In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: June 6, 2017

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SHELAINE HARMON,	No. 12-298V
Petitioner,	Chief Special Master Nora Beth Dorsey
v.	
SECRETARY OF HEALTH AND HUMAN SERVICES,	Entitlement; Off-Table Injury; Human Papillomavirus ("HPV") Vaccine; Gardasil; Central Nervous System ("CNS") Demyelinating Disorder.
Respondent.	
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Edward Kraus, Chicago-Kent School of Law, Chicago, IL, for petitioner.
Robert Paul Coleman, III, United States Department of Justice, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

I. Introduction

On May 8, 2012, Shelaine Harmon ("petitioner") filed a petition under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"),[2] 42 U.S.C. § 300aa-10 et seq. (2012), alleging that she developed a chronic autoimmune demyelinating illness as a result of receiving the Gardasil vaccination for the human papillomavirus ("HPV") (referred to hereafter as "the HPV vaccine") on June 4, 2009. Petition at 1. Respondent recommended against compensation, stating that petitioner had not presented preponderant evidence that the HPV vaccine caused her injuries. Respondent's Report ("Resp. Rep't") dated August 10, 2012 (ECF No. 7) at 16.

[1] Because this ruling contains a reasoned explanation for the action in this case, I intend to post this ruling on the website of the United States Court of Federal Claims, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 note (2012)(Federal Management and Promotion of Electronic Government Services). As provided by Vaccine Rule 18(b), each party has 14 days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b).

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 -34 (2012). All citations in this decision to individual sections of the Vaccine Act are to 42 U.S.C. § 300aa.

Each party submitted several reports in support of their position. Petitioner filed several reports from Dr. Yehuda Shoenfeld, a clinical immunologist. Petitioner's ("Pet.") Exhibits ("Exs.") 40, 51, 52. Petitioner also filed a report from Dr. Nizar Souayah, a neurologist. Pet. Ex. 70. Respondent filed two expert reports from Dr. Thomas P. Leist, as well as reports from Dr. J. Lindsay Whitton and Dr. Edward W. Cetaruk. Resp. Exs. A, C, E, G, I. An entitlement hearing was held on July 20, 2016. Petitioner and Dr. Souayah testified for petitioner. Dr. Leist testified for respondent. Respondent filed his post-hearing brief on November 21, 2016. Brief dated Nov. 21, 2016 (ECF No. 97). Petitioner filed her post-hearing brief on November 22, 2016. Brief dated Nov. 22, 2016 (ECF No. 98). This matter is now ripe for adjudication.

After carefully analyzing and weighing all of the evidence and testimony presented in this case in accordance with the applicable legal standards, the undersigned finds that petitioner has met her legal burden. Petitioner has put forth preponderant evidence that the HPV vaccine caused her to suffer a chronic autoimmune demyelinating illness. Furthermore, respondent has failed to put forth preponderant evidence that petitioner's injury was in fact caused by factors unrelated to the HPV vaccine. Accordingly, petitioner is entitled to compensation.

II. Issues to be Decided

In their joint pre-hearing submission, filed on July 8, 2016, the parties stipulated that: petitioner had not received an HPV vaccination prior to June 4, 2009; petitioner received the HPV vaccine on June 4, 2009; and petitioner has suffered from a central nervous system ("CNS") inflammatory demyelinating condition since at least early August 2009. The parties identified two initial factual issues: the precise diagnosis of petitioner's inflammatory demyelinating condition; and the onset of petitioner's symptoms. Joint Submission dated July 8, 2016 (ECF No. 83) at 1. Further, the parties asked the undersigned to resolve whether the HPV vaccine administered to petitioner on June 4, 2009, was the cause of her CNS inflammatory demyelinating condition. Id.

III. Procedural History

Petitioner filed her petition for compensation on May 8, 2012. Petition dated May 8, 2012 (ECF No. 1). On August 10, 2012, respondent filed a report under Vaccine Rule 4(c), stating that this case was not appropriate for compensation because petitioner had not presented sufficient evidence of causation. Resp. Rep't (citing Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005). Respondent argued that petitioner had offered no theory of how the HPV vaccine caused her atypical autoimmune demyelinating illness. Id. at 15. Respondent also argued that none of petitioner's treating physicians attributed her condition to the HPV vaccine. Id. Respondent further argued that petitioner's first episode occurred within two months of the vaccination, but her subsequent episodes were too remote in time to be related. Id. Finally, respondent asserted that petitioner did not demonstrate that other possible causes were less likely. Id.

