In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 15-1380V

Filed: April 18, 2023

ANSEL WALTERS and SHAKIMA DAVIS-WALTERS, Natural Parents of K.S.S.W., a minor, Petitioners, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	TO BE PUBLISHED Diphtheria, Tetanus and Acellular Pertussis ("DTaP") Vaccine; afebrile seizures

Phyllis Widman, Widman Law Firm, LLC, Northfield, NJ, for Petitioners
Sarah Black Rifkin, U.S. Department of Justice, Washington, DC, for Respondent

DECISION ON ENTITLEMENT[1]

Oler, Special Master:

On November 16, 2015, Ansel Walters and Shakima Davis-Walters ("Petitioners"), as parents of K.S.S.W., filed a petition for compensation under the National Vaccine Injury Compensation Program, 42 U.S.C. § 300aa-10, *et seq*.[2] (the "Vaccine Act" or "Program"). Petitioners allege that K.S.S.W. suffered a Table encephalopathy or, in the alternative a seizure disorder or epilepsy caused-in-fact or significantly aggravated by the diphtheria, tetanus, acellular

[1] Because this Decision contains a reasoned explanation for the action in this case, it must be made publicly accessible and will be posted 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, I agree that the identified material fits within this definition, I will redact such material from public access.

[2] National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

pertussis ("DTaP") vaccine he received on January 16, 2013.[3] Petition at 1, ¶ 10, ECF No. 1.

Upon review of the evidence filed in this case, I find that Petitioners have failed to show that K.S.S.W.'s condition meets the requirements for a Table encephalopathy or that it was caused or significantly aggravated by the DTaP vaccine he received on January 16, 2013. The petition is accordingly dismissed.

I. Procedural History

Ansel Walters and Shakima Davis-Walters filed their petition on November 16, 2015.[4] Over the subsequent eight-month period, they filed an affidavit from Ms. Davis-Walters and the medical records required by the Vaccine Act. Exs. 1-32, ECF Nos. 8-12, 15-16, 18, 20, 23, 31, 36, 41; *see* Section 11(c). They also filed updated medical records. Exs. 33-34, ECF Nos. 43, 46.

On August 30, 2016, Respondent filed a Rule 4(c) Report, setting forth his objections to compensation. ECF No. 37. During the subsequent year, the parties filed expert reports and medical literature to support their assertions. Exs. 35-84 (expert report, curriculum vitae ("CV"), and medical literature from Yuval Shafrir, M.D., a pediatric neurologist), ECF Nos. 47-51; Exs. A-CC, (expert reports, CVs, and medical literature from Neil D. Romberg, M.D., a pediatric immunologist, and Kristin W. Barañano, M.D., Ph.D., a pediatric neurologist), ECF Nos. 57, 59-62. I set an entitlement hearing for November 13-14, 2019.

In May and June 2019, Petitioners filed updated medical records, affidavits from Mr. Walters and Deborah Summey, K.S.S.W.'s maternal grandmother, and an expert report and supporting medical literature from Omid Akbari, Ph.D., a professor of immunology. Exs. 85-142, ECF Nos. 66, 68, 70, 74-80. Respondent then filed a responsive expert report and medical literature from Dr. Romberg. Exs. DD-MM, ECF No. 88. Two weeks later, on August 13, 2019, Petitioners requested that I delay the entitlement hearing so Dr. Akbari could respond to Dr. Romberg's supplemental report and K.S.S.W. could be seen by an additional specialist. ECF No. 89. I granted Petitioners' request and cancelled the planned hearing.

In early December 2019, Petitioners filed Dr. Akbari's supplemental expert report and supporting literature. Exs. 143-57, ECF Nos. 92-93. Two months later, Respondent filed a third expert report and supporting medical literature from Dr. Romberg. Exs. NN-RR, ECF No. 95. On April 2, 2020, Petitioners filed updated medical records, including the medical records from a different pediatrician, who saw K.S.S.W. in late May and June 2019. Exs. 158-162, ECF No. 98. A few months thereafter, in July 2020, I set an entitlement hearing for January 21-22, 2021.

Over the subsequent six-month period, Petitioners filed updated medical records (Ex. 163),

[3] K.S.S.W. also received the haemophilus influenza type b ("Hib") and inactivated polio ("IPV") vaccines at this visit. Ex. 3 at 4. He had received a first round of all three vaccines, as well as the pneumococcal vaccine, on November 26, 2012. *Id.*

[4] Initially assigned to now-retired Special Master George Hastings, this case was reassigned to my docket on December 5, 2017. ECF No. 65.

pictures and video of K.S.S.W. (Exs. 164-65), a second expert report from Dr. Shafrir (Ex. 166), a Power Point presentation from Dr. Akbari (Ex. 182), updated CVs (Exs. 168, 185) and reference summaries (Exs. 167, 181) from both experts, and additional medical literature (Exs. 169-80). ECF Nos. 107-08, 110-12, 128. Respondent filed a fourth expert report from Dr. Romberg (Ex. FFF), a second expert report from Dr. Barañano (Ex. JJJ), updated CVs (Exs. CCC-EEE) and reference summaries (Exs. SS, BBB) from both experts, and additional medical literature (Exs. TT-AAA, GGG-III). ECF Nos. 117, 120, 126.

In early January 2021, the parties filed updated exhibit lists and pre-hearing briefing. Exhibit Lists, ECF Nos. 127, 130; Petitioners' Pre-Hearing Submission ("Pet. Pre-Hearing Br."), ECF No. 114; Respondent's Pre-Hearing Submission ("Res. Pre-Hearing Br."), ECF No. 122; Petitioners' Reply to Res. Pre-Hearing Brief ("Pet. Pre-Hearing Reply"), ECF No. 125. They also filed a joint pre-hearing submission. ECF No. 121.

At the entitlement hearing, held as scheduled on January 21-22, 2021, I heard testimony from Ms. Davis-Walters and all four experts. *See* Transcripts, ECF Nos. 133-34. Over the subsequent eleven-month period, the parties filed their post-hearing briefing. Petitioners' Post-Hearing Submission ("Pet. Post-Hearing Br."), ECF No. 136; Respondent's Post-Hearing Submission ("Res. Post-Hearing Br."), ECF No. 144; Petitioners' Reply to Res. Post-Hearing Brief ("Pet. Post-Hearing Reply"), ECF No. 147.

This matter is now ripe for adjudication.

II. Factual History

In their joint pre-hearing submission, the parties stipulated that K.S.S.W. received his second dose of the DTaP vaccine on January 16, 2013; they further stipulated that he "was born with an unbalanced chromosomal translocation, specifically a duplication ([t]risomy) of 5p15.33p13.3 and a deletion (monosomy) of 6q26q27."[5] ECF No. 121. Under the heading of "Facts/Issues in dispute," they listed only "[w]hether [P]etitioners have established the elements of causation-in-fact." *Id.*

Additionally, the factual histories provided by the parties contain no significant differences regarding the events and circumstances involved in K.S.S.W.'s prenatal testing, birth, and medical condition thereafter. *Compare* Ex. 35 at 1-46 (Dr. Shafrir's first expert report); Pet. Pre-Hearing Br. at 3-4 *with* Rule 4(c) Report at 2-10; Res. Pre-Hearing Br. at 3-13; Res. Post-Hearing Br. at 2-12. Except for one disagreement regarding the *interpretation* of test results obtained in late January 2013, Dr. Romberg stated that he "largely agree[d] with Dr. Shafrir's recitation of K.S.S.W.'s medical history." Ex. A at 2-3 (Dr. Romberg's first expert report).

Thus, there is no factual issue regarding the events and circumstances of K.S.S.W.'s medical history which requires adjudication.

[5] As described in more detail in Section V(C)(3)(b) below, this chromosomal abnormality describes an unbalanced anomaly -- specifically an extra copy from 5p15.33 to the tip of the short arm of chromosome 5 and the deletion of the tip of the long arm at band 6q26 and 6q27 of chromosome 6.

A. Medical Records

1. Prenatal

Ms. Davis-Walters's prenatal records show she suffered two miscarriages at six weeks of pregnancy in 2010 and 2011. Ex. 5 at 8. During her pregnancy with K.S.S.W., an ultrasound performed on April 23, 2012, revealed borderline ventriculomegaly[6] and hemivertebrae[7] of the L2-L3. Ex. 5 at 89. Although the overlying skin appeared intact, it was noted that spina bifida aperta[8] could not be ruled out. Ex. 5 at 89-90. Because of these abnormal findings, an ultrasound-guided amniocentesis was performed the next day, on April 24, 2012. Ex. 5 at 86; *see id.* at 25 (ordering testing).

Following a determination that K.S.S.W. likely possessed an unbalanced translocation -- 5p15 duplication and 6q26 deletion, his parents underwent genetic testing and a second ultrasound at the Children's Hospital of Philadelphia ("CHOP") on May 9, 2012. Ex. 4 at 6-9, 16-17. K.S.S.W.'s mother was determined to have reciprocal translocation[9] of the 5p and 6q chromosomes (*id.* at 6-9), and the ultrasound revealed closed spina bifida[10] at the L4-L5, an

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[6] Ventriculomegaly is the "gross enlargement of a ventricle of the brain, as by hydrocephalus." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY (hereinafter "DORLAND'S") at 2048 (32th ed. 2012).

[7] Hemivertebrae is "a developmental anomaly characterized by incomplete development of one half of a vertebra." DORLAND'S at 838.

[8] Spina bifida is "a neural tube defect characterized by defective closure of the vertebral arch, through which the spinal cord and meninges may be protruded (*s. bifida cystica*) or may not (*s. bifida occulta*)." DORLAND'S at 1748. The main two types of spina bifida is further explained on the NIH (National Institute of Health) website:

> Spina bifida occulta, or closed spinal dysraphism, is the mildest form of the neural tube defects (NTD) which involves a hidden vertebral defect and minimal neural involvement. Spina bifida aperta, or open spinal dysraphism, refers to a defect in which neural tissues communicate with the external environment such as meningocele and myelomeningocele. These conditions result in a varied spectrum of neurological effects due to the degree of neuralization. Spina bifida is commonly associated with several other developmental abnormalities which makes a multidisciplinary medical plan paramount to survival and positive outcomes.

https://www.ncbi.nlm.nih.gov/books/NBK559265/ (last visited on Oct. 28, 2022).

[9] As discussed in Section V(C)(3)(b) below, a reciprocal or balanced chromosomal abnormality means the individual still has a normal complement of genetic information -- two copies of every gene.

[10] Closed spina bifida is also known as spina bifida occulta, "spina bifida in which there is a defect of the vertebral arch without protrusion of the spinal cord or meninges." DORLAND'S at 1748.

associated tethered cord[11] terminating at the L4-L5 level, and mild ventriculomegaly (Ex. 4 at 16).

When discussing these results with the CHOP geneticist on May 9, 2012, Petitioners were informed that K.S.S.W.'s chromosomal arrangement was noted to be rare, resulting in numerous conditions including "malformed brain, mental retardation, and seizures." Ex. 4 at 16. They were cautioned that their newborn would likely require special medical attention for his chromosomal, spinal, and ventricular abnormalities. *Id.* at 17. The CHOP geneticist documented that, after being informed of these likely outcomes, "[t]he family is hoping for a miracle and that things will be different at birth, including a normal chromosome complement." *Id.*

Similarly, when seen by her local prenatal specialist the next day, Ms. Davis-Walters was informed K.S.S.W.'s chromosomal abnormalities were "likely to result in significant phenotypic abnormalities including neurologic abnormalities, developmental delay, mental retardation, among others." Ex. 5 at 86. Regarding the spinal and ventricular abnormalities, the specialist indicated K.S.S.W. may develop hydrocephalus[12] with accompanying neurologic and intellectual consequences and explained that surgical treatment of K.S.S.W.'s spinal abnormalities "may be needed but may not restore function." *Id.* Ms. Davis-Walters expressed her understanding that K.S.S.W.'s "prognosis [wa]s likely poor . . . [and] that the child will likely have severe lifelong neurologic or physical impairments." *Id.*

Additional fetal ultrasounds showed progression of K.S.S.W.'s ventriculomegaly and continued spinal abnormality. Ex. 5 at 81, 79, 67, 71 64. Although active movement at the knees and ankles was observed, only limited extension of the hips was seen. *Id.* at 71 (ultrasound performed on July 17, 2012).

2. Birth to Vaccination

K.S.S.W. was born on September 12, 2012, by caesarian section due to his breech presentation. Ex. 2 at 117-18. He weighed seven pounds, two ounces,[13] and exhibited Apgar scores of 8 and 9, at one and five minutes, respectively.[14] Ex. 2 at 117; Ex. 7 at 249. Observed to have

[11] "Tethered spinal cord syndrome is a neurological disorder caused by tissue attachments that limit the movement of the spinal cord within the spinal column." https://www.ninds.nih.gov/health-information/disorders/tethered-spinal-cord-syndrome (last visited on Oct. 28, 2022).

[12] Hydrocephalus is "a condition marked by dilatation of the cerebral ventricles, most often occurring secondary to obstruction of the cerebrospinal fluid pathways . . . and accompanied by an accumulation of cerebrospinal fluid within the skull; the fluid is usually under increased pressure, but occasionally may be normal or nearly so." DORLAND'S at 877

[13] In later records, K.S.S.W.'s weight at birth was increased slightly to eight pounds, three ounces. *E.g.,* Ex. 3 at 74.

[14] An Apgar score is "a numerical expression of the condition of a newborn infant, usually determined at 60 seconds after birth, being the sum points gained on assessment of the heart rate, respiratory effort, muscle tone, reflex irritability, and color." DORLAND'S at 1682.

spinal abnormalities, colpocephaly,[15] and hydrocephalus, he was transferred to the NICU (neonatal intensive care unit). Ex. 3 at 4, 74 (discharge summary). Testing confirmed these results, as well as the expected chromosomal abnormalities. Ex. 7 at 213-16, 235. When discussed with K.S.S.W.'s mother on September 14, 2012, she confirmed she was aware of these issues from the second month of her pregnancy. *Id.* at 26.

On September 17, 2012, K.S.S.W. underwent surgery for V-P (ventriculo-peritoneal) shunt placement to treat his hydrocephalus. Ex. 4 at 72-74 (discharge summary); Ex. 7 at 179-80 (surgical record). The surgery was completed without complication, but it was determined that K.S.S.W. initially should remain intubated. Ex. 4 at 74 (discharge summary); Ex. 7 at 199 (surgical record). Another head ultrasound, performed three days post-surgery on September 20, 2012, revealed stable hydrocephaly and colpocephaly, with a *possibility* of intraventricular hemorrhage at both frontal horns, left greater than right. Ex. 7 at 210-11. After K.S.S.W. failed his hearing test on September 20, his parents were informed that the test should be repeated in one month. *Id.* at 73. At the time of his discharge on September 23, 2012, it was noted that K.S.S.W. suffered from ventriculomegaly, partial trisomy 5p and monosomy 6q chromosomal abnormalities, spina bifida occulta, and tethered cord syndrome, and had undergone V-P shunt placement. *Id.* at 74.

On September 24, 2012, K.S.S.W. attended his first pediatric appointment. Ex. 3 at 4-5. He was seen by a pediatric neurologist three days later, on September 27, 2012. The pediatric neurologist noted that, given the rarity of K.S.S.W.'s genetic abnormality, "it is important for us to follow him over time . . . [and] unclear what his developmental prognosis is." Ex. 31 at 2.[16] K.S.S.W.'s parents expressed their understanding, promising to provide the pediatric neurologist with documentation from the CHOP Genetic Center. *Id.* It appears K.S.S.W. had experienced a slight weight loss as he weighed six pounds, fourteen ounces at these appointments. Ex. 3 at 5; Ex. 31 at 1.

By his third pediatric visit, on October 24, 2012, K.S.S.W.'s weight had increased to eight pounds, five ounces. Ex. 3 at 7. Seen by an ophthalmologist the same day, he was observed to have normal lids, cornea, lens, and discs. Ex. 18 at 21. Although this record is difficult to read and does not include any typed narrative, it appears only a physical examination was performed. It was noted that K.S.S.W. -- one and a half months old at the time of the examination, was sleeping during the appointment. *Id.*

On November 26, 2012, K.S.S.W. received his first dose of DTaP, Hib, IPV, and pneumococcal vaccines. Ex. 3 at 4. No adverse reaction to these vaccines was noted in the medical records. He also underwent audio testing, the results of which were normal. *Id.* at 75.

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[15] Colpocephaly is the "enlargement of the occipital horns of the lateral ventricles, often accompanied by mental retardation, seizures, and visual disturbances that result from hypoplasia of the optic nerve." DORLAND'S at 388. Hypoplasia is the "incomplete development or underdevelopment of an organ or tissue." DORLAND'S at 905.

[16] Because only page two of this record was originally filed, Petitioners filed complete copies of the medical records from this visit in June and August 2016. *Compare* Ex. 3 at 76 *with* Ex. 30 at 1-2; Ex. 31 at 6-8. I will cite to the latest, most complete filing, Ex. 31.

On January 10, 2013, Petitioners took K.S.S.W. to a pediatric neurosurgeon to discuss treatment for his tethered cord syndrome and spondylolisthesis.[17] Ex. 6 at 11. The pediatric neurosurgeon explained that the planned surgery would untether the spinal cord "to release traction on the cord." *Id.* He added that the surgery would be "helpful for the spondyloptosis surgery in the future." *Id.* On Wednesday, January 16, 2013, K.S.S.W. visited his pediatrician for a pre-surgical evaluation. Ex. 3 at 8. At this visit, he received a second DTaP vaccine, alleged as causal in this case, along with a second round of the Hib and IPV vaccines. *Id.* at 4.

