OFFICE OF SPECIAL MASTERS
No. 07-111V
Filed: June 19, 2009

KELLY BUTLAND,	)	**TO PUBLISH**
Petitioner,	)	Opsoclonus-Myoclonus Syndrome following MMR and Varicella Vaccinations; Proof of Entitlement to Compensation
v.	)	
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,	)	
Respondent.	)	

Curtis Webb, Twin Falls, ID, for petitioner.

Rebecca Trinrud, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

CAMPBELL-SMITH, Special Master

[1] Vaccine Rule 18(b) states that all decisions of the special masters will be made available to the public unless the decisions contain trade secrets or commercial or financial information that is privileged or confidential, or the decisions contain medical or similar information the disclosure of which clearly would constitute an unwarranted invasion of privacy. When a special master files a decision or substantive order with the Clerk of the Court, each party has 14 days within which to identify and move for the redaction of privileged or confidential information before the document's public disclosure. If the special master agrees, upon review of the party's motion, that the identified material falls within the described categories of protected information, the special master shall remove that material from the publicly accessible document.

On February 16, 2007, Kelly Butland (Mrs. Butland or petitioner), as the legal representative of her minor daughter Lenzie Butland (Lenzie), filed a petition pursuant to the National Vaccine Injury Compensation Program.[2] 42 U.S.C. §§ 300aa-1 to -34 (2006). Petitioner alleges that MMR (mumps, measles, rubella) and varicella vaccinations[3] administered on December 22, 2004, caused Lenzie to develop Opsoclonus-Myoclonus Syndrome (OMS).[4] See Petition (Pet.) ¶ 3; Petitioner's Exhibit (Pet. Ex.) 1 ¶ 53 (Affidavit of Mrs. Butland).

Mrs. Butland relies on a theory of causation in fact. In particular, she asserts that the MMR and varicella vaccinations substantially contributed to the development of Lenzie's OMS by provoking an autoimmune reaction in Lenzie's central nervous system. In support of her theory of causation, Mrs. Butland has filed: (1) her affidavit; (2) Lenzie's medical records; (3) the expert opinion of Marcel Kinsbourne, M.D., a neurologist; (4) supporting medical literature, and (5) pre-hearing briefs. Respondent challenges Mrs. Butland's theory of causation in the filed expert opinion of John MacDonald, M.D., a neurologist, and respondent's pre-hearing memorandum.

During a recorded proceeding on May 1, 2008, in Boston, Massachusetts, the undersigned heard the testimony of Mrs. Butland and the parties' respective experts. Based upon the developed factual record, the supporting medical literature, and the testimony of the parties' experts and for the reasons set forth in this ruling, the undersigned finds that petitioner has satisfied her burden of proving vaccine causation and, therefore, is entitled to compensation.[5]

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[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C.A. § 300aa-10 et seq. (2006) (Vaccine Act or the Act). All citations in this Decision to individual sections of the Vaccine Act are to 42 U.S.C.A. § 300aa.

[3] Varicella is chickenpox. Dorland's Illustrated Medical Dictionary 2008 (30th ed. 2003).

[4] Opsoclonus-myoclonus syndrome involves movement of the eyes (opsoclonus) and the trunk (myoclonus), occurring in conjunction with a number of conditions, including viral infections, trauma, drug toxicity, tumors, and hypersmolar nonketotic coma (a variation of a diabetic coma). Dorland's at 1827.

[5] The undersigned is mindful of the delay in the issuance of this decision. The matter became ripe for decision while the undersigned completed her decision in Hazlehurst v. Secretary of Health and Human Services, No. 03-654, 2009 WL 332306 (Fed. Cl. Spec. Mstr. Feb. 12, 2009), one of the autism test cases in the Omnibus Autism Proceeding. Upon issuance of the

I. BACKGROUND

The parties do not dispute the facts of this case, which are well-documented in the medical records. What is in dispute between the parties' respective experts, however, is the proper conclusion to be drawn from the facts. The experts have reached different conclusions about what caused Lenzie's condition. To better understand the bases for the expert's offered opinions, a recitation of the relevant facts follows.

The facts of this case are established by the medical records and the testimony of petitioner, Mrs. Butland. Mrs. Butland's testimony during the hearing was consistent with Lenzie's recorded medical history. Mrs. Butland was a highly credible witness.

A. The Facts[6]

Lenzie was born on November 23, 2003. Joint Stipulation ¶ 1 ("Joint Stip"); Pet. Ex. 1. At birth, Lenzie had a heart murmur.[7] Pet. Ex. 1. at 1-2. The day after her birth, an electrocardiogram revealed that Lenzie had mild aortic insufficiency and pulmonary insufficiency. Pet. Ex. 2A at 5. But, at a follow-up cardiology appointment nearly one month later, on December 17, 2003, the findings were essentially normal, and the cardiologist noted that Lenzie continued to have a soft 1/6 heart murmur. Pet. Ex. 4 at 1-2.

Lenzie's medical records indicate that she showed normal progress during each of her well-child exams during her first year. Pet. Ex. 3A at 3-13; Tr. at 6. She was seen, however, at least nine times between May and November of 2004 by her pediatrician, David Dreenen, M.D., for ear pain and episodes of screaming. Id. at 6-13. During an office visit on November 16, 2004, Dr. Dreenen treated Lenzie for ear pain and noted that

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decision on February 12, 2009, the undersigned has turned to pending non-autism matters awaiting decision. The undersigned regrets the delay in the issuance of this decision.

[6] The undersigned ordered the parties to file a "joint stipulation of facts" with their pre-hearing memoranda. This document is cited as the Joint Stipulation. The undersigned cites to the record for all other facts.

[7] A heart or cardiac murmur is defined as a "sound of finite length generated by turbulence of blood flow through the heart." Dorland's at 1182. Murmurs are graded on a scale from 1 to 6 "on the basis of increasing loudness." Id.

she had a temperature of 101.9 degrees.[8] Pet. Ex. 3 at 13. The medical records reflect that Lenzie was evaluated the next day at Southeastern Ear, Nose, and Throat Clinic in Enterprise, Alabama, for her "chronic otitis media."[9] Pet. Ex. 5A at 1. That evaluation revealed that she had immobile tympanic membranes.[10] Id. To resolve Lenzie's ear condition, bilateral myringotomy[11] tubes were inserted, without complication, on December 3, 2004. Pet. Ex. 5B at 6; see also Tr. at 6.

Notwithstanding Lenzie's multiple ear infections, Mrs. Butland characterized Lenzie's general development as "on time." Tr. at 7. She noted that Lenzie had met her physical developmental benchmarks on time, which included rolling over at four months, sitting up at six months, pulling up at nine months, and walking at twelve months. Id.

On December 22, 2004, Lenzie presented at her one-year well-child examination with an upper respiratory infection that, according to her mother, had been present for two weeks.[12] Joint Stip. ¶ 3; Pet. Ex. 3B at 14. Lenzie received her MMR and varicella vaccinations that day. Id. She had no immediate reaction to the vaccinations. Tr. at 8.

But three days later, on December 25, 2004, Lenzie woke up in the morning with full-body tremors that lasted about 15 or 20 minutes. Id. Mrs. Butland described the tremors as "Parkinson's-like," occurring mainly in her hands but also throughout her body. Id. The tremors subsided and, with the exception of her runny nose and her cold, Lenzie appeared fine for the rest of the day and several days thereafter. Id. at 9.

Mrs. Butland testified that Lenzie awakened on December 31, 2004,[13] with a fever of 104 degrees and "could not do anything." Id. at 10. Mrs. Butland called Lenzie's pediatrician and arranged for an office visit. See id. During that office visit, Mrs.

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[8] Unless otherwise indicated, all referenced temperatures are measured in Fahrenheit.

[9] Inflammation of the middle ear persisting over a longer period of time. Dorland's at 1339.

[10] A tympanic membrane is commonly known as the eardrum. Dorland's at 1120.

[11] Myringotomy is the creation of a hole in the eardrum. Dorland's at 1217.

[12] Lenzie was thirteen months old at the time of her one-year well-child exam.

[13] The medical records reflect that this office visit occurred on December 30, 2004, and that Lenzie had a fever of 103 degrees, and that she had been "shaking a lot x ½ week." Pet. Ex. 3B at 14.

Butland reported that Lenzie had a one-half week history of shaking,[14] a runny nose, red tonsils, and, on the day of the exam, a temperature of 103 degrees. Joint Stip. ¶ 4; Pet. Ex. 3B at 14. The treating pediatrician diagnosed Lenzie with stomatitis[15] and an upper respiratory infection. Pet. Ex. 3B at 14.