Thereafter, the case proceeded on a litigation track where the parties filed expert reports. On November 7, 2012, petitioner filed a report from Dr. Yehuda Shoenfeld. Pet. Ex. 36 dated Nov. 7, 2012 (ECF No. 11). Petitioner subsequently filed supporting medical literature.

On May 1, 2013, respondent filed expert reports and curricula vitae from Dr. J. Lindsay Whitton and Dr. Thomas P. Leist. Resp. Exs. C, D. On June 27, 2013, respondent filed an expert report and supporting medical literature from Dr. Edward W. Cetaruk. Resp. Ex. E.

On November 5, 2013, petitioner filed Dr. Shoenfeld's second report in response to Dr. Cetaruk and his third report in response to Dr. Whitton. Pet. Exs. 51, 52. On May 9, 2014, respondent filed responsive reports and additional medical literature from Dr. Whitton and Dr. Cetaruk. Resp. Exs. E, G.[3]

On February 10, 2015, petitioner filed an expert report from Dr. Nizar Souayah. Pet. Ex. 70. Petitioner filed additional medical records on June 15, 2015. ECF No. 51. On August 10, 2015, respondent filed a second report from Dr. Leist. Resp. Ex. I (ECF No. 57).

On September 3, 2015, the special master then presiding over the case scheduled an entitlement hearing for July 20 and 21, 2016. Prehearing Order dated Sept. 3, 2015 (ECF No. 59). Petitioner filed her initial pre-hearing submissions on April 27, 2016. On May 31, 2016, the case was transferred to the undersigned. Petitioner filed additional prehearing submissions and medical literature on May 25, 2016. Respondent filed pre-hearing submissions and one additional piece of medical literature on May 25, 2016. Petitioner filed a reply to respondent's pre-hearing submissions on June 9, 2016.

On July 8, 2016, the parties filed a joint pre-hearing submission. Resp. Joint Prehearing Sub. dated July 8, 2016 (ECF No. 83). On the same day, they also filed a joint list of terms. A hearing was held on July 20, 2016, during which the undersigned heard testimony from petitioner, petitioner's expert Dr. Souayah, and respondent's expert Dr. Leist. Updated curriculum vitae for Dr. Souayah and Dr. Leist were filed on August 5, 2016. Respondent filed his post-hearing brief on November 21, 2016, and petitioner filed her post-hearing brief the following day. Accordingly, this matter is now ripe for adjudication.

IV. Summary of Relevant Facts[4]

Petitioner was born on October 26, 1987. Pet. Ex. 1 at 1. According to the medical records, petitioner's father's side of the family had a history of cerebral palsy and her mother had a history of atypical migraines. Pet. Ex. 24 at 69; Pet. Ex. 32 at 6. Petitioner stated that she had "frequent" headaches but "[her] mother is the one that had the migraines." Tr. 37. Petitioner stated that when she was fourteen years old, she began consuming tobacco and marijuana. Pet. Ex. 22 at 31. She smoked "one pack per day in high school," and "1/2 ppd" at the time of the vaccination. Pet. Ex. 24 at 69; Pet. Ex. 22 at 31. She reported smoking marijuana "once in a month." Pet. Ex. 22 at 31. In June 2009, petitioner was 21 years old, living independently, and working full-time as an assistant manager of a retail jewelry store. Pet. Ex. 39, Petitioner's Affidavit, ("Pet. Aff.") at 1; Tr. 6.

[3] The expert reports of Dr. Shoenfeld, Dr. Whitton, and Dr. Cetaruk all discuss petitioner's first causation theory, which focused on autoimmune inflammatory syndrome (also known as the "ASIA" theory). During a status conference held on May 5, 2015, petitioner clarified that she intended to abandon this theory and proceed only on the theory of causation as presented by Dr. Souayah. Order dated May 5, 2015 (ECF No. 48). Once petitioner abandoned the ASIA theory of causation, the expert opinions of Dr. Whitton and Dr. Cetaruk were no longer relevant and thus they were not called to testify at the hearing.

[4] Although the undersigned considered the record as a whole in reaching her decision, this section reviews only the most relevant facts. A more detailed recitation of the facts may be found in respondent's Rule 4(c) Report and the parties' pre-hearing submissions.

