United States Court of Appeals for the Federal Circuit

LAURA OLIVER AND EDDIE OLIVER, JR., PARENTS AND LEGAL REPRESENTATIVES OF E.O., III,
Petitioners-Appellants

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,
Respondent-Appellee

2017-2540

Appeal from the United States Court of Federal Claims in No. 1:10-vv-00394-EDK, Judge Elaine Kaplan.

Decided: August 17, 2018

CLIFFORD JOHN SHOEMAKER, Shoemaker and Associates, Vienna, VA, argued for petitioners-appellants.

DANIEL ANTHONY PRINCIPATO, Torts Branch, Civil Division, United States Department of Justice, Washington, DC, argued for respondent-appellee. Also represented by CHAD A. READLER, C. SALVATORE D'ALESSIO, CATHARINE E. REEVES, HEATHER LYNN PEARLMAN.

Before NEWMAN, LOURIE, and WALLACH, *Circuit Judges.*

Opinion for the court filed by *Circuit Judge* WALLACH.

Dissenting opinion filed by *Circuit Judge* NEWMAN.

WALLACH, *Circuit Judge*.

Appellants Laura Oliver and Eddie Oliver, Jr. (together, "the Olivers"), parents and legal representatives of E.O., III ("E.O."), sued the Secretary of Health and Human Services ("the Government") for compensation under the National Childhood Vaccine Injury Act of 1986 ("Vaccine Act"), Pub. L. No. 99-660, 100 Stat. 3755 (codified as amended at 42 U.S.C. §§ 300aa-2–300aa-33 (2012)). The Olivers allege that E.O. developed Dravet syndrome[1] as a result of certain vaccinations. The Chief Special Master of the U.S. Court of Federal Claims determined that, inter alia, the Olivers "failed to show by preponderant evidence that E.O.'s injuries were caused by his . . . vaccinations," such that the Olivers were not entitled to compensation. *Oliver v. Sec'y of Health & Human Servs.* (*Oliver I*), No. 10-394V, 2017 WL 747846, at *2 (Fed. Cl. Feb. 1, 2017). The Olivers filed a motion for review in the Court of Federal Claims, and the Court of Federal Claims denied it. *See Oliver v. Sec'y of Health & Human Servs.* (*Oliver II*), 133 Fed. Cl. 341, 344 (2017); *see also* J.A. 52 (Judgment).

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[1] According to a 2010 study on the relation between vaccination and Dravet syndrome, "Dravet syndrome, formerly severe myoclonic epilepsy of infancy (SMEI), is characterized by prolonged febrile seizures starting at about the age of [six] months." J.A. 1221. "Mutations in [the] SCN1A [gene] can be identified in the majority of patients, and epileptic seizures in the setting of fever are a clinical hallmark" of Dravet syndrome. J.A. 1221 (italics omitted).

The Olivers appeal. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(3) (2012). We affirm.

BACKGROUND[2]

On April 9, 2009, E.O. visited a pediatrician for his six-month visit and received vaccinations for Diphtheria-Tetanus-acellular Pertussis, Hepatitis B, Inactivated Poliovirus, Pneumococcal Conjugate, and Rotavirus. *Oliver I*, 2017 WL 747846, at *4. At approximately 11:30 PM that night, Mrs. Oliver "found E.O. seizing in his bed" and called 9-1-1. *Id.* (citation omitted). When he arrived at the emergency room, E.O. presented with "a fever of 101.3 degrees, red eyes with discharge from his right eye, and a runny nose." *Id.* (internal quotation marks and citation omitted). The emergency room physician diagnosed E.O. with a febrile seizure and discharged E.O. with instructions to see his pediatrician. *Id.* On April 10, 2009, E.O.'s pediatrician recorded E.O.'s temperature as 97.1 degrees and diagnosed E.O. with "complex febrile seizure and conjunctivitis in the right eye." *Id.* (citation omitted).