The next day,[16] Mrs. Butland took Lenzie to the emergency room and reported that she seemed to be "unbalanced" and that she fell "over when trying to pull up." Joint Stip. ¶ 5; Pet. Ex. 6 at 2. Lenzie was referred to Jean-Ronel Corbier, M.D., a neurologist. Pet. Ex. 6 at 5. Dr. Corbier diagnosed her with cerebellar ataxia[17] and indicated that the ataxia could have been caused by either the MMR vaccination or a viral infection. Joint Stip. ¶ 6; Pet. Ex. 3B at 15; Pet. Ex. 7A at 8. The results of Lenzie's subsequent testing (a follow-up electroencephalogram (EEG))[18] on January 4, 2005, were normal. Pet. Ex. 8B at 12.

About a month later, on February 8, 2005, James Izer, M.D., an ophthalmologist, examined Lenzie. Mrs. Butland informed Dr. Izer that Lenzie's left eye had begun "turning in toward her nose" four days prior to the ophthalmologic visit. Joint Stip. ¶ 7; Pet. Ex. 9 at 1; Tr. at 13. Dr. Izer noted that Lenzie's left eye "always had matter in it," and he diagnosed her with esotropia[19] of undetermined cause. Pet. Ex. 9 at 1.

About two weeks later, Lenzie received a further neurological evaluation during her four-day stay at Children's Hospital in Birmingham, Alabama. Pet. Ex. 14. Mrs. Butland reported that Lenzie had a two-month history of "losing milestones and shaking

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[14] To the extent Mrs. Butland's testimony that Lenzie was "fine," Tr. at 9, contradicts the notes in the contemporaneous medical records that Lenzie experienced episodic shaking during the next days after the initial shaking event, the undersigned credits as accurate the contemporaneous medical records. Pet. Ex. 3B at 14.

[15] Stomatitis is the inflammation of the oral mucosa. Dorland's at 1764.

[16] This visit to the emergency room occurred on December 31, 2004. Pet. Ex. 6 at 2.

[17] Cerebellar ataxia is the failure of muscular coordination due to disease of the cerebellum. Dorland's at 170-171.

[18] An EEG is "a recording of the potentials on the skull generated by currents emanating spontaneously from nerve cells in the brain. . . . Fluctuations in potential are seen in the form of waves, which correlate well with different neurologic conditions and so are used as diagnostic criteria." Dorland's at 596.

[19] Esotropia is also called cross-eye. Dorland's at 644.

episodes." Pet. Ex. 14A at 13. Mrs. Butland also reported that Lenzie's eyes had begun to turn inward. Id. Tony McGrath, M.D., the examining pediatric neurologist, made note of Lenzie's earlier diagnosis of acute cerebellar ataxia. Id. at 13-14. According to Dr. McGrath's assessment, Lenzie had "ataxia, hypotonia,[20] and strabismus."[21] Id. at 14.

Five days after Lenzie's discharge from Children's Hospital, Linda Nathanson-Lippitt, M.D., a developmental/behavioral pediatrician at the Children's Habilitation Center in Smyrna, Georgia, saw Lenzie for treatment of her tremors, eye-crossing, and difficulty sitting up, crawling, and walking. Pet. Ex. 10A at 2. In Dr. Nathanson-Lippitt's recorded history for Lenzie was a note that the day after Lenzie received her MMR and varicella vaccinations in December 2004, she was "unable to hold up her head or hold a cup." Pet. Ex. 10B at 15.

On March 7, 2005, about two weeks after Lenzie's neurological evaluation at Children's Hospital, Lenzie had a follow-up visit with Dr. McGrath. Pet. Ex. 11 at 2. Mrs. Butland informed Dr. McGrath that Lenzie's ataxia and irritability has improved, but her eye condition remained unchanged. Id. Dr. McGrath spoke with Lenzie's parents about the possibility that the vaccinations that Lenzie had received were responsible for her physical condition, but Dr. McGrath wrote in his records that "it is difficult to attribute all her symptomatology to her vaccines." Id. at 3.

On March 29, 2005, Lenzie saw Dr. Martin Cogen, an ophthalmologist. Dr. Cogen diagnosed Lenzie with alternating strabismus without nystagmus[22] and noted that she would likely need eye muscle surgery in the future. Pet. Ex. 12 at 5. Nearly two months later, on May 23, 2005, Dr. Cogen performed corrective surgery on the medial rectus muscles of both of Lenzie's eyes. Joint Stip. ¶ 8; Pet. Ex. 12 at 10. By June 21, 2005, Dr. Nathanson-Lippitt reported, during a pediatric visit, that Lenzie's eyes had returned to being "internally rotated," although Lenzie was using both hands equally and showed no signs of tremor. Pet. Ex. 10B at 39-40.

At a subsequent neurology appointment with Dr. McGrath on September 7, 2005, Mrs. Butland reported that Lenzie was able to pull to a stand, but not walk. Pet. Ex. 11 at

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[20] Hypotonia is a condition of diminished tone of the skeletal muscles. Dorland's at 900.

[21] Strabismus is a deviation of the eye which the patient cannot overcome. Dorland's at 1766.

[22] Nystagmus is an involuntary, rapid, rhythmic movement of the eyeball, which may be horizontal, vertical, rotatory, or mixed. Dorland's at 1296.

12. She also informed Dr. McGrath that Lenzie's eyes had begun to turn inward again, her language skills had plateaued, and her left arm would tremble when she was sick with a cold. Id. at 12-13. Dr. McGrath again noted Lenzie's history of ataxia. Id. at 14. Due to the nature of Lenzie's ongoing symptoms, Dr. McGrath ordered a scan of Lenzie's chest, abdomen, and pelvis. Id. That scan revealed that Lenzie had a paraspinal mass with punctuate calcification[23] extending from T7 to T13 on the left side of her spine. Joint Stip. ¶ 9; Pet. Ex. 13 at 1.

On September 9, 2005, Lenzie was admitted to Children's Hospital in Birmingham for the removal of the paraspinal mass. Joint Stip. ¶ 10; Pet. Ex. 13 at 1-9. Testing revealed that the mass was a ganglioneuroblastoma.[24] Joint Stip. ¶ 10; Pet. Ex. 13 at 1-9.

At her follow-up neurology appointment with Dr. McGrath two months later, on November 7, 2005, Mrs. Butland reported that Lenzie was making progress with her cognitive and language skills. Pet. Ex. 11 at 24. Dr. McGrath found no evidence of opsoclonus or nystagmus and noted that Lenzie displayed no ataxia or tremors. Id. Dr. McGrath reported, "[T]his is an almost two year old female with paraneoplastic [25] syndrome of ataxia and esotropia from ganglioneuroblastoma, paraspinal in location, status post-resection. Her neurological exam is significantly improved as compared to the previous times I have seen her. This is very encouraging." Pet. Ex. 11 at 25.

Mrs. Butland testified that Lenzie began to improve after the removal of the tumor and with her subsequent treatment that included IVIG and chemotherapy.[26] Id. at 16. Lenzie's tremors stopped, and she made progress in her speech and walking. Id. at 16, 17. She contrasted Lenzie's condition after the tumor removal with Lenzie's condition prior to the removal of the tumor, explaining that the months preceding the removal of

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[23] Punctuate calcification is the hardening of organic tissue with intermittent dot-like deposits of calcium salts within its substance. Dorland's at 271, 1546.

[24] Ganglioneuroblastoma is a sarcoma (group of tumors) consisting of malignant nerve cells within the brain or spinal cord. It is considered a type of tumor affecting mainly infants and children. Dorland's at 754, 1253.

[25] Paraneoplastic refers to changes produced in tissue remote from a tumor or its metastases. Dorland's at 1367.

[26] Intravenous immunoglobulin (IVIG) therapy is a blood product delivered intravenously containing antibodies extracted from the plasma of donor patients. It is primarily used to as treatment in patients with immune deficiencies, inflammatory or autoimmune disorders, and acute infections. Dorland's at 912, 947.

Lenzie's mass were difficult ones due to Lenzie's prolonged screaming episodes and her episodic shaking for periods of time ranging from 15 minutes to an hour. Tr. at 12-13, 15. Mrs. Butland noted that the shaking episodes were notably worse when Lenzie awakened in the morning or from a nap. Id. at 14.