3. The First Year Post-Vaccination - 2013

Four days later, on the afternoon of January 20, 2013, Petitioners brought K.S.S.W. to the emergency room ("ER"), reporting intermittent episodes of staring off to the left since Wednesday. Ex. 7 at 529. They indicated that, after his mother informed K.S.S.W.'s neurosurgeon of these symptoms and showed him a video she took,[18] he instructed them to bring K.S.S.W. to the ER. *Id.* at 529, 537. In the ER record, it was noted that K.S.S.W. had a medical history of hydrocephalus, V-P shunt surgery, tethered cord syndrome, and immunizations, was in mild distress, and was not experiencing fever, tonic-clonic movements, or vomiting. *Id.* He was assessed as nine out of ten on the FLACC pain scale[19], based upon steady crying, frowning, kicking, and inconsolability, but also received a fully alert score of 15 on the Glasgow Coma Scale.[20] Ex. 7 at 530.

A head CT scan was performed, and K.S.S.W. was admitted for seizures. Ex. 7 at 539-40. When compared to earlier imaging, the CT scan revealed no issues with the shunt and slightly decreased colpocephaly. *Id.* at 539. It was noted that K.S.S.W. was stable, alert, and nontoxic throughout his ER evaluation. *Id.* at 540.

An entry created later that evening indicated that his mother reported K.S.S.W. received vaccinations on Wednesday, January 16th, and experienced an episode of eyes deviating to the left for less than one minute during a 1:00AM feeding on Thursday. Ex. 7 at 625. She reported two to three additional episodes, lasting a few seconds, over the past four days. *Id.*

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[17] Spondylolisthesis is "the forward displacement (olisthy) of one vertebra over another, usually accompanied by rotation of the affected disk." DORLAND'S at 1754.

[18] Petitioners filed five videos taken in early 2013, from January 19 after 5:00PM through January 20 at 4:00PM, into the record in this case. Exs. 165K-165O. Presumably, one of these videos is the one shown to the neurosurgeon.

[19] FLACC which stands for face, legs, activity, and crying, is a behavioral pain assessment scale used for nonverbal or preverbal patients who are unable to self-report their level of pain. NELSON TEXTBOOK OF PEDIATRICS (hereinafter "NELSON PEDIATRICS") at 431-432 (20th ed. 2016).

[20] The Glasgow Coma Scale "is a standardized system for assessing response to stimuli in a neurologically impaired patient; reactions are given a numerical value in three categories (eye opening, verbal responsiveness, and motor responsiveness), and the three scores are then added together. The lowest values are the worst clinical scores." DORLAND'S at 1672. Scores range from 3 to 15. https://www.ncbi.nlm.nih.gov/books/NBK513298/ (last visited on Nov. 7, 2022) (for a detailed discussion of this scale); *see also* NELSON PEDIATRICS at 492.

The next day, K.S.S.W. was examined by Dr. Eric Geller, a neurologist. After recounting his history of hydrocephalus, V-P shunt placement, and spina bifida, Dr. Geller included his mother's account of vaccinations and eye deviations starting at 1:30AM the next day. Ex. 7 at 628. This recitation included a report that, along with the eye deviations, K.S.S.W. also experienced some vomiting Wednesday evening. *Id.* K.S.S.W.'s parents showed the recently taken video to the neurologist and reported that they came to the ER due to the increased frequency of these episodes. *Id.* After reviewing K.S.S.W.'s bloodwork, prior CT scans and MRIs, along with EEG[21] data from overnight, Dr. Geller diagnosed K.S.S.W. with multifocal epilepsy, "most likely related to the underlying hydrocephalus and brain malformation." *Id.* at 629.

Regarding the results of the EEG monitoring, Dr. Geller indicated K.S.S.W. "ha[d] frequent epileptic spikes occurring from multiple regions including the frontal, left parietooccipital and right parietooccipital region." Ex. 7 at 629. He also observed that K.S.S.W. had several seizure episodes which were accompanied by eye deviations, other instances when his parents pressed a button indicating a seizure was occurring without any EEG correlation, and occasions when they ignored electrographic seizures without any clinical presentation, even when holding K.S.S.W. *Id.* When his mother expressed concern that K.S.S.W.'s seizures were connected to his vaccinations, Dr. Geller told her that "because we are seeing EEG seizures without any clinical symptoms, they may have been occurring previously and there was no way to know that seizures were occurring until he had a big enough one to cause physical symptoms." *Id.* Dr. Geller prescribed antiepileptic medication and continued EEG monitoring. *Id.*

During EEG monitoring from January 22-28, 2013, it continued to be difficult to identify K.S.S.W.'s seizure activity. Ex. 7 at 740. The EEG results showed "electrographic and electroclinical seizures, . . . dysfunction and postictal slowing in the left temporal head region, . . . [and] cortical irritability and potential epileptogenicity in the left frontal F3 and right parietal P8 head region." *Id.* at 741.

On January 23, 2013, K.S.S.W.'s ophthalmologist was asked for an assessment of his eye deviations and staring spells. Ex. 18 at 20. After viewing the video taken by K.S.S.W.'s mother and noting his history of hydrocephalus and seizures, the ophthalmologist designated the eye movements as nystagmus[22] related to his seizures. Ex. 18 at 20. Like the earlier record from this

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[21] EEG is the abbreviation for electroencephalogram, "a recording of the potentials on the skull generated by currents emanating spontaneously from nerve cells in the brain." DORLAND'S at 630. It

> is a graphic recording of the electrical activity of the brain. EEG electrodes are placed on the scalp overlying multiple areas of the brain to detect and record electrical impulses within the brain. This study is invaluable in the investigation of epileptic states, in which the focus of seizure activity is characterized by rapid, spiking waves seen on the graph.

MOSBY'S MANUAL OF DIAGNOSTIC AND LABORATORY TESTS at 490 (6th ed. 2018).

[22] Nystagmus is "an involuntary, rapid, rhythmic movement of the eyeball, which may be horizontal, vertical, rotatory, or mixed." DORLAND'S at 1307. There are numerous subcategories for this condition. *Id.* at 1307-08.

ophthalmologist, there is no accompanying typed narrative, but a diagnosis of abnormal vision is clearly stated.[23] Ex. 18 at 20.

During this January 2013 hospitalization, K.S.S.W.'s treating physicians tried several different antiepileptic medications, including Keppra, Dilantin, and Trileptal. Ex. 7 at 305. K.S.S.W. was discharged on February 5, 2013, in stable condition, taking Trileptal and Keppra. His parents were instructed to follow-up with neurology in a few weeks. *Id.*

K.S.S.W. was hospitalized twice in February 2013, on February 7 and 27, as his treating physicians attempted to control his seizures. Ex. 7 at 1075, 1079, 1086, 1091, 1198-99, 1384, 1408, 1734-35. EEG monitoring continued to show seizure activity originating in the left hemisphere, and K.S.S.W. was prescribed varying dosages of Keppra, Dilantin, and Topamax. *Id.* at 1199, 1735.

K.S.S.W. continued to see other specialists as well. A cardiac examination performed on March 15, 2013, revealed only minor, benign findings. Ex. 22 at 2. During an ophthalmology examination on April 9, 2013, K.S.S.W. was observed as having a normal, healthy optic nerve, retina, and anterior segment" but was lacking any response, such as a blink, to stimulation by a very bright light and "no obvious tracking occurring." Ex. 18 at 16. The ophthalmologist theorized this lack of reaction could be due to the antiepileptic medication K.S.S.W. was taking or could be "a possible sign of some neurologic blindness." *Id.*

Seen by his neurologist on April 11, 2013, K.S.S.W. was reported to have experienced only one seizure in the past two weeks. Ex. 29 at 6. However, he was assessed as having partial epilepsy and epileptic syndromes "with mention of intractable[24] epilepsy." *Id.* at 7. This record indicates that K.S.S.W. was being evaluated for early intervention. *Id.* at 6.

K.S.S.W.'s previously delayed tethered cord surgery was performed on April 12, 2013. Ex. 7 at 1629-30, 1704-05 (operative report). The surgery proceeded without complications, and K.S.S.W. was noted to be doing well two days post-surgery. *Id.* at 1636.

Throughout the remainder of the year, K.S.S.W. continued to receive treatment for and EEG monitoring of his seizure activity. After a prolonged seizure in June 2013 -- despite being medicated with Dilantin, K.S.S.W. was admitted for a week-long EEG monitoring. Ex. 29 at 10. Multiple seizures were noted each day of monitoring. *Id.* at 10-11. Showing that "all seizures arose from the left side," the EEG study supported K.S.S.W.'s diagnosis of partial seizure epilepsy. *Id.* at 12. In response to the activity observed, K.S.S.W.'s medication was again adjusted. *Id.*

At an ophthalmology appointment on July 1, 2013, K.S.S.W. was referred for early intervention. Ex. 18 at 10-11. A few weeks later, the ophthalmologist informed K.S.S.W.'s parents that "he still [was] not able to get a response to tracking the light." *Id.* at 9. The ophthalmologist diagnosed him with abnormal vision and potential blindness. *Id.*

[23] There also is an entry stating, "ET Optic Neuro…", with the remainder being unreadable. Ex. 18 at 20.

[24] Intractable means "resistant to cure, relief, or control." DORLAND'S at 953.

During July 2013, K.S.S.W. also attended a follow-up appointment with his neurologist. Ex. 29 at 4-5. The neurologist observed that K.S.S.W. had experienced only one seizure since his June hospitalization for prolonged monitoring and adjustments to his medication. *Id.* at 4. He included information provided by K.S.S.W.'s mother about his sleepiness during the morning and some vomiting in response to the inclusion of phenobarbital in his medications. *Id.* The neurologist noted that K.S.S.W. attended weekly physical and occupational therapy and was eating solid food and taking his bottle without problems. *Id.*

At K.S.S.W.'s next appointment in September 2013, the neurologist remarked on the difficulties K.S.S.W. had experienced tolerating the newly added phenobarbital and accompanying attempts to find the proper dosage. Ex. 29 at 2. EEG monitoring continued to show some seizure activity. *E.g.,* Ex. 14 at 32-33 (results from monitoring in November 2013 showing one clinical seizure during the first 24 hours and twelve during 48 hours). At this visit, K.S.S.W.'s neurologist observed that he could sit with some support, not on his own, and was "[n]ot bearing weight well on [his] legs." Ex. 29 at 2. The fact that K.S.S.W. exhibited global developmental delays was echoed in his pediatric records. Ex. 3 at 83-95.

During September through November 2013, K.S.S.W. was also seen for failure to thrive. Ex. 10. In December 2013, he attended several early intervention appointments for evaluation of his feeding abilities. Ex. 25 at 54-73. It was noted that K.S.S.W. had oral dysphagia[25] which was exacerbated by his seizure disorder. *Id.* at 71. The stated goal for the planned treatment was for K.S.S.W. to consume age-appropriate food. *Id.* at 73.

4. The Second Year Post-Vaccination - 2014

Unable to assess K.S.S.W.'s vision in November 2013 because he was sleeping, his ophthalmologist provided a detailed report following a visit on January 8, 2014. Ex. 18 at 4-5. He noted that K.S.S.W. had been visited by representatives of the Commission for the Blind, who had promised special toys, and had participated in three early intervention visits since November 2013. *Id.* at 4. The ophthalmologist diagnosed K.S.S.W. with optic atrophy, nystagmus, and legal blindness, and referred him to a neuro-ophthalmologist. *Id.* at 5; Ex. 16 at 20.

K.S.S.W. was able to visit this specialist six days later, on January 14, 2014. Ex. 16 at 20-22. In the record from this visit, the neuro-ophthalmologist mentioned K.S.S.W.'s diagnosis of developmental delay and possible blindness, as well as his mother's observation that "he clearly will reach for things and his attention will be directed at newly presented objects." *Id.* at 20. Although he could not assess K.S.S.W. because he was sleeping, he expressed his general feeling that children with developmental delay are often mistakenly diagnosed with visual issues. *Id.* at 21.

On March 17, 2014, K.S.S.W. visited a pediatric physiatrist for an initial evaluation. Ex. 24 at 20-28. The referral was made by his physical therapist due to a concern about K.S.S.W.'s ability to bear his weight. *Id.* at 20. Observing that K.S.S.W. had good movement at his ankles and no issues with his hips warranting x-rays, the physiatrist recommended repetitive exercises and braces to provide standing support. *Id.* at 23-24. He rejected the use of a stander *at this time*, noting

[25] Dysphagia is "difficulty in swallowing." DORLAND'S at 579.

that, although it would facilitate normal hip development by putting weight on K.S.S.W.'s hips, it would not help him walk. *Id.* at 23.

At his next appointment in May 2014, the neuro-ophthalmologist remarked that K.S.S.W. "continued to have problems with recurrent seizures." Ex. 16 at 17. Around this time, K.S.S.W. underwent additional EEG monitoring which showed a similar amount of seizure activity as was seen in November 2013. Ex. 14 at 59-62. He also attended multiple early intervention sessions for help with feeding from May through September 2014. Ex. 25 at 5-53.

K.S.S.W. again visited the pediatric physiatrist in September 2014. Ex. 24 at 12-19. At this visit, he was observed to be sitting up, able to roll to a sitting position and hold himself up, and to be working on weight bearing. *Id.* at 12. The physiatrist checked K.S.S.W.'s orthotics and discussed the insurance company's denial of a stander, which he had recently recommended, with K.S.S.W.'s mother. *Id.* at 13. Reiterating his opinion that a stander would now be beneficial for K.S.S.W., he ordered spinal X-rays and instructed K.S.S.W.'s mother to continue repetitive exercises, including standing, and to watch for any irritation from the braces. *Id.* at 13-14, 16; *see id.* at 18 (x-ray results).

By K.S.S.W.'s last 2014 neurology appointment, he showed little seizure activity. Ex. 14 at 58, 62. The record from this December 2014 visit indicated that he had not experienced a seizure for six months, and the neurologist was considering weaning him off Dilantin. *Id.*

The neuro-ophthalmologist repeated this positive news at K.S.S.W.'s next appointment in late December 2014, writing that K.S.S.W.'s seizures "[we]re coming under better control." Ex. 16 at 11. And, at this visit, the neuro-ophthalmologist was able to perform a more comprehensive evaluation. Observing that K.S.S.W. "moved to mirror movements more than half the time and reacted to a bright flashing light in a very dark room most of the time," the neuro-ophthalmologist concluded he had some residual vision. *Id.* at 12.

5. The Third Year Post-Vaccination - 2015

In early March 2015, K.S.S.W. was seen again by his pediatric physiatrist. Ex. 24 at 5-11. His parents had obtained a stander which K.S.S.W. was able to use for about an hour each day. *Id.* at 5. The physiatrist also discussed school programs with K.S.S.W.'s mother, who was researching the subject. *Id.* at 6.

At his next appointment, the physiatrist noted that K.S.S.W. recently began attending school. Ex. 28 at 24. In the results of a school assessment, performed on October 20, 2015, K.S.S.W. was described as "transitioning nicely into the school program." *Id.* at 5.

6. Most Recent Care

K.S.S.W.'s visual abilities are described in more recent school evaluations. In early May 2018, he was observed as exhibiting less of a past practice of keeping his eyes closed and titling his head to look up. Ex. 161 at 2. He was assessed as being aware of objects near him and motivated by lit objects and music. *Id.* This record indicates that K.S.S.W. was diagnosed by his most recent

ophthalmologist as having cortical visual impairment ("CVI") secondary to his congenital hydrocephalus. *Id.* at 3. This school assessment was accepted without change for the 2019 through 2020 school year. *Id.* at 1.

On May 30, 2019, Ms. Davis-Walters took K.S.S.W. to see a new pediatrician for his yearly physical. Ex. 162 at 3. The reason for the visit was noted to be a routine annual physical for a child with abnormal findings. *Id.* at 4. The listed conditions were an under-immunization status, congenital hydrocephalus, chromosomal abnormality, and unspecified convulsions. *Id*.

One week later, on June 6th, K.S.S.W. and his mother returned to the pediatrician to discuss his chromosomal abnormalities. Ex. 162 at 2. The pediatrician opined that after reviewing additional information, K.S.S.W.'s "chromosomal abnormalities could account for his current systems/development, [u]nless mom can give hx/documentation that seizures started right after a vaccine was given." *Id.* Based upon that assessment, she informed K.S.S.W.'s mother that she would need to sign a vaccine refusal form if she chose not to vaccinate K.S.S.W. *Id.* In response, K.S.S.W.'s mother indicated she did not believe and could not sign what was written on the form. Stating that vaccine studies had not been performed on children with chromosomal abnormalities, she expressed her belief that the vaccines K.S.S.W. received had worsened and caused his current condition. *Id.* at 4.

On June 13, 2019, K.S.S.W.'s mother spoke to the pediatrician again regarding her belief that K.S.S.W. suffered an adverse vaccine reaction. Ex. 162 at 1. The record from this visit indicates she recounted that K.S.S.W. received a "combo vaccine" at four months of age and that, "as soon as he got home," she observed his "eyes roll[ing] inward, not eating, crying." *Id.* She further reported that she contacted both his pediatrician who told her to wait a few days and his neurosurgeon who told her to take K.S.S.W. to the ER immediately, where he was diagnosed with seizures. *Id.* K.S.S.W.'s mother added that she "has been dx with same chromosome abnormality[26] and yet does not suffer from seizures." *Id.* Based upon this history, the pediatrician wrote that she now understood the "timeline of seizures and vaccine" but also discussed "if mom would want to consider Var[icella] or MMR for the future." *Id.* Based upon this history, the pediatrician assessed K.S.S.W. with "Vaccines adverse reaction". *Id.*

Performed in 2018, 24-hours of EEG monitoring showed no clinical seizure activity. Ex. 163 at 79. And, during neurology visits and EEG testing performed in 2019 and 2020, K.S.S.W. was noted to be doing well, except for a three-week long period of breakthrough seizures in January 2019, attributed to dental problems he experienced. *Id.* at 6, 12-13, 209-10, 252, 255, 267. At his last visit in August 2020, it was noted that K.S.S.W. had experienced two seizures in October and November 2019. *Id.* at 267.