On June 4, 2009, petitioner presented to her gynecologist, Dr. Nelson Lehrer, with complaints of vaginal discharge, and she was diagnosed with molluscum contagiosum[5] of the vulva. Pet. Ex. 2 at 3. Dr. Lehrer did not see any signs of HPV. Id. He then administered the first dose of the HPV vaccine. Id. Petitioner stated that there was "no discussion about the vaccine being delayed because of [her] having molluscum contagiosum." Tr. 8.

"A few days, or a week or two later," petitioner began experiencing "pain shooting from [her] right hip down into her foot." Pet. Aff. at 1; Tr. 10. "A couple of weeks after that, sometime around mid-July of 2009, [her] hip stopped hurting," but she "began experiencing numbness in [her] right foot." Pet. Aff. at 1; Tr. 10. Petitioner "had not done anything to injure [her] foot." Pet. Aff. at 1; Tr. at 11. She was concerned about these symptoms but did not go to a doctor at that time because she did not have health insurance. Pet. Aff. at 1; Tr. 11. Instead, she "tried to change how [she] walked to accommodate for the numbness." Pet. Aff. at 1; Tr. 12.

On August 2, 2009, petitioner woke with a terrible headache, photosensitivity, and nausea. Pet. Aff. at 2; Pet. Ex. 22 at 20, 30. On August 3, 2009, she went to work, but "couldn't get anything done because [she] couldn't see people in [her] periphery and [she] kept stumbling on things on or around the floor." Pet. Aff. at 2. She "nearly fell off a ladder when [her] right leg went limp." Id.

On August 4, 2009, petitioner again awoke with a terrible headache, which she described as a "wicked migraine." Tr. 15. That day, based on the headaches and continuing difficulty with her peripheral vision, petitioner decided to seek medical attention. Id. at 13-15; Pet. Aff. at 2. She first went to a walk in clinic, where an optometrist "said there was nothing wrong with [her] eyes." Tr. 12-13. Petitioner was then transferred to the emergency room at John H. Stroger, Jr. Hospital in Chicago, Illinois. Pet. Aff. at 2; Pet. Ex. 22 at 22-23; Tr. 37. Petitioner reported to her treating physician, Dr. Asbury, that she had experienced a headache for about three days and that she had lost her peripheral vision in her left eye. Pet. Ex. 22 at 28. She stated that approximately three weeks prior,[6] she awoke feeling "woozy" and her limbs felt heavy, which then transitioned into tingling in her right leg and foot. Id. at 28-29. She further reported that the tingling in her leg and foot eventually transitioned to numbness in the top of her foot and her second and third toes. Id. at 29. Dr. Asbury described petitioner in his assessment as:

> Young healthy woman with two neurologic episodes,[7] the second suggesting lesion in right visual pathway between chiasm and temporal lobe, but without any other associated deficits. Given her age and two separate episodes, strongly suspect [multiple sclerosis] ("MS"). Tumor is a possibility, though head CT negative.

[5] Molluscum contagiosum is defined as "a common, benign, usually self-limited viral infection of the skin and occasionally the conjunctivae by a poxvirus, transmitted by autoinoculation [or] close contact." Dorland's Illustrated Medical Dictionary ("Dorland's") (32d ed. 2012) at 1174.

[6] Three weeks prior would have been mid July 2009.

[7] Based on the history documented by Dr. Asbury, his reference to two neurological episodes indicates that the first episode occurred three weeks prior, in July, when petitioner's limbs felt heavy and she began having tingling in her right leg and foot. The second episode appears to be the events in August, including headache and visual loss.

> Cerebrovascular event unlikely given age but has a family history of [cerebrovascular accident] ("CVA"). Anneurysm [sic] with small bleed?

Id. Dr. Asbury ordered magnetic resonance imaging ("MRI") and computed tomography ("CT") scans, a neurology consult, and a lumbar puncture "for confirmatory studies." Id. The CT scan, performed that day, was unremarkable. Pet. Ex. 21 at 119-34; Pet. Ex. 22 at 30-32. On August 5, 2009, petitioner underwent MRIs of the brain with and without contrast. Pet. Ex. 23 at 36-37. The reading radiologist, Dr. Anuj Patel, wrote:

> Cerebral and cerebellar hemispheres are morphologically unremarkable. There is no acute hemorrhage or hydrocephalus.
>
> There is a 13 x 12 mm focus of high T2, high flair signal in the deep white matter of the left parietal high convexity, extending to the subcortical white matter. This lesion demonstrates restricted diffusion. There is subtle, interrupted peripheral contrast enhancement, without significant perilesional edema.
>
> There is an additional small focus of high T2, high flair signal in the medial aspect of the left occipital lobe, which does not demonstrate contrast enhancement.
>
> No mass effect or midline shift. No other regions of abnormal contrast enhancement.

