. had an "excessive cytokine reaction that produced [] the initial seizures" but these "did not persist or [] progress into epileptic encephalopathy." Tr. 110; see also Tr. 116.

After J.W.'s second vaccination, his condition became "much more severe," which Dr. Shafrir "presume[d]" was caused by the "production of autoantibodies . . .and then autoreactive cells," and that after the initial cytokine reaction, there were "several mechanisms by which the epileptic encephalopathy [] could persist." Tr. 110. One of these mechanisms was "the effect of the seizures themselves." Id. This mechanism, known in neurology research as "seizure beget seizures," is based on the "negative effect of the seizures [] on the surrounding brain area," resulting in more seizures. Tr. 111; see also Tr. 117.

Addressing other mechanisms, Dr. Shafrir opined that the mechanism of molecular mimicry and production of autoantibodies leads to autoimmunity in the brain. Tr. 111. In

[22] Kawar R. Talaat et al., Rapid Changes in Serum Cytokines and Chemokines in Response to Inactivated Influenza Vaccination, 12 Influenza & Other Respiratory Viruses 202 (2018).

[23] Dr. Shafrir's references to "the vaccine" or "vaccine" in the singular form is presumably to the DTaP vaccine.

support of this mechanism, Dr. Shafrir referenced studies about homology between proteins in the DTaP vaccine with proteins in nerve transmitter receptors in the brain. Pet. Ex. 24 at 65 (citing Pet. Ex. 24, Tab zFF);[24] see also Tr. 111. Dr. Shafrir also provided a paper by Lucchese et al.,[25] who reported that "the tetanus neurotoxin and human epilepsy antigens share an ample pentapeptide platform," which "support[s] the possibility that immune cross-reactions may occur between [tetanus toxin] and epilepsy-related proteins." Pet. Ex. 24, Tab zGG at 2.

Relative to J.W.'s negative autoimmune encephalopathy panel, Dr. Shafrir opined that the negative results do not indicate that he did not have an inflammatory response or an immune reaction.[26] Tr. 112-13. Regardless, Dr. Shafrir opined that J.W.'s negative autoimmune panel "does not affect [his] theory." Tr. 114. This is because the "absence of an identifiable autoantibody does not rule out an immune reaction." Tr. 115; see also Tr. 437-39.

He acknowledged, however, that J.W. did not have autoimmune encephalitis, but instead had a milder condition, "autoimmune encephalopathy." Tr. 113. Dr. Shafrir did not explain the significance of this distinction in diagnosis as it relates to the absence of identifiable autoantibodies. See id. He also did not define or explain how J.W.'s clinical course was consistent with autoimmune encephalopathy.

Regarding lack of fever, Dr. Shafrir opined that there are a "minority of patients who clearly have . . . afebrile seizures after DTaP vaccination." Tr. 442. He added, "[b]ut if there is no fever, there is something else" that causes the seizure. Tr. 443. This "something else" could be "environmental and immunological causes that cause the patient to have seizures after the vaccination." Id. For example, according to Dr. Shafrir, in Dravet syndrome,[27] "cytokines [] go[] from the area of the vaccination into the brain and cause patients who have major susceptibility for seizures because of the SCN1A mutation . . . to have seizures." Id.

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[24] Darja Kanduc, Peptide Cross-Reactivity: The Original Sin of Vaccines, 4 Frontiers Biosci. 1393 (2012).

[25] Guglielmo Lucchese et al., The Peptide Network Between Tetanus Toxin and Human Proteins Associated with Epilepsy, 2014 Epilepsy Rsch. & Treatment 236309.

[26] J.W.'s CSF panel from December 2018 reported that no inflammatory autoantibodies were detected. Tr. 115 (citing Pet. Ex. 69 at 23).

[27] Dravet syndrome is a form of epileptic encephalopathy associated with SCN1A genetic mutations. Resp. Ex. H at 4 (Markus von Deimling et al., Epileptic Encephalopathies—Clinical Syndromes and Pathophysiological Concepts, 17 Current Neurology & Neurosci. Reps. 1 (2017) (Respondent's expert, Dr. Marsh is a named author)). "[S]eizures in Dravet syndrome start in the first year of life, as unilateral clonic or generalized tonic-clonic febrile seizures that are often prolonged . . . ." Id. "Patients often have significant developmental delay and cognitive dysfunction with most patients developing unremarkably in their first year of life, before cognitive functions plateau or decline in the second year of life." Id. J.W. has not been diagnosed with Dravet syndrome. Tr. 151.

The concept of challenge-rechallenge was also discussed by Dr. Shafrir. Tr. 117. Dr. Shafrir defined the concept as abnormal events which occur after both exposure and re-exposure. Tr. 118. If the abnormal event is a "definite reaction" to vaccination, it is "challenge-rechallenge" which is used in "clinical medicine to define [a] definite reaction" to an exposure to medication or vaccination. Tr. 119, 179-80. He noted that, according to Petitioner, J.W. had "two episodes of similar and abnormal[] seizures following each [set of] vaccine[s]." Tr. 118. He further opined that J.W.'s seizures after each vaccination represented challenge-rechallenge. Tr. 119. Dr. Shafrir testified that rechallenge occurred after the second set of vaccinations because the "seizure became more severe." Tr. 180.

Specific to how inflammation in the brain can cause epileptic encephalopathy, Dr. Shafrir cited a paper by Shandra et al.[28] Tr. 120 (citing Pet. Ex. 24, Tab zAA). Although the focus of the paper is a specific type of infantile epileptic encephalopathy, West Syndrome, Dr. Shafrir cited the paper for the mechanisms of inflammation and neuroinflammation. Tr. 120-23. The authors stated that "prior studies" have "associated elevated levels of proinflammatory cytokines with seizures, the pathogenesis of epilepsy, and pathologies manifesting epilepsy." Pet. Ex. 24, Tab zAA at 3. The authors reviewed the current literature about inflammation pathways in the brain of children which can cause seizures and epilepsy. Id. at 3-5. They also discuss treatment, including "inhibition of inflammation" and "ketogenic diet." Id. at 11. However, the paper does not reference vaccination, or cytokine induction of neuroinflammation caused by vaccination.

Turning to animal studies, Dr. Shafrir referenced a study by Lassmann et al.,[29] where mice were immunized with complete Freund's adjuvant and pertussis toxin to induce central nervous system ("CNS") immune pathology resulting in "clinical disease" characterized by loss of activity, mild tremors, and motor changes. Pet. Ex. 24, Tab zKK at 1; Tr. 124. Dr. Shafrir opined that the study showed that components of the DTP vaccine can enhance brain inflammation. Tr. 127. Lassman et al. opined their study findings "strongly suggest[ed] that the cytokine milieu of a tissue can dramatically influence the development of intrinsic immune responses and associated pathology." Pet. Ex. 24, Tab zKK at 2, 5. However, Dr. Shafrir did not show that the vaccinations administered here contained complete Freund's adjuvant or *Mycobacterium*, which is not given to humans due to its toxicity. See id. at 3.

[28] Oleksii Shandra et al., Inflammation in Epileptic Encephalopathies, 108 Advances Protein Chemistry & Structural Biology 59 (2017).

[29] Silke Lassmann et al., Induction of Type 1 Immune Pathology in the Brain Following Immunization Without Central Nervous System Autoantigen in Transgenic Mice with Astrocyte-Targeted Expression of IL-12, 167 J. Immunology 5485 (2001).

Although Dr. Shafrir agreed it is "hard to know" the mechanism, he opined the DTP[30] vaccine has the ability to "produce epileptic discharges in the EEG." Tr. 129. He cited Nouno et al., for the proposition that the DTP vaccination can cause "epileptic discharges in the EEG." Tr. 128-29 (citing Pet. Ex. 24, Tab J).

Nouno et al. studied post vaccination EEG results in children with pre-existing epilepsy/convulsive disorders or febrile seizures from 1986 to 1988. Pet. Ex. 24, Tab J at 2. Of the 61 children, the majority were on anticonvulsant medication. Id. "Of the 116 immunizations given, in 21 cases (18.1%) there were epileptic spikes on EEG's examined immediately before immunization." Id. at 3. Of the 67 children who received DPT vaccines (acellular), there was a "reappearance of epileptic spikes was observed in [nine] (13.4%) and increase of epileptic spikes in [eight] (11.9%)." Id. at 4. However, in children without seizures, "no EEG changes were observed . . . after . . . [the] combined pertussis and diphtheria vaccine." Id. at 5. The authors did not attribute the post-vaccination seizures in the children with pre-existing seizure disorders to cytokines driven inflammation or the other mechanisms discussed by Dr. Shafrir.

Although Dr. Shafrir opined that J.W.'s condition was progressive, he disagreed that J.W.'s microcephaly began at birth. Tr. 443. He opined that J.W.'s head circumference at birth was 44% and the last measurement before the onset of his encephalopathy was 17%.[31] Id. And then it went from 11% to 17%. Tr. 444. Dr. Shafrir explained that in microcephaly there is steady decline, not a decline and then increase. Id. Dr. Shafrir did not appear to address the overall decline in head circumference from 44% to 17%. See Tr. 443-44.

