In the United States Court of Federal Claims

No. 10-394V

(Filed Under Seal: July 14, 2017 | Reissued for Publication: July 31, 2017)[*]

LAURA OLIVER *and* EDDIE OLIVER, JR., *parents and legal representatives of* E.O., III, Petitioners, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	Keywords: Vaccine Act; Motion for Review; Dravet syndrome; SCN1A mutation.

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OPINION AND ORDER

KAPLAN, Judge.

The petitioners in this case are Laura Oliver and Eddie Oliver, Jr. They seek review of a decision issued under the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-1 to -34 ("Vaccine Act" or "Act"), as amended, dismissing their petition for compensation which they filed on behalf of their son, E.O. III (E.O.). Oliver v. Sec'y of HHS, No. 10-394V, 2017 WL 747846 (Fed. Cl. Spec. Mstr. Feb. 1, 2017) (hereinafter the "Decision" or "Dec."). The Chief Special Master dismissed the petition based on her conclusion that the Olivers did not establish by preponderant evidence that certain vaccines that E.O. received on April 9, 2009, caused him to develop Dravet syndrome, a chronic complex partial seizure disorder.

In their Motion for Review, the Olivers argue that the Chief Special Master committed error when, without holding an evidentiary hearing, she rejected the opinion of the Olivers' expert, credited the opinions of the government's experts, and concluded that the cause of E.O.'s

[*] Pursuant to Vaccine Rule 18(b), this opinion was initially filed on July 14, 2017, and the parties were afforded 14 days to propose redactions. The parties did not propose any. Accordingly, this opinion is reissued in its original form for publication.

Dravet syndrome was a mutation of his SCN1A gene, and not the vaccinations he received. The government responds that the Chief Special Master correctly applied the law and that her conclusion that the Olivers did not establish causation by preponderant evidence is supported by the record.

For the reasons set forth below, the Court agrees that the Chief Special Master's decision reflects a careful examination of the record, that her conclusions are neither arbitrary, nor capricious, nor contrary to law, and that she acted within her discretion in deciding the case without an evidentiary hearing. Therefore, the motion for review is **DENIED** and the Decision is **SUSTAINED**.

BACKGROUND

I. Medical History

The Chief Special Master's decision contains a thorough and accurate summary of the background facts of this case. To briefly recapitulate, E.O. was born on October 2, 2008, at St. Mary's Hospital in Athens, Georgia. Pet'rs' Ex. 16 at 34, ECF No. 17-2.[1] According to E.O.'s mother, E.O. was healthy and developing normally until April 9, 2009, when he saw Dr. Jeanne Martin for his six-month well-baby visit and received his Diphtheria-Tetanus-acellular Pertussis (DTaP), Hepatitis B, inactivated Poliovirus, pneumococcal conjugate, and rotavirus vaccinations. See Pet'rs' Ex. 15 ¶¶ 6–8, ECF No. 16-2; Pet'rs' Ex. 8 at 3, 19, ECF Nos. 9-9 & 9-10. At approximately 11:30 P.M. that evening, Ms. Oliver heard "repetitive grunting sounds" through the baby monitor and found E.O. seizing in his bed. Pet'rs' Ex. 15 ¶ 9. E.O.'s seizure lasted approximately four to five minutes. Pet'rs' Ex. 26 at 3, ECF No. 39-3.

E.O. was taken to the Banks-Jackson-Commerce Medical Center, where he arrived at 12:19 A.M. on April 10, 2009. Id. at 1, 3. He had "a fever of 101.3 degrees, red eyes with discharge from his right eye, and a runny nose." Dec. at *4 (quotation omitted); see also Pet'rs' Ex. 1 at 13, ECF No. 9-2. E.O.'s parents reported to the ER physician that he had received vaccinations the previous day. Pet'rs' Ex. 1 at 13. E.O. was diagnosed with a febrile seizure, was prescribed pediatric Tylenol and Motrin, and was discharged with instructions to follow up with his pediatrician. Dec. at *4.

On April 10, 2009, Dr. Martin saw E.O. for a follow-up exam. See Pet'rs' Ex. 8 at 18. Dr. Martin found his condition normal on examination except for a tearing right eye. Id. His temperature was 97.1 degrees with no fever. Id. Dr. Martin diagnosed E.O. with a complex febrile seizure and conjunctivitis in the right eye. Id.

E.O. had no seizures or other health issues over the next two months. See Pet'rs' Ex. 19 at 190, 198, ECF No. 27-4. On June 16, 2009, however, Ms. Oliver noticed that E.O. was not moving his right side and failed to interact with her for about ten minutes. Id. at 192. She took

[1] Citations to the petitioners' exhibits are to the pagination that appears in the lower right-hand corner of the exhibits.

him to the ER at St. Mary's Hospital, where he was seen by Dr. Brewer, who diagnosed him with a "possible seizure" and discharged him in stable condition. Id. at 190.

On June 18, 2009, E.O. was seen for follow up by Dr. Elizabeth Sekul, a pediatric neurologist. Pet'rs' Ex. 4 at 84–87, ECF No. 9-5. On examination, she described E.O. as "alert, playful, interactive, very socially engaging . . . [and] in no apparent distress." Id. at 85. In a letter to Dr. Brewer, Dr. Sekul reported that E.O. had "normal development [and] has had two events"; the first event, she noted, was "associated with his immunizations," and the second "was only some transient hemiparesis, most likely secondary to a Todd." Id. at 86.[2] After reviewing E.O.'s medication history of Diastat 2.5 mg, Dr. Sekul prescribed Trileptal. Id.