Pet. Ex. 23 at 37. Dr. Patel wrote that these findings suggested "active MS plaque versus less likely vasculitis or low grade neoplasm." Id. On August 7, 2009, Dr. Asbury, who first evaluated petitioner in the ER, wrote that the enhancing lesion in the parietal area "might be [consistent with] right leg/ foot sensory changes, though not left temporal hemianopsia."[8] Id. at 1.

On August 6, 2009, petitioner underwent a lumbar puncture, during which cerebrospinal fluid ("CSF") was obtained for analysis.[9] Pet. Ex. 23 at 23-28. The analysis found an elevated immunoglobulin G ("IgG")[10] index and at least three oligoclonal bands in the CSF, compared to none in the serum sample.[11] Id. at 28. Petitioner remained in the hospital, did not improve, and was discharged on August 11, 2009. Pet. Ex. 22 at 25. The primary discharge diagnosis was MS. Id. at 26.

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[8] Hemianopsia is defined as "defective vision or blindness in half of the visual field of one or both eyes." Dorland's at 835.

[9] A CSF analysis is an "evaluation for the presence of blood, bacteria, and malignant cells, as well as quantification of the amount of glucose and protein present." It can assist in diagnosing demyelinating disorders and autoimmune diseases. Mosby's Manual of Diagnostic and Laboratory Tests 683-84 (4th ed. 2010).

[10] IgG is a glycoprotein that functions as an antibody. Dorland's at 919.

[11] Oligoclonal bands are "discrete bands of immunoglobulins … their appearance in … cerebrospinal fluid when absent in the serum is a sign of possible multiple sclerosis or other diseases of the central nervous system." Dorland's at 197.

Petitioner returned to work, but on her first day back, she realized that she could not see well enough to perform her duties. Pet. Aff. at 2; Tr. 16. Over the next two months, petitioner experienced headaches of increasing intensity. Pet. Ex. 21 at 64. On October 19, 2009, she developed slurred speech. Id. On October 20, 2009, she awoke with flailing movement in her limbs that eventually transitioned to a "terrible burning pain" and complete paralysis of the left side of her body, particularly affecting her face, arm, and leg. Id. at 64; Pet. Aff. at 2. Petitioner presented at the emergency room at Stroger Hospital the same day, where she was noted to have dysarthria;[12] left-sided weakness; paresthesia;[13] allodynia;[14] deficits in attention, concentration, and memory; and difficulty swallowing solid food. Pet. Aff. at 2; Pet. Ex. 18 at 9; Pet. Ex. 19 at 35, 44; Pet. Ex. 21 at 1, 6.

An MRI performed on October 21, 2009, showed a new, larger white matter lesion present in the right hemisphere with some progression and worsening of the previous left hemisphere lesion first identified on August 5, 2009. Pet. Ex. 21 at 3, 39, 95-96; Pet. Ex. 19 at 30. The interpreting radiologist reported, "right frontal and parietal and occipital cerebral white matter as well as[,] to a lesser extent[,] left frontoparietal and occipital cerebral white matter diffuse and confluent high T2/FLAIR/DWI/eADC and low ADC lesions,"… with the lesions "not demonstrat[ing] contrast enhancement." Pet. Ex. 21 at 3.

During this stay at the hospital, petitioner received five days of high dose intravenous ("IV") steroid treatment. Pet. Ex. 21 at 42. The treatment did not produce meaningful improvement and was discontinued after it seemed to induce psychosis. Id. at 12, 31, 39-40, 49. After the steroid treatment was withdrawn, petitioner's mental status improved significantly. Id. at 12. On November 2, 2009, she began seven cycles of plasmapheresis, which seemed to slowly improve her condition. Id. at 25, 29, 31, 39. Based on her non-response to steroids and her limited response to plasmapheresis, the treating physicians questioned the diagnosis of multiple sclerosis and suggested performing an open brain biopsy to assess the diagnosis. Pet. Ex. 13 at 31-42.

By November 14, 2009, petitioner was able to move her left leg and the fingers in her left hand. Pet. Ex. 21 at 12. A few days later, on November 17, 2009, petitioner was discharged from Stroger to begin acute rehabilitation at Oak Forest Hospital. Pet. Aff. at 2. On December 8, 2009, petitioner was discharged from Oak Forest Hospital as a modified independent. Id. at 3. Petitioner was able to ambulate for short distances with an ankle-foot orthosis ("AFO") on her left ankle and a quad cane but was still unable to use her left arm and required assistance from others with daily activities, including dressing, bathing, and cutting food to eat. Id.; Tr. 20.