In summary, Dr. Shafrir opined that the vaccines that J.W. received on August 3 and October 11, 2016 were the cause of his seizure disorder and resulting encephalopathy. Tr. 132. His opinion is based on the "lack of other causes and the fact that [J.W.] must have some propensity to [development of seizures and epileptic encephalopathy] that we have not yet identified." Id. While Dr. Shafrir "[a]bsolutely agree[d]" that the best fit for J.W.'s condition is genetic, there has been "no genetic explanation found" in the extensive genetic workup. Tr. 133-34. A developmental genetic epilepsy is "definitely . . .the first thing that" that he would consider when he sees "a child like J.W.," however, here, "a genetic cause was not found, period." Tr. 134. Because a genetic cause was not found, Dr. Shafrir concluded that, more likely than not, that J.W.'s epileptic encephalopathy was caused by the two vaccinations. Tr. 135; see also Tr. 148 (disagreeing that genetic abnormality can be the "only cause" for J.W.'s condition).

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[30] Dr. Shafrir used "DTP" without explicitly noting that it contains to whole cell pertussis. Tr. 127-29. However, in the Japanese study by Nouno et al., the authors used the abbreviation "DPT" for an acellular form of the vaccine. See Pet. Ex. 24, Tab J at 2 (Shin Nouno et al., Adverse Effects on EEG and Clinical Condition After Immunizing Children with Convulsive Disorders, 32 Acta Paediatrica Japonica 357 (1990)). Additionally, Dr. Shafrir noted DTP contains whole cell pertussis in earlier testimony. See, e.g., Tr. 105.

[31] Dr. Shafrir also testified that three days after birth, J.W.'s head circumference was documented at 22%, down from 44% at birth, and asserted that this showed "the measurement is not that accurate." Tr. 443.

On cross-examination, Dr. Shafrir agreed that J.W.'s treating physicians did not attribute his epileptic encephalopathy to an immune dysfunction. Tr. 138-39. However, the fact that they tested J.W. for autoantibodies meant to Dr. Shafrir that the physicians thought J.W. could have an immune dysfunction. Tr. 139. Other than the testing for autoantibodies, Dr. Shafrir agreed that none of J.W.'s treating physicians opined that he had autoimmune dysfunction. Id. And he conceded that none of J.W.'s treating physicians ever diagnosed J.W. with autoimmune encephalopathy. Id.

Other than a ketogenic diet,[32] Dr. Shafrir agreed that J.W.'s treating physicians did not treat him for an autoimmune condition or prescribed immunomodulating medications. Tr. 140. Moreover, if Dr. Shafrir had been J.W.'s treating neurologist from November 2016 through April 2017, he would not have prescribed immune treatment or steroids unless J.W.'s spinal fluid showed high protein levels.[33] Tr. 143-44.

An important point that Dr. Shafrir agreed with is that J.W. did not have a febrile seizure. Tr. 151. He further agreed that J.W. did not have evidence of an exaggerated cytokine response after vaccination. Tr. 152. J.W. had irritability and some fever that last for several days, as well as redness of the vaccine site, but he acknowledged that these signs and symptoms occur in many children who do not develop epilepsy. Id. The only evidence of any overreaction of the innate immune system here is Dr. Shafrir's hypothesis of how the vaccines caused J.W.'s epileptic encephalopathy. Id. In other words, Dr. Shafrir maintained the evidence for an exaggerated cytokine response is based on the fact that J.W. "developed seizures." Tr. 153. He further asserted that the specific cytokines involved in J.W.'s epileptic encephalopathy were IL-1, IL-6 and IL-2, although Dr. Shafrir conceded he did not have "any material evidence" to support this opinion. Tr. 153.

Dr. Shafrir opined that J.W. was "a congested child" with breathing problems. Tr. 161. On cross-examination, he also agreed that between the two-month and four-month vaccinations, there was clinical evidence that J.W. had an URI. Id. However, later in his testimony, on redirect, he opined that J.W. did not have "red throat or anything" to suggest that he had an URI. Tr. 178. He also testified that J.W. did not receive any medication for treatment of a URI during this timeframe. Tr. 179. Lastly, Dr. Shafrir acknowledged that infections can cause cytokine reactions and trigger autoimmune encephalopathy. Tr. 162.

ii. Althen Prong Three

[32] A ketogenic diet "is a high-fat, adequate-protein and low carbohydrate diet proven to be an effective and safe treatment for refractory epilepsy." Pet. Ex. 34, Tab 14 at 1 (Fen-Fen Ni et al., The Effects of Ketogenic Diet on the Th17/Treg Cells Imbalance in Patients with Intractable Childhood Epilepsy, 38 Seizure 7 (2016)). The diet has "anticonvulsant and anti-inflammatory effects." Id. at 6.

[33] No CSF testing was performed during J.W.'s November 2016 hospitalization.

In his first expert report, Dr. Shafrir noted that J.W. had two episodes of leg twitching. Pet. Ex. 24 at 60. The first episode occurred after his two-month vaccines on August 3, 2016, and the second episode after his four-month vaccines on October 11, 2016. Id. He based these opinions on Petitioner's affidavit and the records from J.W.'s admission to CHOP on November 8, 2016. Id.

At the hearing, Dr. Shafrir testified that "[u]nfortunately, we don't have an accurate timetable for the onset of the seizures in relation to the vaccine." Tr. 133. He testified that "the jerks started in mid-October . . . probably a few days after the [second] vaccination[s]." Id. Based on Petitioner's affidavit, averring that the seizures began in October (after the second set of vaccinations), the second video, and the video EEG, Dr. Shafrir opined that the seizures started mid-October, "a few days after the vaccination[s]" on October 11, 2016. Id.

When questioned about the video taken August 20, 2016, and whether it showed seizures that manifest as unilateral leg jerking, Dr. Shafrir initially testified that "[he] couldn't look at this video and say that [J.W.] has a seizure. [He] would say [J.W. was] just kicking." Tr. 155. Dr. Shafrir added that the only way to say that the August 20, 2016 video shows a seizure is "based on . . . what happens after that." Id. Upon continued questioning, he ultimately opined that more likely than not, J.W. had seizures after his first vaccination in August 2016. Tr. 156. But he was unable to say whether there was a disappearance of the seizure activity after the first vaccination, and a recurrence after the second vaccination. Id. If there was worsening after the second vaccination, he characterized it as a rechallenge. Tr. 156-57.

Relative to the onset of encephalopathy, Dr. Shafrir testified that the first indication of J.W.'s encephalopathy was after his admission to CHOP, when his neurological examination revealed hypotonia. Tr. 136-37. Dr. Shafrir compared J.W.'s clinical course to Dravet's syndrome,[34] where encephalopathy begins slowly, when the child becomes delayed and hypotonic.[35] Tr. 137. Here, Dr. Shafrir initially testified that J.W.'s "first clinical symptom of encephalopathy" was his irritability the night after the first set of vaccines. Tr. 136. He then opined the first clinical manifestation of encephalopathy was after November 8, 2016. Tr. 138.

[34] For additional information about Dravet Syndrome and other encephalopathies, see Resp. Ex. H. Dr. Shafrir also provided a case report describing a child with Dravet syndrome who, like J.W., had seizures triggered by diaper changes. See Pet. Ex. 36, Tab 1 (Puneet Jain et al., Perineal Stimulation Triggering Seizures in a Child with Dravet Syndrome, 62 Seizure Eur. J. Epilepsy 106 (2018)).

[35] Although Dr. Shafrir did not identify any onset date for hypotonia or developmental delays, the medical records first reference hypotonia on January 25, 2017, when a neurology examination noted mild decrease in muscle tone in J.W.'s lower extremities. Pet. Ex. 8 at 82. On February 27, 2017, a physical therapy evaluation first noted that J.W. was delayed in developmental milestones and documented low tone (hypotonia) throughout. Pet. Ex. 9 at 3-4.

2. Petitioner's Expert, Omid Akbari, Ph.D.[36]

a. Background and Qualifications

Dr. Akbari is a professor of immunology and professor of medicine at the University of Southern California, Keck School of Medicine. Pet. Ex. 34 at 2; Tr. 182. He received a Ph.D. in cellular and molecular immunology at the National Institute for Medical Research in London, United Kingdom. Tr. 182. Thereafter, he completed a postdoctoral fellowship at Stanford University. Id. Dr. Akbari's research focuses on the "investigating and characterizing the mechanisms underlying the regulation of the acquired and innate immune response." Pet. Ex. 34 at 2. His laboratory research includes multiple studies regarding how an "antigen, allergen, or vaccine can result in an appropriate or dysregulated immune response and inflammation." Id. at 2-3. Dr. Akbari serves as an associate editor and reviewer on several journals. Id. at 2. He has authored or co-authored numerous publications. Id. Dr. Akbari was offered and admitted as an expert in immunology without objection. Tr. 185.

b. Opinions

Dr. Akbari opined that the two sets of vaccinations received by J.W. directly contributed to the "induction" of his "epileptic seizure" and epileptic encephalopathy. Tr. 186, 426. Dr. Akbari is not a medical doctor, so his focus and area of expertise was immunology.

i. Althen Prong One[37]

Dr. Akbari opined that there are "a variety of ways that the immune response can cause a seizure" but focused on cytokines.[38] Tr. 196. He explained that cytokines are very small, "so they can pass [the] blood brain barrier." Id. According to Dr. Akbari, cytokines can also "act on the dendrons of the nervous system" and conduct "signal[s] to the CNS." Id. Cytokines can "actively import[] proinflammatory cytokines and chemokines inside" the blood-brain barrier.