E.O. had several more seizures over the summer, all of which necessitated trips to the ER. See Pet'rs' Ex. 19 at 153, 168; Pet'rs' Ex. 5 at 3, ECF No. 9-6. On August 17, 2009, he was evaluated by Dr. Jun Park, a pediatric neurologist in Atlanta, Georgia. See Pet'rs' Ex. 2 at 5–6, ECF No. 9-3. Dr. Park reported that E.O. had experienced six "sporadic" seizures, with the first event "at six months of age on the night after the six-month vaccination," and the last event on the preceding Wednesday. Id. at 5. Dr. Park diagnosed E.O. with focal epilepsy. Id. at 6. He ordered a repeat EEG, id., which was normal and showed "no focal features or epileptiform discharges," id. at 2. Dr. Park prescribed Diastat and instructed petitioners to follow up in six weeks. Id. at 6.

Beginning in March 2010, E.O. began to experience prolonged seizures, all of which resulted in visits to the ER. See Pet'rs' Ex. 3 at 2–8, ECF No. 9-4; Pet'rs' Ex. 4 at 3–5, 15–28, 33–35, 54–56. The first seizure, on March 1, 2010, lasted approximately two hours and led to E.O.'s admission to the pediatric intensive care unit at the Medical College of Georgia (MCG). Pet'rs' Ex. 4 at 54–56. Dr. Suzanne Strickland diagnosed him with a seizure and status epilepticus, and prescribed Keppra 250 mg twice a day, Trileptal 240 mg twice a day, and Diastat 7.5 mg as needed for seizures. Id. at 56. During another ER visit a week later, on March 8, 2010, Dr. Strickland reported that E.O. continued to have "daily seizures" and that "[t]he episodes have become progressively worse with increase in duration as well as frequency." Id. at 33. Dr. Strickland updated E.O's prescriptions to include Keppra 300 mg twice a day, Dilantin 25 mg twice a day, and Diastat 7.5 mg as needed. Id. at 34–35.

On April 9, 2010, E.O. returned to the ER at MCG after suffering a prolonged seizure that lasted forty-five minutes. Id. at 18. During this episode, E.O. did not respond to Diastat. Id. at 16–18. Upon discharge from MCG, E.O. exhibited additional seizure symptoms and required extra doses of Diastat and Dilantin. Id. at 3. On April 24, 2010, Dr. Park diagnosed E.O. with "[i]ntractable epilepsy from possible left frontal epileptic foci." Id. at 4. Dr. Park prescribed

[2] Todd's paralysis is a "hemiparesis or monoparesis lasting for a few minutes or hours, or occasionally for several days, after an epileptic seizure." Dorland's Illustrated Medical Dictionary 1378 (32d ed. 2012). Hemiparesis is defined as "muscular weakness or partial paralysis affecting one side of the body." Id. at 837. Monoparesis means "paresis of a single limb." Id. at 1178.

Keppra 3.5 mL twice a day, Klonopin 0.5 mg twice a day, Dilantin 25/25/50 mg three times a day, and Diastat 7.5 mg as needed. Id.

On April 26, 2010, Dr. James Wheless, a pediatric neurologist at LeBonheur Children's Medical Center ("LeBonheur") in Memphis, Tennessee, evaluated E.O. See Pet'rs' Ex. 9 at 2–5, ECF No. 9-11. Dr. Wheless reported that E.O.'s parents had stated that "[d]evelopmentally, [E.O.] continues to be on track for his age." Id. at 4. He noted, however, that E.O.'s seizures had increased dramatically over the prior two to three months, and were occurring on a daily basis. Id. at 2. He described E.O.'s seizures over the preceding two months as "characterized by brief cessation of his ongoing activity or brief pauses, with eye blinks." Id. at 7. Dr. Wheless noted that E.O.'s seizures had not adequately responded to treatment with Trileptal, Dilantin, Keppra, Klonopin, Ativan, Topamax, or Depakote. Id. After a full diagnostic evaluation, Dr. Wheless diagnosed E.O. with "intractable cryptogenic complex partial seizures." Id. at 5.

On June 1, 2010, E.O. returned to LeBonheur for further evaluation. Id. at 31. He had a prolonged seizure at the time of admission that lasted fifty minutes. Id. at 37–38. During that admission to LeBonheur, E.O. underwent a genetic test which revealed an SCN1A defect. See id. at 36–37.[3] At the time of E.O.'s discharge on June 4, 2010, he was diagnosed with "[i]ntractable, symptomatic absence and partial new onset seizures of independent hemisphere origin and episodes of status epilepticus," as well as a "sodium channelopathy due to SCN1A gene defect." Id. Dr. Wheless prescribed Carnitor 1.5 mL three times a day, Keppra 500 mg three times a day, and Diastat 7.5 mg as needed, as well as a ketogenic diet plan and calcium and multivitamin supplements. Id. at 38.

On July 19, 2010, E.O., then 21 months old, was seen by Dr. Wheless for follow-up. See Pet'rs' Ex. 18 at 25–27, ECF No. 22-4. E.O.'s mother reported that he had continued to have frequent absence seizures, along with one prolonged complex partial seizure, which occurred on June 13, 2010. Id. at 26. E.O.'s parents also reported that they now had "slightly more concern with [E.O.'s] development in regards to speech." Id. Dr. Wheless performed a general physical exam, a neurologic exam, and a motor exam. Id. His impression was "[i]ntractable, symptomatic childhood absence and complex partial seizures of independent hemisphere origin secondary to

[3] As the Chief Special Master explained in her decision:

> The SCN1A gene encodes for a sodium channel, which is "a portion of a channel that allows the transport of sodium molecules across cell membranes in the neurons." Resp's Ex. A at 6–7. The flow of sodium molecules permits appropriate transmission of information from one cell to another. Id. at 6. SCN1A gene mutations affect neuron cells in various ways, depending on the particular mutation, and how the mutation affects the structure and function of the sodium channel. Id. So far, several neurological conditions have been associated with the SCN1A gene mutation, including . . . E.O.'s condition, Dravet syndrome. Id. at 5–7.