During the beginning of 2010, petitioner was stable and managed a few improvements. Her walking abilities had improved to the point that she could ambulate approximately 90 feet and, at certain times, move around her home without the use of a cane. Pet. Ex. 14 at 28, 30. And, while a January 7, 2010 MRI revealed that lesions in the left hemisphere remained unchanged from the October 21, 2009 MRI, lesions involving the right frontal, parietal, temporal, and occipital areas had

[12] Dysarthria is "a speech disorder consisting of imperfect articulation due to loss of muscular control after damage to the central or peripheral nervous system." Dorland's at 575.

[13] Paresthesia is "an abnormal touch sensation, such as burning, prickling, or formication, often in the absence of an external stimulus." Dorland's at 1383.

[14] Allodynia is "pain resulting from a non-noxious stimulus to normal skin." Dorland's at 51.

all progressed further. Id. at 23; Pet. Ex. 12 at 23. A lumbar puncture performed on January 20, 2010, demonstrated glucose 57, protein 24, chloride 127, red cells 1225, and white cells 207. Pet. Ex. 14 at 12-16.

Petitioner experienced a relapse on March 4, 2010, when she awoke and was unable to move her right arm. Pet. Aff. at 3. Although she was able to walk to Stroger Hospital, her symptoms escalated to painful muscle spasms. Id. She presented to the hospital with right upper extremity paralysis and spastic movement of the left side of the body. Pet. Ex. 11 at 4. A CT scan showed a new left precentral gyrus lesion and an MRI revealed worsening lesions with new demyelination on the left side of the parietal lobe. Pet. Ex. 9 at 20; Pet. Ex. 12 at 6; Pet. Ex. 13 at 23.

During this hospitalization, it was noted that the lesions' "size, location, and relative lack of response… to steroids [were] atypical for multiple sclerosis." Pet. Ex. 11 at 24. Therefore, an infectious disease consult was ordered. Dr. Audrey French, an infectious disease specialist, approved the following opinion written by a medical student:

> In general, this would be atypical for an infectious or post-infectious disorder because of the relapsing course. A primary infection would most likely worsen progressively in the absence of therapy and especially in the presence of high-dose steroids.[15] A post-infectious demyelinating disorder would come on acutely, often would improve with steroid and would be unlikely to relapse.
>
> That having been said, this is a case that hasn't easily fit into diagnostic categories and it is reasonable to consider infectious possibilities even if unlikely. Acute disseminated encephalomyelitis is a demyelinating disorder that can occur after a variety of infections such as HSV, VZV, CMS, measles, influenza, enteroviruses and also some vaccinations. It doesn't sound as if she had an infection immediately prior to the onset of the illness but would be worth checking . . .

Id. On March 11, 2010, petitioner underwent a brain biopsy. Pet. Ex. 13 at 7-8. The findings were "not consistent with a demyelinating plaque of multiple sclerosis." Id. at 8. It was considered whether petitioner had a vasculopathy, "such as a treated vasculitis or CADASIL syndrome."[16] Id. However, "no active vasculitis was identified." Id. Subsequent genetic testing ruled out CADASIL. Id. at 14.

On March 24, 2010, petitioner was transferred from Stroger Hospital to Oak Forest Hospital for acute inpatient rehabilitation where she experienced insignificant improvement in the mobility of the right side of her body. Pet. Ex. 9 at 46; Pet. Ex. 25 at 3. Furthermore, she continued to suffer mild dysphagia, as well as dystonia in her left arm and left leg. Pet. Ex. 25 at 3. Nonetheless, she was discharged from Oak Forest Hospital on April 10, 2010. Id. at 1.

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[15] As previously noted, petitioner received five days of steroid treatment in October 2009, which did not have any impact on her condition except for inducing psychosis, and was therefore withdrawn. See Pet. Ex. 21.

[16] CADASIL is an abbreviation for Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy, a hereditary stroke disorder. Pet. Ex. 13 at 8.