After Lenzie's tumor removal, she suffered several relapses. Id. at 17. Symptoms of ataxia reappeared in early March 2006. Pet. Ex. 15 at 92. Mrs. Butland consulted Dr. McGrath, who ordered additional scans, but found no evidence of recurrent disease. Pet. Ex. 15 at 95-98. Lenzie's symptoms persisted throughout the month, and, on March 27, 2006, Dr. Crawford, a pediatric hematologist/oncologist, added high dose adrenocorticotropic hormone (ACTH)[27] to Lenzie's prescriptive treatment, which proved effective. Id. at 120, 131.

Mrs. Butland testified that Lenzie's treating physician at the time sought the advice of Dr. Michael Pranzatelli, a pediatric neurologist and professor at the Southern Illinois University School of Medicine who studies OMS, and that Dr. Pranzatelli suggested the ACTH injections that Lenzie began receiving in the middle of March 2006. Tr. at 17. Mrs. Butland recalled that Lenzie's condition dramatically improved after she began receiving the injections. Id. at 18. By Lenzie's follow-up appointment with Dr. Crawford on May 22, 2006, Lenzie's symptoms appeared to have resolved completely, with the exception of her disjunctive gaze. Pet. Ex. 15 at 166.

Several months later, in August of 2006, petitioner reported that Lenzie's symptoms of irritability and ataxia had returned. Pet. Ex. 15 at 194. Mrs. Butland elaborated during the hearing that during that particular relapse, Lenzie exhibited the same symptoms that characterized her earlier relapse: falling down, attacks of rage, insomnia, crossed eyes, and tremors. Tr. at 18-19. In response, Dr. Crawford prescribed rituximab[28] to suppress Lenzie's immune system and to prevent an immune-mediated attack on her brain. Id.; Tr. at 19. Dr. Crawford also scheduled another scan. Pet. Ex. 15 at 194. That scan did not reveal any new tumor. Id. at 201-203.

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[27] Adrenocorticotropic hormone or ACTH is a corticosteroid used to reduce inflammation and relieve symptoms in a variety of disorders, including the suppression of immune responses. Dorland's at 33, 425.

[28] Rituximab (the generic version of Rituxan) is a chimeric, monoclonal antibody against the CD20 antigen, used in the treatment of B-cell non-Hodgkin's lymphoma., B-cell leukemias, and some autoimmune disorders. See Rituxan, Physician's Desk Reference for Prescription for Drugs.

Early the next month, Dr. Crawford noted in Lenzie's medical records a "dramatic improvement in her physical symptoms." Id. at 228. Mrs. Butland related that Lenzie was walking without ataxia and no longer cried out in her sleep. Id. At a subsequent visit to Dr. Crawford, on September 21, 2006, Lenzie's parents reported that they had no additional concerns or complaints about Lenzie to address. Id. at 232.

But, Lenzie suffered another relapse in January 2007. Tr. at 19. That relapse was marked by the same symptoms as her prior relapses and was treated again with rituximab. Id.

Mrs. Butland added that in the few months preceding the hearing, Lenzie had several sinus infections. Id. at 127. With the infections or with any sickness, Mrs. Butland has noticed that Lenzie experiences increased instances of rage attacks and falling over. Id. Mrs. Butland observed that Lenzie's general physical stability is negatively affected when she is sick. Id. at 128. Moreover, Lenzie's doctors have indicated that an upper respiratory infection could trigger a relapse of her OMS symptoms. See Tr. at 20.

Mrs. Butland testified that Lenzie was "doing okay," and that her development was normal for a four-year-old. Id. But in some areas, Mrs. Butland acknowledged, Lenzie is "a little behind." Id. Lenzie returns to the doctor every three months to check her OMS, and Lenzie still experiences eye-crossing. Id. at 20.

II. DISCUSSION

A. Legal Standards

The Vaccine Injury Table lists certain injuries and conditions that if found to occur within a prescribed time period create a rebuttable presumption of causation between the administered vaccine and the injury or medical condition alleged by a petitioner. 42 U.S.C. § 300aa-14(a). Because Opsoclonus Myoclonus Syndrome is not included among the injuries and conditions listed on the Vaccine Injury Table, this is not a Table Injury case, and no presumption of vaccine causation attaches to petitioner's claim. Rather, petitioner must prove causation. See id.

To satisfy the burden of proving causation in an off-Table case, petitioner must show that "the vaccination brought about [the vaccinee's] injury 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 the vaccination and the injury."

Althen v. Sec'y of Health and Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005). Petitioner bears the burden of proving causation by preponderant evidence. See 42 U.S.C. § 300aa-13(a)(1)(A).

Petitioner has an affirmative duty to prove causation. Evidence merely showing "an absence of other causes" is insufficient to establish actual or legal causation of vaccine-related injury. Grant v. Sec'y of Health and Human Servs., 956 F.2d 1144, 1149 (Fed. Cir. 1992). While the imposed affirmative duty does not require petitioner to show that the vaccine was solely responsible or even the predominant cause of the injury, the burden rests with petitioner to establish that "the vaccine was not only a but-for cause of the injury, but a substantial factor in bringing about the injury." Shyface v. Sec'y of Health and Human Servs., 165 F.3d 1344, 1352 (Fed. Cir. 1999); see also Pafford v. Sec'y of Health and Human Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006) (stating that "[u]nder this court's precedent, [petitioner] must prove by preponderant evidence both that her vaccinations were a substantial factor in causing the illness, disability, injury or condition and that the harm would not have occurred in the absence of the vaccination").

Petitioner must support her theory of causation with a "sound and reliable medical or scientific explanation." Knudsen v. Sec'y of Health and Human Servs., 35 F.3d 543, 548 (Fed. Cir. 1994). A medical or scientific theory is not valid, however, simply because an expert offers the theory during his or her testimony. The Supreme Court has instructed in Daubert v. Merrell Dow Pharmaceutical, Inc., that the reliability of the offered testimony must be considered. 509 U.S. 579, 592 (1993). The reliability of an expert's theory may be evaluated by considering: (1) whether the theory or technique 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 (4) whether the theory or technique enjoys general acceptance within the scientific community. Daubert, 509 U.S. at 592-95; see also Kumho Tire Co. v. Carmichael, 526 U.S. 137, 138 (1999) (internal quotation and citation omitted) (noting that the general principles of Daubert apply broadly to "scientific, technical, or other specialized knowledge" and that offered testimony must have "a reliable basis in the knowledge and experience of [the relevant] discipline"); General Elec. Co. v. Joiner, 522 U.S. 136, 145 (1997) ("Nothing, either in Daubert or the Federal Rules of Evidence[29] requires a district court to admit opinion

[29] Although the Federal Rules of Evidence do not apply in vaccine cases, see Vaccine Rule 8(c), the Federal Circuit has affirmed efforts by special masters to examine the underpinnings of an offered theory of vaccine causation for a "sound and reliable medical or scientific explanation." Knudsen, 35 F.3d at 548; Terran v. Secretary of Health and Human Servs., 195 F.3d 1302 (Fed. Cir. 1999) (affirming a special master's denial of compensation on the ground that the special master's application of Daubert principles in excluding an expert's

evidence that is connected to existing data only by the ipse dixit [30] of the expert. A court may conclude that there is simply too great an analytical gap between the data and the opinion proffered.")(footnotes added).

Although petitioner must provide a "sound and reliable medical or scientific explanation," see Knudsen, 35 F.3d at 548, petitioner need not provide particular types of evidence (such as medical literature or epidemiologic studies), see Capizzano v. Sec'y of Health and Human Servs., 440 F.3d 1317, 1324 (Fed. Cir. 2006). The Federal Circuit has observed that requiring petitioners to present particular types of evidence would "prevent[] the use of circumstantial evidence envisioned by the preponderance standard and negate[] the system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants."[31] Capizzano, 440 F.3d at 1324.

Once petitioner makes the requisite showings, she establishes a prima facie case of vaccine-related causation. In the absence of evidence that rebuts petitioner's case, petitioner is entitled to an award of Program compensation. Compare Pafford, 451 F.3d at 1355 with Walther v. Sec'y of Health and Human Servs., 485 F.3d 1146, 1150 (Fed. Cir. 2007) (addressing the issue of which party bears the burden of ruling out potential non-vaccine causes of the alleged injury); see also De Bazan v. Sec'y of Health and Human Servs.., 539 F.3d 1347, 1352-1353 (Fed. Cir. 2008) (discussing what evidence a special master may consider when deciding whether petitioner has satisfied her threshold burden of proving causation).

B. The Parties' Experts' Opinions Regarding Causation

Both parties proffered the opinion of a medical expert regarding what caused Lenzie's OMS.

1. Petitioner's Expert's Opinion

Dr. Marcel Kinsbourne, a pediatric neurologist, testified for petitioner. Dr.