Dec. at *7.

SCN1A gene defect (borderline SMEI syndrome)," and "[e]ncephalopathy characterized by speech delay." Id.

Severe Myoclonic Epilepsy of Infancy, or SMEI syndrome, is a distinct epilepsy syndrome which is sometimes referred to as Dravet syndrome. See Pet'rs' Ex. 40 at 1, ECF No. 58-15. Dravet syndrome is extremely rare, with a frequency of one in 40,000 children. Pet'rs' Ex. 28 at 12, ECF No. 58-2. According to one study published in the medical journal Lancet Neural, "[a]bout 70-80% of children with Dravet syndrome have mutations in SCN1A." Pet'rs' Ex. 36 at 1, ECF No. 58-11; see also Pet'rs' Ex. 41 at 2, ECF No. 58-16 ("Of the cases with Dravet syndrome, 70–80% are caused by SCN1A mutations . . . ."); Pet'rs' Ex. 32 at 2, ECF No. 58-6 (journal article noting that "[m]any other studies have confirmed the finding of SCN1A gene mutations in most of the patients affected by SME but not in all"); but see Pet'rs' Ex. 28 at 12 (Dr. Shafrir asserting that the rate of identification of an SCN1A defect in SMEI cases ranged from 33% to 45%). The time frame in which the disease first presents overlaps with the schedule of routine childhood vaccinations. Pet'rs' Ex. 40 at 1. Dravet syndrome is "characterized by onset of recurrent febrile and/or afebrile hemiclonic or generalized seizures . . . in a previously healthy infant." Pet'rs' Ex. 41 at 2. The hemiclonic or generalized seizures evolve into "multiple seizure types generally resistant to anti-epileptic drugs." Id. By the second year of life, children usually have an encephalopathy with cognitive, behavioral, and developmental delays. See id.; Pet'rs' Ex. 55 at 2.

II. Procedural Background

A. Proceedings Before the Chief Special Master

On June 25, 2010, approximately a month before Dr. Wheless diagnosed E.O.'s Dravet syndrome, the Olivers filed a petition alleging that the vaccinations that E.O. received on April 9, 2009, caused him to develop "a fever and febrile seizures . . . [and] a chronic complex partial seizure disorder." Pet. ¶¶ 5–6. Over the next year, the Olivers compiled and submitted E.O.'s medical records for consideration in connection with their petition.

On July 29, 2011, the Secretary of Health and Human Services filed a Rule 4(c) Report, recommending against compensation on the ground that the petitioners had not established causation in fact by preponderant evidence. See Resp't's Rule 4(c) Report at 1, 15, ECF No. 40. Specifically, the Secretary observed that E.O. "had tested positive for a SCN1A gene defect," and that "[E.O.'s] own treating neurologist, Dr. Wheless . . . attributed [E.O.'s] seizure disorder not to the vaccines, but to a mutation in his SCN1A gene." Id. at 10, 14.

On April 16, 2012, petitioners submitted an expert report prepared by Dr. Yuval Shafrir, along with his curriculum vitae and seventeen medical articles referenced in his report. ECF No. 58.[4] Dr. Shafrir stated that he "definitely agree[d] with Dr. Wheless that this case is very

[4] Dr. Shafrir is a pediatric neurologist in private practice in Baltimore, Maryland. Pet'rs' Ex. 46 at 3, ECF No. 59-3. He is board-certified in neurology with a specialty in pediatric neurology, and in neurophysiology. Id. at 2. He has served as an Assistant Professor in Neurology and Pediatrics at multiple academic and medical institutions. Id. at 3. Dr. Shafrir has conducted

reminiscent of Dravet's syndrome," and that E.O. "has Dravet's syndrome." Pet'rs' Ex. 28 at 11–12. As discussed in greater detail below, however, Dr. Shafrir also opined that there was an association between the vaccinations E.O. received and the onset of his Dravet syndrome. See id. at 12–22.

On December 17, 2012, the Secretary filed expert reports prepared by Dr. Gerald Raymond[5] and Dr. Rajesh Sachdeo,[6] along with their curricula vitae and relevant medical literature. See ECF No. 65. Dr. Raymond and Dr. Sachdeo both opined that E.O.'s SCN1A gene mutation, rather than the vaccines, was more likely the cause of his Dravet syndrome. Resp't's Ex. A at 13; Resp't's Ex. C at 6.

On September 22, 2014, the Secretary filed a motion for a ruling on the record. ECF No. 93. She argued that the petition should be dismissed because petitioners had failed to distinguish their case from previously dismissed cases in which other special masters concluded, and the Federal Circuit affirmed, that the SCN1A gene mutation, and not a vaccination, was the cause of petitioners' Dravet syndrome or other seizure disorders. Resp't's Mot. for a Ruling on the R. at 10–13 (citing Snyder v. Sec'y of HHS, 553 F. App'x. 994 (Fed. Cir. 2014); Deribeaux ex rel. Deribeaux v. Sec'y of HHS, 717 F.3d 1363 (Fed. Cir. 2013); Stone v. Sec'y of HHS, 676 F.3d 1373 (Fed. Cir. 2012); Barnette v. Sec'y of HHS, 110 Fed. Cl. 34 (2013); and Waters v. Sec'y of HHS, No. 08-76V, 2014 WL 300936 (Fed. Cl. Spec. Mstr. Jan. 7, 2014)).