On August 19, 2010, petitioner was admitted to Stroger Hospital for Cytoxan infusions which she had been routinely receiving since March 2010. Pet. Ex. 3 at 6; Pet. Ex. 26 at 19. On August 23, 2010, an MRI "showed bilateral frontal/parietal/occipital periventricular subcortical [white matter] foci on T2/Flair," and progression of the lesions in the corpus callosum. Pet. Ex. 26 at 19. Petitioner reported improvement with her right side hemiparesis, and on August 25, 2010, she was discharged to Schwab Rehabilitation Center for inpatient rehabilitation. Id. at 71; Pet. Ex. 3 at 6. On September 22, 2010, when petitioner was 22 years old, she was transferred for continuing care at East Ann Arbor Health and Geriatrics Center in Ann Arbor, Michigan, which was closer to her family. Pet. Ex. 3 at 1, 61; Pet. Aff. at 3; Tr. at 26.

On October 1, 2010, petitioner had an initial consult with Dr. John Fink, a specialist at the Neurogenetics Clinic at the University of Michigan. Pet. Ex. 1 at 1. Dr. Fink hypothesized that the nature of the illness, namely, the exacerbating and remitting course, the multifocality of the lesions, and the CSF findings, were most consistent with MS. Id. at 1-2. Dr. Fink then referred petitioner to Dr. Evanthia Bernitsas at the University of Michigan MS Clinic, who saw her on October 19, 2010. Pet. Ex. 24 at 68. Dr. Bernitsas suggested a diagnosis of vasculitis of autoimmune etiology, but requested an angiogram "to see the typical changes of vasculitis," and to "confirm the diagnosis." Id. at 70. At another appointment on November 12, 2010, Dr. Bernitsas further opined that petitioner had "primary angitis[17] of the central nervous system, since no secondary etiology is found." Id. at 57.[18] On January 7, 2011, Dr. Fink saw petitioner again and noted that he would "defer the treatment of [petitioner's] autoimmune vasculitis to Dr. Bernitsas." Id. at 30-31.

In March 2011, Dr. Joseph Hornyak at the University of Michigan's Physical Medicine and Rehabilitation Clinic noted that, despite undergoing both physical therapy and serial casting, petitioner's ankle did not tolerate the casting because of increasing tone. Pet. Ex. 28 at 11. He recommended Botox shots to her tibilias posterior, left gastrocnemius, and soleus muscle in hopes it would work on the dystonic posturing. Id. at 11. Petitioner continued receiving Botox injections in the lateral and medial head of her gastrocnemius and soleus, but the treatment was deemed unsuccessful. Id. at 72, 75. Finally, in September 2011, an orthopedist recommended tendon-lengthening surgery which petitioner eventually underwent. Pet. Ex. 30 at 5. As a result, the doctor noted marked improvement of the ankle. Pet. Ex. 66 at 67.

On September 20, 2011, Dr. Vessela Giger-Mateeva of the University of Michigan MS Center ordered MRIs of petitioner's brain and cervical spinal cord. Pet. Ex. 30 at 29. The brain MRI revealed "localized hyperintense signals … in the subcortical and deep white matter of the left frontoporietal region," as well as confluent hyperintense signals in the subcortical of the right side, with more localization of the signals in the subcortical on the left. Id. Overall, while the lesions appeared more prominent on the right side than the left, their distribution had not changed significantly since the prior MRI on October 28, 2010. Id. Furthermore, the spinal MRI revealed no lesions, T2 hyperintense signals, or morphological changes since the prior MRI. Id.

[17] Angitis (or "angiitis") is another term for vasculitis. Dorland's at 83.

[18] There is no medical record of petitioner undergoing an angiogram in or after October 2010. It is not clear whether this procedure ever occurred, although Dr. Bernitsas had recommended it in order to "confirm the diagnosis" of vasculitis.

Petitioner sought an additional opinion as to her diagnosis and management from Dr. Robert Lisak at the Detroit Medical Center, Harper Neurology Clinic. Pet. Ex. 32 at 9. Her first appointment with Dr. Lisak was on September 21, 2011. Id. Dr. Lisak recorded that petitioner "had a complicated medical history." Id. He mentioned that prior to onset, petitioner "was doing OK and had a HPV vaccine in July of 2009." Id. Petitioner had "white matter hyperintensities" of "unclear" etiology. Id. at 12. His three possible explanations were (1) vasculitis, (2) MS, or (3) "Schilder's disease, which is not an absolute entity and likely represent[s] several diseases."[19] Id. After the first visit, Dr. Lisak reviewed petitioner's MRI images. Id. at 1.