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[36] Dr. Akbari testified at the entitlement hearing and submitted one report. Tr. 181-220, 229-56, 420-27; Pet. Ex. 34.

[37] Dr. Akbari's discussion of the implications of the genetic finding of mTOR is not included herein, as Dr. Niyazov opined that there is no genetic finding or major genetic causative factor that has been identified as a cause or contributing factor of J.W.'s epilepsy or epileptic encephalopathy. Pet. Ex. 34 at 12-16 (discussing mTOR); Tr. 84-85 (interpreting genetic testing to show that mTOR is not contributing to a developmental phenotype in J.W.'s case, because J.W.'s genetic variant is likely benign and the function of the mTOR gene is "unaffected"). Further, the undersigned does not discuss the other experts' opinions about the mTOR pathway as it is not relevant since there is no foundational support to show that J.W. has this abnormality.

[38] For an overview of cytokines, see Resp. Ex. A, Tab 11 (Annamaria Vezzani & Barbara Viviani, Neuromodulatory Properties of Inflammatory Cytokines and Their Impact on Neuronal Excitability, 96 Neuropharmacology 70 (2015)).

Id. And they allow other cells of the immune response (macrophages or T cells) to pass into the blood-brain barrier. Tr. 196-97.

As an overview, Dr. Akbari opined that vaccinations are intended to initiate immune cells, including regulatory T cells (Tregs) and regulatory pathways. Tr. 199. In many autoimmune conditions there is a "dysregulated immune response." Tr. 200. Dr. Akbari compared immunization to "the initiation of a fire" with Tregs and "immunoregulatory pathways" acting as "fire extinguishers." Tr. 199. When a dysregulated immune response occurs, Dr. Akbari explained that it is not because "the fire is too big. Sometimes it's because the fire extinguishers are not working property." Tr. 200. He stated that genetic factors can cause Tregs to be less functional, and their dysfunction can result is a lack of appropriate effector function. Id. When there is a dysregulated immune response with a "massive induction of inflammation" and stress at the blood-brain barrier, the innate immune response attracts many cells. Tr. 200-01. He opined this was followed by the adaptive immune response and molecular mimicry. Tr. 201. Immune privilege sites allow immune cells to enter, with "a variety of cytokines" and when "any of these . . . get impaired" and are not able to work properly, the result is neuroinflammation. Tr. 202.

Further, Dr. Akbari opined that the induction of inflammasomes[39] causes fever and redness at the site of injection. Tr. 202. The "vaccination . . .brings the immune cells to the certain other level . . . much higher than normal, and . . . the extinguishers or Tregs cannot really contain the fire, and they started to see dysregulated immune responses." Tr. 203. After the induction of inflammasome, Dr. Akbari opined that there is an "emergence of [] molecular mimicry." Tr. 205. "[A]utoreactive T cells start to [] produce antibodies . . . [and] migrate to the part that they recognize part of self." Tr. 206. Dr. Akbari noted that the "induction of inflammasome is a major effect in initiation of seizure." Id.

To illustrate his opinions, Dr. Akbari referenced an article by Quan.[40] Tr. 209-10 (citing Resp. Ex. A, Tab 12 at 6). The article describes four scenarios that cause neuroinflammation. Tr. 209, 421. During neuroinflammation, cells pass the blood-brain barrier, and molecules "actively pass the inflammatory signals to the [CNS]." Tr. 209-10. Dr. Akbari noted that first, "peripheral nerves at the site of inflammation . . . at the site of [vaccine] injection . . . can transmit inflammation to the brain." Tr. 421. Second, he asserted that small cytokines, like IL-6, can cross the blood brain barrier and enter the brain. Tr. 421-22. Third, the blood-brain barrier has receptor cells or other molecules that can "bring the cytokines in." Tr. 422. And fourth, Dr. Akbari agreed that the cytokines have a very short half-life, but he opined that "they activate the cells, because it's the language of the immune response." Id. Dr. Akbari acknowledged that two

[39] Inflammasomes are "a complex of . . . proteins, found in phagocytic cells and related to the body's system of innate immunity. Assembly of the inflammasome leads to activation of . . . [an] inflammatory response." Inflammasome, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition? id=25203 (last visited July 25, 2025).

[40] Ning Quan, In-Depth Conversation: Spectrum and Kinetics of Neuroimmune Afferent Pathways, 40 Brain Behavior & Immunity 1 (2014).

days after vaccination, there will no longer be IL-1-beta because it gets "used up." Tr. 426. He agreed with Dr. McCusker that the half-life of IL-1-beta is only "a few minutes." Id.

In J.W.'s case, Dr. Akbari testified that there was inflammasome induction at the site of vaccination, where there was redness. Tr. 423. Dr. Akbari made it clear that he never suggested there was fever. Id.

Lastly, he opined that response to vaccination is heterogenous and varies from patient to patient. Tr. 425. The Treg response is also different from one individual to another. Id. "In a very rare occasion . . . we can see that sometimes the immune system, whether they are Tregs or massive inflammasome induction, these things cannot really handle very well, and that's why the adverse effects after vaccination, particularly multiple vacation, is pretty rare." Id.

3. Petitioner's Expert, Dmitriy Niyazov, M.D.[41]

a. Background and Qualifications

Dr. Niyazov is a clinical geneticist and associate professor in medical genetics at Duke University. Tr. 68-69; Pet. Ex. 49 at 2. He holds a specialty certification from the American College of Medical Genetics and Genomics. Pet. Ex. 49 at 1. He received his M.D. from Rochester University and subsequently completed a genetics residency at Emory University. Tr. 69. His clinical research is focused on mitochondrial diseases and lysosomal storage disorders. Tr. 70. Dr. Niyazov also sees patients with "mitochondrial and lysosomal storage diseases, developmental delay, intellectual disability, chromosomal disorders, congenital defects, short stature, failure to thrive and adult genetic disorders" in outpatient and inpatient setting. Pet. Ex. 46 at 1; Tr. 70. He has authored or co-authored various publications on genetic disorders. Pet. Ex. 49 at 3-7. Dr. Niyazov was offered and admitted as an expert in genetics without objection. Tr. 71.

b. Opinions

Dr. Niyazov offered brief testimony at the hearing to explain J.W.'s genetic testing and the significance of the tests results. Tr. 71-86.

During the pendency of this case, J.W. underwent genetic tests, including whole exome gene sequencing in 2018 by GeneDx, that showed a "variant of unknown significance in the mTOR gene." Tr. 71-72. To determine whether this finding was relevant, there was parental testing, followed by reanalysis of the results using the results of the parental tests. Tr. 72. This

[41] Dr. Niyazov testified at the entitlement hearing and submitted one report. Tr. 68-86; Pet. Ex. 46. The opinions and testimony of Dr. Niyazov, that genetic testing has not identified any genetic abnormality to explain J.W.'s condition, renders earlier opinions held by some of the other experts no longer relevant. Such opinions were offered before genetic testing was completed and Dr. Niyazov submitted his expert report. The undersigned finds any contrary prior opinions are no longer relevant because they are based on inaccurate foundational evidence. Accordingly, the undersigned does not discuss these opinions in this Decision.

later set of tests showed the mTOR variant was maternally inherited, so it was "downgraded to likely benign since [his] mother does not have any of the features that J.W. has." Id. Dr. Niyazov opined that J.W. has not been diagnosed with a mitochondrial disease or metabolic disorder. Tr. 78-79. Further, Dr. Niyazov testified that the mTOR variant was not causing J.W. any immune dysfunction because it is a likely benign variant. Tr. 79-82. As a likely benign variant, he expected "that mTOR is functioning correctly and fully" and noted the "protein is likely unaffected and should function normally." Tr. 82, 85.

The whole exome sequencing in 2018 also showed a variant of uncertain significance in the MT-CYB gene. Tr. 72. Later maternal testing showed that J.W. and his mother had similar levels of heteroplasmy for MT-CYB, so this genetic variant was also not thought to be significant. Tr. 72, 75-76.