During a status conference on March 3, 2015, the Chief Special Master denied the Secretary's motion for a ruling on the record. See Order, ECF No. 102. She asked the parties to provide additional information about E.O.'s SCN1A mutation, and requested that the petitioners submit E.O.'s updated pediatric neurological records, his parents' genetic testing results, and an evaluation from his genetic specialist. Id. at 1–2. She also ordered both parties to submit supplemental expert reports. Id.

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numerous clinical studies in pediatric neurology and has published more than twenty peer-reviewed articles and abstracts. Id. at 3–6.

[5] Dr. Raymond is a pediatric neurologist who has completed fellowships in both developmental neuropathology and genetics and teratology. Resp't's Ex. B at 1. Dr. Raymond is board-certified in pediatrics, clinical genetics, and neurology with a special competency in child neurology. Id. He has extensive clinical, instructional, and research experience in the fields of neurology, pediatrics, and genetics. See id. at 1–2, 9–10. Dr. Raymond has peer reviewed and published numerous articles in these fields. See id. at 2–9. He is currently a professor in neurology at Johns Hopkins University, the director of neurogenetics research at the Kennedy Krieger Institute, and on the staff of the pediatrics and neurology department at Johns Hopkins Hospital. Id. at 1.

[6] Dr. Sachdeo is a neurologist who specializes in epilepsy. See Resp't's Ex. D at 1, 3–4. He has been board-certified in neurology since 1982. Id. at 3. Dr. Sachdeo is active in clinical research and has conducted more than fifty studies on epilepsy and has an active clinical practice addressing pediatric epilepsy. See id. at 1, 4–8. He has seen and treated patients with Dravet syndrome. Resp't's Ex. C at 1.

Subsequently, on March 28, 2016, the petitioners filed a motion for a ruling on the record. ECF No. 126. On February 1, 2017, the Chief Special Master denied the petitioners' motion, finding that they had not established a causal relationship between the vaccinations E.O. received and his Dravet syndrome. Dec. at *2. Accordingly, she dismissed their petition for compensation. Id. at *28.

B. The Present Motion for Review

Petitioners filed their motion for review of the Chief Special Master's Decision with this Court on March 3, 2017. ECF No. 131. In their motion, the Olivers argue that the Chief Special Master "impermissibly raised E.O.'s burden of proof by improperly applying Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579, 580, 590 (1993) when evaluating expert testimony." Mot. for Review at 3. They also contend that in deciding the case without an evidentiary hearing, the Chief Special Master "improperly us[ed] estoppel to deny both a full and fair hearing, in an abuse of her discretion, as well as a finding of causation." Id. In response, the Secretary argues that the Chief Special Master's ruling on causation was based on a careful weighing of the evidence of record, in light of the applicable case law, and that the motion for review should be denied. Resp't's Mem. in Resp. to Pet'rs' Mot. for Review at 1–2, ECF No. 133.

For the reasons set forth below, the Court concludes that the petitioners' motion for review lacks merit. Accordingly, the motion for review is **DENIED** and the Decision is **SUSTAINED**.[7]

DISCUSSION

I. Jurisdiction and Standard of Review

Congress established the National Vaccine Injury Compensation Program in 1986 to provide a no-fault compensation system for vaccine-related injuries and deaths. Figueroa v. Sec'y of HHS, 715 F.3d 1314, 1316–17 (Fed. Cir. 2013). The Vaccine Act is remedial legislation that should be construed in a manner effectuating its underlying spirit and purpose. Id.

A petition seeking compensation under the Vaccine Act is filed in the Court of Federal Claims, after which the Clerk of Court forwards it to the chief special master for assignment to a special master. 42 U.S.C. § 300aa-11(a)(1). The special master to whom the petition is assigned "issue[s] a decision on such petition with respect to whether compensation is to be provided under the [Vaccine Act] Program and the amount of such compensation." Id. § 300aa-12(d)(3)(A).

The Vaccine Act grants the Court of Federal Claims jurisdiction to review the record of the proceedings before a special master, and authority, upon such review, to:

[7] The Court has determined that oral argument is unnecessary in this case. Accordingly, its decision is based on the record, the Chief Special Master's opinion, and the parties' briefs.

1) Uphold the findings of fact and conclusions of law of the special master and sustain the special master's decision;

2) Set aside any findings of fact or conclusion of law of the special master found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law and issue its own findings of fact and conclusions of law; or

3) Remand the petition to the special master for further action in accordance with the Court's direction.

Id. § 300aa-12(e); see also Vaccine Rule 27.

On review of the special master's decision, the court applies the arbitrary and capricious standard to factual findings and the "not in accordance with law" standard to legal rulings. Moberly ex rel. Moberly v. Sec'y of HHS, 592 F.3d 1315, 1321 (Fed. Cir. 2010). The court's scope of review is a narrow one. The court "do[es] not reweigh the factual evidence, assess whether the special master correctly evaluated the evidence, or examine the probative value of the evidence or the credibility of the witnesses," because those "are all matters within the purview of the fact finder." Porter v. Sec'y of HHS, 663 F.3d 1242, 1249 (Fed. Cir. 2011) (citing Broekelschen v. Sec'y of HHS, 618 F.3d 1339, 1345 (Fed. Cir. 2010)). "[A]s long as a special master's finding . . . is 'based on evidence in the record that [is] not wholly implausible,'" the Court must uphold it. Id. (quoting Cedillo v. Sec'y of HHS, 617 F.3d 1328, 1338 (Fed. Cir. 2010) (alteration in original)). "'[T]he standard of review is uniquely deferential'" to special masters' decisions; if a special master "'has considered the relevant evidence of record, drawn plausible inferences and articulated a rational basis for the decision,' then reversible error is 'extremely difficult to demonstrate.'" Milik v. Sec'y of HHS, 822 F.3d 1367, 1376 (Fed. Cir. 2016) (first quoting Hodges v. Sec'y of HHS, 9 F.3d 958, 961 (Fed. Cir. 1993), then quoting Hines v. Sec'y of HHS, 940 F.2d 1518, 1528 (Fed. Cir. 1991)).