"E.O. did not have any health issues or seizures for the next two months." *Id.* However, E.O. had several seizures over the summer of 2009 and began to experience prolonged seizures in March 2010, with each seizure resulting in an emergency room visit. *Id.* at *5. In April 2010, E.O. was referred to a pediatric neurologist, who diagnosed E.O. with an SCN1A gene defect in June 2010. *Id.* at *5–6. In July 2010, E.O. began to exhibit develop-

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[2] The relevant facts and procedural history are largely undisputed and are set forth in the Chief Special Master's and Court of Federal Claims' decisions below. *See Oliver II*, 133 Fed. Cl. at 344–48; *Oliver I*, 2017 WL 747846, at *1–9. For convenience, we cite those opinions in outlining the undisputed facts relevant to this appeal.

mental delay, and the pediatric neurologist performed general physical, neurological, and motor examinations, which demonstrated "intractable, symptomatic childhood absence and complex partial seizures of independent hemisphere origin secondary to SCN1A gene defect (borderline SMEI syndrome) and encephalopathy characterized by speech delay." *Id.* at *6 (internal quotation marks and citation omitted).

DISCUSSION

I. Standard of Review and Legal Standard

"We review an appeal from the Court of Federal Claims in a Vaccine Act case de novo, applying the same standard of review [as the Court of Federal Claims] applied in reviewing the special master's decision." *Milik v. Sec'y of Health & Human Servs.*, 822 F.3d 1367, 1375 (Fed. Cir. 2016) (citation omitted). "Although we review legal determinations without deference, we review the special master's factual findings under the arbitrary and capricious standard." *Id.* at 1376 (citation omitted). This standard is "uniquely deferential" and "difficult for an appellant to satisfy with respect to any issue, but particularly with respect to an issue that turns on the weighing of evidence by the trier of fact." *Id.* (internal quotation marks and citations omitted). "[A]s long as the special master's conclusion is based on evidence in the record that is not wholly implausible, we are compelled to uphold that finding as not being arbitrary or capricious." *Id.* (internal quotation marks, brackets, and citation omitted).

Where, as here, a petitioner alleges an injury not found on the Vaccine Injury Table ("the Table"),[3] they

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[3] The Table is published in 42 U.S.C. § 300aa-14. For injuries listed in the Table, i.e., "Table Injuries," "causation is presumed when a designated condition

"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." *Moberly*, 592 F.3d at 1321 (internal quotation marks and citation omitted). To demonstrate causation, the petitioner's "burden is to show by preponderant evidence" each of the requirements set forth in *Althen v. Secretary of Health and Human Services* ("the *Althen* prongs"): "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." 418 F.3d 1274, 1278 (Fed. Cir. 2005). "If [the petitioner] satisfies this burden, she is entitled to recover unless the [G]overnment shows, also by a preponderance of evidence, that the injury was in fact caused by factors unrelated to the vaccine." *Id.* (internal quotation marks, brackets, and citation omitted).

II. The Court of Federal Claims Did Not Err in Sustaining the Chief Special Master's Determination

The Chief Special Master determined that the Olivers failed to satisfy their burden as to each of the *Althen* prongs. *Oliver I*, 2017 WL 747846, at *11–21. The Olivers aver that the Chief Special Master erred in her evaluation of the *Althen* prongs by: (1) "misappl[ying] *Daubert* [*v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993)] and thus appl[ying] an evidentiary standard not in accordance with law," Appellants' Br. 17 (capitali-

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follows the administration of a designated vaccine within a designated period of time." *Moberly ex rel. Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010). For "all other injuries alleged to be caused by a vaccine" that are not listed in the Table, i.e., "off-Table injuries," "causation must be proved in each case." *Id.* (citation omitted).

zation modified); *see id.* at 17–33; and (2) "improperly using estoppel and a faulty scientific premise to deny both a full and fair hearing, in an abuse of her discretion, as well as a finding of causation," *id.* at 34 (italics omitted); *see id.* at 34–43. We disagree with the Olivers.