After this additional testing, and because the testing did not show any genetic diagnosis, Dr. Niyazov recommended whole genome analysis, "most advanced currently available clinically genetic testing," to look for "metabolic disorders, mitochondrial diseases, and . . . single gene disorders that could potentially explain" J.W.'s condition. Tr. 72. No additional genetic variants were identified. Tr. 73. Thus, Dr. Niyazov testified that the tests did not find anything causative, and therefore, he concluded that "currently there is no genetic explanation of J.W.'s regression from the vaccines—after the vaccines." Tr. 73.

In summary, based on the testing, Dr. Niyazov opined that currently J.W. does not have "any genetic etiology that would predispose his to the proposed effect of the vaccines." Tr. 76. He added that there is no further "clinically available genetic testing that can further identify the problem in J.W." Tr. 77.

4. Respondent's Expert, Eric D. Marsh, M.D., Ph.D.[42]

a. Background and Qualifications

Dr. Marsh is professor of neurology and pediatrics at the University of Pennsylvania, the director of the neurogenetics clinic at CHOP[43] and the director of the Orphan Disease Center at the University of Pennsylvania. Tr. 258-59. He is board-certified in neurology and held a board-certification in clinical neurophysiology. Tr. 259; Resp. Ex. N at 2. Dr. Marsh received his M.D. and a Ph.D. in physiology and neuroscience from New York University. Tr. 258. He completed a pediatrics residency at New York University followed by a child neurology residency at CHOP and the University of Pennsylvania. Id. Thereafter, he completed an epilepsy fellowship at CHOP as well as post-doctoral work in epilepsy development and research. Id. In his practice, he treats patients with neurogenetic conditions and has trained junior facility on the evaluation of neurogenetic conditions. Tr. 259. His clinical research is

[42] Dr. Marsh testified at the entitlement hearing and submitted one expert report. Tr. 258-339; Resp. Ex. F.

[43] Although Dr. Marsh is a clinical director and cares for patients at CHOP, he confirmed that he did not provide patient care to J.W.

focused on the "mechanisms of generation of seizures in the developing brain, particularly how different genetic mutations alter brain development to lead to epilepsy." Tr. 261. He has published extensively on topics involving epilepsy. Id.; Resp. Ex. N at 7-27.

Dr. Marsh was admitted as an expert in pediatric neurology and with specializations in epilepsy and neurogenetics, over the objection of Petitioner,[44] based on his training, education, and his position as the clinical director of the neurogenetics program at CHOP. Tr. 262-64, 268.

b. Opinions

Dr. Marsh opined that the vaccines at issue did not cause J.W.'s epileptic encephalopathy. Tr. 269. He further opined that J.W.'s condition was instead most consistent with "a presumed genetic epileptic encephalopathy" based on feeding issues early in life, his history of congestion, lack of head growth, the development of his epilepsy over his first months of life, and his clinical course and outcome. Id.

Regarding the onset of J.W.'s seizures, Dr. Marsh reviewed the August 20, 2016 video, taken 17 days after J.W.'s two-month vaccinations, and agreed with Dr. Shafrir's testimony that J.W.'s movements did not appear to be seizures but "just normal baby movements." Tr. 270 (citing Pet. Ex. 71).

Dr. Marsh offered the same opinions about the video of J.W. taken August 29, 2016, 26 days after J.W.'s two-month vaccinations. Tr. 270 (citing Pet. Ex. 64). Dr. Marsh testified that there was no suggestion that J.W. was having seizures, and instead, it looked like "he was playful." Id. According to Dr. Marsh, it is also possible that J.W. could have experienced seizures prior to the vaccinations, and they were not noticed, or dismissed as normal baby movements. Tr. 297-98.

Dr. Marsh opined that the first documentation of seizures is the video taken between the four-month vaccines and his November 8, 2016 hospital admission, when J.W.'s movements were "fairly consistent with seizures." Tr. 325 (citing Pet. Ex. 65).

Dr. Marsh disagreed with Dr. Shafrir's opinion that during J.W.'s initial hospital admission in November 2016, the initial EEG showed frequent seizures, "consistent with acute

[44] Petitioner objected to Dr. Marsh's qualifications neurogenetics on the basis that he "didn't have any formal training in genetics." Tr. 263-64. However, Dr. Marsh is the director of the neurogenetics clinic at CHOP and has held this position since 2011. Tr. 259. In this position he oversees the general neurogenetics program, sees patients with neurogenetic conditions, and trains junior faculty on the "evaluation and treat[ment] of individuals with neurogenetic conditions." Id. His clinical duties at CHOP involve "primarily neurogenetic patients" including those with "developmental epileptic encephalopathies." Tr. 260. He also studies "the mechanisms of generations of seizures in the developing brain, particularly how different genetic mutations alter brain development [and] lead to epilepsy." Tr. 260-61. As the undersigned noted at the entitlement hearing, "the expertise of Dr. Marsh [] speak[s] for itself" and he is well-qualified to discuss neurogenetics. Tr. 267-68.

brain insult." Tr. 285 (quoting Pet. Ex. 36 at 2). Dr. Marsh did not agree with Dr. Shafrir's opinions in this regard because J.W. had no baseline EEG for comparison, and there may have been abnormalities for earlier in life, but no EEG was done. Tr. 285-86. Additionally, since J.W. was having seizures at the time of the EEG, an abnormal EEG was to be expected. Tr. 286. Further, there was a period of fluctuation, when J.W.'s EEG would be abnormal and then normal, until it became persistently abnormal. Id. For these reasons, Dr. Marsh disagreed that J.W.'s initial EEG provided evidence of an "acute insult." Id.

Turning to the onset of J.W.'s encephalopathy, Dr. Marsh opined it was difficult to discern onset exactly, but it was probably later when his "focal seizures became more generalized and he started to show frank signs of developmental delay." Tr. 271. He defined encephalopathy as "a diffuse brain disorder, where the brain is not functioning properly." Id. A patient with epileptic encephalopathy has fairly normal development until the emergence of seizures. Tr. 273. "During the emergence of seizures, there is a slowing of the child's development," and often a decrease in head growth, along with the onset of other problems, such as reflux and hypotonia. Tr. 274. Seizures become worse, and "medically refractory." Id. This process leads to lifelong disabilities, including motor and cognitive impairments. Id.

J.W. was seven months old when he showed the first sign of developmental delay. Tr. 328. On January 25, 2017,[45] he was seen at CHOP, and his parents expressed concerns about behavior beginning in mid-December which indicated developmental issues. Tr. 328-29 (citing Pet. Ex. 8 at 108-13).

He disagreed with Dr. Shafrir that J.W.'s microcephaly was only present after his epileptic encephalopathy, or that it was more suggestive of an acquired as opposed to a genetic etiology. Tr. 297. Dr. Marsh noted that J.W.'s head circumference was 22nd percentile at birth, then it decreased to the tenth percentile and then down to second percentile after he turned two years of age. Id. He explained that this course illustrates a decline over the child's age, which started before he received the vaccines here, and is consistent with a genetic or a presumed genetic epileptic encephalopathy. Id.; see also Tr. 318-20 ("[H]is head circumference goes from 22nd at birth[,] down to 17, down to 12, down to [fifth], down to [second], and that starts prior to any vaccines being given. . . . [I]n most cases there is a genetic cause preventing the head from growing.").

As explained by Dr. Marsh, J.W.'s progression is distinct from that of an acute encephalopathy which is characterized by a "change in the mental status and the functioning of the child immediately after vaccine, often in association with febrile seizures." Tr. 277. He defined a febrile seizure as a seizure occurring between three months and five years of age associated with an ongoing fever, where fever is greater than 100.7 degrees. Tr. 335. Typically, fevers associated with febrile seizures are in the range of 102 degrees or higher. Id. They are further defined as "simple febrile seizures" if they are brief and self-limited. Tr. 335-36. "Complex febrile seizures" are prolonged or associated with developmental issues. Tr. 336.

[45] In the hearing testimony, this visit is identified as taking place on February 1, 2017; however, the cited medical records show that the visit took place on January 25, 2017. Pet. Ex. 8 at 108.

Febrile seizures occur in approximately five to 10% of children. Id. "Low-grade fever" is used "when children are warm" but the child's temperature is less than 100.7 or 101 degrees. Id.

J.W.'s seizures were afebrile. Tr. 279. Dr. Marsh opined there is no evidence in the record that he had a fever during his seizures. Id. While J.W. could have had a low-grade fever after vaccination,[46] there is no evidence he had a fever at the time that he began to have unilateral leg jerking. Tr. 306-08. Dr. Marsh agreed that in rare situations, the DTaP vaccine can cause seizure with fever, or febrile seizures. Tr. 300. But he opined that vaccines do not cause afebrile seizures. Tr. 300-01, 306. Further, he does not believe that is evidence to support the idea that the DTaP vaccine can cause a progressive encephalopathy. Tr. 304.

Dr. Marsh acknowledged that J.W. has received genetic testing and that a genetic cause has not been found for his condition. Tr. 281. He testified that a genetic basis is found in about 40% of those with epileptic encephalopathy. Tr. 281, 284. In time, Dr. Marsh believes a genetic cause will be found in most of these patients, including in J.W. Tr. 281-84.