No additional medical records pertinent to this analysis have been filed.

[26] As discussed throughout this Decision, K.S.S.W.'s chromosomal translocation is not the same as Ms. Davis-Walters' balanced translocation.

B. Affidavits and Testimony

1. Ms. Shakima Davis-Walters – K.S.S.W.'s Mother

When testifying at the entitlement hearing on January 21, 2021, K.S.S.W.'s mother described the prenatal testing performed in the second trimester of her pregnancy and resulting abnormal findings. Transcript ("Tr.") at 11-12. Characterizing K.S.S.W. as "fine" after birth, she testified that he breastfed, looked at her, and moved his arms and legs within 48 hours of birth. Tr. at 14-15. Regarding the placement of the shunt, she indicated she believed this was a positive step, a safe procedure, and that K.S.S.W. "would still be okay and nothing would bother him." Tr. at 15.

In her affidavit, executed in January 2014, Ms. Davis-Walters maintained that, prior to vaccination, K.S.S.W. could make cooing sounds, could view pictures without any crossing of his eyes, would put one foot in front of the other in a walking motion when held upright, and was moving around on a mat, performing army crawls. Ex. 1 at ¶ 4. She echoed her description of K.S.S.W. cooing and making walking movements during her testimony, adding that K.S.S.W. could focus on and track her; interact with her, his father, and his grandmother; grasp his rattle and activate his toys; watch specific programs on television; and respond to noises and other stimuli. Tr. at 17-19. Indicating that she bought a piano to place at the foot of his bassinet "so he could learn how to kick and play the notes" (Tr. at 18), she characterized K.S.S.W. as adorable and lively (Tr. at 17), maintaining that he would smile and wiggle when she sang to him (Tr. at 21). To show K.S.S.W. smiling, Petitioner's counsel played a video from late November 2012. Tr. at 20-22 (showing video labeled Ex. 165G).

Regarding K.S.S.W.'s condition post-vaccination, his mother indicated he became ill within three to four hours. Ex. 1 at ¶¶ 9-10. After he vomited that evening, she gave him Pedialyte as his pediatrician recommended. *Id.* at ¶ 11. At the hearing, she testified K.S.S.W. was crying, lethargic, often sleeping, and had a blank stare. Tr. at 25.

Ms. Davis-Walters maintained that, in the following days, K.S.S.W.'s eating habits and body movements changed. Ex. 1 at ¶ 12. She stated that he seemed sluggish, not focused or cooing as much, and "had a lot of eye jumping movements." *Id.* at ¶ 13. She testified that, when babysitting on January 17 or 18, her mother observed an episode during which K.S.S.W. clenched his fist, brought it to his chest, and closed his eyes which seemed "off." Tr. at 26. The next day, Ms. Davis-Walters viewed jerky movements of K.S.S.W.'s eyes which she filmed and sent to his pediatrician on January 20. Tr. at 26-27; Ex. 1 at ¶ 14. She testified that she was particularly concerned about these symptoms since K.S.S.W. was scheduled to undergo tethered cord surgery. Tr. at 27.

Ms. Davis-Walters recalled that, after bringing her son to the ER based upon his pediatrician's instructions and showing the video she took to the ER physician, K.S.S.W. was diagnosed as experiencing seizures. Ex. 1 at ¶¶ 14-16; Tr. at 27-28. At the hearing, Petitioner's counsel played the video which Ms. Davis-Walters took on January 20. Tr. at 29 (showing video labeled Ex. 165N). Ms. Davis-Walters described the subsequent five-week hospital stay, during which different medications were tried to control K.S.S.W.'s seizures. Tr. at 28, 30; Ex. 1 at ¶ 17. She added that K.S.S.W.'s tethered cord surgery was postponed, and it was recommended that he

participate in an early intervention program. Ex. 1 at ¶ 19.

During the remainder of her direct testimony, Ms. Davis-Walters described K.S.S.W.'s medical treatment, condition, lack of developmental progress, and future prognosis. Tr. at 30-37. She reported that K.S.S.W. could no longer track with his eyes or hold his own bottle. Tr. at 31. Explaining that she continues to feed and to carry K.S.S.W., now eight years old, she testified that she has been informed that K.S.S.W. will never talk or walk. Tr. at 32-35. In both her affidavit and testimony, Ms. Davis-Walters communicated her belief that the vaccines her son received when four months old caused his current condition, adding that he no longer receives any vaccinations. Tr. at 35; Ex. 1 at ¶¶ 23-24.

During Ms. Davis-Walters' cross examination, Respondent's counsel focused on her recollection of the results of her prenatal testing, specifically the genetic abnormalities it revealed, and her observation of K.S.S.W.'s jerky eye movements. Tr. at 37-50. Ms. Davis-Walters insisted that she did not recall being told that K.S.S.W. could develop seizures, only that he would require a shunt to treat his hydrocephalus, could have abnormal features, may suffer from mental retardation and require special schooling, and would need to seek follow-up treatment from several specialists. Tr. at 30-47. Regarding K.S.S.W.'s eye movements, Ms. Davis-Walters confirmed that the movement was quick, lasting only a few minutes until K.S.S.W. returned to baseline after being stimulated, and that it occurred two to three times between January 17-20, 2013. Tr. at 47-50.

2. Mr. Ansel Walters – K.S.S.W.'s Father

Characterizing his son as a "typical baby boy" prior to receiving his four-month vaccinations (Ex. 85 at ¶ 3), Mr. Walters emphasized that K.S.S.W. "met all standards that are set for a baby's development" (*id.* at ¶ 4). He maintained that his son enjoyed being rolled over; would communicate effectively, by babbling and using body and facial expressions, when he disliked something; could make eye contact, provide a responsive smile, and change his facial expression in response to a cue; and would hold his own bottle while feeding himself. *Id.* at ¶¶ 5-8.

Mr. Walters insisted that his son changed after receiving his four-month-old vaccinations, stating "it looked like someone hit the reset button on my son." Ex. 85 at ¶ 11. He maintained that K.S.S.W. "no longer made eye contact, he was unable to hold his bottle, he didn't smile anymore and no more scolding actions when he did not like something I did." *Id.* at ¶ 12. Emphasizing that that neither he, his wife, nor any family member suffers from a seizure disorder (*id.* at ¶ 15), Mr. Ansel stated that he "truly believe[s] that the vaccinations [his] son received on January 16, 2013 caused his injuries" (*id.* at ¶ 14).

3. Ms. Deborah Summey – K.S.S.W.'s Maternal Grandmother

As K.S.S.W.'s maternal grandmother (Ex. 86 at ¶ 1), Ms. Summey indicated she "spent a great deal of time with him" (*id.* at ¶ 2). She provided her recollection of K.S.S.W. before receiving his four-month-old vaccinations. Describing the same type of walking movement when being held upright as her daughter, Ms. Summey also insisted that K.S.S.W. would "track [her] moves with his eyes" (*id.* at ¶ 3), look around with his eyes wide open, and eat food eagerly from a spoon. *Id.* at ¶¶ 3-6.

Regarding K.S.S.W.'s condition post-vaccination, Ms. Summey recalled the January 17 instance which she found troubling and related to her daughter, involving K.S.S.W.'s holding closed fists to his chest and closing his eyes. Ex. 86 at ¶¶ 7-8, 10. Characterizing the change in her grandson's condition as "like night and day" (*id.* at ¶ 12), she recalled that he no longer ate solid mashed food, constantly closed his eyes and looked off in the distance instead of at her, slept all the time, and would no longer put one foot in front of the other. *Id.* at ¶¶ 14-16.

III. Applicable Law

A. Overall Burden in Vaccine Program Cases

Under the Vaccine Act, a petitioner may prevail on her claim if she has "sustained, or endured the significant aggravation of any illness, disability, injury, or condition" set forth in the Vaccine Injury Table (the Table). § 11(c)(1)(C)(i). The most recent version of the Table, which can be found at 42 C.F.R. § 100.3, identifies the vaccines covered under the Program, the corresponding injuries, and the time period in which the particular injuries must occur after vaccination. § 14(a). If a petitioner establishes that she has suffered a "Table Injury," causation is presumed.

If, however, a petitioner suffered an injury that either is not listed in the Table or did not occur within the prescribed time frame, she must prove that the administered vaccine caused injury to receive Program compensation. § 11(c)(1)(C)(ii) and (iii). In such circumstances, petitioner asserts a "non-Table or [an] off-Table" claim and to prevail, a petitioner must prove her claim by preponderant evidence. § 13(a)(1)(A). This standard is "one of . . . simple preponderance, or 'more probable than not' causation." *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274, 1279-80 (Fed. Cir. 2005) (referencing *Hellebrand v. Sec'y of Health & Hum. Servs.*, 999 F.2d 1565, 1572-73 (Fed. Cir. 1993). The Federal Circuit has held that to establish an off-Table injury, a petitioner must "prove . . . that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury." *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1351 (Fed. Cir 1999). The received vaccine, however, need not be the predominant cause of the injury. *Id.* at 1351.

The Federal Circuit has indicated that a petitioner "must show 'a medical theory causally connecting the vaccination and the injury'" to establish that the vaccine was a substantial factor in bringing about the injury. *Shyface*, 165 F.3d at 1352-53 (quoting *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992)). The Circuit Court added that "[t]here must be a 'logical sequence of cause and effect showing that the vaccination was the reason for the injury.'" *Id.* The Federal Circuit subsequently reiterated these requirements in its *Althen* decision. *See* 418 F.3d at 1278. *Althen* requires a petitioner demonstrate by preponderant evidence that the vaccinations she received caused her injuries by providing: "(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.* All three prongs of *Althen* must be satisfied. *Id.* "Unlike an on-Table case, proof of causation in an off-Table case must comprise more than just a literal temporal association between the onset of the injury and the vaccination." *Pafford v. Sec'y*

of Health & Hum. Servs., 64 Fed. Cl. 19, 24 (Fed. Cl. 2005); *see also Grant*, 956 F.2d at 1148.

The Federal Circuit has instructed that a petitioner may satisfy her evidentiary burden by relying either on "medical records or medical opinion." *Althen*, 418 F.3d at 1279 (emphasis in original). Any offered expert testimony must be scientifically reliable and may be analyzed using the four factors enumerated by the Supreme Court in *Daubert*. *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1301, 1316 (Fed. Cir. 1999) (referring to *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579 (1993)). Circumstantial evidence also might be used. *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1325-26 (Fed. Cir. 2006). Evidence that satisfies one prong might assist in proving another prong as well. *Id.* at 1326.

B. Analysis of Expert Testimony

Establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of her claim. *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert*, 509 U.S. at 594-96. *See Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (*citing Terran*, 195 F.3d at 1316). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592-95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora. *Daubert* factors are employed by judges to exclude evidence that is unreliable and potentially confusing to a jury. In Vaccine Program cases, these factors are used in the weighing of the reliability of scientific evidence. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g., Snyder*, 88 Fed. Cl. at 743. In this matter, (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts of his own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)). A "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly v. Sec'y*

of Health & Hum. Servs., 592 F.3d 1315, 1324 (Fed. Cir. 2010). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Id.* at 1325-26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs.*, 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

C. Consideration of Medical Literature

Although this decision discusses some but not all of the medical literature in detail, I reviewed and considered all of the medical records and 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.'" (citation omitted)), *aff'd*, 601 F. App'x 982 (Fed. Cir. 2015).

IV. Expert Opinions

Petitioners submitted two expert reports from Dr. Yuval Shafrir, a pediatric neurologist, and two expert reports from Dr. Omid Akbari, a professor of immunology. Exs. 35, 166 (hereinafter "First Shafrir Rep.", "Second Shafrir Rep."); Exs. 89, 143 (hereinafter "First Akbari Rep.", "Second Akbari Rep."). In response, Respondent submitted four expert reports from Dr. Neil Romberg, a pediatric immunologist, and two expert reports from Dr. Kristin Barañano, a pediatric neurologist. Exs. A, DD, NN, FFF (hereinafter "First Romberg Rep.", "Second Romberg Rep.", "Third Romberg Rep.", "Fourth Romberg Rep."); Exs. B, JJJ (hereinafter "First Barañano Rep.", "Second Barañano Rep."). Regarding the CVs provided, I will refer only to the most recent updated CV for each expert. Exs. 168, 185, DDD, EEE (hereinafter "Shafrir CV", "Akbari CV", "Barañano CV", "Romberg CV").

A. Qualifications

1. Petitioners' Expert: Yuval Shafrir, M.D.

Dr. Shafrir received his medical training at the Sackler School of Medicine, Tel Aviv University, Israel. Shafrir CV at 1; Tr. at 53. After graduating *magna cum laude,* he completed a pediatric residency and neonatology rotation at several hospitals in Israel. Dr. Shafrir completed another pediatric residency at a New York hospital affiliated with the Cornell University Medical School and fellowships in pediatric neurology and pediatric neurophysiology and epileptology in Missouri and Florida, respectively. Shafrir CV at 1; Tr. at 53-54.

Dr. Shafrir is currently board certified in neurology and clinical neurophysiology. Shafrir CV at 2; Tr. at 54-55. Although he has been board certified in pediatrics in the past, he chose not

to pursue that renewal in 1998, due to the amount of time and expense needed and the fact that he was primarily working as a pediatric neurologist. Tr. at 54.

After testifying that he had practiced in general pediatrics for about seven years, Dr. Shafrir explained that he currently is the neurologist for the Maryland School for the Blind. Tr. at 55. Since 1993 and until the COVID-19 pandemic, he also worked in private practice, traveling to areas where temporary help was needed. Tr. at 56.

Due a recent interest in epilepsy, autism, and developmental disorders, Dr. Shafrir indicated that he "ha[s] a lot of patients with neuro-immune problems, mainly a disorder identified as PANDAS[27] and autoimmune encephalitis and other autoimmune conditions of the brain." Tr. at 55. His CV states that he worked at the Latimer Neurology Center – run by Dr. Beth Latimer who touts experience with PANS/PANDAS,[28] from April through October 2019, and has had a private practice in two different residential areas in Maryland since January 2020. Shafrir CV at 3-4.

Dr. Shafrir indicated that he originally testified in vaccine cases for the government, but now testifies for petitioners. Tr. at 56-57. He estimated he has done so in approximately 30 to 40 vaccine cases. *Id.* He stressed that he has always been accepted as a qualified expert. Tr. at 57. I recognized him as an expert in the fields of pediatric neurology and epileptology. *Id.*

2. Petitioners' Expert: Omid Akbari, Ph.D.

Educated in London, England, Dr. Akbari earned a B.S. in Microbiology in 1993, an M.S. in Medical and General Microbiology in 1995, and a Ph.D. in Cellular and Molecular Immunology in 1998. Akbari CV at 1; Tr. at 124. After working as a research associate scientist in pediatric allergy and immunology at Stanford University from 2001-2004, he served as an assistant professor in immunology at Children's Hospital, Harvard Medical School until 2008. Akbari CV at 2; First Akbari Rep. at 1-2. From 2008 to the present, he has been a tenured professor at the Keck School of Medicine in Los Angeles, California, and a full professor since 2015. Akbari CV at 2; Tr. at 125. He also served as a visiting associate professor at Harvard Medical School from 2008 until 2012 and is currently a visiting professor at Chiba University in Japan. Akbari CV at 2.

Dr. Akbari has received many awards and honors, has supervised and mentored numerous fellowship participants and individuals earning their master's and doctorate degrees; and has acted as a reviewer for NIH, many medical journals, and several grant programs, and as an editor on

[27] "PANDAS is short for Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections, a disorder which occurs in reaction to a strep infection." *See* https://www.nimh.nih.gov/health/publications/pandas (last visited on Nov. 4, 2022). Due to the strep bacteria's ability to mimic molecules in a child's own tissues, antibodies produced by the child's immune system in response to the strep infection will also attack human host molecules. "The symptoms are usually dramatic, happen "overnight and out of the blue," and can include motor or vocal tics or both and obsessions, compulsions, or both. In addition to these symptoms, children may become moody or irritable, experience anxiety attacks, or show concerns about separating from parents or loved ones." *Id.*

[28] *See* https://www.bethlatimermd.com (clinic's website, last visited Nov. 4, 2022).

several journals; and has lectured, nationally and internationally, on topics in immunology, including allergy and inflammation. Akbari CV at 1, 3-5, 7; First Akbari Rep. at 2; Tr. at 125-27. In his bibliography, he listed 70 publications. Akbari CV at 8-13.

Citing several journals which have published his studies, Dr. Akbari described his research as "focused on the role of immune tolerance and how immune cells induce autoimmune and allergic diseases." First Akbari Rep. at 2. He added that his current research involves "multiple research studies . . . currently conducted with the aim to understand the medical explanations and theories involved in regard to immunization, which may result in appropriate or dysregulated immune responses causing unwanted inflammation and adverse effects." *Id.* I recognized him as an expert in the field of immunology. Tr. at 127.

3. Respondent's Expert: Neil Romberg, M.D.

Dr. Romberg earned his medical degree from Pennsylvania State University in 2004. Romberg CV at 1; Tr. at 209. He then completed a pediatric residency at New York University School of Medicine, spending an extra year there as chief resident. After a three-year fellowship in Allergy and Clinical Immunology at Yale University School of Medicine, which included laboratory research, he was offered a faculty appointment. *Id.* He testified that Yale's immunobiology research division is "very elite," one of the top three immunobiology programs in the world. Tr. at 209.