II. The Merits

To secure compensation under the Vaccine Act, a petitioner must prove by a preponderance of the evidence that the injury at issue was caused by a vaccine. See 42 U.S.C. §§ 300aa-11(c)(1), -13(a)(1). Where a petitioner sustains an injury in association with a vaccine listed in the Vaccine Injury Table, causation is presumed. Broekelschen, 618 F.3d at 1341–42 (citing 42 U.S.C. § 300aa-11(c)(1)(C)(i) and Andreu v. Sec'y of HHS, 569 F.3d 1367, 1374 (Fed. Cir. 2009)). Where, as in this case, the injury is not listed in the Table, the petitioner must prove causation in fact. Id. at 1342 (citing Moberly, 592 F.3d at 1321). To discharge that burden, "a petitioner must show that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Stone, 676 F.3d at 1379 (quotation omitted). "Once the petitioner has demonstrated causation, she is entitled to compensation unless the government can show by a preponderance of the evidence that the injury is due to factors unrelated to the vaccine." Broekelschen, 618 F.3d at 1342 (citing Doe v. Sec'y of HHS, 601 F.3d 1349, 1351 (Fed. Cir. 2010) and 42 U.S.C. § 300aa-13(a)(1)(B)).

The three-pronged test that the Federal Circuit announced in Althen v. Secretary of Health and Human Services, 418 F.3d 1274 (Fed. Cir. 2005) guides the causation determination. Under that test, to demonstrate that a vaccination caused the petitioner's injury, he or she must provide: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Id. at 1278.

In this case, the Chief Special Master found that petitioners had failed to demonstrate causation in fact. Indeed, she concluded, it was more likely than not that E.O.'s SCN1A mutation was the sole cause of his Dravet syndrome. For the reasons set forth below, the Court finds that the Chief Special Master's conclusions were well-supported by the record and entitled to deference. The Court further finds that the petitioners' objections to her Decision lack merit.

A. Reliable Theory of Causation—Althen Prong One

As the Chief Special Master observed, to satisfy prong one of the Althen test, the petitioners were required to set forth a medical theory explaining how the vaccines E.O. received could have caused his injury. Dec. at *11 (citing Andreu, 569 F.3d at 1375 and Pafford v. Sec'y of HHS, 451 F.3d 1352, 1355–56 (Fed. Cir. 2006)) (noting that prong one addresses whether the vaccine at issue can cause the type of injury alleged). "Petitioners' theory of causation need not . . . be medically or scientifically certain; however, it must be informed by a 'sound and reliable medical or scientific explanation.'" Id. (quoting Knudsen ex rel. Knudsen v. Sec'y of HHS, 35 F.3d 543, 548 (Fed. Cir. 1994)).

In this case, the petitioners relied upon the opinion of their expert, Dr. Shafrir, to establish the existence of a medical theory under which the vaccines E.O. received could cause an individual to develop Dravet syndrome. Dr. Shafrir's view was that an SCN1A mutation is a necessary but not sufficient precondition to the development of Dravet syndrome. Pet'rs' Ex. 74 at 1–2, ECF No. 98-2. Further, according to Dr. Shafrir, the possession of the SCN1A mutation does not necessarily lead to the development of Dravet syndrome. See id. He posed two alternative theories under which the DTaP vaccination E.O. received might have interacted with his SCN1A mutation to cause E.O.'s Dravet syndrome. Pet'rs' Ex. 68 at 4–6, ECF No. 90-2; Pet'rs' Ex. 102 at 5–8, ECF No. 121-2; Pet'rs' Ex. 47 at 3–4.

Dr. Shafrir's first proposed theory of causation was a "second hit" theory. Citing a study by Klassen et al., Dr. Shafrir observed that for many diseases, including cancer, it has "been hypothesized that the appearance and severity of the disorder are a simple result of the net accumulation of genetic variants or 'hits' in a disease pathway, where crossing an undefined risk threshold divides affected from unaffected individuals." Pet'rs' Ex. 47 at 3 (internal quotation omitted). Dr. Shafrir opined that "the occurrence of a single seizure, which here, was clearly induced by vaccination, make[s] the brain more prone to seizures from other causes." Id. at 8. Thus, Dr. Shafrir observed, a "single seizure can cause dramatic changes in gene expression in the brain, which may serve as the second hit mentioned by Klassen." Id.

Alternatively, Dr. Shafrir proposed a second mechanism "based on an immune-mediated response to the DTaP vaccination." Dec. at *13. Citing a number of studies, Dr. Shafrir suggested the possibility that one of the immune responses at play in E.O.'s case was the

mechanism of molecular mimicry. Id. (citing Pet'rs' Ex. 68 at 5 and Mem. in Supp. of Mot. for Ruling on the R. at 18). Specifically, he opined that "components of the DTap [sic] vaccination contain multiple areas of homology with multiple brain proteins, including multiple ion channels in epilepsy related genes." Id. (citing Pet'rs' Ex. 102 at 5). In other words, Dr. Shafrir asserted that E.O.'s seizures could be the result of the body's immune response to the vaccination, in the form of antibodies which, because of molecular mimicry, result in the body attacking the "component of the sodium channel coded by the SCN1A gene." See Pet'rs' Ex. 102 at 6.