First, although the Olivers claim that the Chief Special Master misapplied *Daubert*, their argument amounts to no more than a challenge to the weight afforded to their expert's testimony and supporting evidence.[4] *See id.* at 17–33. The Chief Special Master thoroughly evaluated both parties' evidence as to each *Althen* prong and found the Government's more persuasive. *See Oliver I*, 2017 WL 747846, at *11–21. For example, regarding the first *Althen* prong, the Chief Special Master found that "none of the articles cited by [the Olivers' expert] suggest that vaccines can cause . . . or change the clinical course of Dravet syndrome, and several come to the opposite conclusion," whereas the Government's expert "provide[d] strong evidence [in the form of animal studies] that Dravet syndrome will develop in children with the SCN[1]A mutation, whether or not they receive vaccinations." *Id.* at *16; *see id.* at *11–16 (reviewing the parties'

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[4] While the Chief Special Master referenced *Daubert* in the "Standards for Adjudication" section of her opinion, *see Oliver I*, 2017 WL 747846, at *10, she did not exclude either parties' evidence and made no reference to *Daubert* when weighing the parties' evidence to determine whether the Olivers had satisfied their burden of establishing each of the *Althen* prongs, *see id.* at *11–21. Nevertheless, the Government acknowledges that the Chief Special Master *implicitly* conducted a *Daubert* analysis in finding the Olivers' expert's testimony and supporting evidence unpersuasive. *See* Oral Arg. at 18:39–19:17, http://oralarguments.cafc.uscourts.gov/default.aspx?fl=2017-2540.mp3.

evidence as to the first *Althen* prong). In light of these findings, the Chief Special Master determined that the Olivers' expert "did not provide a 'sound and reliable' medical theory to explain how the vaccinations at issue cause Dravet syndrome." *Id.* at *16. The Chief Special Master made similar findings with respect to the second and third *Althen* prongs. *See id.* at *16–20 (reviewing the parties' evidence as to the second *Althen* prong), *20 (finding, with respect to the second *Althen* prong, that the Olivers' expert's testimony was "not persuasive" in light of the Government's expert's testimony and E.O.'s medical records, such that the Olivers "failed to prove by a preponderance of the evidence a logical sequence of cause and effect showing that the vaccines E.O. received caused his Dravet syndrome"), *20–21 (reviewing the parties' evidence as to the third *Althen* prong), *21 (finding, with respect to the third *Althen* prong, that, "[w]hile the proximity between vaccination and seizure onset might suggest a causal relationship between the two events, E.O. did not develop Dravet syndrome until . . . more than a year after these vaccinations," such that the Olivers' evidence "[wa]s not sufficient to establish a causal link").

The Olivers repeatedly fault the Chief Special Master for failing to afford greater weight to their expert's testimony and supporting evidence. *See, e.g.*, Appellants' Br. 25 (stating that "the [Chief] Special Master is highly dismissive of all of [their expert]'s testimony"), 26 (stating that the Olivers' expert's "theory and . . . mechanisms were, in fact, *supported* by the literature even if his conclusions were not yet published"), 33 (stating that the Chief Special Master "essentially reject[ed]" their expert's supporting evidence). We cannot review such challenges. *See Milik*, 822 F.3d at 1376 ("[W]e do 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—these are all matters within the purview of the fact find-

er." (internal quotation marks and citation omitted)); *Lampe v. Sec'y of Health & Human Servs.*, 219 F.3d 1357, 1362 (Fed. Cir. 2000) (stating that "assessments of the credibility of the witnesses and the relative persuasiveness of the competing medical theories of the case" "are virtually unchallengeable on appeal"). Therefore, we hold that the Chief Special Master did not misapply *Daubert* in weighing the parties' experts' testimony and supporting evidence and that the Chief Special Master's factual findings were neither arbitrary nor capricious. *See de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 n.4 (Fed. Cir. 2008) (rejecting similar arguments on the grounds that "*Daubert* is inapposite here because the special master did not exclude any expert evidence under *Daubert*" and, instead, "admitted and weighed both parties' evidence but simply decided that the [G]overnment's evidence was more persuasive"); *Terran ex rel. Terran v. Sec'y of Health & Human Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999) (affirming a "[s]pecial [m]aster's analysis . . . using *Daubert*[] . . . as a tool or framework for conducting the inquiry into the reliability of the evidence," where the special master's "application of the *Daubert* factors [was] reasonable," because "[t]he [s]pecial [m]aster found that the *Daubert* inquiry raised serious questions about the [petitioner's expert's] testimony," such that "the proffered theory of causation was not sufficiently reliable").[5]