On January 18, 2012, Dr. Lisak saw petitioner again and recorded that the MRIs were "not classic for multiple sclerosis." Pet. Ex. 32 at 1. But he also expressed "significant doubts" about the diagnosis of vasculitis, because the MRIs "did not look like even longstanding CNS vasculitis" and the blood vessels from the brain biopsy did not show any vasculitis. Id. Dr. Lisak stated, "[Petitioner] has what one might expect from the classic Schilder's disease. As you know, she described what we now think are several entities including [Subacute Sclerosing Panencephalitis "(SSPE")],[20] [Adrenoleukodystophy ("ALD"],[21] and then perhaps [Acute Disseminated Encephalomyelitis ("ADEM")],[22] and then the final entity being probably some peculiar variant of MS, although I suppose in this modern era, we would say that she had not ruled out vasculitis, either." Id. at 3. Dr. Lisak decided to advance the administration of baclofen, while continuing azathioprine and low-dose steroids. Id. Dr. Lisak also included a note regarding the possible cause of petitioner's condition: "Her mother is convinced that since her first episode came on after a[n] HPV viral vaccination, that that might be related, but she clearly had her second episode quite remote from that." Id. at 2.

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[19] Schilder's disease is defined as "a subacute or chronic form of leukoencephalopathy of children and adolescents, characterized by massive destruction of the white substance of the cerebral hemispheres with cavity formation and glial scarring. Clinical symptoms include blindness, deafness, bilateral spasticity, and progressive mental deterioration. The disease as a separate diagnostic entity has been disputed." Dorland's at 542.

[20] SSPE is "a rare and devastating form of leukoencephalitis usually affecting children and adolescents. Insidious in onset, it characteristically produces progressive cerebral dysfunction over several weeks or months and death within a year. There is also demyelination with intranuclear inclusion bodies in nerve cells and oligodendroglia." Dorland's at 1368.

[21] ALD, also known as Addison-Schilder disease, is "an X-linked recessive disease of childhood … in which deficient peroxisomal fatty acid degradation results in the accumulation of very long chain fatty acids in the tissues. It is marked by progressive adrenal dysfunction and diffuse abnormality of the cerebral white matter, with neurologic degeneration leading to severe dementia and deterioration of speech, vision, hearing, and gait. Death occurs within a few years of onset." Dorland's at 32.

[22] ADEM is an acute or subacute encephalomyelitis or myelitis characterized by perivascular lymphocyte and mononuclear cell infiltration and demyelination …. It is believed to be a manifestation of an autoimmune attack on the myelin of the central nervous system. Symptoms include fever, headache, vomiting; sometimes tremor, seizures, and paralysis; and lethargy progressing to coma that can be fatal." Dorland's at 613.

On July 13, 2012, petitioner was seen by Dr. Giger-Mateeva at the University of Michigan MS Center. Pet. Ex. 42 at 41. Dr. Giger-Mateeva wrote:

> Initially, [petitioner] was given a diagnosis of [MS], which after the brain biopsy was changed to possible CNS vasculitis. Most recently, Dr. Lesak [sic], her local neurologist in [Detroit Medical Center,] … suggested that her diagnosis is Schilder's disease, a[n] MS spectrum disorder, and not CNS vasculitis. We agree that her clinical and radiological course are suggestive of relapsing-remitting MS, with extensive white matter lesions, as seen in Schilder's disease.

Id. at 42-43.

From 2012 until early 2015, petitioner was stable. Tr. 30. However, in spring 2015, petitioner was diagnosed with a respiratory infection, suffered a relapse, and presented to Detroit Medical Center. Pet. Ex. 72 at 39. Dr. Lisak saw her on an urgent basis on April 27, 2015. Pet. Ex. 72 at 39. He commented that petitioner's "original MRI scan… resembled the Schilder variant of multiple sclerosis," but "over the past few years, it actually improved, although it is still markedly abnormal." Id. A brain MRI on the following day, April 28, 2015, showed progression of the previously identified lesions as well as new lesions in the right pons, right posterior medulla, and the right temporal lobe. Pet. Ex. 73 at 23, 31. Prior to the relapse, petitioner had chosen to stay "off any disease-modifying therapies." Id. at 31. After the relapse, in May 2015, petitioner agreed with Dr. Lisak to start fingolimod and ACTH gel. Id.

At the entitlement hearing in July 2016, petitioner stated that in April or May 2016, she had another MRI which "came back better."[23] Tr. 32. She also testified that she lives in an apartment with her fiancé, who provides assistance for her. Id. Because she qualifies for disability services, which includes eight hours of care a day, her fiancé is compensated for his aid. Id. at 33. Without his help, petitioner believes she would be forced to return to a nursing facility to receive assistance as well as her regular physical, occupational, and rehabilitation therapy. Id.