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causation-in-fact testimony was not improper).

[30] Ipse dixit refers to the Latin phrase "he himself said it." It refers to something asserted but not proved. Black's Law Dictionary 833 (7th Ed. 1999).

[31] Should petitioner elect to provide such evidence, however, the reliability of the offered evidence must be considered. See Knudsen, 35 F.3d at 548 (requiring that petitioner provide a "sound and reliable" medical or scientific explanation).

Kinsbourne holds medical licenses in the United Kingdom, Canada, North Carolina, and the Commonwealth of Massachusetts. He has held numerous teaching positions and hospital appointments in various capacities at universities in each of the aforementioned locations. Additionally, he has authored and edited many medical articles, books, and medically-related literature over his lengthy career as a neurologist.

Of particular relevance in this case, Dr. Kinsbourne published in 1962 a report of six pediatric cases of "a hitherto undescribed condition." Pet. Ex. 28 at 276 (1962 Kinsbourne article).[32] The condition was marked by the acute onset, during infancy, "of incoordination due to the frequent, widespread, and irregular intrusion of myoclonic jerking." Id. Dr. Kinsbourne is credited with first describing cases involving this "motor disorder of a highly distinctive type" characterized by (1) the irregular, involuntary movements of the limbs as well as the eyes; (2) a protracted, but non-progressive and self-limiting course; and (3) the "striking symptomatic relief" obtained from treatment with ACTH, an immunosuppressive corticosteroid. Id. at 275, 276. This disorder is now known as childhood OMS or Kinsbourne syndrome. See Pet. Ex. 20 at 1 (2004 Pranzatelli article);[33] Pet. Ex. 28 (1962 Kinsbourne article).

In this case, Dr. Kinsbourne opined that certain viral infections or attenuated viral vaccines may act in concert with certain tumors to cause the immunological disturbances that lead to the development of OMS. See Pet. Ex. 23 at 3-4; see also Tr. at 35-38. During his hearing testimony, he offered a reasoned explanation for his opinion.

At the hearing, Dr. Kinsbourne described the condition of OMS. He discussed the differences between OMS and ataxia. He addressed the role of tumors in the development of OMS and identified other triggers for OMS. He testified about the combined effect of a tumor and a virus or vaccination in causing OMS generally and specifically in Lenzie's case. These aspects of Dr. Kinsbourne's opinion are now set forth in more detail.

a. What is OMS?

Dr. Kinsbourne testified that childhood OMS is an immune disorder that affects a child's brainstem and usually presents in children between the ages of nine months to two

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[32] M. Kinsbourne, Myoclonic encephalopathy in infants, 25 J. Neurol. Neurosurg. Psychiatry 271-276 (1962).

[33] M. Pranzatelli, et al., CSF B-Cell Expansion in Opsoclonus-Myoclonus Syndrome: A Biomarker of Disease Activity, 19 Movement Disorders 7:770-777 (2004).

years. Tr. at 25. The disorder is thought to result from an attack on proteins within the child's cerebellum, the part of the brain responsible for muscular coordination and posture stability. Id. Dr. Kinsbourne testified that while the nature of the attack is yet unknown, evidence indicates that the humoral arm of the immune system is overactive.[34] Id. More specifically, evidence indicates that antibodies are formed that attack specific proteins contained in the cerebellum. Id. There is also evidence that the T-cell-mediated arm of the immune system is implicated.[35] See Tr. at 26.

In support of Dr. Kinsbourne's position, petitioner submitted literature (filed as Petitioner's Exhibit 17) that characterized OMS as "an important conceptual part of the spectrum of putative autoimmune neurologic disorders." Pet. Ex. 17 at 35-36 (1996 Pranzatelli review article).[36] Dr. Kinsbourne's opinion and testimony reflect a heavy reliance on the review article filed as Petitioner's Exhibit 17 and four other submissions (filed as Petitioner's Exhibits 16, 18, 19 and 20), all of which were authored or co-authored by Michael Pranzatelli, M.D., a neurologist who has studied OMS and who founded the National Myoclonus Pediatric Center in 1985.[37] See Pet. Ex. 17 at 18, 20, 35-36.

The 1996 Pranzatelli review article filed as Petitioner's Exhibit 17 addresses the criteria for an autoimmune disease stating that "[t]here are five classical strict criteria for an autoimmune disease."[38] Pet. Ex. 17 at 2. After identifying the five classical criteria,

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[34] The humoral arm of the immune system provides immunity through the production of antibodies (secreted by B cells). See Dorland's at 910; see also Pet. Ex. 16D at 15-16.

[35] The T cell-mediated arm of the immune system provides immunity through the release of non-antibody proteins and the targeted killing (or exerted cytotoxicity) of specially identified invader cells. See Dorland's at 471, 910, 1078; see also Pet. Ex. 16D at 16-17.

[36] M. Pranzatelli, Review: The Immunopharmacology of the Opsoclonus-Myoclonus Syndrome, 19 Clinical Neuropharmacology 1:1, 35-36 (1996).

[37] Respondent's expert, Dr. MacDonald, discounted the weight of Dr. Pranzatelli's articles because Dr. MacDonald does not regard Dr. Pranzatelli as an expert on the syndrome. Tr. at 94. But, as noted in Section I.A (the facts section) of this decision, Dr. Crawford, one of Lenzie's treating physicians, consulted Dr. Pranzatelli regarding treatment for Lenzie.

[38] The identified criteria are:

> [First, a] defined circulating antibody or cell-mediated immunity to autoantigens is required, but most patients with OMS do not exhibit detectable levels of suspect circulating antibodies. The second criterion is the definition of

Dr. Pranzatelli concludes that OMS, like most other putative autoimmune disorders, does not meet these criteria. Id.

But Dr. Pranzatelli observes that there is circumstantial evidence that may support the finding of an immunologic basis for OMS. Id. The circumstantial evidence to which Dr. Pranzatelli referred in the review article included: (1) the finding of immunologic abnormalities in the cerebrospinal fluid of OMS patients, which suggests that an immunogenic mechanism is involved in the pathophysiology of OMS, id. at 3-4, and (2) the successful treatment of OMS through modulation of the immune system, which also suggests that an immunogenic mechanism is involved, id. at 26. Dr. Pranzatelli posits that viral infections may have a role in aggravating the immunologic dysregulation that seems to occur in cases of OMS. Id.

Petitioner filed two additional articles, Petitioner's Exhibits 19[39] and 20,[40] that

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> the specific autoantigen: given that both peripheral neoplasms and various viruses are the typical etiologies of OMS, an apparent common denominator is unknown. The next three criteria require an animal model, which is lacking in OMS. First, the disease must be produced in an experimental animal by passive transfer of the antibody or the self-reacting cells. The disease then must be produced by immunization with the self-antigen in the presence of complete Freund's adjuvant. [Such adjuvant is "a water-in-oil emulsion incorporating antigen, in the aqueous phase, into lightweight paraffin oil with the aid of an emulsifying agent. On injection, this mixture induces strong persistent antibody formation." See Dorland's at 33, 740.]. Last [of the three criteria that require an animal model], such [produced] immunization must be able to generate the autoantibodies or the self-reacting cell.

Pet. Ex. 17 at 2.

[39] Filed as Petitioner's Exhibit 19 is a 2004 article listing Dr. Pranzatelli as the lead author. The citation for the article is M. Pranzatelli, et al., B and T-cell markers in opsoclonus-myoclonus syndrome: Immunophenotyping of CSF lymphocytes, 62 Neurology 1526-1532 (May 2004). The article reports the findings of a study involving thirty-six children with OMS and eighteen control subjects. Pet. Ex. 19 at 2-3. Samples of cerebrospinal fluid from each of the study participants were obtained and analyzed for an expression of immunological markers of the OMS disorder. Id. The investigators found that abnormalities existed in a percentage of various B-cells and T-cells in each of the OMS cases. Id. at 3-4. The discovered immunophenotype in the study subjects with OMS was not affected by the presence of a tumor or the administration of treatment. Id. The investigators noted that "[b]ecause both B-cell and T-cell abnormalities were linked to neurologic dysfunction, [the cellular abnormalities] could account for relapses and disease progression." Id. at 5. Although the investigators recognized the risks of "draw[ing]

support a finding that an immunogenic mechanism is involved in the condition of OMS. Although there is mounting evidence of an immunogenic component in the development of OMS, the immunobiology of OMS is admittedly not yet well-understood. Pet. Ex. 17 at 1 (stating in the opening sentence of the article that "so little is known about the immunobiology" of the condition).

b. The difference between OMS and ataxia

Dr. Kinsbourne explained the difference between muscle movement in an OMS patient and muscle movement in an ataxic patient. The symptoms of OMS include instability of the muscles that manifests as tremors. Tr. at 26. OMS characteristically involves the irregular trembling of the muscles. Id. By contrast, acute cerebellar ataxia involves a rhythmic tremor of the muscles. Id.