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[5] At oral argument, the Olivers asked the court to take judicial notice of an extra-record scientific article published in 2017 ("the 2017 Article"). Oral Arg. at 10:12–11:41; *see* Reply Br. 20 & n.8 (discussing Valentina Cetica et al., *Clinical and Genetic Factors Predicting Dravet Syndrome in Infants with* SCN1A *Mutations*, 88(11) Neurology 1037, 1037 (2017), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5384833/

(exploring the "prognostic value of initial clinical and mutational findings in infants with SCN1A mutations" and concluding that, "[i]n individuals with SCN1A mutations, age at seizure onset appears to predict outcome better than mutation type" (italics omitted)). The Olivers allege that this article demonstrates that one "can have the SCN1A [gene] and *not* develop Dravet syndrome" and that E.O.'s "vaccination *triggered* the onset of seizures within his first [twelve] months" and, thus, was a but-for cause of his injuries because it "*did* impact his clinical course." Reply Br. 21.

Scientific "theories that are so firmly established as to have attained the status of scientific law, such as the laws of thermodynamics, properly are subject to judicial notice under Federal Rule of Evidence 201." *Daubert*, 509 U.S. at 592 n.11; *see* Fed. R. Evid. 201(b) ("The court may judicially notice a fact that is not subject to reasonable dispute because it: (1) is generally known within the trial court's territorial jurisdiction; or (2) can be accurately and readily determined from sources whose accuracy cannot reasonably be questioned."). However, the Olivers have failed to establish that this theory has garnered such widespread acceptance, as evidenced by the Chief Special Master's extensive discussion of articles with contradictory findings. *See, e.g.*, *Oliver I*, 2017 WL 747846, at *15 (discussing "studies show[ing] that the occurrence of febrile seizures following vaccinations does not change the clinical course or outcome of Dravet syndrome"). Therefore, we decline to take judicial notice of the 2017 Article. *See Brown v. Piper*, 91 U.S. 37, 42–43 (1875) (explaining that a courts' power to take judicial notice "is to be exercised . . . with caution," that "[c]are must be taken that the requisite notoriety exists," and that "[e]very reasonable doubt upon the subject should be resolved promptly in the negative"). To the extent the Olivers ask us to consider findings in the 2017 Article, "studies that were not

Second, the Chief Special Master did not apply estoppel to either deny a fair hearing or bar the Olivers' theory of causation. The Olivers assert that the Chief Special Master "effectively estopped the [Olivers] from fully presenting [their] case," Appellants' Br. 39, by noting that, "[t]o date, there have been at least [fifteen] other . . . cases which involved children with SCN1A mutations[] and compensation has been denied in all of these cases," *Oliver I*, 2017 WL 747846, at *1 (footnote omitted); *see id.* at *1 n.3 (listing the prior cases); *see also Estoppel*, Black's Law Dictionary (10th ed. 2014) (defining estoppel as, inter alia, "[a] bar that prevents the relitigation of issues"). However, one reference to other cases rejecting similar claims does not constitute the application of estoppel. *Cf. Waymo LLC v. Uber Techs., Inc.*, 870 F.3d 1350, 1361 (Fed. Cir. 2017) ("We will not find legal error based upon an isolated statement stripped from its context." (internal quotation marks and citation omitted)). Indeed, the Chief Special Master made no reference to estoppel, *see generally Oliver I*, 2017 WL 747846, and the Olivers concede that they cannot identify where the Chief Special Master applied estoppel to bar their claims, *see* Oral Arg. at 2:04–41 (acknowledging that the Chief Special Master's opinion did not apply equitable estoppel and failing to identify any authority for finding an improper application of equitable estoppel under those circumstances). As we explained above, the Chief Special Master thoroughly considered the parties' evidence and found the Government's more persuasive, *Oliver I*, 2017 WL

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before the [Chief S]pecial [M]aster are not appropriate for consideration on appellate review." *Whitecotton ex rel. Whitecotton v. Sec'y of Health & Human Servs.*, 81 F.3d 1099, 1104–05 (Fed. Cir. 1996) (citation omitted).