Dr. Marsh does not find any evidence to support an autoimmune cause of J.W.'s epileptic encephalopathy. Tr. 290-91. He opined it is unusual to see autoimmune causes in babies. Tr. 291. And here, no immunomodulating therapy was prescribed, which suggests that the treating physicians did not suspect an autoimmune etiology. Id. Additionally, Dr. Marsh explained that children with autoimmune causes usually have other systemic problems, such as skin, cardiac, or gastrointestinal problems, whereas J.W. does not have any of these features. Tr. 311-12. Dr. Marsh also does not attribute J.W.'s condition to his exposure to various viruses or infections. Tr. 294. Instead, J.W. has "a very classic picture of a presumed genetic developmental epileptic encephalopathy." Tr. 294, 313-15.

5. Respondent's Expert, Christine McCusker, M.D.[47]

a. Background and Qualifications

Dr. McCusker is a professor of pediatrics at McGill University in Canada and a "clinician scientist" at McGill University Health Centre Research Institute. Tr. 341. She was board-certified in pediatrics by the American Board of Pediatrics and holds equivalent certifications in pediatrics and allergy and clinical immunology in Canada. Tr. 343. Dr. McCusker received M.Sc. in molecular biology and completed three years of a Ph.D. program in immunology at McMaster University before attending medical school. Resp. Ex. A at 1; Resp. Ex. O at 1. She received her M.D. from McMaster University. Resp. Ex. A at 1; Resp. Ex. O at 1. She then completed a pediatric residency, fellowship in immunology, and a fellowship in allergy and immunology. Resp. Ex. O at 2. Dr. McCusker's "research focus is the regulation of the immune

[46] Dr. Marsh reviewed the medical records and testified that the maximum temperature recorded was 99.5 degrees, which "is not [a] fever." Tr. 310. He also testified that there is no evidence as to the low-grade fevers. Id.

[47] Dr. McCusker testified at the entitlement hearing and submitted two expert reports. Tr. 340-418; Resp. Exs. A, E.

responses." Resp. Ex. A at 1. She treats an average of 50-120 children per week in allergy and clinical immunology as well as urgent care general pediatrics. Id. at 2. Throughout her career, she has held various university and hospital appointments, and she has authored or co-authored over 100 publications. Resp. Ex. O at 3-4, 33-46. Dr. McCusker was offered and admitted as an expert in the field of pediatric immunology without objection. Tr. 348.

b. Opinions

Dr. McCusker opined that the Petitioner's theory is not reliable and does not explain J.W.'s clinical picture. Tr. 349. She summarized Petitioner's theory as follows: J.W.'s two-month vaccines resulted in cytokine release which caused seizures to develop a couple of days following vaccination, and these were influenced by the next set of vaccines at four months that led to the onset of epileptic encephalopathy. Tr. 348. Additionally, Petitioner's experts posited that molecular mimicry played a role and that autoimmunity could have developed. Tr. 348-49.

She described cytokines as small protein that "act as a communication molecule," noting there are over one hundred different types of cytokines. Tr. 349-50. Dr. McCusker opined that vaccination results in a needle injury to the skin and local tissue, which triggers the release of mediators from damaged cells that initiates innate immune responses. Tr. 349-50. The classic triad of cytokines that result include IL-6, IL-1-beta and TNF-alpha. Tr. 350. These cytokines cause symptoms such as redness and pain at the injection site, fever, and malaise. Resp. Ex. A at 4; Tr. 351. This is a localized response. Tr. 351. Subsequently, in about four days, the cytokines bind to a receptive cell, and in the context of an inflammatory event, create a complex called inflammasome which is a "cascade of signaling molecules" that tell a cell what to do. Tr. 352.

Dr. McCusker explained that Dr. Akbari posited it is possible for the inflammasome to "turn on" but fail to appropriately "turn off" resulting in the ongoing production of inflammation and proinflammatory cytokines. Tr. 353. However, Dr. McCusker opined that after vaccination, the inflammatory event occurs and then ends. Tr. 354. It does not lead to "excessive or uncontrolled cytokine release." Id. If there was an excessive or uncontrolled cytokine response, there would be very high fever. Tr. 354-55. She opined that temperatures of 104 to 106 degrees can occur during excessive cytokine responses in children. Tr. 355. Additionally, the child would be irritable, not eating, and inconsolable. Id.

In short, Dr. McCusker agreed that a vaccination "activates immune responses . . . through cytokine upregulation." Resp. Ex. A at 5. But she disagreed that cytokines produced in response to vaccination occur at levels that are high enough to "lower seizure thresholds" so as to cause "cytokine-mediated afebrile seizures." Id. (citing Resp. Ex. A, Tab 6);[48] Tr. 355-59.

Dr. McCusker specifically disagreed with Dr. Akbari's opinions that there are four ways that vaccination can cause neuroinflammation as described in the Quan article. Tr. 362-63; see

[48] Yasuyo Kashiwagi et al., Production of Inflammatory Cytokines in Response to Diphtheria-Pertussis-Tetanus (DPT), Haemophilus Influenzae Type B (Hib), and 7-Valent Pneumococcal (PCV7) Vaccines, 10 Hum. Vaccines & Immunotherapeutics 677 (2014).

Pet. Ex. 12, Tab A at 6. She explained that cytokines from outside do not come into the brain, instead, the microglia in the brain produce their own cytokines. Tr. 366-67. She also explained that scenario 4 in the Quan article is "sepsis." Tr. 367. In that situation, the baby has a very high fever, is obtunded, hypotensive, has liver injury, and is very sick. Id. This scenario is not relevant to the facts here, involving a baby who has had a vaccination and has redness at the site of vaccination.[49] Tr. 368.

Dr. McCusker agreed that after his two-month vaccinations on August 3, 2016, J.W. was fussy and had redness at the vaccination site, which Dr. McCusker agreed was evidence of local inflammation. Resp. Ex. A at 5. These symptoms were not documented after J.W.'s four-month vaccines on October 11, 2016, and thus, Dr. McCusker suggested J.W.'s "innate system was activated to a lesser extent" following the second set of vaccinations. Id.

Dr. McCusker agreed that cytokines can cross the blood brain barrier, and influence "cytokine expression in the CNS." Resp. Ex. A at 6-7. She agreed that cytokines IL-1-beta and IL-6 are produced by microglia "in response to tissue stressors in the brain," and that they play roles in "development of CNS connections" and "act as neurotransmitters." Id. at 7. She agreed there are "increased levels" of these cytokines in epilepsy, and that levels of IL-1-beta increase within four hours of the onset of seizures. Id. And she agreed that at "super-physiological amounts," IL-1-beta can cause seizures ("has epileptogenic potential"). Id. However, at "levels expected to be induced by vaccination," Dr. McCusker opined that IL-1-beta appears to cause "an antiepileptic effect." Id.

Dr. McCusker cited Li et al.[50] for the proposition that CNS increases in cytokines are associated with lower seizure thresholds. Resp. Ex. A at 7-8 (citing Resp. Ex. A, Tab 18). However, she noted that medical literature suggests that increases in cytokines seen with seizures are "in response" to the seizures rather than a cause of the seizures. Id. at 8-9; see, e.g., Resp. Ex. Tab 18; Resp. Ex. A, Tab 20;[51] Pet. Ex. 24, Tab zPP.[52] She also noted that IL-1-beta has "a very short half-life," of 19 minutes and any unused serum IL-1-beta would be inactivated within 19 minutes. Resp. Ex. A at 9.

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[49] Dr. McCusker provided a paper by Capuron and Miller that describe sickness behaviors associated with cytokines in the context of microbial infections. Resp. Ex. A, Tab 4 at 2-3 (Lucile Capuron & Andrew Miller, Immune System to Brain Signaling: Neuropsychopharmacological Implications, 130 Pharmacology & Therapeutics 226 (2011)). These behaviors include "fatigue, psychomotor slowing, decreased appetite, sleep alterations, and increased sensitivity to pain." Id. at 2.

[50] Gang Li et al., Cytokines and Epilepsy, 20 Seizure 249 (2011).

[51] Annamaria Vezzani & Tallie Baram, New Roles for Interleukin-1 Beta in the Mechanisms of Epilepsy, 7 Epilepsy Currents 45 (2007).

[52] Valentina Lori et al., Modulation of Neuronal Excitability by Immune Mediators in Epilepsy, 26 Current Op. Pharmacology 118 (2016).

Dr. McCusker concluded that there is "no persuasive evidence" vaccination induces cytokines that can trigger epilepsy in general, or that they did so in J.W. Resp. Ex. A at 9. In conclusion, cytokines expressed in the periphery are not thought to cause afebrile seizures. Tr. 369.

Turning to the Petitioner's theory based on the adaptive immune system (molecular mimicry), Dr. McCusker noted that J.W. was not diagnosed with autoimmune encephalopathy. Resp. Ex. A at 10. Further, she explains that the role of autoantibodies in the cause of autoimmune epilepsies is not known at this time. Id. at 11. Further, J.W. was tested for autoantibodies and found to be negative. Id.