The government's expert, Dr. Raymond, took issue with Dr. Shafrir's proposed theories of causation. He opined that the SCN1A mutation was the "sole cause" of E.O.'s Dravet syndrome. Resp't's Ex. A at 13. Dr. Raymond rejected Dr. Shafrir's theories of causation on three general grounds. First, Dr. Raymond summarized a number of medical studies and other literature which he asserted establish that a significant alteration in the SCN1A gene alone is sufficient to cause Dravet syndrome. See Resp.'s Ex. E at 1, 3–4, ECF No. 92-1. Dr. Raymond explained that Dr. Shafrir's theories were not supported by scientific evidence because the studies he cited were not specific to SCN1A, or were retrospective studies with methodology problems. See id. Second, as the Chief Special Master summarized, Dr. Raymond reported that "animal models have demonstrated significant abnormalities of SCN1A mutation that 'mirror the human condition,' and in these studies the animals spontaneously developed seizures without any triggers." Dec. at *15 (citing Resp't's Ex. E at 3–4). Third, Dr. Raymond cited studies conducted by McIntosh et al. and Berkovic et al., which he explained showed that, contrary to Dr. Shafrir's theories, "the occurrence of febrile seizures following vaccinations does not change the clinical course or outcome of Dravet syndrome." Id. (citing Resp't's Ex. A at 11).

The Chief Special Master found Dr. Raymond's views more persuasive than those of Dr. Shafrir. See id. at *16, *20. Petitioners contend that in so finding, the Chief Special Master "raised E.O.'s burden of proof," and failed to properly apply the standards set forth in Daubert. See Mot. for Review at 8–17. Specifically, they argue that her Decision was inconsistent with Daubert because she focused on whether there was scientific support for the conclusions Dr. Shafrir reached, rather than on whether the principles and methodology he used to reach his conclusions were scientifically reliable.

It is not entirely clear to the Court why the Daubert decision (which concerns the admissibility of expert testimony) is relevant to this case. The Chief Special Master did not exclude Dr. Shafrir's opinion from consideration on the grounds that it failed to meet Daubert's standards. To the contrary, she carefully evaluated the seven reports Dr. Shafrir prepared, as well as the medical literature submitted in support of his opinions and weighed them against the opinions of the other experts. Cf. de Bazan v. Sec'y of HHS, 539 F.3d 1347, 1352 n.4 (Fed. Cir. 2008) (finding Daubert inapposite where the special master did not exclude any expert evidence but "[r]ather . . . admitted and weighed both parties' evidence [and] simply decided that the government's evidence was more persuasive").

Moreover, as the court of appeals has observed, "[w]hile Daubert does not require that the experts' ultimate conclusions be generally accepted in the scientific community, and the focus of a Daubert inquiry must generally be 'on principles and methodology, not on the conclusions they generate,' 'conclusions and methodology are not entirely distinct from one another . . . . A court may conclude that there is simply too great an analytical gap between the

data and the opinion proffered.'" Cedillo, 617 F.3d at 1339 (quoting Gen. Elec. Co. v. Joiner, 522 U.S. 136, 146 (1997) (observing that "[t]rained experts commonly extrapolate from existing data" but that "nothing in . . . Daubert . . . requires a district court to admit opinion evidence that is connected to existing data only by the ipse dixit of the expert")).

In this case, the Chief Special Master's Decision reflects a thorough examination of the entire record in support of her ultimate conclusion that there was a substantial analytical gap between the data upon which Dr. Shafrir's theories of causation relied and the conclusions he reached. Thus, in contrast to the sources cited by Dr. Raymond, the Chief Special Master observed, "none of the articles cited by Dr. Shafrir suggest that vaccines can cause Dravet syndrome or change the clinical course of Dravet syndrome, and several come to the opposite conclusion." Dec. at *16. She also observed that "[w]hile some studies demonstrate an association between vaccination and fever, and thus the onset of seizures in children with Dravet syndrome, the existing medical literature has established that vaccination does not affect the clinical course or prognosis of Dravet syndrome." Id. In fact, she noted, "[t]he animal models, as presented by Dr. Raymond, provide strong evidence that Dravet syndrome will develop in children with the SCN1A mutation, whether or not they receive vaccinations." Id.

Additionally, the Chief Special Master rejected Dr. Shafrir's "second hit" theory because the Klassen article upon which he relied "suggest[ed] that mutations may combine to cause disease, [but] did not examine vaccines or other environmental factors or draw conclusions about the theories proposed by Dr. Shafrir." Id. at *12. As far as molecular mimicry, she found that the studies which Dr. Shafrir cited in support were either not pertinent or not persuasive for a variety of reasons, explained in detail in her opinion. See id. at *13–*16.

As the court of appeals has noted, "[f]inders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them . . . ." Moberly, 592 F.3d at 1326. Specifically, it has explained that:

> Congress assigned to a group of specialists, the Special Masters within the Court of Federal Claims, the unenviable job of sorting through these painful cases and, based upon their accumulated expertise in the field, judging the merits of the individual claims. The statute makes clear that, on review, the Court of Federal Claims is not to second guess the Special Masters['] fact-intensive conclusions; the standard of review is uniquely deferential for what is essentially a judicial process . . . . That level of deference is especially apt in a case in which the medical evidence of causation is in dispute.