747846, at *11–27, and we may not reweigh that evidence on appeal, *see Milik*, 822 F.3d at 1376.[6]

CONCLUSION

We have considered the Olivers' remaining arguments and find them unpersuasive. Accordingly, the Judgment of the U.S. Court of Federal Claims is

AFFIRMED

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[6] To the extent the Olivers contend that, even if the Chief Special Master did not improperly apply estoppel, the Chief Special Master abused her discretion by denying their request for an evidentiary hearing, *see* Appellants' Br. 39, we disagree. Special masters have "wide discretion" to determine whether to hold an evidentiary hearing. *Burns ex rel. Burns v. Sec'y of Dep't of Health & Human Servs.*, 3 F.3d 415, 417 (Fed. Cir. 1993); *see* 42 U.S.C. § 300aa-12(d)(3)(B)(v) (providing that the special master "may conduct such hearings as may be reasonable and necessary"); Rule 8(d) of App. B to the Rules of the Court of Federal Claims (permitting the special master to "decide a case on the basis of written submissions without conducting an evidentiary hearing"). Because the record was fully developed and the Olivers have not identified any factual or legal errors by the Chief Special Master that would have necessitated an evidentiary hearing, we conclude that the Chief Special Master acted within her discretion in denying the Olivers' request for such a hearing. *See Burns*, 3 F.3d at 417.

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v.

SECRETARY OF HEALTH AND HUMAN SERVICES,
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2017-2540

Appeal from the United States Court of Federal Claims in No. 1:10-vv-00394-EDK, Judge Elaine Kaplan.

NEWMAN, *Circuit Judge*, dissenting.

Infant E.O. was described by his pediatrician, at his 6-month well-baby visit on April 9, 2009, as developing normally, temperature 97.4° F. He was given the third dose of the DTaP[1] vaccine. At about 11:30 that night he was found convulsing and with a fever. He was rushed by ambulance to the emergency room, where a temperature of 101.3° F was recorded. By August 2009 E.O. had six observed seizure episodes. By the following year seizures

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[1] Diptheria-Tetanus-acellular Pertussis. J.A. 2.

were occurring daily, and normal mental and physical development were affected.

E.O.'s parents obtained genetic analysis of both his and their DNA. E.O. was found to have a mutation of the SCN1A gene, which has become associated with "severe myoclonic epilepsy in infancy," also called "Dravet syndrome," as characterized by Dr. Dravet in 1978.[2] The Petitioners duly sought the benefits of the Vaccine Act, but the Special Master held that since E.O. has this genetic mutation, any vaccine relationship is irrelevant and the Vaccine Act does not apply. My colleagues now affirm this ruling.

I respectfully dissent, for this is a classic case of vaccine injury, within the purpose, policy, and text of the Vaccine Act. Advances in scientific understanding of why some infants experience vaccine-related seizures and their tragic consequences, support the statutory plan.

DISCUSSION

It was known that about one half of one percent of apparently normal infants experience a serious adverse reaction to vaccine. *See* S. Hrg. 98-1060, at 21 (1984). Vaccine injury of healthy infants has long been believed to be affected by some aberration within the infant; advances in genetic science now are enabling exploration of such aspects.

The Special Master held that E.O.'s "destiny" is to be mentally and physically disabled because of his SCN1A gene mutation. The Special Master held that it is irrelevant that E.O. experienced a classic Vaccine Act injury, and irrelevant whether the vaccine triggered or contributed to his ensuing disability. The Special Master discarded

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[2] The record states that E.O.'s parents do not have the mutation.

the studies that show at least half of the persons found to have the SCN1A mutation never manifest Dravet syndrome. The Special Master deemed it irrelevant that 20–30% of persons afflicted with Dravet syndrome do not have the SCN1A mutation.

The reported studies found that vaccination within the first 6 months of infancy almost always produced seizures and led to Dravet syndrome for infants having the SCN1A mutation, while vaccination after 12 months never produced seizures and Dravet syndrome. The studies show that both vaccination and the mutation have a role in Dravet syndrome. Nonetheless, my colleagues hold that if a genetic relationship to the injury can be found, the triggering role of vaccination is irrelevant.