According to Dr. Kinsbourne, Mrs. Butland's description of Lenzie's behavior was consistent with what are the known clinical manifestations of OMS. Compare Tr. at 26 (Dr. Kinsbourne's testimony) with id. at 8, 13, 15, 19 (Mrs. Butland's testimony); see also

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conclusions about the functional properties of immune cells from their phenotypic markers alone," the investigators observed that the cytotoxic capacity of the immune cells (identified as abnormal in OMS subjects) may have a role in the pathophysiology of the disorder. Id. at 7.

[40] Filed as Petitioner's Exhibit 20 is another 2004 article listing Dr. Pranzatelli as the lead author. The citation for this article is M. Pranzatelli, et al., CSF B-cell Expansion in Opsoclonus-Myoclonus Syndrome: A Biomarker of Disease Activity, 19 Movement Disorders 7:770-777 (2004). This article reports the findings of a study involving fifty-six children with OMS and twenty-six pediatric control subjects. Pet. Ex. 20 at 2. Samples of cerebrospinal fluid from each of the study participants were obtained and analyzed for evidence of B-cell expansion. Id. Acknowledging that no autoantibody specific for OMS has been identified to date, the investigators devised a study that shifted the focus from looking for an antibody to looking at the source of the antibody production, specifically the B lymphocyte. Id. at 1-2. In particular, the investigators decided to look for evidence of B-cell expansion in cerebrospinal fluid. Id. Noting that in normal circumstances, cerebrospinal fluid is "nearly devoid of B-cells in adults," the investigators posited that a finding of B-cell expansion in cerebrospinal fluid that could be linked as well to severe neurological symptoms "would help substantiate" an autoimmune basis for the disorder of OMS. Id. at 2. Focusing on two different B-cell markers, the investigators found evidence of B-cell expansion in the cerebrospinal fluid that correlated with neurological severity in the OMS cases that was much greater than measured B-cell expansion in the control subjects. See id. at 4-7. The findings of "significant B-cell recruitment to the central nervous system and the potential for autoantibody production" in pediatric OMS cases contributes to the growing evidence that the disorder involves long-term immunological abnormalities. See id. at 2, 4, 6.

Pet. Ex. 16E at 21 (describing symptoms of OMS). Specifically, a child suffering from OMS will wake up very irritable, upset, and shaking. Id. at 26. Dr. Kinsbourne explained that the tremors vary in severity, but could be strong enough to shake the crib containing the child. Id. Dr. Kinsbourne observed that while a child suffering with OMS remains cognitively aware, oftentimes the child will not want to undertake certain physical actions, like raising a glass to the lips, due to the unsteadiness created by tremors. Id. at 27. Dr. Kinsbourne described how the tremors extend to the muscles surrounding the eyes, and result in a jerking of the eyeballs. Id. The muscles controlling the eyeballs will also jerk in an unpredictably irregular manner, both horizontally and vertically. Id. Because of the irregular eye movement, the syndrome has also been referred to as "syndrome of the dancing eyes." Id. at 28.

Dr. Kinsbourne noted that Lenzie's eyes were described as crossed rather than dancing. Id. He explained that there may be some variability in how the condition presents and that the difference in the described abnormality in Lenzie's eyes cast no doubt on his opinion that she suffered from OMS. Id.. In Dr. Kinsbourne's view, Lenzie's initial diagnosis of cerebellar ataxia was a misdiagnosis. Id. at 26.

c. The onset of Lenzie's OMS

In Lenzie's case, Mrs. Butland first observed that Lenzie had an ataxic gait on December 31, 2004, nine days after the receipt of the vaccinations at issue. Tr. at 10; Pet. Ex. 3B at 15. Before she developed an ataxic gait, however, she had awakened with tremors on the morning of December 25, 2004, just three days after receiving her vaccinations.

Dr. Kinsbourne identified Lenzie's ataxia as her first symptom of OMS, Tr. at 38-39. When asked whether Lenzie's tremors, which preceded the appearance of her ataxia, could have been the first symptom of her OMS, Dr. Kinsbourne replied that the described symptom of shaking could not be "ignored." Tr. at 38. But he observed that in most cases, the shaking does not "go away" once it begins. Id. at 38-39. Because Lenzie's mother testified that Lenzie's shaking stopped for a period of days, Dr. Kinsbourne opined that the correct onset of Lenzie's condition was later, when the symptom "came back with a vengeance." Id. at 39.

Dr. Kinsbourne's testimony reflected some confusion about the sequence of Lenzie's initial symptoms. His testimony indicated that he incorrectly believed that Lenzie's first observed shaking occurred before she received the vaccinations. See id. at 39. Additionally, his testimony indicated that he incorrectly believed that Lenzie's ataxia

first appeared two days after her vaccinations.[41] See Tr. at 38-39; Pet. Ex. 23 at 2, 4. As described in the medical records and during the testimony of Mrs. Butland, however, Lenzie's first symptom of concern was her shaking. See Joint Stip. ¶ 4; Pet. Ex. 3B at 14; Tr. at 8. Accordingly, the undersigned credits as more accurate than Dr. Kinsbourne's factual account the description of Lenzie's earliest symptoms contained in the contemporaneous medical records and reiterated during petitioner's testimony.

That Dr. Kinsbourne's testimony did not accurately reflect what Lenzie's earliest symptoms were had no material impact in this case because the earliest manifested symptoms after Lenzie's vaccinations were symptoms of OMS. As described in the literature filed in support of petitioner's claim, the earliest neurological symptom of OMS identified in rank order is ataxia. Pet. Ex. 18 at 3. The fourth symptom of OMS identified in rank order is tremor. Id. In this case, Lenzie exhibited both symptoms within days of her receipt of the vaccinations of interest in this Program claim, and petitioner's own expert acknowledged that the noted shaking episode could not be "ignored." See Tr. at 38. Moreover, the earliest symptoms occurred within the time frame that Dr. Kinsbourne believed was critical to implicate the vaccinations. See Section II.C.2.

d. The Role Tumors Have in OMS

Dr. Kinsbourne testified that a sizeable minority of OMS cases (on average, 1 in 4 children) involves an underlying tumor, in particular, either a ganglioneuroma or neuroblastoma.[42] Pet. Ex. 23 at 3; Tr. at 32. He acknowledged that some studies (particularly the later conducted studies) have reported that between forty to sixty percent of OMS cases are caused by neuroblastoma, but he attributes the higher estimates to a bias in the selection of the study subjects. See Tr. at 42. He explained that the studies reporting higher percentages involve subjects who have been referred from specialized centers rather than subjects from the general population. Id.

Dr. Kinsbourne stated that of the children who have a neuroblastoma, only two to three percent of them develop OMS. Id. at 32. He described a neuroblastoma as "a

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[41] Lenzie received her vaccinations on December 22, 2004, three days before Christmas Day.

[42] A neuroblastoma is a tumor consisting of malignant neuroblasts. Dorland's at 1253, 1657. Neuroblasts are embryonic cells that develop into nerve cells. Id. at 1253. A neuroma is a more benign form of the tumor growing from a nerve. See id. at 1256; see also Tr. at 32.

common tumor of childhood" that triggers a reaction by the child's immune system against the abnormal cells in the tumor and that immunological reaction "sometimes . . . can actually cause the tumor to regress , and . . . even disappear." Id. at 32-33. In contrast to the commonness of the neuroblastoma tumor, Dr. Kinsbourne described the condition of OMS as a "rare disorder of childhood." Id. at 32. He posited that the development of OMS as a complication of an underlying neuroblastoma is "very unusual" because the chance that the immune system of a child with a neuroblastoma would react to the tumor as well as against the child's brain is "pretty low." Id. at 33 (stating that "it is very unusual for th[e] immune response to the tumor also to overflow onto a response against [the cells of the child's own brain which] . . . are called self-antigens").

e. Other Triggers for OMS

In his submitted report and during his testimony, Dr. Kinsbourne identified several viruses and immunizations as possible "triggers" for the immunologic process that precipitates OMS. Pet. Ex. 23 at 3; Tr. at 31-32. He stated that "[t]here are no known differences" between the clinical presentation of, on one hand, an OMS patient with an underlying neuroblastoma and no identifiable antecedent infection or vaccination and, on the other hand, that of an OMS patient with a preceding viral infection or immunization but no detected tumor. Tr. at 34. Moreover, the same treatments may be effective in OMS cases involving a neuroblastoma and in cases without a detected tumor. Id. at 34-35.