While at Yale, Dr. Romberg studied B cell development and tolerance, specifically in patients with genetic problems of the immune system. Tr. at 210. He also studied the function and evaluation of T regulatory ("Treg") cells, including patients who lacked or had function issues with T reg cells. *Id.* He also became interested in a structure called inflammasome, "a highly inflammatory micro-organ within a cell that produces fever cytokines, . . . and . . . is the reason why alum adjuvants are used in vaccines." *Id.*

In 2015, Dr. Romberg accepted an assistant professor position at the University of Pennsylvania, which included starting a research laboratory at CHOP. Romberg CV at 1; Tr. at 209. Describing an expertise in the humeral immune system, he stated he had "discovered several monogenic diseases of the immune system" and was well-known in the field. Tr. at 211-12. Since 2015, he has served as the Jeffrey Modell Chair of Pediatric Immunology Research. Romberg CV at 2; Tr. at 213-14. He recently won the Lady Barbara Colyton Prize for Autoimmune Research, a cash award given annually to the University of Pennsylvania researcher "who has performed the most exemplary research in the field of autoimmunity." Tr. at 216-17. He also pursues NIH grants, which are very competitive, to fund his research. Romberg CV at 6; Tr. at 214.

Dr. Romberg is board certified in allergy and immunology. Romberg CV at 2; Tr. at 211. Like Dr. Shafrir, he has allowed his pediatric board certification to lapse due to the time and cost of its renewal. Tr. at 211. Dr. Romberg has lectured extensively, authored approximately 30 peer reviewed publications, and acted as an *ad hoc* reviewer for different publications. Romberg CV at 3-12.

Regarding the character of his current work, Dr. Romberg testified that he spends about 20

percent of his time seeing patients, usually those with rare diseases. Tr. at 211-13. The remainder is spent performing research with a small portion devoted to administrative work and teaching. *Id.* at 212. He testified that his current funding and research regarding the epigenetics of human lymphocytes, including B cells and T cells, is particularly relevant to Petitioners' experts' theory "that "K.S.S.W.'s unique genetic anomaly . . . has changed the structure of his chromatin, has changed his gene expression." *Id.* at 216. I recognized him as an expert in the fields of clinical pediatric immunology and pediatric immunology and autoimmune disease research. *Id.* at 219.

4. Respondent's Expert: Kristin Barañano, M.D., Ph.D.

After eight years at Johns Hopkins University School of Medicine, Dr. Barañano earned her medical degree and doctorate in pediatrics and pediatric neurology in 2004. Barañano CV at 1; Tr. at 300-01. After completing residencies in pediatrics and pediatric neurology, she spent a year in private practice in Atlanta, Georgia, while her husband completed his fellowship. Barañano CV at 1; Tr. at 301. She then returned to Johns Hopkins to complete a fellowship in neurogenetics at the Kennedy Kreiger Institute in Baltimore, Maryland. *Id.*

In 2011, Dr. Barañano joined the faculty at Johns Hopkins. Barañano CV at 1; Tr. at 301. Her "area of expertise is neurogenetics, . . . trying to understand the genetic contribution to neurologic disease." Tr. at 301. She is board certified in adult neurology with special certification in child neurology. *Id.* at 302. Like Dr. Romberg, she sees patients, but estimated that she spends 80 percent of her time on direct patient care. *Id.* For six weeks each year, she is the attending neurologist for pediatrics at Johns Hopkins. Twenty percent of her time is spent on academia and research. *Id.*

Dr. Barañano indicated that she has lectured frequently, has published 25 peer-reviewed articles regarding pediatric neurology and neurogenetics, and has acted as an *ad hoc* reviewer for several journals. Barañano CV at 1-4, 6; Tr. at 304-05. Particularly relevant to this case, several of these articles involved children with genetic disorders. Tr. at 304. Dr. Barañano indicated she has testified in one other vaccine case. *Id.* at 305. I recognized her as an expert in the fields of pediatric neurology and neurogenetics. *Id.* at 306.

B. Expert Reports and Testimony

There were three phases of expert evidence in this case. The first involved Dr. Shafrir's initial expert report, followed by responsive reports from Dr. Romberg and Dr. Barañano. First Shafrir Rep., First Romberg Rep., First Barañano Rep. Petitioners then produced an expert report from Dr. Akbari, leading to multiple exchanges between Dr. Akbari and Dr. Romberg set forth in two reports from each expert. First Abkari Rep., Second Romberg Rep., Second Akbari Rep., Third Romberg Rep. During the month prior to the entitlement hearing, Dr. Shafrir, Dr. Romberg, and Dr. Barañano all filed supplemental expert reports. Second Shafrir Rep., Fourth Romberg Rep., Second Barañano Rep. All four experts testified at the entitlement hearing.

1. Phase One: Dr. Shafrir, Dr. Romberg, and Dr. Barañano

a. *Petitioners' Expert: Dr. Shafrir*

In his first report, Dr. Shafrir opined that K.S.S.W. developed epileptic encephalopathy after receiving his second DTaP vaccine on January 16, 2013, followed by persistent and intractable seizures and worsening of his developmental and visual functions. First Shafrir Rep. at 46, 60. He theorized that K.S.S.W. experienced an excessive inflammatory response of the innate immune system due to the aluminum adjuvant contained in the DTaP vaccine and/or dysfunction of the adaptive immune system -- specifically molecular mimicry involving cross reaction between the DTaP vaccine proteins and several brain proteins involved in electrical activity, whose dysfunction could produce seizures. *Id.* at 58-60.

To support the different stages of his theory and his overall assertion that K.S.S.W. developed epileptic encephalopathy following vaccination, Dr. Shafrir cited medical literature discussing links between the DTaP vaccine and epileptic discharges, encephalopathy, autoimmune encephalitis, and autoimmune disease; and an autoimmune basis for encephalitis.[29] First Shafrir Rep. at 55, 57. Dr. Shafrir stated that his "proposed mechanism is heavily based on the framework suggested by Tishler and Sh[oe]nfeld" -- specifically, molecular mimicry. *Id.* at 58. Regarding the stage involving molecular mimicry, he relied upon the work performed by a group headed by Professor Darja Kanduc at the University of Bari in Italy.[30] First Shafrir Rep. at 56. Although he

[29] Ex. 56: Nouno, et al., *Adverse Effects on EEG and Clinical Condition after Immunizing Children with Convulsive Disorders*, 32 ACTA PAEDIATRICA JAPONICA 357-60 (1990) (hereinafter "Nouno"); Ex. 57: 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 United Kingdom Department of Health and Social Security, Whooping Cough:* REPS. FROM THE COMMITTEE ON SAFETY OF MEDS. AND THE JOINT COMMITTEE ON VACCINE AND IMMUNISATION 79–184 (1981) (hereinafter "NCES"); Ex. 58: 42 C.F.R. § 100.3 (2005) (Vaccine Injury Table from 2005); Ex. 64: Irani, et al., *N-methyl-D-aspartate antibody encephalitis: temporal progression of clinical and paraclinical observations in a predominantly non-paraneoplastic disorder of both sexes,* 133 BRAIN 1655–67 (2010); Ex. 65: Hofmann, et al., *Anti-NMDA receptor encephalitis after TdaP-IPV booster vaccination: cause or coincidence?*, 258 J. NEUROL. 500-01 (2011); Ex. 66: Tenembaum, et al., *Acute disseminated encephalomyelitis,* 68:2 NEUROL. S23–S36 (2007); Ex. 67: Downes, et al., *Acute Autoimmune Hemolytic Anemia Following DTP Vaccination: Report of a Fatal Case and Review of the Literature,* 40 CLIN. PEDS. 355-58 (2001); Ex. 51: Roberson, et al., *Electroencephalograms of Children with Permanent Cortical Visual Impairment*, 13 CAN. J. NEUROL. SCI. 256-61 (1986); Ex. 52: Brodsky, *Preictal, Ictal, or Postictal Phenomena:* PED. NEURO OPHTHALMOLOGY 18-19 (2nd ed. 2010); Ex. 59: Carvalho, et al, *Generalized Epilepsies: immunologic and inflammatory mechanisms*, 3 SEMS. IN PED. NEUROL. 214-20 (2014); Ex. 62: Takahashi, et al., *Vaccination and infection as causative factors in Japanese patients with Rasmussen syndrome: Molecular mimicry and HLA class I,* 13 CLIN. & DEV. IMMUNOLOGY, 381–87 (2006); Ex. 63: Specchio, et al., *Epileptic encephalopathy in children possibly related to immune-mediated pathogenesis*, 32 BRAIN & DEV. 51–56 (2010).

[30] Ex. 69: Kanduc, et al., *Peptide cross reactivity and vaccine,* FRONTIERS IN BIOSCI. 1393-1401 (2014) (hereinafter "Kanduc"); Ex. 70: Lucchese & Kanduc, *The Peptide Network between Tetanus Toxin and Human Proteins Associated with Epilepsy,* EPILEPSY RES. & TREAT. 1-11 (2014) (hereinafter "Lucchese); Ex. 71: Bavaro, et al., *Pentapeptide sharing between Corynebacterium diphtheria toxin and the human neural protein network,* 33(2) IMMUNOPHARMACOLOGY & IMMUNOTOXICOLOGY, 360-72 (2011) (hereinafter "Bavaro"); Ex. 72: Capone & Kanduc, *Peptide sharing between Bordetella pertussis proteome and human sudden death proteins: a hypothesis for a causal link*, 8(8) FUTURE MICROBIOL. 1039-48 (2013).

acknowledged the theoretical nature of this work, he maintained that it "shows that the potential for humeral cellular autoimmune reaction as a result of molecular mimicry is huge." *Id.* Pointing to the study described in Lucchese, he claimed the article "shows multiple areas of homology between the tetanus toxin and proteins that are directly implicated as caus[ing] genetic epilepsy." *Id.* He also cited a more recent study involving autistic children which he claimed showed antibodies of a specific brain protein "were implicated in autoimmune epilepsy." *Id.* (citing Ex. 73: Obregon, et al., *Potential Autoepitope within the Extracellular Region of Contactin-Associated Protein-like 2 in Mice*, 4(1) BR. J. MED. & MED. RES. 416-23 (2014)).

When providing proof that K.S.S.W. suffered a vaccine related injury, Dr. Shafrir relied heavily upon his assertion that K.S.S.W.'s brain and chromosomal abnormalities -- known to lead to developmental, motor, and cognitive disabilities and seizures -- made him more vulnerable to the deleterious effects of the DTaP vaccine, but, by themselves, would not have resulted in his post-vaccination condition. First Shafrir Rep. at 46-54, 60. Specifically, he insisted that K.S.S.W.'s "colpocephaly, his shunted hydrocephalus, and his chromosomal anomaly cannot, by themselves, explain his clinical picture . . . [but] make him more prone to deleterious effects of the vaccine." *Id.* at 60; *accord id.* at 46.

To support this assertion, Dr. Shafrir emphasized K.S.S.W.'s mother's lack of symptoms related to her balanced chromosomal abnormality and cited numerous studies involving individuals with either a chromosome 6 deletion or chromosome 5 duplication who suffered seizures and epilepsy which were milder and controlled with medication.[31] First Shafrir Rep. at 46-54. He also theorized that, due to what he characterized as the rarity of cortical blindness related to complications of congenital hydrocephalus,[32] K.S.S.W.'s blindness must, instead, be due to epileptic encephalopathy. First Shafrir Rep. at 52-53. He criticized the conclusions of a neurologist, who treated K.S.S.W. during his initial January 2013 hospitalization, that K.S.S.W.'s seizures were due to his hydrocephalus and brain malformation, rather than the vaccinations he received, including the treating physician's opinion that K.S.S.W. likely experienced prior, but unnoticed, seizure activity. *Id.* at 54.

b. *Respondent's Expert: Dr. Romberg – Response to Dr. Shafrir*

In his first expert report, Dr. Romberg opined there was "no basis to reasonably conclude that the administration of the DTaP vaccine triggered an *exaggerated* innate inflammatory response injuring K.S.S.W.'s central nervous system . . . [or] evidence of an adaptive immune response responsible for K.S.S.W.'s neurologic symptoms." First Romberg Rep. at 6 (emphasis

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[31] *See infra* note 32. Respondent's expert Dr. Barañano's citation of many of these same studies. The parties agree that these studies show seizure activity in individuals suffering only one of K.S.S.W.'s chromosomal abnormalities tends to be less severe.

[32] To support his assertion regarding the rarity of cortical blindness related to congenital hydrocephalus, Dr. Shafrir revealed that his literature search produced only one case report. First Shafrir Rep. at 52 (citing Ex. 48: Smith, et al., *Cortical Blindness in Congenital Hydrocephalus,* 62(2) PERIPHERAL FUNDI IN RETINOBLASTOMA 252-57 (2016).

added). He also opined that K.S.S.W.'s disease timeline was not consistent with the mechanisms Dr. Shafrir proposed. *Id.*

Specifically, Dr. Romberg emphasized that K.S.S.W. did not exhibit symptoms or test results indicative of an excessive innate immune system response, such as local injection site reaction, increased fever, suspected hypotension, leukocytosis, or increased presence of immature neutrophils and platelet concentrations. First Romberg Rep. at 3-4. He noted that these symptoms and testing would have occurred within four days of vaccination. *Id.* at 4.

Regarding Dr. Shafrir's reliance on molecular mimicry, Dr. Romberg first mentioned that it "is a theory considered by experts in the field of autoimmune disease to be largely unproven." First Romberg Rep. at 4. He acknowledged only one instance of possible molecular mimicry due to the cross reactivity between *campylobacter jejuni* associated Guillain-Barré syndrome ("GBS") with IgM, IgA, or IgG autoantibodies. *Id.* However, based upon that example, as well as the usual delay associated with the activation of the adaptive immune system, Dr. Romberg maintained that K.S.S.W.'s neurologic symptoms, which occurred only one day after vaccination, would be too rapid to have occurred in conjunction with an adaptive immune response. *Id.*

Additionally, Dr. Romberg provided several criticisms of the medical literature Dr. Shafrir cited to show potential cross reactivity between the proteins found in the DTaP vaccine and the brain. First Romberg Rep. at 5; *see supra* note 29 (for referenced medical literature). He maintained that the study in Lucchese utilized an overly simplistic two-dimensional model to search for similar sequences and was subject to confirmation bias associated with the experimental design. *Id.* at 5. He also mentioned that this literature was published in a "low-impact pay-to-publish journal" and, to his knowledge, had not been cited by any other researcher. *Id.*

c. *Respondent's Expert: Dr. Barañano – Response to Dr. Shafrir*

In her first expert report, Dr. Barañano opined that "it is more likely than not that K.S.S.W.'s seizure activity is attributed to his chromosomal abnormality and not related to his receipt of a vaccination." First Barañano Rep. at 5. To illustrate the connection between the two significant chromosomal abnormalities K.S.S.W. suffers, 6q deletion and 5p duplication, and the seizures he experienced, she cited multiple articles showing individuals suffering from either chromosomal abnormality were more likely to suffer seizures.[33] Acknowledging that these seizures are often well-controlled with medication, she emphasized that seizures experienced by individuals showing trisomy of the 5p "can prove hard to control." First Barañano Rep. at 4 (citing Ex. AA: Grosso, et al., *De Novo Complete Trisomy 5p: Clinical and Neuroradiological Findings*, 112 AM. J. MED. GENETICS 56–60 (2002). To explain the intractable nature of K.S.S.W.'s seizures, Dr. Barañano opined that, based upon her clinical experience, it was safe to assume that the effects of multiple unbalanced translocations, as K.S.S.W. possessed, were likely to be additive. *Id.* at 5.

[33] Ex. V: Bertini, et al., *Clinical Report Isolated 6q Terminal Deletions: An Emerging New Syndrome*, 140(A) AM. J. MED. GENETICS 74–81 (2006); Ex. W: Elia, et al., *6q Terminal Deletion Syndrome Associated with a Distinctive EEG and Clinical Pattern: A Report of Five Cases*, 47(5) EPILEPSIA, 830–38, (2006); Ex. X: Striano, et al., *Clinical Phenotype and Molecular Characterization of 6q Terminal Deletion Syndrome: Five New Cases*, 140A AM. J. MED. GENETICS 1944–49 (2006).

2. Stage Two: Dr. Akbari and Dr. Romberg

a. *Petitioners' Expert: Dr. Akbari*

After providing an overall discussion of the immune system and molecular mimicry, Dr. Akbari described how K.S.S.W.'s chromosomal abnormalities made him susceptible to immune dysfunction through the immune deviation of T ("Th") helper cells which direct other cells involved in the immune process, and reduction and/or impairment of Treg cells which can protect the host from autoimmune disease. First Akbari Rep. at 4-13. He provided a visual depiction of this theory, accompanied by a written description, labeled Figure 1. *Id.* at 11.

Regarding K.S.S.W.'s chromosome 5p trisomy, Dr. Akbari theorized it would result in the "over expression of type two cytokines and Granulocyte-Macrophages Colony Stimulation (GMC-CSF) . . . [which] may lead to increase in number of eosinophils and contribute to the formation of atypical lymphocytes and inflamed macrophages." First Akbari Rep. at 11; *see id.* at 10. Acknowledging that there was no direct measurement of K.S.S.W.'s cytokine levels, he cited the results of a blood test performed during K.S.S.W.'s hospitalization in late February/early March 2013, which showed a higher number of eosinophils. *Id.* at 12 (citing Ex. 7 at 1491-92, 1734-35).