Science is at last providing answers to why some infants manifest a severe reaction to vaccination. However, these are the infants for whom the Vaccine Act was enacted. Instead, HHS and the courts now exclude these infants from the Vaccine Act—in contravention of the statute and the legislative purpose.[3]

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[3] Congress recognized the consequences of government-mandated vaccination when it instituted a compensation scheme. *See* S. Hrg. 98-1060, at 5 (1984) ("In all of our States, vaccination is required before a child will be allowed to enter public school. Federal, State, and local government officials urge all parents to immunize their children. For all practical purposes, immunization programs have become obligatory. Should a child sustain injury as a consequence of such an immunization program, it hardly seems fair that that child or its parents should sustain the entire burden of the consequences which may follow."). Congress was also well aware that the DTP vaccine could cause the injuries sustained by E.O. *See* S. Hrg. 98-350, at 1 (1983) ("The occurrence of

THE EVOLVING SCIENCE OF VACCINE INJURY

HHS acknowledges that E.O.'s 6-month DTaP vaccination produced an immediate reaction of seizures and fever, squarely within the statutory vaccine injury.[4] However, HHS insists that vaccine injury is irrelevant if the SCN1A mutation is present.

The Petitioners cite several scientific articles that report studies of the role of vaccination when the SCN1A mutation is present. These articles illustrate evolving understanding, drawing on the capabilities of DNA analysis. I have placed these publications in chronological order, for they illustrate the growth of this area of scientific knowledge, as well as the continuing uncertainties.

1.

M. Nieto-Barrera et al., *Severe Myoclonic Epilepsy in Infancy. An Analytical Epidemiological Study*, 30 REV. NEUROL. 620–24 (2000).

The authors report their study of patients afflicted in infancy with Severe Myoclonic Epilepsy (SMEI, referred to as "Dravet's syndrome" by the early 2000s). The article recites the history of vaccine-related convulsions, and traces the appearance and effects of infant myoclonic epilepsy. The authors state:

> Our study emphasizes, however, the high frequency in which the first convulsion is related with the DTP vaccination (six times with the first

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occasional central nervous system reactions to pertussis vaccines is well-established, ranging from simple, short-lived convulsions to encephalopathy with permanent brain damage and, rarely, death.").

[4] The Vaccine Act establishes a presumption of vaccine injury when fever and seizure occur within 3 days after immunization, 42 U.S.C. §§ 300aa-14(a); 14(b)(2).

> dose, eight with the second and two with the third), [a] fact that we consider, with discrete reservations, something more than a coincidence. The relation between the vaccine DTP and the convulsions has been discussed extensively. It is considered by some as mere coincidence etárea, is estimated that the majority of the seizures that follow to the pertussis vaccination are associated with the fever . . . .

J.A. 1197 (internal citations omitted). The authors state that "[a] relative increase has been verified of the incidence of convulsions in the three first days that follow to the vaccination," *id.*, and that "[w]ith independence of the differences among vaccines of the diverse manufacturers . . . sufficient experimental data exist to imply to the endotoxin and to the germ pertussis in the neurological adverse reactions to the pertussis vaccination." *Id.*

2.

Charlotte Dravet et al., *Severe myoclonic epilepsy in infancy (Dravet Syndrome)*, in *Epileptic Syndromes in Infancy, Childhood and Adolescence* 89–113 (J. Roger et al. eds., 4th ed. 2005).

The authors review the scientific literature and describe "Dravet syndrome." They note that some studies have concluded that "in a significant number of SME cases a genetic aetiology is likely . . . ." *Id.* at 90. The authors report that many studies confirm that the syndrome does not manifest exclusively in individuals with the SCN1A mutation. *Id.* at 108. The authors discuss their attempts to understand the biophysical properties of SCN1A gene mutations and find phenotype/genotype correlations, and state that the relationship between genotype and phenotype is "complex." *Id.* at 91. The authors state that:

> afebrile seizures usually occur in the context of a vaccination or of an infectious episode, or after a bath. Later on, they are associated with febrile seizures in 80 per cent of the patients. Nieto-Barrera *et al.* (2000) emphasized the coincidence between the first seizure and the DTP (diphtheria-tetanus-polio) vaccination.

Id. at 92.

3.

Samuel F. Berkovic et al., *De-novo mutations of the sodium channel gene SCN1A in alleged vaccine encephalopathy: a retrospective study*, 5 LANCET NEUROL. 488–92 (2006).