Dr. Kinsbourne's testimony on these points was supported by literature filed by petitioner as Exhibits 16 and 18. Exhibit 16 is comprised of pages from the website of the National Pediatric Myoclonus Center. See http://www.omsusa.org. Dr. Pranzatelli, who is a staff neurologist and Professor of Neurology and Pediatrics at Southern Illinois University School of Medicine, founded the Center. The website addresses, among other matters, the causes of OMS. Pet. Ex. 16C at 7. As explained on the relevant page of the website, when the disorders of opsoclonus and myoclonus occur in combination, the "rather specific" causes are tumors and infections. Id. Among the documented viral infections associated with OMS are Epstein-Barr, Coxsackie B, and St. Louis encephalitis. Id. Described as "neurotropic," these viruses have a selective affinity for nerve tissue. See Pet. Ex. 18 at 2; Dorland's at 1260. Additionally, the wild-type varicella virus (or chicken pox) has been associated with "severe cerebellar ataxia" in some children. Pet. Ex. 16G at 30.

Petitioner's Exhibit 18 is a 1996 article that Dr. Pranzatelli co-authored.[43] In the article, Dr. Pranzatelli and his co-authors observe that "a viral etiology is inferred" in pediatric OMS cases that occur "without a demonstrated tumor." Pet. Ex. 18 at 1. The article documents the results of a study of 105 children who were recruited to participate in the study based on their diagnosed condition of OMS. Id. The variables of interest in the study were: (1) whether the OMS occurred with or without a detected tumor; (2) what was the age of OMS onset; and (3) what was the course of treatment. Id. at 2. The study indicated that the majority of the cases occurred, with or without a detected tumor, in children under the age of two years. Id. at 5, Fig. 2. The most common of the symptoms (known as prodromal symptoms) preceding the onset of OMS were irritability, crying, coughing or sneezing, fever and ear infection. Id. at 6, Fig. 3. The prodromal symptoms did not differ greatly between the two etiologic subgroups, specifically, the no-tumor group and the tumor group. Id. Nor did the neuropsychiatric signs that appeared in the OMS patients (the most common of which were tremulousness, staggering, behavior problems, slurred speech, and eye jerks) differ greatly between the two etiologic subgroups. Id. at 8, Fig. 4. Treatment protocols that included high dose ACTH appeared to yield the best initial response rates in both subgroups. Id. at 10. In discussing the results of the study, the investigators noted the possibility that tumors in pediatric OMS cases may be significantly "underdiagnosed." Id. at 10. But, the investigators concluded that whether or not an underlying tumor is ever detected in an OMS patient, immunotherapy is an essential component of treatment once the autoimmune process has been activated in the patient.

Also reported in Petitioner's Exhibit 18 is the finding that more than 85 percent of the 105 children with OMS recruited through the National Pediatric Myoclonus Center over a thirteen year period had received immunizations prior to the onset of their neurological symptoms. See Pet. Ex. 18 at 3. Listed among the immunizations that the affected children had received was the MMR. Id. The varicella vaccine was not listed. Id. But, on the website of the National Pediatric Myoclonus Center, Dr. Pranzatelli urges parents of children with OMS to weigh the risks of immunization (particularly with attenuated viral immunizations) against the risks of infection. See Pet. Ex. 16G at 30-31.

Dr. Kinsbourne relies on the research conducted by Dr. Pranzatelli as the principal support for his theory that OMS is an immunologically-based disorder that may be triggered by viral infections or vaccinations. Tr. at 31; Pet. Ex. 23 at 3. Dr. Kinsbourne identified Lenzie's MMR and varicella vaccinations (both of which are attenuated, viral

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[43] The citation for the article is D.T. Tate, et al., Neuroepidemiologic Trends in 105 U.S. Cases of Pediatric Opsoclonus-Myoclonus Syndrome, 19 Clinical Neuropharmacology 1:1-47 (1996).

vaccines) as substantial causal factors in the development of her OMS. Pet. Ex. 23 at 3.

f. The Combined Effect of a Virus or Vaccination and a Neuroblastoma in Causing OMS

Dr. Kinsbourne opined that either a viral infection or an administered vaccination could work in concert with a neuroblastoma to cause OMS:

> "[T]he fact that almost every child with neuroblastoma does not get this condition needs an explanation . . . so there should be [. . .] some second factor . . . and there is a general opinion that a second factor could be always a further challenge to the immune system, such as a substantial infection or immunization, which is given deliberately to operate the immune system."

Id. at 35-36. Dr. Kinsbourne testified that in cases involving a neuroblastoma, an antecedent vaccination or an antecedent virus could be a factor substantially contributing to the development of OMS. Id. at 36.

Important to Dr. Kinsbourne's theory in this case is the time between Lenzie's vaccinations and the development of the symptoms of her OMS. As discussed in Section II.B.1.c of this opinion, Dr. Kinsbourne identified Lenzie's ataxia as her first symptom of OMS. Tr. at 38-39. He testified that the appearance of Lenzie's symptoms after her vaccinations (both of which contain attenuated viruses) suggested that the vaccinations substantially contributed to the development of her OMS. Tr. at 36-37, 39. He further testified that live viral infections are particularly apt "to cause the kind of relapses" that Lenzie experienced. Id. at 38. Dr. Kinsbourne asserted that a child with OMS should never be given an attenuated viral vaccination (also known as a live virus vaccination). Id.

He opined that Lenzie's vaccinations interacted with her neuroblastoma to trigger Lenzie's OMS. Tr. at 39, 63-65; Pet. Ex. 23 at 4. In Dr. Kinsbourne's view, Lenzie's neuroblastoma had been present for a long time before it was discovered. Pet. Ex. 23 at 4. The presence of the subclinical neuroblastoma in Lenzie's body had stimulated an immune response. Id. The received vaccinations created an additional challenge to Lenzie's immune system that "destabilized" the already mounted immune response and raised the immune response "to a clinical level of autoimmunity." Id. That induced autoimmunity led to the development of Lenzie's OMS. Id.

Dr. Kinsbourne discounted the effect of the "incessant succession of infections and

runny noses" that Lenzie had prior to and around the time of her vaccinations on the development of her OMS. Id. at 40. He asserted that the infections were an unlikely trigger for Lenzie's OMS because he would have expected Lenzie to have reacted to those infections earlier in time. Id. Lenzie was treated at least nine times between May and November 2004 for painful ear infections; she received the vaccinations at issue in this case in late December 2004. See Pet. Ex. 3B at 3-13; Joint Stip., ¶ 3; Pet. Ex. 3B at 14. Dr. Kinsbourne testified that had the infections been a contributing factor in the development of Lenzie's OMS, he would have expected Lenzie to have reacted "as much as two months earlier at the very least." Tr. at 40. During cross-examination, Dr. Kinsbourne further testified that the viral infection that preceded the development of Lenzie's OMS was not identified. Tr. at 46. He reasoned that because the commonest virus that affects the upper respiratory system is the adenovirus, which is not a neurotropic virus (the type of virus more likely to trigger OMS), he had less confidence that the antecedent viral infections "were the provocative factor." Tr. at 40-41, 46.

2. Respondent's Expert Opinion

Challenging the opinion expressed by Dr. Kinsbourne, respondent offered the opinion and testimony of John MacDonald, M.D., a board-certified pediatric neurologist. Tr. at 67; Resp't. Ex. B. Dr. MacDonald works primarily at the University of Minnesota; but he still has a part-time private practice that he is in the process of phasing out. Tr. at 67. At the University, Dr. MacDonald's responsibilities include covering inpatient services, seeing outpatients, and seeing children with neurological problems. Id. Engaged in clinical practice for more than 37 years,[44] Dr. MacDonald is well-qualified to address neurological matters. Resp. Ex. B at 1. His testimony was clear and direct.

Dr. MacDonald does not dispute that the eventual diagnosis of Lenzie's condition as OMS was proper one. However, in his opinion, Lenzie's OMS was not caused by the vaccinations she received on December 22, 2004. Tr. at 70, 73, 75.