Deribeaux, 717 F.3d at 1366–67 (quoting Hodges, 9 F.3d at 961); see also de Bazan, 539 F.3d at 1354 (upholding the special master's determination that respondent's expert testimony was more credible and probative than that of the petitioner's expert); Lampe v. Sec'y of HHS, 219 F.3d 1357, 1361–62 (Fed. Cir. 2000) (upholding the special master's determination that the Secretary's medical expert was more persuasive than the petitioners' medical expert because "[t]hose findings, which are at the core of the special master's decision in this case, are largely

based on his assessments of the credibility of the witnesses and the relative persuasiveness of the competing medical theories of the case. As such, they are virtually unchallengeable on appeal.").

In this case, as noted, the Chief Special Master applied her expertise and conducted a painstaking review and analysis of the expert reports and the supporting literature. Her conclusion that Dr. Shafrir's theories were not supported by the scientific studies upon which he relied, and her decision to instead credit the opinions of the government's experts, were entirely reasonable and well-supported by the record before her. Accordingly, the Court rejects the petitioners' argument that her ruling was contrary to Daubert and that she erred when she concluded that the petitioners' theories of causation were not supported by sound and reliable science.

B. Prongs Two and Three of the Althen Test

Prong one of Althen, as explained above, requires a petitioner to supply a theory of causation that is scientifically sound and reliable. In this case, the Chief Special Master found that the petitioners did not satisfy prong one. That failure alone is sufficient to justify dismissing the petition. But even if petitioners had provided a plausible theory of causation, their claim would nevertheless be untenable given the Chief Special Master's conclusions that they failed to satisfy prongs two and three of the Althen test, and that, in fact, the government produced preponderant evidence that E.O.'s injuries were attributable to another cause—the defect in his SCN1A gene.

As noted above, under prong two, petitioners must prove by a preponderance of the evidence that there is a "logical sequence of cause and effect" showing that the vaccination was in fact the reason for E.O.'s injury. Capizzano v. Sec'y of HHS, 440 F.3d 1317, 1324 (Fed. Cir. 2006) (quoting Althen, 418 F.3d at 1278); see also Pafford, 451 F.3d at 1356 (stating that "petitioner[s] 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'"). And under the third prong, petitioners must prove by preponderant evidence that the onset of E.O.'s Dravet syndrome "occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." See de Bazan, 539 F.3d at 1352.

As with prong one, the Chief Special Master's conclusions that the petitioners failed to provide preponderant evidence to support prongs two and three were based upon a thorough and well-reasoned analysis of the conflicting opinions of the experts. Thus, with respect to prong two, she concluded that petitioners failed to prove that there was a logical sequence of cause and effect showing that the vaccines E.O. received caused his Dravet syndrome. She observed that the essence of the article that Dr. Shafrir relied upon to demonstrate that the vaccinations may have triggered E.O.'s earlier seizures was actually "that neither vaccines nor time of seizure onset changes the clinical course or outcome in children with Dravet syndrome." Dec. at *20. Further, "Dr. Shafrir's calculations of the relative risks for immunization were based on an article that lacked accurate data of gene positive rates, and he cited articles that were not relevant to E.O.'s situation." Id. Moreover, the Chief Special Master found that "E.O.'s medical records do not support evidence of cause and effect." Id. "Although E.O.'s treating physicians and EMS caregivers reported that his initial seizure was temporally associated with vaccinations," the Chief Special Master observed, "none of them attributed his development of Dravet syndrome to

the vaccines." Id. On the contrary, as the Chief Special Master noted, "Dr. James Wheless, E.O.'s pediatric neurologist, first diagnosed him with complex partial seizures 'secondary to SCN1A gene defect' at the age of 21 months." Id. (citing Pet'rs' Ex. 18 at 26).

The Chief Special Master also found that the petitioners did not satisfy prong three of the Althen test. To be sure, E.O.'s first seizure occurred within 24 hours of his six-month vaccinations. But the Chief Special Master rejected Dr. Shafrir's opinion that E.O.'s first seizure marked the onset of his encephalopathy. See id. at *21. Instead, she credited Dr. Raymond's conclusion that E.O.'s Dravet syndrome did not manifest until he was twenty-one months old. See id. He based that conclusion on the fact that after his initial seizure, "E.O. recovered and returned to baseline, and he did not show evidence of any injury that was temporally associated with the vaccines." Id. (citing Resp't's Ex. A at 9). The manifestation of his encephalopathy at approximately twenty-one months of age, Dr. Raymond opined, "is consistent with the temporal profile of [Dravet syndrome] and not to an adverse event subsequent to a brief seizure following immunization." Resp't's Ex. A at 9. Crediting Dr. Raymond, the Chief Special Master concluded that "[w]ithout evidence of a causal mechanism or evidence of injury, the temporal relationship between the vaccination and the first seizure alone is not sufficient to establish a causal link." Dec. at *21.

Moreover, the Chief Special Master found that petitioners had not only failed to establish a prima facie case of causation but that even if they had, the government rebutted it by proving that "E.O.'s SCN1A mutation, a factor unrelated to the administration of the vaccines, is the agent solely responsible for causing E.O.'s Dravet syndrome and resultant neurological injuries." Id. at *26. This conclusion is supported by the reports of the Secretary's experts, Drs. Raymond and Sachdeo, who opined that E.O.'s SCN1A mutation was the sole cause of his Dravet syndrome, and that E.O.'s clinical outcome was not altered by his receipt of the vaccines administered on April 9, 2009. Id. at *26–*27. The Chief Special Master observed that "[t]he medical articles and studies filed in this case establish that the international medical community generally agrees that vaccinations are not the cause of Dravet syndrome and that the SCN1A mutation is responsible for causing the disease." Id. at *26.