The authors state that "[v]accination, particularly for pertussis, has been implicated as a direct cause of an encephalopathy with refractory seizures and intellectual impairment." *Id.* at 488 (Summary). They trace the association with SCN1A mutations, and state that "[t]he mechanism by which SCN1A mutations cause SMEI is unknown." *Id.* at 491. The authors state that some patients with the SCN1A mutation may develop the syndrome without a vaccine trigger, and also state:

> In the presence of SCN1A mutations, vaccination can still be argued to be a trigger for the encephalopathy, perhaps via fever or an immune mechanism.

Id. The authors state that this study was not designed to address that question.

4.

Anne M. McIntosh et al., *Effects of vaccination on onset and outcome of Dravet syndrome: a retrospective study*, 9 LANCET NEUROL. 592–98 (2010).

The authors, reviewing the scientific literature, state that about 70–80% of children with Dravet syndrome have the SCN1A gene mutation, and about 20–30% do not have the mutation. *Id*. at 592. They report that about one-third of children with Dravet syndrome exhibited onset in less than 3 days after vaccination. The authors state that "[v]accination might trigger earlier onset of Dravet syndrome in children who, because of an SCN1A mutation, are destined to develop the disease." *Id*. at 592.

5.

Blanca Tro-Baumann et al., *A retrospective study of the relation between vaccination and occurrence of seizures in Dravet syndrome*, 52(1) EPILEPSIA 175–78 (2011).

The authors state that for infants with SCN1A mutations,

> epileptic seizures in the setting of fever are a clinical hallmark. Fever is also commonly seen after vaccinations and provocation of epileptic seizures by vaccinations in patients with Dravet syndrome has been reported, but not systematically assessed.

Id. at 175 (Summary). They report that "[t]he majority of seizures occurred after DPT vaccinations and within 72 h after vaccination." *Id*.

The authors state that seizures after vaccination are "a common feature in Dravet syndrome and emphasize the need for preventive measures for seizures triggered by vaccination or fever in these children." *Id*. at 175.

6.

Meral Özmen et al., *Severe myoclonic epilepsy of infancy (Dravet syndrome): Clinical and genetic*

***features of nine Turkish patients*, 14(3) ANNALS OF INDIAN ACADEMY OF NEUROLOGY 178 (2011).**

The authors studied patients having the SCN1A mutation, and discuss the complexities of the relation to vaccines. They summarize past studies, and state:

> Sudden occurrence of seizures and developmental regression after the pertussis vaccine in previously healthy children may confound as that it may be related with vaccination. There are several reasons for seizures and developmental regression in infancy. Some of them were incorrectly identified as vaccine encephalopathies. However, later studies did not support the link between permanent brain damage and vaccines. On the other hand, similarities were observed between clinical progressions of SMEI and vaccine encephalopathy as more data was gained about special epilepsy syndromes like SMEI. Berkovic et al. detected SCN1A gene mutations in 11 out of 14 patients who were diagnosed with vaccine encephalopathy. It was reported that the cause of vaccine encephalopathy was not vaccination but rather the genetically determined age-specific epileptic encephalopathy. In our patients, convulsions started after whole cell pertussis vaccination. Similarly, recent data from a study by McIntosh et al. showed that 37 patients out of 40 in the cohort had their first seizure after at least one DTP vaccination. They concluded that while the pertussis vaccine is a trigger for earlier onset of the disease, it does not affect its outcome.

J.A. 1310 (internal citations omitted). The authors conclude that:

> Pertussis vaccination acts as a trigger for the onset of [SMEI]. Neuro-developmental delay and behavioral problems that appear after two years

> of age should be expected in all patients as long-term complications of the disease.

J.A. 1311.

7.

Nelia Zamponi et al., *Vaccination and Occurrence of Seizures in SCN1A Mutation–positive Patients: A Multicenter Italian Study*, PEDIATRIC NEUROLOGY xxx 1–5 (2013).