Dr. MacDonald testified that Lenzie's condition falls into the category of "paraneoplastic syndromes." Id. at 67. Such syndromes, Dr. MacDonald explained, involve an autoimmune reaction to a specific tumor. Id. He disagreed with Dr. Kinsbourne's view that the vaccinations substantially aggravated Lenzie's underlying immunological condition causing OMS. He asserted that "the clear-cut obvious cause to me is [the] neuroblastoma [. . . .] [T]he search for a tumor is . . . the most important part of [addressing] this [condition]." Id. at 68. He described the cause of Lenzie's illness in

[44] Dr. MacDonald completed his pediatric fellowship in 1971. Respondent's Exhibit (Resp. Ex.) B at 1.

explicit terms: "In this case, the neuroblastoma caused [Lenzie's] neurological picture." Id. at 70. Dr. MacDonald explained that the antigens[45] in Lenzie's neuroblastoma matched the antigens in Lenzie's cerebellum and triggered an immunological attack on that region of her brain. Id.

Dr. MacDonald's theory of causation involved "three actors," specifically, the normal immune system, the tumor, and the nervous system, to produce the neurological effects associated with OMS. Id. at 69, 73. Rejecting Dr. Kinsbourne's testimony that the received vaccinations further challenged Lenzie's immune system--which was already primed by the presence of a neuroblastoma and an ongoing viral infection, Dr. MacDonald stated:

> Unlike Dr. Kinsbourne, I don't need another actor on the stage. I don't care about the virus. I don't care about the vaccine. I have enough just because it's a neuroblastoma. . . [I]f I'm being asked to be reasonable to a medical degree of certainty, all I need is the tumor. This explains it. . . . The rest of it to me is, at best, academic."

Id. Dr. MacDonald explained that the presence of the tumor is what induces the normal immunological system to produce anti-neural antibodies. Id. at 74. In a small number of cases, the anti-neural antibodies produced by a neuroblastoma adversely affect the brains of the individuals with the tumors. Id. No additional "triggering" factor is necessary, according to Dr. MacDonald. Id. The biological mechanism triggering Lenzie's OMS symptoms was the tumor and not the immunizations or the infections. Id. at 75.

When asked to address the nine-month period of time during which Lenzie exhibited various neurological symptoms before the discovery of her neuroblastoma, Dr. MacDonald explained that given the size of the central nervous system, a significant period of time can elapse before a tumor is discovered even though the tumor might be causing noticeable symptoms. Id. at 79. He further explained that "the tumor elicits the expected response from the normal immune system . . . [a]nd then for some reason, some chemical part of that tumor overlaps with another area, typically the brain. And then as the immune system finds that, the symptoms start. The tumor may take a long time to otherwise make itself known." Id. at 80. Responding to additional questioning about the

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[45] An antigen is "any substance capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T lymphocytes, or both." Dorland's at 103.

onset of Lenzie's symptoms, Dr. MacDonald commented that the timing of Lenzie's onset was not curious and that Lenzie's clinical presentation was normal for a neuroblastoma. Id. at 82-83.

Dr. MacDonald expressed skepticism about the causal relationship, proposed by Dr. Kinsbourne, between Lenzie's vaccinations and the onset of her OMS. Id. at 83. But upon further questioning by the undersigned, Dr. MacDonald acknowledged the possibility of a causal relationship between a viral infection and OMS in the absence of a neuroblastoma, but he refused to credit viruses or vaccines as the most significant causal factors in the development of OMS. Id. at 96-97. He noted that viral exposure is not infrequent in young children and young children typically are exposed to multiple infections, most of which are viral. See id. at 86-87. Moreover, he stated:

> I haven't been convinced [that vaccines can cause OMS]. But I'm willing to say they're possible, in some cases maybe. We blame viruses, usually. They're blamed for[] anything we don't know[,] we blame on a virus it seems. . . . I think if you're going to blame a vaccine, or a virus, it would be a little more [] convincing for me if this was a patient that had AIDS, or this was a patient that had some other innate problem with their immune system.

Tr. 84-86. (emphasis added).

Of the opinion that viruses are not the likely triggers for OMS in individuals who do not have a neuroblastoma and who do not have severely compromised immune systems, Dr. MacDonald asserted, "[T]he only cause [of OMS] that I have confidence in, to a reasonable degree of medical certainty[,] is tumors." Id. at 98. Accordingly, he expressed doubt about petitioner's theory that Lenzie suffered relapses of her OMS symptoms after the removal of her neuroblastoma as a result of her subsequent viral infections. Id. at 100-01.

C. Evaluating the Presented Evidence

As stated earlier, petitioner must prove causation by showing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing the vaccination was the reason for the injury; and (3) a proximate temporal

relationship between the vaccination and the injury. Althen, 418 F.3d at 1278. The undersigned addresses each of the prongs of the Althen standard in turn.

1. Petitioner's Offered Medical Theory

In support of the medical theory of causation proposed by petitioner, petitioner's expert, Dr. Kinsbourne, relied primarily on articles that were authored by Dr. Pranzatelli and were filed as exhibits in this case. In the filed articles, Dr. Pranzatelli considered whether OMS might have an immunologic basis. See Pet. Ex. 17 at 2. He further considered the possibility that viruses and vaccinations might have a role in triggering the autoimmune-type process that leads to the development of OMS. See Pet. Ex. 16C at 7 (identifying tumors and viral infections as causes of OMS); Pet. Ex. 18 at 1-3; Pet. Ex. 19 at 17 (identifying neuroblastoma and viral infections as the most common causes of OMS in children).

Respondent's expert, Dr. MacDonald, acknowledged the possibility that in particular cases, viruses could cause OMS in the absence of a tumor. The particular cases to which he referred were ones involving either AIDS patients or patients with innate immunological problems; in either event, the particular circumstances that he contemplated involved patients with compromised immunological systems. Dr. MacDonald made clear, however, that although he was willing to entertain the possibility that in certain immunologically susceptible patients, viruses could contribute to the development of OMS, he was not persuaded that vaccinations could have the same effect.

The support for a finding that viruses and, according to petitioner, vaccinations as well might contribute to the development of OMS derives from the opinions of the parties' experts and the opinion of Dr. Pranzatelli on whose opinion Dr. Kinsbourne has based his opinion. It appears that in the absence of a more complete understanding of OMS, support for the offered opinions is derived, in part, by reports that, in some cases, viral symptoms or immunizations have preceded the onset of OMS symptoms. See Pet. Ex. 17 at 16, 19-20, 22; see also Pet. Ex. 18 at 1-2 (viral etiology inferred in OMS cases in children without "a demonstrated tumor . . . often based on a 'viral prodrome' consisting of upper respiratory or gastrointestinal symptomatology"). Petitioner has presented evidence that supports a finding that viruses and vaccinations containing attenuated viruses can cause OMS. Having presented a medical theory with biological plausibility, petitioner has satisfied the first prong of Althen.

2. The Sequence of Cause and Effect

The Federal Circuit has observed that an offered medical theory is persuasive when accompanied by "'proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury[,]' the logical sequence being supported by 'reputable medical or scientific explanation [,]' i.e., 'evidence in the form of scientific studies or expert medical testimony[.]'" Althen, 418 F.3d at 1278 (quoting Grant, 956 F.2d at 1148)).

Both petitioner and respondent have filed literature indicating that OMS has been associated with both tumors and viruses. Pet. Ex. 17 at 26; Pet. Ex. 18 at 1-2; Respondent's Exhibit (Resp. Ex.) A3 at 1. As Dr. Pranzatelli observed in Petitioner's Exhibit 17, "[g]iven the diversity of etiologic agents in OMS, the most economical interpretation of the data is that the mechanism of anti-tumor or anti-viral immunity, however different at the outset, may share the same final common pathway, one that leads to an autoimmune brain disorder." Pet. Ex. 17 at 20.

A review of the supporting literature filed in this case indicates that most of the medical literature filed in this case that addresses the non-tumor causes of OMS is either authored by or co-authored by Dr. Pranzatelli. That the weight of petitioner's supporting evidence comes primarily from one source is not necessarily disqualifying. Petitioner need only support her theory with a "sound and reliable medical or scientific explanation." Knudsen, 35 F.3d at 548. That such evidence comes from one source may be sufficient provided that the offered opinion supported by that source is connected to existing data by more than the mere statement that there is a connection. See General Elec. Co. v. Joiner, 522 U.S. at 145. In evaluating the reliability of the views held by Dr. Pranzatelli, an important consideration to the undersigned is that the research performed by Dr. Pranzatelli has not been discredited, to the knowledge of the undersigned, in the last three years.