Dr. Akbari also proposed that, due to his chromosome 6q monosomy, K.S.S.W. would lack "genes essential for immune cells proper function including Interferon gamma receptor [("IFNGR")], ATG5, and CCR6." First Akbari Rep. at 12; *see id* at 11-13. He theorized this deficiency would result in immune deviation -- from Th1 to Th17 and Th2 cells -- associated with inflammation and epilepsy, and a reduction and impairment of Treg cells. *Id.* at 11-13. As evidence that these effects occurred in K.S.S.W.'s case, he contrasted K.S.S.W.'s more severe seizures right after vaccination with the lower occurrence of unprovoked epilepsy and seizures in patients with only 6q monosomy and the lack of any seizure activity in K.S.S.W.'s mother. *Id.* at 14 (citing Ex. 145: Engwerda, et al., *The phenotypic spectrum of proximal 6q deletions based on a large scale cohort derived from social media and literature reports,* 26 EUR. J. OF HUMAN GENETICS 1478-89 (2018) (hereinafter "Engwerda")).

Dr. Akbari also discussed a proposed role of the immune system in epilepsy and seizures, asserting "[i]t is generally accepted that the activation of the immune system can be the cause of seizures." First Akbari Rep. at 13-14 (citing Exs. 135-39).[34] He maintained that the timing between the vaccination K.S.S.W. received and the onset of his seizure activity coincided with "what is known about the timing of epilepsy and neurological disorders resulting from the DTaP vaccination, particularly as it is likely in these patients [in which] immune related genes are impaired." First Akbari Rep. at 14.

[34] Ex. 135: Ong, et al., *Population-Level Evidence for an Autoimmune Etiology of Epilepsy*, 71(5) JAMA NEUROL. 569–74 (2014); Ex. 136: Korff & Scheffer, *Epilepsy classification: a cycle of evolution and revolution*, 26(2) CURRENT OPINION NEUROL. 163-67 (2013); Ex. 137: Vezzani, *Epilepsy and Inflammation in the Brain: Overview and Pathophysiology*, 14(1) EPILEPSY CURRENTS 3-7 (2014); Ex. 138: Vezzani & Ruegg, *Immunity and Inflammation in Epilepsy*, 52 EPILEPSIA 1-4 (2011); Ex. 139: Vezzani, et al., *The role of inflammation in epilepsy*, 7(1) NAT. REV. NEUROL. 31–40 (2011).

b. *Respondent's Expert: Dr. Romberg – Response to Dr. Akbari*

In response to Dr. Akbari's report, Dr. Romberg filed a second expert report. As an initial matter, he criticized the depiction by Dr. Akbari of the possible DTaP vaccine response in K.S.S.W.'s case, contained in Figure 1 of his expert report, indicating that it "diverges from the prevailing view on how the DTaP vaccine generates protective immunity." Second Romberg Rep. at 1. Although he questioned Dr. Akbari's understanding of the DTaP vaccine, he acknowledged an awareness of the work performed by Dr. Akbari's team "on murine ICOS-ICOSL interactions and airway hyperreactivity," which he characterized as "well-designed investigations [that] added significantly to our field." *Id.* He observed that Dr. Akbari's prior experience was studying "murine models of asthma and allergic diseases but not vaccine studies." *Id.*

Regarding Dr. Akbari's opinion in this case, Dr. Romberg observed that, "[l]ike Dr. Shafrir, Dr. Akbari's theory of injury by vaccine revolves around an inflammatory mechanism." Second Romberg Rep. at 1. However, he noted that Dr. Akbari had introduced a new aspect to the theory when he proposed that K.S.S.W.'s chromosomal abnormalities, which made him more susceptible to seizures, also "made him especially susceptible to vaccine-triggered inflammatory disease." *Id.* at 2. Agreeing only that K.S.S.W.'s chromosomal abnormalities and shunted hydrocephalus predisposed him to seizures, Dr. Romberg insisted "there is no evidence his seizures were caused by an immunologic mechanism." *Id.* at 3. He emphasized the lack of evidence showing K.S.S.W. experienced an inflammatory response or that his treating physicians suspected or prescribed treatment for such. *Id.*

Dr. Romberg also provided several specific criticisms of Dr. Akbari's explanation of the potential effects of the chromosomal abnormalities K.S.S.W. suffered on immune system function. Second Romberg Rep. at 2-3. For example, he insisted that, because K.S.S.W. lost only the Chr6q26q27 tip of chromosome 6, he would not have lost the genes encoding IFNGR and ATG5 as Dr. Akbari maintained, but only those encoding CCR6. *Id.* at 3. He also opined that the loss of a copy of CCR6, such as K.S.S.W. experienced, would not have the substantial negative effect that Dr. Akbari proposed and may even cause greater resistance to autoimmune disease. *Id.* at 3 (citing Exs. HH - II).[35] Regarding Dr. Akbari's arguments related to chromosome 5, he observed that the genes encoding type 2 cytokines and/or GMCSF are not located within 5p15.33p13.3 -- the affected area for K.S.S.W. *Id.* at 2.

c. *Petitioners' Expert: Dr. Akbari – Response to Dr. Romberg*

Dr. Akbari then filed a second expert report in response to Dr. Romberg's criticisms. Second Akbari Rep. Emphasizing the lack of studies regarding the effects of the DTaP vaccine on patients with genetic defects, he mentioned a study, cited in his first expert report, involving patients with Down Syndrome which showed a reduced efficacy of the DTaP vaccine. *Id.* at 1, 4

[35] Ex. HH: Chen, et al., *The RNA-binding protein HuR contributes to Neuroinflammation by promoting C-C chemokine receptor 6 (CCR6) expression on Th17 cells*, 292 J. BIOL. CHEM. 14532-43 (2017) (hereinafter "Chen"); Ex. II: Reboldi, et al., *C-C chemokine receptor 6–regulated entry of TH-17 cells into the CNS through the choroid plexus is required for the initiation of EAE*, 10 NATURE IMMUNOLOGY 514-23 (2009) (hereinafter "Reboldi").

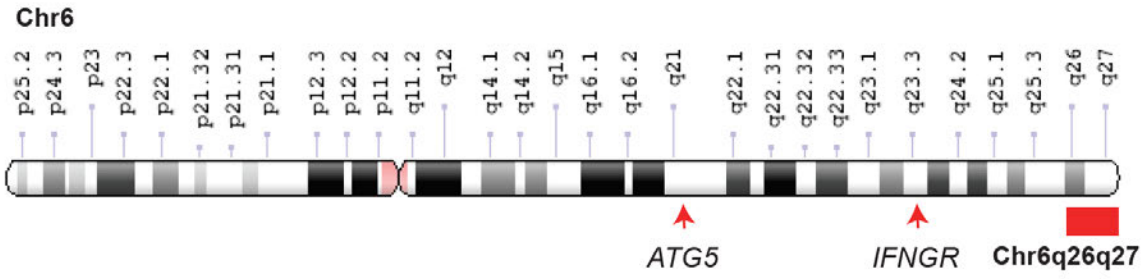
(citing Ex. 141: Kusters, et al., *Intrinsic defect of the immune system in children with Down syndrome: a review*, 156 CLIN. & EXPER. IMMUNOLOGY 189–93 (2009) (hereinafter "Kusters")).

Additionally, asserting that Dr. Romberg agreed with his identification of three missing genes and the importance of one gene (CCR6) to Treg cells, Dr. Akbari challenged Dr. Romberg to provide his opinion regarding the missing or duplicated genetic material in K.S.S.W.'s case and to address the research he cited showing the greater susceptibility to seizure in CCR6 deficient mice. Second Akbari Rep. at 1-3 (citing Ex. 150: Liu, et al., *Altered expression of neuronal CCR6 during pilocarpine induced status epilepticus in mice,* 126 EPILEPSY RES. 45-52 (2016) (hereinafter "Liu"); Ex. 154: Scharschmidt, et al., *Commensal Microbes and Hair Follicle Morphogenesis Coordinately Drive Treg Migration into Neonatal Skin*, 21(4) CELL HOST MICROBE 467–77 (2017) (hereinafter "Scharschmidt"). Specifically, Dr. Akbari stated, "I am glad that at least on few of those genes, we are in agreement with Dr. Romberg. I only here focus on the genes that Dr. Romberg agreed to be involved in minor KSSW including ATG5, CCR6 and IFNγR …" Second Akbari Rep. at 1-2.

Expanding on his hypothesis, Dr. Akbari described recent studies of potential indirect effects of any genetic defect, termed genetic variegation. Second Akbari Rep. at 3. He indicated that the genetic defects "may affect the chromatin structure and therefore, affect the expression of other genes independent of the distance." *Id.* He maintained that several studies showed that in patients with genetic defects, chromosome rearrangements changed the surrounding chromatin environment, significantly influencing and altering gene expression. Second Akbari Rep. at 3 (citing Ex: 155: Sullivan, et al., *Human centromere repositioning within euchromatin after partial chromosome deletion*, 24(4) CHROMOSOME RES. 451–66 (2016) (hereinafter "Sullivan")).

d. *Respondent's Expert: Dr. Romberg – Response to Dr. Akbari*

In his response, Dr. Romberg again disputed Dr. Akbari's assertion concerning the genes encoding ATG5 and IFNγR. Referring to Dr. Akbari's prior expert report, he opined, "I find this an odd statement as my last report refuted, with text and illustration, Dr. Akbari's original claim that ATG5 and IFN-GR were within or proximate to KSSW's chromosome 6q26q27 deletion." Third Romberg Rep. at 2. Dr. Romberg again inserted the below illustration, demonstrating that K.S.S.W.'s deletion of a portion of chromosome 6q did not include the genes that encode ATG5 and IFNγR.



Id. Dr. Romberg clarified that "CCR6 is the only gene Dr. Akbari and I agree was plausibly within K.S.S.W.'s chromosome 6 deletion." *Id.* And he reiterated his belief that this abnormality would

not significantly affect and may even provide a greater resistance to autoimmune encephalitis. *Id.* at 2-3 (citing Reboldi). To further support this assertion, he reported that a search he performed using the Genome Aggregation Database showed a score of only 0.01, noting that "a score of zero essentially excludes deleterious effects and one guarantees them." *Id.* at 2.

When addressing Dr. Akbari's reliance on research involving CCR6-deficient mice, Dr. Romberg contested the relevance of the first -- which involved Treg cell trafficking to neonatal hair follicles, and the characterizations and conclusions Dr. Akbari espoused regarding the second study -- which did not involve CCR6-deficient mice. Third Romberg Rep. at 3-4 (citing Scharschmidt and Liu). He also criticized Dr. Akbari's depiction of Sullivan, noting it involved studies restricted to the centromeric chromatin[36] which is not interchangeable with the deletions and duplications K.S.S.W. suffers. *Id.* at 4. Regarding Dr. Akbari's reliance on the study involving patients with Down Syndrome, Dr. Romberg stressed the distinction between vaccine efficacy and safety. *Id.* at 1 (referring to Kusters).

3. Stage Three: All Experts

a. *Petitioners' Expert: Dr. Shafrir*

In his second expert report, filed shortly before the entitlement hearing, Dr. Shafrir provided additional information and argument regarding the excessive innate immune response he maintains K.S.S.W. experienced and the deleterious effect of his early seizure activity on his abnormal brain. Second Shafrir Rep. at 1-2. He theorized that K.S.S.W.'s second DTaP vaccination "produced abnormal cytokine[] response with markedly increased level of epileptogenic cytokines, which caused his initial episode of repetitive seizures and encephalopathy." *Id.* at 1. Adding that this "overstimulation of the innate immune system by the vaccinations subsequently involved the adaptive immune system, with possible production of antibodies affecting the brain as well as cell-mediated immunity," he maintained this process, along with the effects of continued seizure activity, caused K.S.S.W. to suffer "progressive epileptic encephalopathy, with intractable seizures, developmental arrest, cortical blindness and inability to respond appropriately to his environment." *Id.* at 2. Based upon representations from K.S.S.W.'s mother, that his epileptic encephalopathy began several hours post-vaccination, Dr. Shafrir argued that this timing would correlate to the timing of any increased cytokine response. *Id.*

Along with his second expert report, Dr. Shafrir provided some additional medical literature. Second Shafrir Rep. at 2-3. In particular, he cited an article containing the list of known genes located in K.S.S.W.'s deleted segment -- noting that several have important roles in immune regulation. *Id.* (citing Ex. 169: De Cinque, et al., *Developmental Coordination Disorder in a Patient with Mental Disability and a Mild Phenotype Carrying Terminal 6q26-qter Deletion,* 8 FRONTIERS IN GENETICS article 206 (2017)). Another cited article discussed "the negative effect of seizures during early infancy on brain function and cognition." Second Shafrir Rep. at 3 (citing Ex. 177: Holmes, Gregory L., *Effect of Seizures on the Developing Brain and Cognition*, 23(2) SEMS. IN PED. NEUROL. 120-26 (2016).

[36] Centromere is "the region of the chromosome at which the sister chromatids are joined and by which the chromosome is attached to the spindle during cell division." DORLAND'S at 329.

Dr. Shafrir repeated these theories and assertions during the entitlement hearing. However, he added additional information regarding his theory that K.S.S.W. suffered an exaggerated innate response post-vaccination, explaining that "the cytokines can ooze into the system and then get to the brain." Tr. at 83. As an example of this process, he cited the IL-1 cytokine, which is produced following vaccination, travels to the hypothalamus, and interacts with other cells -- creating fever. *Id.*

During his testimony, Dr. Shafrir also discussed K.S.S.W.'s CVI. Emphasizing the results of the eye exam performed prior to the vaccination alleged as causal, he characterized K.S.S.W.'s CVI as acquired later, not from birth. Tr. at 93-95. Thus, he theorized that the blindness would have to be related to K.S.S.W.'s epileptic encephalopathy, rather than his chromosomal abnormalities or hydrocephalus. *Id.* at 93-97.

b. *Petitioners' Expert: Dr. Akbari*

Although Dr. Akbari did not provide an additional expert report in January 2021, he testified at the entitlement hearing held that month. Focusing on the gene both he and Dr. Romberg agreed is missing from K.S.S.W.'s chromosome 6 -- CCR6 -- he explained its role as a chemokine[37] and importance in trafficking Treg cells, as well as the proposed deviation in Th cells caused by its diminished presence. Tr. at 132-38 (citing Ex. 133: Yamakazi, *CCR6 Regulates the Migration of Inflammatory and Regulatory T Cells*, 181(12) IMMUNOLOGY 8391–8401 (2008); Ex. 134: Wang, *The roles of CCR6 in migration of Th17 cells and regulation of effector T-cell balance in the gut,* 2(2) MUCOSAL IMMUNOLOGY 173-83 (2009). He also gave his Power Point presentation discussing the role of the immune system in epilepsy and seizures and theories related to molecular mimicry. Tr. at 143-62; *see* Ex. 182 ("Presentation"). Regarding this proposed link, he relied in part upon an article regarding the results of a 2017 meeting of the International League against Epilepsy. Tr. at 145-46 (citing Ex. 140: Korff & Dale, *The Immune System in Pediatric Seizures and Epilepsies Pediatrics,* 140(3) PEDS. 1-15 (2017). Expounding on his previous mention of the importance of genetic variegation, Dr. Akbari proposed that the *absence* of a gene would affect this ability as well, decreasing the instances of genes sharing information or "cross talking." Tr. at 159.

During recross, Dr. Akbari was asked whether K.S.S.W. was ever diagnosed with an autoimmune disease or had testing which would indicate an inflammatory reaction. Tr. at 177-79. He also was challenged further on his reliance on K.S.S.W.'s mother's lack of seizure activity and the January 2013 test result revealing elevated eosinophils. *Id.* at 182-86. On several occasions, Dr. Akbari confirmed that he was not a clinician or neurologist, and that he did not have a medical degree. *Id.* at 170-71, 202.

In response to my questions, Dr. Akbari acknowledged that not all epilepsies are immune mediated. Tr. at 190-91, 196. He also confirmed that he was basing his opinion on the complexity of the DTaP vaccine, the variety of the genes K.S.S.W. is missing, and eosinophil test results -- this time referencing results from early March 2013. *Id.* at 191-96. He characterized the absolute

[37] Chemokines "are regulators of the immune system and may also play roles in the circulatory and central nervous systems." DORLAND'S at 340.

eosinophil results as most meaningful. *Id.* at 201.

c. *Respondent's Expert: Dr. Romberg*

In his last expert report, filed in January 2021, Dr. Romberg addressed the claims made by Dr. Shafrir in his second, most recent report. Fourth Romberg Rep. at 1. Although he agreed with the assertion that K.S.S.W.'s chromosomal abnormalities and hydrocephalus made him more susceptible to seizures, he disputed any notion that they also made him prone to immune dysregulation. *Id.* at 2. He maintained that there was no evidence that K.S.S.W. suffered from an abnormal cytokine response or that his adaptive immune system contributed to his seizures. *Id.* at 2-3. Emphasizing that seizures by themselves are not evidence of an excessive immunological response, he observed that typical symptoms such as fever or vaccine site reaction were not present in K.S.S.W.'s case. He also maintained that the timing was too soon for involvement of the adaptive immune system. *Id.* at 4.

During his direct testimony, Dr. Romberg repeated the opinions and information set forth in his expert reports. Clarifying that vaccines are designed to elicit a local inflammatory response and to generate a systemic event, he stressed that symptoms such as fever would have been observed in K.S.S.W. if his local immune response had been too robust, as Dr. Shafrir and Dr. Akbari claimed. Tr. at 224-25. Specifically, he testified that had the excessive local cytokines "leaked out of the local site into the systemic circulation and circulated to the brain," K.S.S.W.'s brain would have sensed the cytokines and responded with symptoms associated with a febrile response. *Id.* at 225. Regarding the elevated eosinophil levels that Dr. Akbari identified as evidence of an excessive immune response, Dr. Romberg opined that, from his perspective as a clinician, the levels reported for K.S.S.W. were not remarkable and that the mild deviation was likely due to the seizure activity and vomiting K.S.S.W. had experienced. *Id.* at 233-34.