Dr. McCusker concluded that J.W. had his first seizures in November 2016, two to three weeks after his second set of vaccinations. Resp. Ex. E at 8. Prior to his vaccinations, she opined that J.W. had microcephaly, "which has persisted." Resp. Ex. A at 12. There is no evidence that he had "innate immune dysregulation" or any "persuasive evidence that vaccinations led to his seizure disorder." Id. at 12; see also Tr. 386-88.

Dr. McCusker did not disagree that there was a temporal association between vaccination and seizures. See Resp. Ex. A at 12. However, she explained that "the incidence of epilepsy is highest during infancy and the onset of seizures in the first year of life most commonly occurs before the age of [seven] months." Id. Further, while there is a temporal association, vaccinations are not linked with epilepsy in large, controlled studies. Id. Regarding the onset of encephalopathy, Dr. McCusker opined that J.W was "probably born with [it] and that continues to develop and/or progress with time." Tr. 391. She did not opine on when clinical manifestation of encephalopathy first occurred.

She cited several studies in support of her opinions. Resp. Ex. A at 12. Verbeek et al.[53] a large Dutch study of children who had seizures in temporal association with vaccination, found that most children had underlying genetic or structural etiologies that accounted for their epilepsy. Resp. Ex. A, Tab 35 at 1. There was a finding of vaccine-related febrile seizures in some children, particularly those with "genetically determine[d] fever-sensitive epilepsies." Id. at 7. Huang et al., the largest study to examine DTaP and seizures, found no increased risk of seizures within three days of DTaP vaccination. Resp. Ex. C, Tab 6 at 1, 6. Sun et al.,[54] a subsequent large scale study, reported that vaccination with DTaP/Hib/IPV was "not associated with an increased risk of epilepsy." Resp. Ex. A, Tab 16 at 1.

Regarding the literature cited by Petitioner, Dr. McCusker distinguishes the articles from the facts here because they relate to vaccines that were not given to J.W., like the whole cell

[53] Nienke E. Verbeek et al., Etiologies for Seizures Around the Time of Vaccination, 134 Pediatrics 658 (2014).

[54] Yuelian Sun et al., Risk of Febrile Seizures and Epilepsy After Vaccination with Diphtheria, Tetanus, Acellular Pertussis, Inactivated Poliovirus, and Haemophilus Influenzae Type B, 307 JAMA 823 (2012).

pertussis vaccine, or the studies did not use unvaccinated control subjects, rendering the results less reliable. Resp. Ex. A at 9-10 (criticizing Pet. Ex. 24, Tabs J-N).[55]

Dr. McCusker concluded by stating that the vaccines were not the cause of J.W.'s epileptic encephalopathy. Tr. 391. She opined he likely was born with a condition that progressed over time which caused his clinical course. Id.

IV. LEGAL STANDARDS

A. Standards for Adjudication

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Hum. Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). 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, Petitioner must prove 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)); see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner who satisfies this burden is entitled to compensation unless respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B). However, if a petitioner fails to establish a prima facie case, the burden does not shift. Bradley v. Sec'y of Health & Hum. Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

"Regardless of whether the burden ever shifts to the [R]espondent, the special master may consider the evidence presented by the [R]espondent in determining whether the [P]etitioner has established a prima facie case." Flores v. Sec'y of Health & Hum. Servs., 115 Fed. Cl. 157, 162-63 (2014); see also Stone v. Sec'y of Health & Hum. Servs., 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."); de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the [P]etitioner's evidence on a requisite element of the [P]etitioner's case-in-chief."); Pafford, 451 F.3d at 1358-59 ("[T]he presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the

[55] Dr. McCusker also testified about some of the medical literature relied upon by Dr. Akbari and Dr. Shafrir regarding cytokines, and why it was not relevant. See Tr. 375-83.

vaccination. . . . [T]he Special Master properly introduced the presence of the other unrelated contemporaneous events as just as likely to have been the triggering event as the vaccinations.").

B. Factual Issues

Petitioner must prove, by a preponderance of the evidence, the factual circumstances surrounding her claim. § 13(a)(1)(A). To resolve factual issues, the special master must weigh the evidence presented, which may include contemporaneous medical records and testimony. See Burns v. Sec'y of Health & Hum. Servs., 3 F.3d 415, 417 (Fed. Cir. 1993) (explaining that a special master must decide what weight to give evidence including oral testimony and contemporaneous medical records).

Medical records, specifically contemporaneous medical records, are presumed to be accurate and generally "warrant consideration as trustworthy evidence." Cucuras v. Sec'y of Health & Hum. Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). But see Kirby v. Sec'y of Health & Hum. Servs., 997 F.3d 1378, 1382 (Fed. Cir. 2021) (rejecting the presumption that "medical records are accurate and complete as to all the patient's physical conditions"); Shapiro v. Sec'y of Health & Hum. Servs., 101 Fed. Cl. 532, 538 (2011) ("[T]he absence of a reference to a condition or circumstance is much less significant than a reference which negates the existence of the condition or circumstance." (quoting Murphy v. Sec'y of Health & Hum. Servs., 23 Cl. Ct. 726, 733 (1991), aff'd per curiam, 968 F.2d 1226 (Fed. Cir. 1992))), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 503 F. App'x 952 (Fed. Cir. 2013). The weight afforded to contemporaneous records is due to the fact that they "contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium." Id. To overcome the presumptive accuracy of medical records, a petitioner may present testimony which is "consistent, clear, cogent, and compelling." Sanchez v. Sec'y of Health & Hum. Servs., No. 11-685V, 2013 WL 1880825, at *3 (Fed. Cl. Spec. Mstr. Apr. 10, 2013) (citing Blutstein v. Sec'y of Health & Hum. Servs., No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)), mot. for rev. denied, 142 Fed. Cl. 247 (2019), vacated on other grounds & remanded, 809 F. App'x 843 (Fed Cir. 2020).

There are situations in which compelling 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) ("[L]ike 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 v. Sec'y of Health & Hum. Servs., No. 03-1585V, 2005 WL 6117475, at *19 (Fed. Cl. Spec. Mstr. Dec. 12, 2005) ("[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 v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1379 (Fed. Cir. 2009); Bradley, 991 F.2d at 1575.

Despite the weight afforded medical records, special masters are not bound rigidly by those records in determining onset of a petitioner's symptoms. Valenzuela v. Sec'y of Health &

Hum. Servs., No. 90-1002V, 1991 WL 182241, at *3 (Fed. Cl. Spec. Mstr. Aug. 30, 1991); see also Eng v. Sec'y of Health & Hum. Servs., No. 90-1754V, 1994 WL 67704, at *3 (Fed. Cl. Spec. Mstr. Feb. 18, 1994) (Section 13(b)(2) "must be construed so as to give effect also to § 13(b)(1) which directs the special master or court to consider the medical records (reports, diagnosis, conclusions, medical judgment, test reports, etc.), but does not require the special master or court to be bound by them").

C. Causation

Petitioner alleges a causation-in-fact claim. To prevail on this claim, Petitioner must prove that a vaccine J.W. received caused his injury. To do so, Petitioner must establish, by preponderant evidence: (1) a medical theory causally connecting the vaccine and J.W.'s injury ("Althen Prong One"); (2) a logical sequence of cause and effect showing that the vaccine was the reason for J.W.'s injury ("Althen Prong Two"); and (3) a showing of a proximate temporal relationship between the vaccine and J.W.'s injury ("Althen Prong Three"). Althen, 418 F.3d at 1278; § 13(a)(1).

The causation theory must relate to the injury alleged. Petitioner must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen, 35 F.3d at 548-49. Petitioner cannot establish entitlement to compensation based solely on her assertions; rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether Petitioner is entitled to compensation, the special master shall consider all material in the record, including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in Petitioner's favor when the evidence weighs in her favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in Petitioner's favor).

Testimony that merely expresses the possibility—not the probability—is insufficient, by itself, to substantiate a claim that such an injury occurred. See Waterman v. Sec'y of Health & Hum. Servs., 123 Fed. Cl. 564, 573-74 (2015) (denying Petitioner's motion for review and noting that a possible causal link was not sufficient to meet the preponderance standard). The Federal Circuit has made clear that the mere possibility of a link between a vaccination and a petitioner's injury is not sufficient to satisfy the preponderance standard. Moberly, 592 F.3d at 1322 (emphasizing that "proof of a 'plausible' or 'possible' causal link between the vaccine and the injury" does not equate to proof of causation by a preponderance of the evidence); Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019). While certainty is by no means required, a possible mechanism does not rise to the level of preponderance. Moberly, 592 F.3d at 1322; see also de Bazan, 539 F.3d at 1351.