Moreover, respondent has not filed any evidence that squarely contradicts petitioner's position. Rather, respondent has elected to focus on one particular causal factor known to lead to the development of OMS. Specifically, respondent maintains that the presence of the tumor alone is sufficient for causation. Although respondent has preferred to focus narrowly on the established association between a detected neuroblastoma and the development of OMS, respondent's expert did acknowledge the possibility that viruses could cause OMS in certain cases in which no tumor was found.

Moreover, as stated earlier, the authors of one of the articles filed by respondent acknowledge that the condition of OMS is associated with viral infections and particular tumors. See Resp. Ex. A3 at 1.[46]

Petitioner's expert, Dr. Kinsbourne, made clear during his testimony that in the absence of medical certainty, the evidence supporting a finding of vaccine-related causation was "circumstantial." Tr. at 47. He stated that Lenzie's immune system was activated initially by the presence of a yet undetected neuroblastoma and by an "incessant succession of ear infections and runny noses" between October 9, 2004 and December 22, 2004, the date of Lenzie's vaccinations. See Tr. at 40, 45-46, 52, 54 (pointing to Lenzie's tumor and the "panoply of infections" that she endured during the ten weeks preceding the receipt of her vaccinations as contributing factors to Lenzie's injury but not "the provocative factor"); see also Pet. Ex. 23 at 3-4 (noting that at the time that Lenzie received the vaccines at issue here, her immune system was in an already activated state due to the presence of a yet undiscovered tumor). When Lenzie presented to her pediatrician's office for her scheduled examination and to receive the MMR and varicella vaccines, Lenzie had a runny nose (rhinorrhea) and an upper respiratory infection. Pet. Ex. 23 at 1; Pet. 3B at 14. Dr. Kinsbourne explained that the vaccinations Lenzie received further "up-regulated" her already "up-regulated" immune system to cause a self-directed attack on her nervous system. See Tr. at 47, 52; see also Pet. Ex. 23 at 4. Dr. Kinsbourne emphasized that the appearance of the clinical condition of OMS provides no information about the nature of the cause--whether a tumor or a virus or a vaccination. See Tr. at 50. He opined, to a reasonable degree of medical probability, that Lenzie's vaccinations were causal factors that substantially contributed to her neurological condition. See id.; Tr. at 39. He also opined that but for the receipt of the MMR and varicella vaccinations, Lenzie was unlikely to have developed OMS. Tr. at 37.

Dr. MacDonald discounted the theory that a viral infection and/or an attenuated viral vaccination could work synergistically with a pre-existing tumor to trigger an overreactive immune response that leads to an autoimmune-type response and in turn, to the development of OMS. See Tr. at 72-75, 78-79, 84. Acknowledging his own interest in providing treatment rather than ascertaining what causal factors lead to the development of OMS, Dr. MacDonald dismissed as speculative the presented evidence that cases of OMS have been reported in which no tumor was found and the onset of the disorder followed a viral infection. Tr. at 93-94, 96. Dr. MacDonald stated that in such

[46] The full citation of the article is A. Klein, et al., Long-term Outcome of Ten Children with Opsoclonus-Myoclonus Syndrome, Eur. J. Pediatr. 166:359-363 (2007).

circumstances, he would worry that a tumor did exist but had eluded detection. See id.

In the view of the undersigned, the vehemence of Dr. MacDonald's expressed concern that OMS in the absence of a tumor suggests only that one has not yet found the tumor makes him a valued practitioner but does not render petitioner's theory a less than likely one. Consistent with the requirements of Althen, petitioner has offered a medical explanation that logically links a vaccine-related cause and to the observed injury in this case, see Althen, 418 F.3d at 1278; see also Grant, 956 F.2d at 1148, and the offered explanation is biologically plausible albeit not medically certain, see Knudsen, 35 F.3d at 548-49. As the Federal Circuit observed in Althen, 418 F.3d at 1280, "the purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof of how vaccines affect the human body."

On examination of the facts of this case and in the absence of evidence that demonstrates otherwise,[47] the undersigned is persuaded that petitioner has presented a

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[47] As the Federal Circuit stated in Knudsen, "[c]ausation in fact under the Vaccine Act is . . . based on the circumstances of the particular case." 35 F.3d at 548. The Federal Circuit later reiterated in Althen that "[t]he special master's role is to assist the courts by judging the merits of individual claims on a case-by-case basis." Althen, 418 F.3d at 1281. A review of vaccine claims involving the injury of OMS reflects that, in fact, case-by-case determinations have been made.

In Mulvaney v. Secretary of the Department of Health and Human Services, No. 05-556 V, 2006 WL 2438454 (Fed. Cl. Spec. Mstr. 2006), the vaccinee received his first MMR vaccination at one year of age and received a second MMR (as well as DTaP and inactivated polio vaccinations) when he was five years of age. He fell nine days later, and twenty days after he received the vaccinations, his mother took him to be evaluated because he had been falling frequently for the last five days. The child was diagnosed as having OMS. The parties presented the expert testimony of two neurologists, Dr. Marcel Kinsbourne for petitioners and Dr. Michael Kohrman for respondent. The special master concluded that petitioner's theory of causation, similar to the theory advanced in this case, supported a finding of entitlement on the facts of the case.

In contrast, in Tosches v. Secretary of the Department of Health and Human Services, No. 06-192 V, 2008 WL 440285 (Fed. Cl. Spec. Mstr. 2008), the vaccinee received his fourth dose of DTaP, a third inactivated polio, and a fourth Hib vaccination at eighteen months of age. Petitioners implicated only DTaP in the vaccine claim. Ten days after vaccination, the child began to exhibit symptoms of ataxia and was eventually diagnosed with OMS. The parties presented the expert testimony of two pediatric neurologists, Dr. Marcel Kinsbourne for petitioners and Dr. John MacDonald for respondent. Additionally, the parties presented the

logical sequence of cause and effect that satisfies the second prong of Althen.

3. The Temporal Relationship between the Vaccination and the Injury

Petitioner must show more than a proximate temporal relationship between the vaccination and the injury to satisfy the burden of showing actual causation. Althen, 418 F.3d at 1278; see also Grant v. Secretary of Health and Human Services, 956 F.2d 1144, 1148 (Fed. Cir. 1992). Specifically, petitioner must demonstrate that the first symptoms of Lenzie's OMS occurred in a time frame that would be consistent with an immune-mediated disorder caused by the vaccinations at issue.

Dr. Kinsbourne testified that the appropriate period of time within which an autoimmune response might be expected is within six weeks of the event or exposure generating an immune response. See Tr. at 54, 58-59. He added that "most . . . events occur within the first . . . two weeks." Id. at 59.

An important component of Dr. Kinsbourne's theory of causation was the timing between Lenzie's vaccinations that, according to Dr. Kinsbourne, enhanced the immunological effects of the existing tumor, and the onset of Lenzie's symptoms of OMS. See Tr. at 38-39. Lenzie had a shaking episode three days after her receipt of the vaccinations, and she developed a noticeable ataxic gait nine days after she received the MMR and varicella vaccinations. Tr. at 8; Pet. Ex. 3b at 14; Pet. Ex. 6 at 2. Lenzie's earliest symptoms of OMS occurred within the medically appropriate time frame for an autoimmune-type reaction triggered by the received vaccinations.

Additionally, another important component of Dr. Kinsbourne's theory of causation was the onset of Lenzie's OMS within the appropriate "window of

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expert testimony of two immunologists, Dr. Vera Byers for petitioners and Dr. Christine McCusker for respondent. The special master found the testimony of respondent's immunologist far more persuasive than that of petitioners' immunologist and declined to find entitlement on the facts of that particular case.

Of further note, the facts in Tosches are distinguishable from the facts in Mulvaney and in the instant case by the nature of the involved vaccine. In Tosches, the implicated vaccine was the DTaP vaccine which does not contain an attenuated live virus as do the MMR and varicella vaccines.

vulnerability." See Tr. at 54. That window of vulnerability is between nine months and two to three years of age. See Tr. at 55. Because Lenzie was twenty-five months of age when she presented with symptoms of OMS, see Joint Stip. ¶¶ 1, 3, 5, she was in the "right" developmental stage when she developed OMS, see Tr. at 55.

Here, petitioner has established a temporal association between Lenzie's vaccinations and her injury that satisfies the third prong of Althen.

II. CONCLUSION

For the foregoing reasons, the undersigned finds that petitioner has established entitlement to Program compensation for Lenzie's opsoclonus-myoclonus syndrome. The parties shall contact the undesigned's law clerk, Camille Collett, at (202) 357 - 6361 **on or before July 24, 2009**, to schedule a status conference to address the determination of damages.

IT IS SO ORDERED.

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Patricia E. Campbell-Smith
Special Master