During cross, Dr. Romberg acknowledged that, given the lapse of five days between vaccination and K.S.S.W.'s initial ER visit, any local vaccine site response may have faded. Tr. at 284-85. In response to my follow-up questions, he also confirmed that vomiting may be an indication of an excessive innate system response, adding that he would not expect it to be the only symptom observed. *Id.* at 287-88.

Regarding molecular mimicry, Dr. Romberg discussed recent criteria, proposed by leaders in the field of adaptive immunity, to determine when a disease may involve molecular mimicry. Tr. at 226. According to Dr. Romberg, these criteria include "an epidemiologic relationship suggesting cause and effect, . . . the identification of an [sic] either antibody or a T cell receptor which recognizes both the microbe and a self-antigen, . . . [and] the recapitalization of the phenomena in a mouse." *Id.* at 227.

d. *Respondent's Expert: Dr. Barañano*

In her second expert report, Dr. Barañano reiterated her belief that K.S.S.W.'s "chromosomal anomalies alone more likely than not explain his epilepsy and developmental disabilities." Second Barañano Rep. at 2. She also stressed the lack of medical evidence showing an adverse event occurred in response to the DTaP vaccine K.S.S.W. received. *Id.*

When testifying, Dr. Barañano offered a thorough explanation of K.S.S.W.'s chromosomal anomalies, which she characterized as significant, as well as his brain and spinal abnormalities. Tr. at 307-13. She then discussed the literature related to children exhibiting only one of the chromosomal abnormalities K.S.S.W. possesses and the additive effect she would expect to see in K.S.S.W.'s case. *Id.* at 313-18, 326.

Additionally, Dr. Barañano criticized Dr. Shafrir's liberal use of the term epileptic encephalopathy "without really giving any good evidence that K.S.S.W.'s ultimate neurologic outcome was specifically impacted by the course of his epilepsy independent of his chromosomal anomaly." Tr. at 323. After providing her understanding of epileptic encephalopathy, she opined that K.S.S.W. "does not fit the diagnosis." *Id.* at 355.

During cross examination, Dr. Barañano confirmed that she also believed K.S.S.W.'s "chromosomal anomaly is [a] sufficient explanation for his cortical visual impairment." Tr. at 348. She explained that CVI "is a problem with processing in the visual cortex." *Id.* at 349. When asked about the claim by his parents that post-vaccination K.S.S.W. exhibited a loss of eye contact, Dr. Barañano questioned the accuracy of their assessment of his prior capabilities, explaining that a four-month-old child would not play the piano in any meaningful way but only randomly kick at a mat, like the one in K.S.S.W.'s crib, and would not be able to reliably hold a bottle. *Id.* at 364-65. Dr. Barañano further discussed the difficulty of assessing CVI in this case, in part because "tracking does not equate to whether or not someone has cortical visual impairment. The ability to track is a lower visual processing function and so that's why it's so challenging at such a young age to determine if a child will ultimately be diagnosed with cortical visual impairment." *Id.* at 351, 366-67.

V. Analysis

A. Credibility of the Experts

I will note at the outset that while all experts involved in this case were qualified to testify in this proceeding, I found the opinions of Respondent's experts more persuasive for a number of reasons; first, they were based upon a more accurate recitation of K.S.S.W.'s medical history.[38] At important junctures, both Dr. Shafrir and Dr. Akbari substantially misstated or ignored significant aspects of K.S.S.W.'s symptoms, condition, and care. They also consistently ignored the evidence provided by the contemporaneously created medical records, for example, regarding the lack of medical evidence showing any type of excessive inflammatory response in K.S.S.W.'s case. In multiple instances, they accepted as accurate accounts which deviated from those contained in the medical records.

Throughout their expert reports and testimony, Dr. Shafrir and Dr. Akbari repeatedly

[38] Medical opinions on causation based upon factually incorrect medical histories may be afforded less weight. *Burns by Burns v. Sec'y of Health & Hum. Servs.*, 3 F.3d 415, 417 (Fed. Cir. 1993); *Snyder ex rel. Snyder v. Sec'y, Health & Hum. Servs.*, No. 01–0162V, 2009 WL 332044 (Fed. Cl. Spec. Mstr. Feb. 12, 2009), *aff'd*, 88 Fed. Cl. 706 (2009).

overstated K.S.S.W.'s prior abilities, exaggerated his condition post-vaccination, and confused specific timing and facts. For example, Dr. Shafrir's described onset repeatedly deviated from that depicted in the contemporaneously created medical records. He often shortened the amount of time between vaccination and K.S.S.W.'s first symptoms of epileptic encephalopathy -- characterizing it as a period of a few hours, presumably to better provide the timing needed to support the innate immune system response he espoused. Second Shafrir Rep. at 2; Tr. at 67, 81, 120, 373.

Displaying a similar misunderstanding of K.S.S.W.'s condition post-vaccination, Dr. Akbari described him as "projectile vomiting" during his February 2013 hospitalizations, an assertion not supported by the contemporaneously created medical records. First Akbari Rep. at 4. Instead, according to the medical records, K.S.S.W. was not vomiting when initially assessed during an ER visit on February 7, 2013. Ex. 7 at 1067. Three days later, on February 10, K.S.S.W. vomited a moderate amount of fluid several times, consequences attributed to his seizure medication. *Id.* at 1083, 1089. There is a notation of an incident of vomiting in conjunction with seizure activity on February 28, 2013. *Id.* at 1505. Otherwise, there are no entries describing episodes of vomiting, certainly not projectile vomiting.

When asserting that K.S.S.W.'s CVI was not congenital but occurred post-vaccination, Dr. Shafrir exhibited substantial confusion regarding the timing and results of the only pre-vaccination eye exam. Although he initially stated that the exam was performed in October 2012 (Tr. at 65), Dr. Shafrir later testified that the pre-vaccination exam was performed on January 8, 2014, the date of one of K.S.S.W.'s post-vaccination eye exams which included a diagnosis of legal blindness. Tr. at 93; *see* Ex. 18 at 4-5 (exam performed on January 8, 2014, almost one-year post-vaccination). Dr. Shafrir may have mistakenly believed the pre-vaccination eye exam was performed in early January 2013, just before the January 16 vaccinations and when K.S.S.W. was almost four months old, making its results more relevant. However, the medical records clearly reveal that the only eye exam performed prior to vaccination occurred on October 24, 2012, when K.S.S.W. was sleeping and very young, only one and one half months old. Ex. 18 at 21.

The fact that the opinions of Dr. Shafrir and Dr. Akbari are based upon a depiction of K.S.S.W.'s pre- and post-vaccination statuses which deviate from that portrayed in the contemporaneously created medical records diminishes their probative value. Contemporaneously created medical records are presumed to be accurate because they are created close in time to the events being described and for the purposes of obtaining medical treatment. *See Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). They are considered more trustworthy than after-the-fact witness statements prepared in connection with this matter. *Id.* When experts make incorrect factual assumptions, it makes their expert opinions less persuasive. *Dobrydnev v. Sec'y of Health & Hum. Servs.*, 566 Fed.App'x 976, 982 (Fed. Cir. 2014) (giving little weight to expert opinions that are based on erroneous factual assumptions).

Additionally, although highly qualified to opine on certain aspects of this case, the fact that Dr. Akbari is not a medical doctor and thus does not have clinical experience limited his knowledge in certain areas, to include the interpretation of K.S.S.W.'s blood tests and issues surrounding

neurogenetics.[39] Despite later clarifying that he understands the terms are not synonymous, at several points during his testimony, Dr. Akbari appeared to employ the terms encephalitis and encephalopathy interchangeably. Tr. at 177-78, 188-89; *see* DORLAND'S at 612 (encephalitis is "inflammation of the brain"), 614 (encephalopathy is "any degenerative disease of the brain"). And, when asked if K.S.S.W. was ever diagnosed with encephalitis, Dr. Akbari responded that he "was diagnosed with inflammation of the nervous system," which he then equated to seizure activity/epilepsy. Tr. at 178-79.

Dr. Akbari ventured outside of his area of expertise and offered his opinions on the import of certain findings from K.S.S.W.'s bloodwork, and the specifics of K.S.S.W.'s genetic anomaly, areas better left to medical doctors and providers with expertise in neurogenetics, respectively. I have discussed this issue in more detail in section V(C)(3)(a)(i). Special masters may consider an expert's background and expertise when weighing that expert's opinion. *See Depena v. Sec'y of Health & Hum. Servs.*, No. 13-675V, 2017 WL 1075101 (Fed. Cl. Spec. Mstr. Feb. 22, 2017), *mot. for rev. denied*, 133 Fed. Cl. 535, 547-48 (2017), *aff'd without op.*, 730 Fed. App'x 938 (Fed. Cir. 2018); *Copenhaver v. Sec'y of Health & Hum. Servs.*, No. 13-1002V, 2016 WL 3456436 (Fed. Cl. Spec. Mstr. May 31, 2016); *mot. for rev. denied*, 129 Fed. Cl. 176 (2016). Dr. Akbari's willingness to offer his opinion in these areas when he was not qualified to do so reduced the overall persuasiveness of his opinion.

B. Table Encephalopathy

As Dr. Barañano explained during her testimony, in general, the term encephalopathy means any altered state or change in neurologic mental status. Tr. at 352, 356-57. Thus, it can refer to any disease that alters brain function. DORLAND'S at 614. In contrast, a Table encephalopathy is strictly defined with specific requirements which must be met. *Sharpe v. Sec'y of Health & Hum. Servs.,* No. 14-0065V, 2018 WL 7625360, at *23 (Fed. Cl. Spec. Mstr. Nov. 5, 2018) (citing the strictly construed requirements for a Table encephalopathy as discussed in *Miller v. Sec'y of Health & Hum. Servs.*, No. 02-0235V, 2015 WL 5456093, at *24 (Fed. Cl. Spec. Mstr. Aug. 18, 2015)), *aff'd in part, vacated in part on other grounds*, 964 F.3d 1072 (Fed. Cir. 2020).

In addition to their causation-in-fact and significant aggravation claims, Petitioners alleged K.S.S.W. suffered a Table encephalopathy following receipt of the DTaP vaccine. Thus, they must establish that K.S.S.W.'s first symptom or manifestation of onset occurred within 72 hours of vaccination. 42 C.F.R. § 100.3(a)(II)(B). Additionally, they must demonstrate that K.S.S.W.'s condition satisfies the requirements for a Table encephalopathy as set forth in the Qualifications and Aids to Interpretation ("QAI"). 42 C.F.R. § 100.3(c)(2). Specifically, Petitioners must prove that K.S.S.W. suffered an acute and chronic encephalopathy as defined in 42 C.F.R. § 100.3(c)(2)(i)(A) and 42 C.F.R. § 100.3(d)(1), respectively.

Most problematic for Petitioners is the requirement that K.S.S.W. suffered an acute encephalopathy. The primary requirement of an acute encephalopathy for a child less than 18 months of age is a decreased level of consciousness lasting at least 24 hours, which cannot be

[39] An examination of the publications and lecture topics listed in Dr. Akbari's CV supports Dr. Romberg's observation that much of Dr. Akbari's past work often involved asthma and allergic diseases. *See* Akbari CV at 7-13.

attributed to seizure activity. 42 C.F.R. § 100.3(c)(2)(i)(A). The contemporaneously created medical records are devoid of any such evidence.

When his parents brought K.S.S.W. to the ER on January 20, 2013, they described only temporary decreases in consciousness, lasting only a few seconds. Ex. 7 at 529, 625, 628. His mother recounted that K.S.S.W. received his four-month vaccinations five days ago and, beginning at 1:00AM the next day, experienced several episodes of eye deviation to the left. *Id.* at 561. She reported that each episode lasted less than a minute, and that K.S.S.W. would return to baseline when stimulated. *Id.* Although observed to be crying, kicking, squirming, and inconsolable when assessed for pain, K.S.S.W. also was assessed as fully alert, receiving the highest score of 15 on the Glasgow Coma Scale. *Id.* at 530. It was noted that he was stable, alert, and nontoxic throughout his ER evaluation. *Id.* at 540.

Petitioners appear to acknowledge this shortcoming as they expended little time asserting their Table claim. They provided argument only regarding their causation-in-fact claim. Pet. Pre-Hearing Br.; Pet. Pre-Hearing Reply; Pet. Post-Hearing Br.; Pet. Post-Hearing Reply. And they mentioned the existence of a Table encephalopathy injury following administration of the DTaP vaccine only as evidence for their causation-in-fact claim or to undermine the credibility of Respondent's experts. Tr. at 74-75, 292, 359-60, 363; Pet. Post-Hearing Br. at 20.

Due to Petitioners' inability to satisfy a basic requirement for a Table encephalopathy -- that K.S.S.W. suffered a decreased level of consciousness for more than 24 hours, I find they have failed to provide preponderant evidence to support their allegation of a Table encephalopathy claim.

C. Causation: Three-Pronged *Althen* Test

1. Legal Standards of Three-Pronged *Althen* Test

To receive compensation under the Vaccine Act, Petitioners must prove causation by satisfying the three-pronged test set forth in *Althen* by the preponderance of evidence standard required in the Vaccine Act. 418 F.3d at 1278. In *Althen,* the Federal Circuit described this standard "as one of proof by a simple preponderance, of 'more probable than not' causation." *Id.* at 1279.

Although the first and second prongs of *Althen* appear to be similar, these analyses involve different inquiries. *See Doe 93 v. Sec'y of Health & Hum. Servs.*, 98 Fed. Cl. 553, 566-67 (2011). The first prong focuses on general causation, whether the administered vaccine can cause the particular injury suffered, and the second prong focuses on specific causation, whether the administered vaccine did cause the injury. *Pafford v. Sec'y of Health & Hum. Servs.,* 451 F.3d 1352, 1355-56 (Fed. Cir. 2006). This distinction "has been described as the 'can cause' vs. 'did cause' distinction." *Stapleton v. Sec'y of Health & Hum. Servs.*, No. 03-234V, 2009 WL 1456441, at *18 (Fed. Cl. Spec. Mstr. May 1, 2009).

Under the first prong of *Althen*, Petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citations omitted). To satisfy this prong, Petitioners' theory must be based on a "sound

and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs*., 35 F.3d 543, 548 (Fed. Cir. 1994). Proof that the proffered medical theory is reasonable, plausible, or possible does not satisfy Petitioners' burden. *Boatmon v. Sec'y of Health & Hum. Servs*., 941 F.3d 1351, 1359-60 (Fed. Cir. Nov. 7, 2019).

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). Additionally, they are not required to describe the exact mechanism of causation. *Knudsen,* 35 F.3d at 549. However, special masters are "entitled to require some indicia of reliability to support the assertion of the expert witness." *Boatmon*, 941 F.3d at 1360, *quoting Moberly*, 592 F.3d at 1324.

To satisfy the second prong of the *Althen* test, a petitioner must establish a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." *Althen*, 418 F.3d at 1278. The sequence of cause and effect need only be "logical and legally probable, not medically or scientifically certain." *Knudsen*, 35 F.3d at 548-49; *accord Capizzano*, 440 F.3d at 1326. In establishing that a vaccine did cause the injury in question, the opinions and views of treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("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).

Petitioners are not required to eliminate alternative causes when establishing their prima facie case. *Doe 11 v. Sec'y of Health & Hum. Servs.*, 601 F.3d 1349, 1357-58 (Fed. Cir. 2010); *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). To support an argument regarding causation, Petitioners may, however, introduce evidence of the lack of an alternative cause. *Walther v. Sec'y of Health & Hum. Servs.*, 485 F.3d 1146, 1149-50 (Fed. Cir. 2007). Respondent also may introduce evidence of the presence of an alternative cause to rebut evidence regarding causation. *Doe 11*, 601 F.3d at 1358; *de Bazan*, 639 F.3d at 1353.

Once Petitioners have established a prima facie case, the burden shifts to respondent to show by preponderant evidence that petitioner's injury was "due to factors unrelated to the administration of the vaccine." § 13(a)(1); *see also DeBazan*, 639 F.3d at 1352-54; *Walther*, 486 F.3d at 1150.

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* The timing prong contains two parts. First, a petitioner must establish the "timeframe for which it is medically acceptable to infer causation" and second, she must demonstrate that the onset of the disease occurred in this period. *Shapiro v. Sec'y of Health & Hum. Servs.,* 101 Fed. Cl. 532, 542-43 (2011), *recons. denied after remand on other grounds*, 105 Fed. Cl. 353 (2012), *aff'd without op.,* 503 F. App'x 952 (Fed. Cir. 2013). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Shapiro*, 101 Fed. Cl. at 542; *Koehn v. Sec'y of Health & Hum. Servs*., No. 11-355V, 2013 WL 3214877

(Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

2. Nature of K.S.S.W.'s Alleged Injury

In his initial expert report, Dr. Shafrir began by declaring "there is no question that following the vaccination on January 16, 2013, KSSW developed epileptic encephalopathy." First Shafrir Rep. at 46. Based upon later provided definitions from both Dr. Shafrir and Dr. Barañano,[40] Dr. Shafrir's use of the term "epileptic encephalopathy," which he often relies upon when testifying in vaccine cases,[41] has two effects. First, it implies that K.S.S.W.'s later observed conditions -- developmental delay and CVI, are attributable to his seizure activity, rather than his preexisting chromosomal abnormalities. Second, it suggests that there is an additional underlying etiology contributing to K.S.S.W.'s overall medical condition.

However, none of K.S.S.W.'s treating physicians diagnosed K.S.S.W. with epileptic encephalopathy. Furthermore, during her testimony, Dr. Barañano disputed this portrayal of K.S.S.W.'s condition, opining that epileptic encephalopathy was not an appropriate diagnosis. Tr. at 355.