V. ANALYSIS

A. Althen Prong One

Under Althen prong one, Petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu, 569 F.3d at 1375; Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by a "sound and reliable" medical or scientific explanation. Boatmon, 941 F.3d at 1359; see also Knudsen, 35 F.3d at 548; Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioner relies upon a medical opinion to support his theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen v. Sec'y of Health & Hum. Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better than the soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

Lack of information about a specific mechanism to prove that a theory is sound and reliable by preponderant evidence does not preclude Petitioner from prevailing. Given the state of current scientific knowledge, there is no way that a petitioner could satisfy such a requirement. And requiring proof of such would require scientific certainty, which is a bar too high. See Knudsen, 35 F.3d at 549 (explaining that "to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program"). However, there must be more than conclusory opinions or speculation. Special masters consistently reject "conclusory expert statements that are not themselves backed up with reliable scientific support." Kreizenbeck v. Sec'y of Health & Hum. Servs., No. 08-209V, 2018 WL 3679843, at *31 (Fed. Cl. Spec. Mstr. June 22, 2018), mot. for rev. denied, decision aff'd, 141 Fed. Cl. 138, aff'd, 945 F.3d 1362 (Fed. Cir. 2020).

Here, Petitioner's experts focus on a cytokine driven theory[56] to explain how vaccinations, and especially the DTaP vaccination, can cause seizures through a process of inflammation/neuroinflammation. Dr. Akbari discussed cytokines at length and asserted that cytokines can pass through the blood brain barrier and/or act on dendrons of the nervous system. Dr. Akbari offered a general tutorial about the immune system, both innate and adaptive. He talked about dysregulated T cells (Tregs) suggesting that here there was a dysregulated immune response, analogizing the facts to a fire that has gotten "too big" because the fire extinguishers are not working. He discusses molecular mimicry generally as well, but again, he offers general information without factual context. There is no evidence here of an autoimmune diagnosis, so

[56] Dr. Shafrir also presented a theory of challenge-rechallenge. However, since onset occurred after the second set of vaccinations, there is no basis for challenge-rechallenge. See infra Part V.C (finding seizure onset occurred in mid-October 2016 following his second set of vaccinations).

Dr. Akbari's cytokine and/or molecular mimicry theory does not fit the factual context. While Dr. Akbari's discussion of the immune system is generally informative, it was not tailored to the facts and circumstances here, were there is no evidence of fever or sickness behaviors to provide foundational evidence that there were proinflammatory cytokine effects on the brain, or facts to support immune dysregulation, or an autoimmune etiology of the seizures and epilepsy.

In contrast, Dr. McCusker's explanation of the immune responses to vaccines, especially those related to cytokines, more closely aligns with the medical literature, and is therefore more persuasive. Citing Kashiwagi et al., Dr. McCusker opines that the data does not support a finding that cytokine levels after vaccination are "sufficient to lower seizure thresholds and influence the development of cytokine-mediated afebrile seizures." Resp. Ex. A at 5 (citing Resp. Ex. A, Tab 6).

Further, Dr. Akbari's reliance on the four scenarios described in the Quan article in support of his cytokine theory is misplaced. At the outset, Quan describes the effect of "direct injection of cytokines into the brain." Resp. Ex. A, Tab 12 at 1. The resulting effect is "fever, prolonged slow wave sleep, . . . reduced food and water intake, and decreased locomotor activity, generally mimicking CNS-controlled sickness symptoms during immune challenge." Id. at 1, 5-6, 6 fig.1. Throughout the paper, Quan refers to fever and sickness behaviors, but these signs of neuroimmune activation are not present here. Respondent's expert, Dr. McCusker persuasively explained why the Quan scenarios are not relevant here, particularly where there is no evidence of excessive cytokine activity. As explained by Quan, a "fully controlled sub-threshold infection" is presented in scenario 1. Id. at 5. There is no evidence of "sub-threshold infection" in this case. Scenario 2 involves activation of the CNS in the context of localized inflammation activating the CNS via the neural route. According to Quan, this scenario is not well understood. Dr. Akbari did not explain how this scenario would cause seizures after vaccination. And if he did, it was not presented in the context of the facts at issue here. In scenario 3, there is "systemic inflammation" of the host. Id. at 5-6. The facts here are not consistent with systemic inflammation. And in scenario 4, there is "systemic inflammation" and "chronic liver inflammation." Id. As explained by Dr. McCusker, Quan's scenario 4 describes sepsis, where a baby has a very high fever, is obtunded, hypotensive, has liver injury, and is very sick. In summary, the Quan scenarios do not reflect the facts and circumstances present in this case involving a baby who had afebrile seizures without evidence of an underlying subclinical or systemic infection. Moreover, Quan does not discuss vaccination, seizures, or epilepsy.

The undersigned has previously found that in certain circumstances, post-vaccination febrile seizures may be associated with an increased risk of subsequent epilepsy, where experts agreed that vaccinations triggered the initial febrile seizure and led to epilepsy. See Ginn v. Sec'y of Health & Hum. Servs., No. 16-1466V, 2021 WL 1558342 (Fed. Cl. Spec. Mstr. Mar. 26, 2021); Fuller ex rel. B.F. v. Sec'y of Health & Hum. Servs., No. 15-1470V, 2019 WL 7576382 (Fed. Cl. Spec. Mstr. Dec. 17, 2019). Here, however, there is no evidence of a fever or that a fever triggered the seizures. Both Dr. Shafrir and Dr. Marsh agree that J.W. did not have febrile seizures associated with his vaccinations. See Tr. 151 (agreeing "there's no evidence . . . that J.W. ever had a febrile seizure"); Tr. 271 (noting "[t]here's no direct evidence" that "J.W. experienced febrile seizures").

Moreover, the undersigned agrees with the reasoning set forth in a line of cases[57] where compensation has been denied by special masters in claims alleging that the DTaP vaccination caused afebrile seizures and epilepsy. See, e.g., McClellan ex rel. L.M. v. Sec'y of Health & Hum. Servs., No. 14-714V, 2019 WL 4072130, at *25-31 (Fed. Cl. Spec. Mstr. July 23, 2019) (finding that Petitioner's theory was deficient where he invoked a cytokine-based causation theory to support the position that vaccination triggered infant child's afebrile seizures); Hargrove ex rel. A.F.M. v. Sec'y of Health & Hum. Servs., No. 17-233V, 2023 WL 8071917, at *33-35 (Fed. Cl. Spec. Mstr. Oct. 27, 2023); Walters ex rel. K.S.S.W. v. Sec'y of Health & Hum. Servs., No. 15-1380V, 2023 WL 3750716, at *30 (Fed. Cl. Spec. Mstr. June 1, 2023), aff'd, 2023 WL 5274006 (Fed. Cl. July 31, 2023), aff'd, 2025 WL 1000404 (Fed. Cir. Apr. 3, 2025); Nance v. Sec'y of Health & Hum. Servs., No. 06-0730V, 2010 WL 3291896, at *13 (Fed. Cl. Spec. Mstr. July 30, 2010) (denying entitlement in a DTaP/seizure disorder case because Petitioner's theory was speculative); Gram ex rel. A.L.M. v. Sec'y of Health & Hum. Servs., No. 15-515V, 2022 WL 17687972, at *1 (Fed. Cl. Spec. Mstr. Nov. 16, 2022); Chavez ex rel. T.C. v. Sec'y of Health & Hum. Servs., No. 16-1479V, 2022 WL 3368502, at *25 (Fed. Cl. Spec. Mstr. July 19, 2022).[58]

Accordingly, the undersigned finds Petitioner has not offered a sound and reliable medical theory in support of her claim. Thus, Petitioner has not met the preponderant evidentiary standard with respect to Althen prong one.

B. Althen Prong Two

Under Althen prong two, Petitioner must prove by a preponderance of the evidence that there is a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1324 (Fed. Cir. 2006) (quoting Althen, 418 F.3d at 1278). "Petitioner must show that the vaccine was the 'but for' cause of the harm . . . or in other words, that the vaccine was the 'reason for the injury.'" Pafford, 451 F.3d at 1356 (internal citations omitted).

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical 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 trustworthy evidence since they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528. The

[57] Older cases involving the whole cell pertussis vaccine, DTP, are distinguished based on the differences in the safety profiles between the whole cell and the acellular form of pertussis.

[58] But see Romero ex rel. Romero v. Sec'y of Health & Hum. Servs., No. 07-671V, 2010 WL 2766761 (Fed. Cl. Spec. Mstr. June 22, 2010). Romero is distinguishable based on its facts; the "onset seizure" was prolonged, lasting between 20-30 minutes. Id. at *2-3. Two days later, the infant had another prolonged seizure lasting more than 30 minutes. Id. Thus, the child had two prolonged seizures within three days of vaccination.

Petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, Petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

Since Petitioner failed to prove Althen prong one, it follows that she cannot prove Althen prong two. However, even if Petitioner had proven a sound and reliable causal mechanism, she failed to prove by preponderant evidence a logical sequence of cause and effect, showing J.W.'s vaccinations caused epileptic encephalopathy for two reasons.