The authors acknowledge the controversy concerning the relation of vaccination to Dravet syndrome ("DS"), and consider whether vaccination should be withheld for infants with the SCN1A mutation. They state:

> The relationship between vaccination and clinical evolution of SCN1A-mutated patients is still controversial. Moreover, the possible advantage to suspend vaccination route in these patients has not been addressed. Recently, some authors have argued that vaccination might trigger the onset of DS in patients carrying a genetic mutation because these patients are genetically inclined to developing the disease. However, according to these studies, vaccination does not seem to affect clinical outcome of DS and therefore it should not be withheld. In contrast, other authors have stated that vaccination, performed either before or after DS onset, might affect clinical outcome of these patients.

Id. at 2 (internal citations omitted). The authors are cautious about extrapolating vaccination recommendations from their results, although they state that "patients who experienced seizures close to vaccination had an earlier seizure onset and a higher frequency of status epilepticus during development." *Id.* at 4.

8.

Valentina Cetica et al., *Clinical and Genetic Factors Predicting Dravet Syndrome in Infants with* SCN1A *Mutations*, 88(11) NEUROLOGY 1037 (2017).

This is a study of 200 persons having the SCN1A mutation, wherein 97 had Dravet syndrome, including borderline forms, and 103 did not have the syndrome. All 200 subjects were more than 24 months of age, which is when Dravet syndrome can usually be diagnosed; the sample had an average age of 18.58 years.

Of these subjects, the relation of seizure occurrence to Dravet syndrome was analyzed, with 182 patients having had seizures as their presenting symptom. The authors report that "age at first seizure and frameshift mutations were associated with Dravet Syndrome. The risk of [developing] Dravet Syndrome was 85% [if the first seizure occurred] in the 0- to 6-month group, 51% in the 6- to 12-month range, and 0% after the 12th month." *Id.* at 1037. The authors report that: "None of the patients who experienced their first seizure after 12 months of age developed Dravet syndrome." *Id.* at 1040. Thus, "an older age at seizure onset represents a protective factor against the risk of developing Dravet syndrome." *Id.*

APPLICATION TO E.O.

The government's position is that "E.O.'s mutation is the sole cause of his Dravet syndrome and his resulting neurological condition." J.A. 2. Although the science is still evolving, it is apparent that this simplistic statement is incorrect.

All of the reported studies show a role of vaccination in producing seizures in infants with the SCN1A mutation. The Petitioners agree that there is a relationship between E.O.'s genetic mutation and his seizures and ensuing disabilities; they argue that "his DTaP vaccination in conjunction, with his SCN1A mutation . . . likely

caused his seizure disorder, encephalopathy, and developmental delays." Reply Br. 1.

It is not known whether E.O. would have manifested Dravet syndrome without the vaccination. The only certainty is that E.O. experienced a dramatic reaction within a few hours of DTaP vaccination, that the seizures continued, and that there were developmental consequences. The Special Master so acknowledged, but leaped to the conclusion that "[a]lthough E.O.'s vaccinations may have caused a fever or otherwise triggered his first seizure, neither that initial seizure nor his vaccinations caused his Dravet syndrome or neurological complications." *Oliver v. Sec'y of Health & Human Servs.*, No. 10-394V, 2017 WL 747846, at *2 (Fed. Cl. Feb. 1, 2017).

This conclusion does not withstand scrutiny. The scientific studies all show a reasonable likelihood that E.O.'s vaccination in his first 6 months triggered the adverse events he suffered. The seizures and fever on the evening of E.O.'s 6-month DTaP vaccination are recognized in the scientific literature as likely to have contributed to or triggered the Dravet syndrome in conjunction with the SCN1A mutation.

"Likelihood" is the standard of Vaccine Act recovery, for the Vaccine Act arose because certainty was not available. Until modern science discovered a genetic foundation for at least some vaccine injury, E.O.'s vaccine response would have been classified as a "Table Injury" and routinely entitled to the support of the Vaccine Act. Though science has begun to understand previously unexplained responses to vaccines, such understanding does not alter the Vaccine Act.

Until every infant is genetically analyzed before vaccination and all aberrant genes are identified, the Vaccine Act is the nation's response to potential vaccine-induced consequences such as Dravet syndrome. HHS is required to administer the Vaccine Act in accord with its text and

purpose. From my colleagues' contrary ruling, I respectfully dissent.