I agree that Dr. Shafrir's use of the term of "epileptic encephalopathy" is not supported by the evidence in this case, especially without any evidence from his treating physicians that the diagnosis is appropriate. Thus, I will avoid using this term during the below *Althen* analysis. Instead, I will utilize the diagnoses and nomenclature employed by K.S.S.W.'s treating physicians which have not deemed to be inaccurate by either party.

Although they disagree upon the first onset, cause, and meaning of many of K.S.S.W.'s symptoms, the parties agree that K.S.S.W. experienced afebrile seizures involving eye deviations of a brief duration, developmental delays, and CVI. They also have stipulated that K.S.S.W.

[40] During her testimony, Dr. Barañano provided her understanding of epileptic encephalopathy as "a condition that's characterized by slowing or regression of development due to seizures or abnormal EEG activity rather than the underlying etiology of the epilepsy." Tr. at 322. She explained that the term has been increasingly used to refer to etiologies involving both severe epilepsy and intellectual disability, thus intertwining the two conditions. Tr. at 323. In response, Dr. Shafrir provided his definition: "encephalopathy associated with seizures, … typically intractable, and the level of encephalopathy cannot be explained by the severity or the frequency of the seizures." Tr. at 369. Agreeing with Dr. Barañano's assertion that there are problems with this definition, he clarified that the term refers to a condition caused by seizures, regardless of the underlying etiology of the seizure activity. Tr. at 370.

[41] *See Mattus-Lang v. Sec'y of Health & Hum. Servs.,* No. 15-0113V, 2022 WL 4242140, at *11 (Fed. Cl. Spec. Mstr. Aug. 30, 2022); *Morales v. Sec'y of Health & Hum. Servs.,* No. 14-1186V, 2019 WL 4047626, at *9 (Fed. Cl. Spec. Mstr. July 30, 2019); *Oliver v. Sec'y of Health & Hum. Servs.,* No. 10-0394V, 2017 WL 747846, at *21 (Fed. Cl. Spec. Mstr. Feb. 1, 2017), *mot. for review den'd*, 133 Fed. Cl. 341 (2017), *aff'd*, 900 F.3d 1357 (Fed. Cir. 2018), *rehearing en banc den'd*, 911 F.3d 1381 (Fed. Cir. 2019); *K.T. v. Sec'y of Health & Hum. Servs.,* No. 12-0477V, 2016 WL 5929954, at *9 (Fed. Cl. Spec. Mstr. Sept. 8, 2016) *aff'd* 132 Fed.Cl. 175 (2017); *Waters v. Sec'y of Health & Hum. Servs.,* No. 08-0076V, 2014 WL 300936, at *17 (Fed. Cl. Spec. Mstr. Jan. 7, 2014).

suffered chromosomal abnormalities, from birth, involving the 5p and 6q chromosomes.

3. Application of Three-Pronged *Althen* Test

a. *Reputable Medical Theory – First Althen Prong "Can It" Analysis*

Although the exact nature of K.S.S.W.'s condition is not essential to any *Althen* analysis in this case,[42] Petitioners are required to provide a reputable medical or scientific explanation that pertains specifically to K.S.S.W.'s circumstances. *Broekelschen*, 618 F.3d at 1345. Thus, to satisfy the first *Althen* prong, Petitioners must provide preponderant evidence of a reliable medical theory involving the DTaP[43] vaccine and symptoms and conditions K.S.S.W. suffered which are alleged to be vaccine-caused.

The question of whether vaccination can trigger seizures has been previously litigated in the Vaccine Program. Prior Program cases have determined that vaccination can trigger a fever, which in turn can provoke *febrile* seizures. *See, e.g., Thompson v. Sec'y of Health & Hum. Servs.*, No. 15-671V, 2023 WL 21234 (Fed. Cl. Spec. Mstr. Jan 3, 2023) (determining that DTaP component of the Pentacel vaccine caused petitioners' infant child to experience complex febrile seizure which in turn caused developmental delay); *Adams v. Sec'y of Health & Hum. Servs.*, 76 Fed. Cl. 23, 41 (2007) (finding an infant who developed febrile seizures within twenty-four hours after pneumococcal vaccination entitled to compensation); *Tembenis v. Sec'y of Health & Hum. Servs.,* No. 03-2820V, 2010 WL 5164324, at *15-16 (Fed. Cl. Spec. Mstr. Nov. 29, 2010) (finding entitlement where child experienced febrile seizure following DTaP vaccination, which resulted in epilepsy and child's subsequent death).

Cases in the Vaccine Program have generally found that a vaccine is not the cause of a seizure that occurs in absence of a fever. *See, e.g., Gram v. Sec'y of Health & Hum. Servs.*, No. 15-515V, 2022 WL 17687972 (Fed. Cl. Spec. Mstr. Nov. 16, 2022) (finding no causal link between MMR and varicella vaccines and afebrile seizures); *Valico v. Sec'y of Health & Hum. Servs.,* No. 00–662V, 2002 WL 508344 at *4 (Fed. Cl. Spec. Mstr. Mar. 11, 2002) (finding Dr. Shafrir, testifying for the Respondent, to be persuasive in opining that the medical literature does not support a connection between the whole cell pertussis vaccine and afebrile seizures.).

Further, decisions from the Court of Federal Claims have affirmed special masters' decisions noting the reduced likelihood that afebrile seizures are vaccine-caused. *See, e.g.*, *K.L. v. Sec'y of Health & Hum. Servs.*, 134 Fed. Cl. 579, 587 (2017) (finding that special master's decision to credit expert testimony "that scientific evidence strongly supports that interleukin–1 beta is the chief cytokine that mediates fever, and, thus, it has been associated with febrile seizures but not afebrile seizures" was not arbitrary or capricious); *Dodd v. Sec'y of Health & Hum. Servs.*, 114

[42] *See Lapierre v. Sec'y of Health & Hum. Servs.*, No. 17-0227V, 2019 WL 6490730, at *16-17 (Fed. Cl. Spec. Mstr. Oct. 18, 2019).

[43] Although Petitioners alleged that K.S.S.W.'s injuries were caused by the DTaP vaccine he received, in their pre-hearing brief, they included the other two vaccines administered on January 16, 2013 -- the Hib and IPV vaccines. Pet. Pre-Hearing Br. at 4. Although my analysis refers only to the DTaP vaccine, I have considered any possible effect involving these other vaccines as well.

Fed. Cl. 43, 55-57 (2013) (finding the special master's determination that evidence concerning febrile seizures had little bearing on alleged vaccine causation of afebrile seizures to be neither arbitrary nor capricious). One case also specifically discusses the importance of this distinction where a cytokine-driven immune response is a main component of petitioner's *Althen* prong one theory. *See, e.g., L.M. by and through McLellan v. Sec'y of Health & Hum. Servs.*, No. 14-714V, 2019 WL 4072130 (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). I agree with the reasoning found in these past Program decisions that distinguishes between febrile and afebrile seizures.

Petitioners' first expert, Dr. Shafrir, presented two variations of a multi-staged medical theory, by which the DTaP vaccine could cause an injury comprised of afebrile seizures, developmental delays, and CVI. Essential to each variant is an excessive innate immune system response caused by the DTaP vaccine and aluminum adjuvant added to help stimulate such as response. Pursuant to one version of the medical theory, the innate immune system response would be substantial enough to directly affect brain function -- due to cytokine stimulation via the immune system (hypothalamus) or possibly more directly through the circulatory system. The alternative version assumes the inclusion of the adaptive immune system in the excessive response. According to both options, the resulting autoimmune process could cause afebrile epileptic seizures such as those suffered by K.S.S.W., which then would produce deleterious effects on the brain, resulting in developmental delay and CVI.

Supplementing Dr. Shafrir's opinion, Dr. Akbari provided rationales for the proposed excessive immune system responses -- both innate and adaptive, involving K.S.S.W.'s 5p and 6q chromosomal abnormalities. He posited that, due to their effects upon Th and Treg cells, these abnormalities would predispose an individual to the excessive immune responses which are integral to Dr. Shafrir's medical theory. He also posited a more indirect effect of the chromosome 5p and 6q defects, involving positional variegation. Tr. at 158-61.

i. Petitioners did not Provide Persuasive Evidence in Support of K.S.S.W.'s Genetically Caused Immune Dysregulation

Much of Dr. Akbari's opinion in this area is based on a misunderstanding of K.S.S.W.'s chromosomal array and the consequences associated with his chromosomal duplication and deletion. With respect to K.S.S.W.'s duplication of a portion of the short arm of chromosome 5, Dr. Akbari theorizes that K.S.S.W., due to his genetic defect, overexpresses genes which encode certain cytokines (IL-5, IL-13, and GM-CSF), leading to increased cytokine production. First Akbari Rep. at 10-11. *See also*, Pet. Post Hearing Brief at 4-5, highlighting Dr. Akbari's opinion that the genes which encode IL-5 and IL-13 are duplicated. However, as Dr. Romberg describes, these genes referenced by Dr. Akbari are not located in the region of K.S.S.W.'s duplication, but instead are found within 5q15, which is 125,000Mb[44] away on the long arm (q) of chromosome 5,

[44] Mb stands for Megabase, "a unit of measurement used to help designate the length of DNA. One megabase is equal to 1 million bases." https://www.genome.gov/genetics-glossary/Megabase (last visited on Nov. 14, 2022).

a substantial distance apart. Tr. at 233. Accordingly, it is not appropriate to conclude that K.S.S.W. overexpresses the genes which encode IL-5, IL-13, and GM-CSF.[45]

Similarly unpersuasive is Dr. Akbari's theory that K.S.S.W.'s deletion of a portion of chromosome 6q increases his susceptibility to inflammatory disease. Specifically, Dr. Akbari theorizes that K.S.S.W. lost genes which encode IFNγR,[46] ATG5,[47] and CCR6. Again, Dr. Akbari misapprehends the location of these genes. The genes which encode IFNγR and ATG5 are not located in the tip of chromosome 6q (K.S.S.W.'s deletion). *See* Second Romberg Rep. at 2-3; Tr. at 232-33.[48] The CCR6 gene is the *only* gene discussed by Dr. Akbari that is located in 6q26q27, the missing piece of the tip of the long arm of chromosome 6. Dr. Romberg persuasively opined that a single CCR6 gene is well tolerated in humans; in other words, K.S.S.W.'s deletion of this CCR6 gene likely had no effect. Third Romberg Rep. at 2-3; Tr. at 237-39 (testifying that NOMAD's probability loss and tolerance score for CCR6 is .01, a "vanishingly small number,

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[45] Dr. Akbari attempts to explain his discussion of seemingly irrelevant genes by describing the limitations of Fluorescence *in situ* Hybridization (FISH) testing. He describes that the FISH test "is a test that 'maps' the genetic material in a person's cells and cannot precisely determine the number of genes missing or present in duplicate in KSSW." Second Akbari Rep. at 1-2. Dr. Romberg responded to Dr. Akbari as follows: "To be clear, the technical limitations of clinical FISH testing, which has an analytical resolution in the range of 100–200 kilobases does not begin to close the massive 125,000 megabase genomic distance between 5q33 and 5p15.33p13.3. Thus what Dr. Akbari considers plausible, I consider pure fantasy." Third Romberg Rep. at 2. I do not find persuasive Dr. Akbari's invocation of FISH testing as a way to suggest that genes outside of K.S.S.W.'s deletion or duplication are involved in his purported abnormal response to the DTaP vaccine.

[46] Dr. Akbari notes that "IFNγ is a cytokine that is critical for innate and adaptive immunity against pathogens and often play an important role in immunization. Modulation of IFNγ as result of direct deletion of a copy or positional variegation may cause immune deviation after DTaP immunization." First Akbari Rep. at 12.

[47] With respect to ATG5, Dr. Akbari opines as follows: "Autophagy related 5 (ATG5) is a protein that, in humans, is encoded by the ATG5 gene located on Chromosome 6q. ATG5 is responsible for maintenance of autophagy. Autophagy is an essential, homeostatic process by which cells break down their own components. Perhaps the most primordial function of this lysosomal degradation pathway is adaptation to nutrient deprivation. However, in complex multicellular organisms, the core molecular machinery of autophagy — the 'autophagy proteins' — orchestrates diverse aspects of cellular and organismal responses to other dangerous stimuli such as infection. Recent developments reveal a crucial role for the autophagy pathway and proteins in immunity and inflammation." First Akbari Rep. at 12.

[48] I note that at the time of the entitlement hearing, Dr. Akbari did not focus on IFNγR and ATG5, and instead primarily testified about CCR6. However, he did make a passing reference to interferon gamma and "ETG-5" (error in the transcript, should read ATG-5). Tr. at 156. Furthermore, Dr. Akbari discussed the overexpression of Th2 cytokines (testifying that "there are a variety of other genes which are in excess number, mainly gene CSF and Th2 cytokines, and there [is] some evidence for that." Tr. at 155; testifying that "IL-5 and IL-13 are expressed as extra copy in this patient." Tr. at 185; *see also* Tr. at 192). The fact that Dr. Akbari *repeatedly* and *erroneously* discussed the duplication and deletion of genes outside of K.S.S.W.'s genetic anomaly as being relevant to K.S.S.W.'s immune response has caused me to give his opinion less weight than the opinion of Dr. Romberg.

very close to zero, suggesting that there is not a biologically deleterious effect of having heterozygous loss of CCR6 in humans.").

Dr. Romberg's additional point that losing one copy of CCR6 does not affect Treg function is also persuasive. Specifically, he testified that loss of CCR6 more likely protects against neuroinflammation than the converse. Tr. at 240. As Dr. Romberg described in his second expert report, "CCR6 is a chemokine receptor expressed by all proinflammatory Th17 lineage cells. The receptor allows Th17 cells to traffic to mucosal sites of inflammation." Second Romberg Rep. at 3. He went on to note that the impaired trafficking of Th17 cells "would reduce, not increase, their ability to participate in inflammatory responses." *Id.* This position is supported by the Chen paper, which found that reduction of CCR6 expression blocks Th17 trafficking to the brain in a murine model. Chen at 14532. Further, the Reboldi paper demonstrates that CCR6 deficient mice are resistant to autoimmune encephalitis. Reboldi at 514.

Ultimately, Dr. Akbari was not persuasive in opining that K.S.S.W.'s unbalanced genetic translocation had any bearing on his immune response to vaccination. I additionally note that Dr. Akbari's opinion was an integral part of Petitioners' causation theory. *See, e.g.,* Pet. Prehearing Reply at 2 ("The deletion of CCR6, as well as the extremely rare anomaly of 5p 6q unbalanced translocation, primed K.S.S.W. to have a reaction to the DTaP vaccine. His reaction was devastating due to his genetic abnormalities, which caused him to be ill-equipped to handle the immune response from the DTaP vaccine. The result of his body's inability to handle the assault was persistent seizures, which developed into epileptic encephalopathy. This encephalopathy ultimately caused severe, irreversible damage."); *See also*, Pet. Posthearing Brief at 3 ("Petitioner's experts, Dr. Akbari and Dr. Shafrir, successfully presented a cohesive explanation setting forth the way in which KSSW's faulty immune system was devastatingly ill-equipped to handle the DTaP vaccination."). Because K.S.S.W.'s chromosomal translocation resulting in immune dysregulation was central to Petitioners' prong one theory, this causation theory fails due to the insufficiency of their showing.

ii. The Remainder of Petitioners' Prong One Theory is not Persuasive

To support their hypotheses in this case, Dr. Shafrir and Dr. Akbari cited medical literature supportive only of broad principles or not applicable to the circumstances of K.S.S.W.'s case. Thus, they do not provide the claimed support. For example, Dr. Shafrir referenced studies which involved the *whole cell* pertussis vaccine -- not administered to K.S.S.W. *E.g.,* Nouno at 358; NCES at 101. Importantly, the children involved in the Nouno study had previously experienced epileptic and/or *febrile* seizures -- a factor not present in K.S.S.W.'s case. *Id.* at 357-58; *see* Tr. at 115-16. Although an increase in EEG activity was seen in 28.8% of the children who had previously experienced epileptic seizures, it was mild enough for the authors to conclude only that follow-up EEG monitoring was necessary. Nouno at 360. The main conclusion of the study was regarding the children who had previously suffered *febrile* seizures; it was recommended that they not be vaccinated until at least three years of age. *Id.*

On numerous occasions, Dr. Shafrir and Dr. Akbari acknowledged the limited support provided by their cited medical literature. After describing an article regarding seizure activity in children suffering from autoimmune encephalitis, Dr. Shafrir acknowledged that K.S.S.W. "did

not have autoimmune encephalitis." Ex. 167 at 11 (Dr. Shafrir's medical literature summary). In response to Dr. Romberg's criticism of his citation of Sullivan as not applicable to this case, Dr. Akbari stressed that he only mentioned this literature as proof of the broad concept of cross talking between genes. Tr. at 391.

The medical literature Dr. Shafrir cited to support his assertions regarding molecular mimicry has been rejected in other vaccine cases. *E.g.*, *Oliver,* 2017 WL 747846, at *21*, mot. for rev. denied*, 133 Fed. Cl. 341 (2017), *aff'd,* 900 F.3d 1357 (rejecting Kanduc and Obergon as inapplicable and Lucchese and Bavaro as unsound and lacking any definitive conclusion). Dr. Romberg expressed a similar assessment of these studies. First Romberg Rep. at 5 (pointing to deficits in Lucchese). I find Dr. Romberg's criticisms of that medical literature, as well as those leveled at the CC6R mice studies -- Liu and Scharschmidt, to be well-founded. *See id.*; Third Romberg Rep. at 3-4. Petitioners and their experts are unpersuasive with respect to this stage of the proposed medical theory.