First, J.W.'s clinical course is not consistent with vaccine causation. There is no evidence that J.W. had a cytokine driven response to either his two-month or four-month vaccinations. Based on the report that he had redness and swelling at the vaccine site[59], one may conclude that J.W. had a localized response to the first set of vaccines. However, there is no evidence that he had a significant fever. And there is no reference to sickness behaviors at the time that he was reported to have seizures after either set of vaccinations. He was not taken to the pediatrician after his two-month vaccinations administered on August 3, 2016, and no problems were documented by his physician following vaccinations. The video taken on August 20, 2016 does not show that J.W. was experiencing any sickness behaviors, and the expert neurologists did not opine that the video showed that J.W. appeared ill, or describe any sickness behaviors seen on the video. J.W. experienced chest congestion in mid-September, but this was one month after the two-month vaccinations and was not attributed to his vaccinations. In September, J.W. was seen for eye redness, but the records do not document any fever or irritability. In short, after his two-month vaccines, there is no indication in the contemporaneous medical records that J.W. experienced any adverse reaction.

J.W. received his four-month vaccinations on October 11, 2016. Petitioner testified that after this set of vaccinations, J.W. had redness and swelling at the vaccine site, but these symptoms were not documented when J.W. was next seen at his pediatrician's office on October 21. At that visit Petitioner reported cough and congestion, with a maximum fever of 99.5 degrees and later 100.3 degrees, which the experts agree did not constitute a fever sufficient to be associated with seizures. At the October 21 visit, J.W.'s treating physician described him as "pleasant and happy." Pet. Ex. 6 at 9. The physician noted that J.W. was "well appearing." Id. at 10.

In summary, there is no evidence that J.W. experienced sickness behaviors or significant fever after either set of vaccinations that would suggest cytokine driven neuroinflammation caused his seizures. Additionally, the contemporaneous records do not support a finding that there was any adverse reaction by J.W. to his vaccinations.

[59] J.W. received multiple vaccinations; however, Petitioner did not identify which of the vaccine sites had redness and swelling. Further, the medical records do not identify the location of the vaccine injections. See, e.g., Pet. Ex. 6 at 4.

Relative to Petitioner's experts' theories that J.W.'s seizures were autoimmune in nature and caused by autoantibodies or molecular mimicry, the undersigned again finds no factual basis for such theory. J.W.'s epilepsy was never diagnosed by any of his treating neurologists as autoimmune in nature, he was not treated with immune modulating therapies, and CSF testing did not reveal inflammatory autoantibodies to confirm an immune reaction.

Moreover, there was no evidence of an "acute insult" precipitated by vaccination. Dr. Marsh's opinions on this point were more consistent with J.W.'s clinical course, and therefore more persuasive that those of Dr. Shafrir.

The second reason that the undersigned finds that Petitioner did not prove Althen prong two by preponderant evidence is based on the records of one of J.W.'s treating physicians. On January 15, 2017, J.W. was seen by Dr. Melissa DiGiovine, a specialist in Epilepsy and Clinical Neurophysiologist in the Pediatric Regional Epilepsy Program at CHOP. See Pet. Ex. 8 at 78. Dr. DiGiovine conducted a thorough review of J.W.'s history, EEG, MRI, and provided recommendations to J.W.'s parents. During this visit, Dr. DiGiovine advised it was "highly unlikely that his vaccines had any effect on [J.W.] developing seizures" and she "strongly advise[d] continuing vaccines to protect him against communicable diseases." Id. at 82.

The opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical 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)). The undersigned gives weight J.W.'s treating physician opinion that it was "highly unlikely" that vaccinations effected the development of his seizures.

Regarding the opinions voiced by Respondent's experts and some of J.W.'s treating physicians that J.W.'s condition was caused by a genetic abnormality, an alternative factor unrelated to vaccination, the undersigned finds that currently, there is insufficient evidence of a likely genetic abnormality. Dr. Niyazov presented clear and cogent opinions establishing that to date, no genetic cause of J.W.'s seizures or epileptic encephalopathy have been found.

Although there is no evidence of a genetic abnormality to explain J.W.'s illness, the undersigned finds that there are independent reasons, as described above, for finding that Petitioner has failed to provide preponderant evidence of a logical sequence of cause and effect required under Althen prong two.

C. Althen Prong Three

Althen prong three requires Petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That term has been equated to mean a "medically acceptable temporal relationship." Id. Petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disease's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352. The explanation for what is a medically acceptable time

frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen Prong One). Id.; Koehn v. Sec'y of Health & Hum. Servs., 773 F.3d 1239, 1243 (Fed. Cir. 2014); Shapiro, 101 Fed. Cl. at 542.

J.W.'s alleged injury is epileptic encephalopathy, and his resulting neurological sequelae. Joint Submission at 3.

The undersigned finds there is preponderant evidence that J.W.'s seizures began mid-October after his second set of vaccinations. There are several reasons for this finding. First, the earliest in time medical records place onset of seizures in mid-October, about one week after his four-month vaccinations. There are at least three entries in the records placing onset in mid-October. In November 2016, during J.W.'s hospitalization, J.W.'s parents reported that beginning in mid-October they noticed occasional twitching of his left leg. Pet. Ex. 8 at 10 ("Beginning in mid-October, his [parents] noticed occasional twitching of his left leg . . . . [H]e had [] received his [four]-month vaccinations [one] week prior to the beginning of these episodes."). Pet. Ex. 14 at 7 (documenting, during admission by ED provider, a history "of intermittent twitching of left leg over past two weeks"). And in December 2016, neurologist Dr. Fung noted that the leg-jerking began two weeks prior to his recent hospitalization, placing onset on approximately October 25. See Pet. Ex. 8 at 52.

Second, the undersigned relies on the opinions about onset offered by the neurology experts. Dr. Shafrir initially testified that J.W.'s seizures began in mid-October, a few days after the second set of vaccinations. After reviewing the video taken August 20, 2016, Dr. Shafrir initially testified that it did not show seizures. Tr. 155 ("I would say he's just kicking."). However, after continued questioning, he ultimately opined that more likely than not, J.W. had seizures after his first vaccinations. Tr. 156.

Dr. Marsh opined that the first documentation of seizures is the video taken between October 11, 2016, date of administration of the four-month vaccines, and November 8, 2016, when J.W.'s movements were "fairly consistent with seizures." Tr. 325. He disagreed that the earlier video taken August 20 showed seizures.

Because Dr. Shafrir initially testified that J.W.'s seizure began in mid-October, but later changed his opinion under continued questioning, the undersigned finds his testimony less reliable than that of Dr. Marsh. Further, Dr. Marsh's opinion is consistent with what was reported in the contemporaneous medical records.

Regardless of when J.W.'s seizures began, the experts agree that the onset of J.W.'s encephalopathy did not occur until later in time. Dr. Shafrir opined that the first indication of J.W.'s encephalopathy was after his admission to CHOP on November 8, 2016, and when his neurological examination revealed hypotonia. Dr. Shafrir compared J.W.'s clinical course to a genetic epileptic encephalopathy called Dravet's syndrome, where encephalopathy begins slowly, when the child becomes delayed and hypotonic. Dr. Marsh agreed with Dr. Shafrir that the onset of J.W.'s encephalopathy was later, when his seizures became more generalized and he showed signs of developmental delay.

The medical records show that when J.W. was seen at CHOP in February 2017, his parents expressed concerns about his behavior beginning in mid-December which suggested developmental issues. On January 25, 2017, at seven months of age, J.W. was seen by neurologist Dr. DiGiovine. At this visit, J.W. was noted to be doing well and continuing to make development gains, however, tone was slightly decreased in the lower extremities. At a PT evaluation on February 27, 2017, J.W. was assessed with low tone (hypotonia) and standardized developmental motor testing revealed poor gross motor results (less than one percentile).

Based on the opinions of the neurology experts, the undersigned finds that the onset of J.W.'s epileptic encephalopathy did not occur with the onset of seizures, but that it occurred later when J.W. exhibited hypotonia and developmental delay, in early 2017, as evidenced by the records cited above.

J.W. received the vaccinations at issue on August 3, 2016 and October 11, 2016. His epileptic encephalopathy manifested in early 2017, approximately five months after the first set of vaccinations and three months after his second set of vaccinations. Petitioner's experts did not explain how either set of vaccinations would result in a progressive course that would take three to five months for the onset of encephalopathy. Therefore, the undersigned finds that Petitioner failed to prove Althen prong three by preponderant evidence.

VI. CONCLUSION

The undersigned extends her sympathy to J.W. and Petitioner for all that they and their family have suffered. The undersigned's Decision, however, cannot be decided based upon sympathy, but rather on the evidence and law.

For all the reasons discussed above, the undersigned finds that Petitioner has not established by preponderant evidence that a vaccination caused J.W.'s condition. Therefore, Petitioner is not entitled to compensation. In the absence of a timely filed motion for review pursuant to Vaccine Rule 23, the Clerk of Court **SHALL ENTER JUDGMENT** in accordance with this Decision.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master