Reliable scientific evidence also supports the conclusion that E.O.'s specific SCN1A mutation is a disease-causing mutation. Thus, Dr. Raymond explained that "splice site mutations" or "splicing defects," like E.O.'s "are a very common cause of human genetic disease and are frequently found as a cause in SMEI." Resp't's Ex. A at 8. Indeed, even Dr. Shafrir agreed that the mutation "probably" "play[ed] a major role in [E.O.'s] condition." Pet'rs' Ex. 74 at 5.

Further, the Chief Special Master noted that Dr. Raymond's theory is supported by current medical research and literature, animal models, and studies demonstrating that febrile seizures following vaccination do not alter the clinical outcome of Dravet syndrome. Dec. at *14–*16. Thus, Dr. Raymond opined, and the Chief Special Master accepted, that the SCN1A mutation is the sole cause of E.O.'s Dravet syndrome. Id. at *26–*27.

In their motion for review, the petitioners merely restate Dr. Shafrir's views, which the Chief Special Master rejected for the reasons set forth above and as further explained in her opinion. Mot. for Review at 10–14. They also take issue with the Chief Special Master's

treatment of the medical literature upon which Dr. Shafrir relied. Id. at 11–14. But this case, at bottom, involves a disagreement among experts regarding what the medical record and literature reveals about the causes of E.O.'s Dravet syndrome. The Chief Special Master carefully considered the entire record, including the opinions of the experts and the medical literature. She explained her reasoning in detail. Under the well-established principles set forth above, this Court defers to the Chief Special Master's ultimate conclusion that the opinions of the government's experts were more persuasive than those of Dr. Shafrir, and that E.O.'s SCN1A gene mutation and not a vaccine was the cause of E.O.'s Dravet syndrome.

C. Estoppel Argument

The petitioners' final contention is that that the Chief Special Master erred by not holding an evidentiary hearing on their claim. They argue that by failing to hold such a hearing she improperly applied estoppel on the basis of prior decisions in which children with SCN1A mutations had been denied compensation under the Vaccine Act. Mot. for Review at 17–20. This contention lacks merit.

The Vaccine Rules explicitly authorize a special master to make findings of fact and decide a case on the basis of the written record without an evidentiary hearing. Vaccine Rule 8(d). A special master is not obliged to hold an evidentiary hearing. See Burns ex rel. Burns v. Sec'y of HHS, 3 F.3d 415, 417 (Fed. Cir. 1993). Rather, the decision whether to hold a hearing is within the discretion of the special master. See 42 U.S.C. § 300aa-12(d)(3)(B)(v).

In this case, petitioners' argument that the Chief Special Master "improperly applied the principle of estoppel contrary to law" when she issued a ruling on the record lacks merit. To be sure, the Chief Special Master observed that "[c]ompensation has been denied in a number of similar cases based upon a finding that the SCN1A mutation was a 'factor unrelated to the administration of the vaccine,' and the agent solely responsible for causing Dravet syndrome in a child."[8] Dec. at *25 (footnote omitted). Nonetheless she did not apply estoppel to prevent petitioners from proving their theories of causation. To the contrary, she carefully evaluated all

[8]See, e.g., Faoro v. Sec'y of HHS, No. 10-704V, 2016 WL 675491 (Fed. Cl. Spec. Mstr.), aff'd, 128 Fed. Cl. 61 (2016); Harris v. Sec'y of HHS, No. 07–60V, 2011 WL 2446321 (Fed. Cl. Spec. Mstr.), rev'd, 102 Fed. Cl. 282 (2011), rev'd sub nom. Snyder v. Sec'y of HHS, 553 F. App'x 994 (Fed. Cir. 2014); Snyder v. Sec'y of HHS, No. 07–59V, 2011 WL 3022544 (Fed. Cl. Spec. Mstr.), rev'd 102 Fed. Cl. 305 (2011), rev'd 553 F. App'x 994 (Fed. Cir. 2014); Hammitt v. Sec'y of HHS, No. 07–170V, 2011 WL 1135878 (Fed. Cl. Spec. Mstr.), aff'd, 98 Fed. Cl. 719 (2011), aff'd sub nom. Stone v. Sec'y of HHS, 676 F.3d 1373 (Fed. Cir. 2012); Stone v. Sec'y of HHS, No. 04–1041V, 2011 WL 836992 (Fed. Cl. Spec. Mstr.), aff'd, 99 Fed. Cl. 187 (2011), aff'd, 676 F.3d 1373 (Fed. Cir. 2012). Thus as noted, with the exception of Faoro (from which no appeal was taken), each decision finding the SCN1A mutation to be the sole cause of the petitioner's Dravet syndrome was affirmed by the court of appeals.

of the evidence, including seven expert reports from Dr. Shafrir, and more than eighty scientific articles submitted by the petitioners. See id. at *3–*9, *11–*16.

Further, petitioners do not point to any specific reason why this case necessitated an evidentiary hearing. Mot. for Review at 17–20. The Chief Special Master's ruling was based on the persuasiveness of the experts' written opinions in light of the extensive medical literature; there was no need for her to personally observe the expert witnesses testify to evaluate their demeanor or truthfulness.

In short, the Chief Special Master's decision not to hold an evidentiary hearing in this matter was an appropriate exercise of her discretion. Accordingly, the petitioners' allegation of error on this basis is rejected.

CONCLUSION

On the basis of the foregoing, the petitioners' motion for review is **DENIED** and the Chief Special Master's Decision is **SUSTAINED**. The Clerk is directed to enter judgment accordingly.

IT IS SO ORDERED.

s/ Elaine D. Kaplan
ELAINE D. KAPLAN
Judge