As Dr. Romberg emphasized, the DTaP vaccine is designed to elicit an immune response of both the innate and adaptive immune systems. He explained that the addition of an aluminum additive is to ensure a sufficient innate immune system response. Pursuant to the medical theory they proposed, Dr. Shafrir and Dr. Akbari submitted that, for an individual possessing chromosomal abnormalities such as K.S.S.W.'s, the resulting immune response would be sufficiently excessive to trigger afebrile seizure activity which would not otherwise occur. Although Petitioners need not provide evidence of an exact mechanism, they must provide some evidence to support their experts' assertions. *Boatman,* 941 F.3d at 1360-61. Petitioners have not done so in this case.

Petitioners have failed to provide preponderant evidence of a reputable medical theory concerning how the DTaP vaccine could cause afebrile seizure activity, developmental delays, and CVI such as K.S.S.W. experienced. They have failed to satisfy the first *Althen* prong.

b. *Logical Sequence of Cause and Effect – Second Althen Prong "Did It" Analysis*

Even if I found Petitioners had provided sufficient evidence to support a reliable medical theory, demonstrating how the DTaP vaccine *could cause* similar symptoms and conditions, they have failed to provide a logical sequence of cause and effect showing the DTaP vaccine *did cause* K.S.S.W.'s afebrile seizures, developmental delays, and CVI, as alleged.

i. K.S.S.W.'s Clinical Signs/Symptoms and Test Results do not Support Petitioner's Causation Theory

As Dr. Romberg observed, there is a dearth of evidence from the medical records indicating that K.S.S.W. was experiencing any type of excessive inflammatory response shortly after vaccination. Tr. at 224-28. Dr. Romberg testified:

> The brain is a very, very, very exquisite detector -- good detector of IL-1 Beta. And when you have IL-1 Beta circulating in the blood, your brain senses it and causes

> the things that we associate with a febrile response. So that's not just fever. That's also tachycardia, malaise, anorexia, the lack of appetite. These are all things that help us mount a multisystem response to an infection.

Tr. at 225. Dr. Romberg went on to testify that there is no evidence that K.S.S.W. experienced an excessive inflammatory response to vaccination. *Id.* at 226. There was no evidence of fever, no evidence he became hypotensive, no elevation in his platelets, and no evidence of swelling or redness at the injection site. *Id.* Given Petitioners' cytokine-based prong one theory, this lack of evidence that K.S.S.W. experienced an excessive inflammatory response undermines their prong two showing.

As supporting evidence for a logical sequence of cause and effect, Dr. Akbari pointed to K.S.S.W.'s eosinophil level test results obtained during hospitalizations in January and early March 2013. First Akbari Rep. at 3; Tr. at 155, 185-86, 193-95. Although he referenced only the March 2013 results in his first expert report, during testimony, he confirmed that he was relying upon results from testing performed on January 20, 2013. *Compare* First Akbari Rep. at 3 (citing March 2013 test results -- Ex. 7 at 1491-92) *with* Tr. at 197-201 (indicating a reliance on January 2013 test results -- Ex. 7 at 538). The January 2013 testing revealed an absolute eosinophil level of 0.8 K/CMM,[49] compared to a normal range of 0.0 to 0.5 K/CMM and a percentage eosinophil level of 6%, compared to a normal range of 0-5%. Ex. 7 at 538. The March test results were 1.2 K/CMM and 8% on 3/2/2013 and 0.7 K/CMM and 5% (a normal result) on 3/5/2013. Ex. 7 at 1492.

In response, Dr. Romberg opined that, as a clinician who is board certified in allergy and immunology, he does not find any of these results to be significant, and testified that the elevated eosinophil levels were likely due to K.S.S.W.'s seizure activity. Tr. at 233-36. Importantly, none of K.S.S.W.'s treating physicians prescribed a course of treatment, or even mentioned the test results. Dr. Romberg persuasively testified, "I don't know any pediatricians who would refer a patient for that mild an increase in eosinophils and I don't know of any allergists or hematologists who would do anything other than offer reassurance for those values…" *Id.* at 233-34.

Emphasizing that lab aberrations are common when a patient is ill, he observed that the January 2013 testing reflected other mildly elevated or decreased levels, such as neutropenia,[50] and elevated potassium and calcium. Tr. at 234-35; *see* Ex. 7 at 538-39 (lab results). Regarding the reported neutropenia (lower level of neutrophils), he remarked that according to Dr. Shafrir and Dr. Akbari's theory, he would expect to see neutrophilia -- too many neutrophils. Tr. at 235-36.

Additionally, Dr. Romberg pointed out another lab finding incongruent with Petitioner's causal theory; he opined that if K.S.S.W.'s genetic anomalies caused him to have a duplication of genes that encode IL-5 and IL-13, then one would expect him to be "eosinophilic all of the time

[49] K/CMM means thousands of cells per cubic milliliter of blood. *See* https://www.cdc.gov (last visited Nov. 11, 2022).

[50] Neutropenia is "the abnormal decrease in the number of neutrophils in the blood." DORLAND'S at 1272.

not just when he's in extremis." *Id.* at 237. Dr. Romberg pointed out that this was not the case, as K.S.S.W.'s CBCs from January 24, 25 and February 3 all showed eosinophils in the normal range. *Id. See*, Ex. 7 at 749. This highly persuasive point was unrebutted by Petitioners.

ii. K.S.S.W.'s Treating Physicians

Although K.S.S.W.'s treating physicians did consider the connection between his seizures and his hydrocephalus or chromosomal abnormalities, none contemplated the possibility that K.S.S.W. was experiencing an underlying autoimmune condition. *E.g.,* Ex. 7 at 629. No treating physician ordered testing, such as a measurement of cytokine levels, or testing for immune cells or antibodies in the CSF, or prescribed treatment typical for autoimmune disease, such as IVIG therapy or steroids. Both Dr. Shafrir and Dr. Akbari acknowledged this deficiency during their testimony. Tr. at 80-81, 109-10, 180-81.

The only treating physician who even considered a connection between the January 2013 DTaP vaccination and K.S.S.W.'s later condition was a pediatrician who first saw K.S.S.W. in May 2019, more than six years post-vaccination. Initially, when responding to his mother's belief that K.S.S.W. suffered a vaccine-related injury, the pediatrician opined that K.S.S.W.'s "chromosomal abnormalities could account for his current symptoms/development." Ex. 162 at 2. She insisted that his mother would need to sign a vaccine refusal form to avoid any future vaccinations. *Id.* It was only after Ms. Davis-Walters described a severe and immediate vaccine reaction in 2013 and represented that she had the *same* chromosomal abnormality without seizure activity that the pediatrician relented, allowing K.S.S.W. to avoid future vaccinations without the usually required parental refusal. *Id.* at 1. However, the pediatrician still suggested administering the MMR (measles, mumps, and rubella) or Varicella vaccines. *Id.* In short, there is no persuasive evidence from K.S.S.W.'s treating physicians which supports causation.

iii. K.S.S.W.'s Chromosomal Abnormalities

When arguing that the record contains sufficient evidence of a logical sequence of cause and effect, Dr. Shafrir relied heavily upon the lack of any alternative cause, asserting that K.S.S.W.'s chromosomal abnormalities would not be sufficient by themselves to result in the seizure activity and subsequent symptoms K.S.S.W. experienced. Tr. at 75, 118-19; First Shafrir Rep. at 60. Consistently characterizing K.S.S.W.'s condition post-vaccination as significant and dramatic (*e.g.*, Tr. at 67, 71), Dr. Shafrir maintained that the drastic change could only be caused by the trigger effect of the DTaP vaccine. He testified "there is absolutely no other cause for this super abrupt and progressive change that occurred in KSSW." Tr. at 75.

Both Dr. Shafrir and Dr. Akbari summarily dismissed the possibility that K.S.S.W.'s seizure activity could be attributed solely to his chromosomal abnormalities. First Shafrir Rep. at 60; Tr. at 87, 118. However, they based their conclusions upon evidence pertaining to individuals possessing only one of the chromosomal abnormalities K.S.S.W. possesses and the lack of seizure activity in his mother who suffers from a balanced translocation of the 5p and 6q chromosomes. First Shafrir Rep. at 46-52; Tr. at 182-85.

Dr. Barañano disagreed.[51] Although she cited similar medical literature, she opined that, based upon her experience as a clinician, she would expect the effects of K.S.S.W.'s dual chromosomal abnormalities to be additive. First Barañano Rep. at 2-5; Tr. at 326. Thus, Dr. Barañano concluded that it was more likely than not that K.S.S.W.'s seizures are solely attributable to his chromosomal abnormalities. First Barañano Rep. at 5; Second Barañano Rep. at 2-3; Tr. at 307; 323-24.

In her first expert report, Dr. Barañano provided a detailed explanation of K.S.S.W.'s specific chromosomal abnormalities. First Barañano Rep. at 2-5. Explaining that each chromosome has a short arm labeled p, and long arm labeled q, she indicated that K.S.S.W. was missing the tip of the long arm of chromosome 6 and possessed an extra piece, comprised of most of the short arm of chromosome 5.[52] *Id.* at 2. She further explained that the monosomy deletion of 6q26q27 means K.S.S.W. is missing the tip of the q arm at band 6q26 and 6q27, representing an omission of 19.4 Mb of information. *Id.* at 3. The duplication trisomy of 5p15.33p13.3 describes an extra copy from 5p15.33 to the tip, representing a gain of 29.2 Mb of information. *Id.*at 4.

Regarding the *balanced or reciprocal* chromosomal abnormality K.S.S.W.'s mother possesses, Dr. Barañano explained why her lack of seizure activity and normal to above normal intelligence was predictable, and not relevant to any discussion of K.S.S.W.'s capabilities. Tr. at 324-25. She clarified that "even though the person with the balanced translocation will have a derivative -- what's called a derivative chromosome, they will still have the normal complement of genetic information. They will still have two copies of every gene." Tr. at 325. She added that "[i]t's only when they go on to have a child, to produce an egg or a sperm, that those chromosomes don't line up with their pair[s] properly and the resulting egg or sperm can get extra or missing pieces of a chromosome." *Id.*

In their testimony, Dr. Shafrir and Dr. Akbari echoed the descriptions provided by Dr. Barañano. Tr. at 59-61, 85-86, 154-55. Praising Dr. Barañano's explanation of meiosis (Tr. at 659), Dr. Shafrir explained that any child is only "in trouble" when, like K.S.S.W., he ends up with an

[51] Dr. Barañano is the only expert who testified at the entitlement hearing with expertise in neurogenetics. By way of background, she has a Ph.D. in neuroscience and completed her fellowship in neurogenetics. Barañano CV at 1. She sees children and adults in a clinical setting to evaluate them for potential genetic contributions to their neurologic disease. Tr. at 301. She teaches medical students, residents, and fellows in genetics. *Id.* at 304. Based on these qualifications, I recognized her as an expert in both pediatric neurology and neurogenetics. *Id.* at 306. Accordingly, in areas of neurogenetics, I have given her testimony more weight than the testimony of Dr. Shafrir and Dr. Akbari, who do not have this specialized training and experience.

[52] Dr. Barañano also mentioned a third chromosomal abnormality involving chromosome 7. However, there is some confusion as to whether this is an abnormality that K.S.S.W. or his father possesses. At different times, Dr. Shafrir entertained both possibilities. *Compare* First Shafrir Rep. at 10 (citing K.S.S.W.'s testing) *with* Tr. at 59 (attributing this test result to K.S.S.W.'s father). The test results from CHOP are also confusing; it is difficult to determine to whom the test results apply. *See* Ex. 4 at 4-9. Because both Dr. Barañano and Dr. Shafrir agreed that the described abnormality – the duplication of a small segment of chromosome 7, was not significant, it is not necessary to eliminate this confusion or to address the issue further.

extra piece of chromosome 5 and a missing piece of chromosome 6 – an *unbalanced* chromosome anomaly. Tr. at 61.

All experts cited numerous articles showing the possibility of seizure activity in relationship to either of the chromosomal abnormalities from which K.S.S.W. suffers, agreeing that the lack of studies addressing the effect of K.S.S.W.'s exact chromosomal abnormalities was likely due to the rarity of his combined defects. First Shafrir Rep. at 46-54; First Barañano Rep. at 3-4. Additionally, they agreed the seizure activity revealed by this medical literature was less severe than what K.S.S.W. experienced. *Id*. However, the percentages of individuals with only one of these abnormalities who subsequently suffered from seizures is still significant -- 30% to 50%. Tr. at 77-79, 84-86, 381-82.

Despite their reliance on similar studies and data, the experts reached different conclusions. Dr. Shafrir and Dr. Akbari assumed that any seizure activity related to K.S.S.W.'s dual abnormalities would be indistinguishable from that experienced by individuals suffering from only one of these chromosomal abnormalities or K.S.S.W.'s mother who had a balanced or reciprocal translocation of chromosomes 5 and 6. First Shafrir Rep. at 60; Tr. at 87, 182-85. In contrast, Dr. Barañano indicated that, based upon her expertise as a clinician, she would assume an additive effect in K.S.S.W.'s case. First Barañano Rep. at 2-5; Tr. at 326.

Dr. Shafrir and Dr. Akbari provided no foundation for their assumption that the dual chromosomal abnormalities suffered by K.S.S.W. would have no additional effect. And medical literature they cited supported the proposition that the more severe the chromosomal abnormality, the more significant the adverse effect. *E.g.,* Engwerda at 1481. Most troubling is their comparison of K.S.S.W.'s circumstances with those of his mother, who suffered only a balanced or reciprocal anomaly. As Dr. Barañano indicated, "[t]his is not a germane point." First Barañano Rep. at 5. Such proposed equivalency strains credulity.

In contrast, Dr. Barañano's opinion that K.S.S.W.'s dual chromosomal abnormalities alone more likely than not produced the seizures he experienced follows from the medical literature provided. Dr. Barañano's opinion is persuasive and reduces the strength of Petitioners' prong two showing. *Stone v. Sec'y of Health & Hum. Servs.*, 676 F.3d 1373, 1379-80 (Fed. Cir. 2012) (finding that special masters can consider other possible sources of injury in making a determination under *Althen* prong two). Dr. Shafrir and Dr. Akbari have failed to provide adequate support for their opinions that, were it not for the DTaP vaccination K.S.S.W. received, his outcome would have been no worse than children who possessed only one of his two chromosomal abnormalities.

Petitioners have failed to provide the evidence needed to establish a *prima facie* case that the DTaP vaccine K.S.S.W. received caused his afebrile seizures and subsequent conditions of developmental delay and CVI. Their attempts to demonstrate causation based upon the lack of an alternative cause are ineffective and were adequately countered by Respondent. Petitioners have failed to satisfy the requirements of the second *Althen* prong.

c. *Proximate Temporal Relationship – Third Althen Prong Analysis*

Lastly, Petitioners have failed to provide a medically appropriate temporal relationship

between K.S.S.W.'s vaccination and the symptoms he experienced thereafter. As discussed earlier in this Decision, Petitioners did not provide a reliable theory for how the DTaP vaccine could cause afebrile seizures, developmental delay, and CVI. Because of this, they cannot satisfy *Althen's* third prong, as the adequacy of the proposed time frame for the vaccine to cause the injury must relate to the proffered medical theory. *Langland v. Sec'y of Health & Hum. Servs.*, 109 Fed. Cl. 421, 443 (2013); *see also*, *Sullivan v. Sec'y of Health & Hum. Servs.*, No. 10-398V, 2015 WL 1404957 (Fed. Cl. Spec. Mstr. Feb. 13, 2015).

Even if they had satisfied the third *Althen* prong, as a result of their cytokine-based theory of causation and the proximity of K.S.S.W.'s seizures to his vaccination (approximately 12-13 hours later), this, without more, is insufficient for Petitioners to meet their burden. "[A] proximate temporal association alone does not suffice to show a causal link between the vaccination and the injury." *Pafford*, 64 Fed. Cl. at 24, citing *Grant*, 956 F.2d at 1148.

Petitioners have failed to demonstrate that a proximate temporal relationship exists in K.S.S.W.'s case, and thus have failed to satisfy the third *Althen* prong.

D. Significant Aggravation

In their petition, Mr. Walters and Ms. Davis-Walters advanced claims of both causation-in-fact and significant aggravation. Petition at 1. However, other than that one mention, they provided no further discussion of or evidence for a claim of significant aggravation.

Additionally, assuming that Petitioners had advanced a significant aggravation theory, I find that theory would have been unpersuasive for the reasons articulated in this Decision. Namely, any significant aggravation theory would have necessarily relied on the same unpersuasive causal mechanism articulated in Petitioners' causation-in-fact claim.

If Petitioners had pursued a significant aggravation claim further, it would be appropriate to discuss the legal standards for such a claim as articulated in *Loving ex rel. Loving v. Sec'y of Health & Hum. Servs.*, 86 Fed. Cl. 135, 144 (2009). Because Petitioners effectively abandoned this argument by not discussing significant aggravation in their briefs and because it is clear such as claim would fail, no further discussion is required.

VI. Conclusion

Petitioners have my deepest sympathy for K.S.S.W.'s ongoing medical condition and for their continued suffering. However, after my careful evaluation of all the evidence submitted in this matter, including the medical records, the testimony, as well as the experts' opinions and medical literature, I conclude that Petitioners have not shown by preponderant evidence that K.S.S.W.'s condition was caused by the vaccines he received. **The petition is therefore DISMISSED. The clerk shall enter judgment accordingly.**[53]

IT IS SO ORDERED.

[53] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by each filing (either jointly or separately) a notice renouncing their right to seek review.

s/ Katherine E. Oler
Katherine E. Oler
Special Master