V. Expert Testimony and Analysis

A. Standards of Adjudication for a Causation Claim

To receive compensation under the Vaccine Act, petitioner must prove either (1) that she suffered a "Table Injury" – i.e., an injury falling within the Vaccine Injury Table – corresponding to one of the vaccinations in question, or (2) that her injury was actually caused by a vaccine (a "non-Table injury"). See §§ 300aa-13(a)(1)(A), 11(c)(1); § 300aa-14(a) as amended by 42 C.F.R. § 100.3; 300aa-11(c)(1)(C)(ii)(I); see also Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1321 (Fed. Cir. 2010); Cappizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1320 (Fed. Cir. 2006). Since no table injury is alleged in this case, petitioner must prove causation in fact.

Petitioner bears the burden of demonstrating actual causation by a preponderance of the evidence. See Cedillo v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1321 (Fed. Cir. 2010); § 300aa-13(a)(1). To do so, petitioner must provide: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal

[23] There are no medical records for this MRI.

relationship between the vaccination and injury." Althen, 418 F.3d at 178. The preponderance of the evidence standard requires a petitioner to demonstrate that it is "more likely than not" that the vaccine caused her injury. Moberly, 592 F.3d at 1322 n.2. Proof of medical certainty is not required. Bunting v. Sec'y of Health & Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, petitioner must demonstrate that the vaccine was "not only [a] but for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). The undersigned must consider the record "as a whole" and may not rule in petitioner's favor solely based on petitioner's own claims "unsubstantiated by medical records or medical opinion." § 13(a)(1).

Causation is determined on a case by case basis, with "no hard and fast per se scientific or medical rules." Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 548 (Fed. Cir. 1994). The Althen court noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. Id. at 1279–80. The court also indicated that, in finding causation, the fact-finder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." Id. at 1280. In other words, any close calls regarding causation must be resolved in favor of the petitioner. Althen, 418 F.3d at 1280.

B. Expert Reports and Testimony

In Vaccine Act cases, expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579, 594-96 (1993); see also Cedillo, 617 F.3d at 1339 (citing Terran v. Sec'y of Health & Human Servs., 195 F.3d 1302, 1316 (Fed. Cir. 1999). "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). In Vaccine Program cases, these factors are used in the weighing of the scientific evidence actually proffered and heard. Davis v. Sec'y of Health & Human Servs., 94 Fed. Cl. 53, 66–67 (Fed. Cl. 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"), aff'd,420 F. App'x 923 (Fed. Cir. 2011). The flexible use of the Daubert factors to determine the persuasiveness and/or reliability of expert testimony in Vaccine Program cases has routinely been upheld. See, e.g., Snyder v. Sec'y of Health & Human Servs., 88 Fed. Cl. 706, 742–45 (2009).

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 & Human Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing Lampe v. Sec'y of Health & Human Servs., 219 F.3d 1357, 1362 (Fed. Cir. 2000)). 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. 146 (1997)). 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. Moberly, 592 F.3d 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 & Human 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").

In the present case, two experts testified at the hearing: Dr. Souayah for petitioner and Dr. Leist for respondent. The experts' respective qualifications and opinions are summarized below.

i. Petitioner's Expert, Dr. Nizar Souayah

1. Qualifications

Petitioner filed one report and presented testimony from Dr. Nizar Souayah. Dr. Souayah gained primary care and family practice experience from 1987 to 1990 at the Medical School of Tunis in Tunisia, from which he obtained his medical degree in 1990. Pet. Ex. 230 at 1. Afterward, he was a resident in internal medicine and vascular disease at a teaching hospital in Strasbourg, France, from 1992 to 1997. Id. at 1. He served as an intern and then resident in internal medicine at the University of Pennsylvania Health System in Philadelphia, Pennsylvania from 1997 to 1999. Pet. Ex. 230 at 1. He was an intern and then resident in neurology from 1999 to 2000, and was the chief resident from 2000 to 2002 at Temple University Hospital in Philadelphia, Pennsylvania. Pet. Ex. 230 at 1. From 2002 to 2003, Dr. Souayah held a fellowship in electromyography and neuromuscular disease with Didier Cros, M.D., the Director of Massachusetts General Hospital at Harvard Medical School in Boston, Massachusetts. Id. From 2003 to 2004, Dr. Souayah held a fellowship in neuroscience, focusing on neuroinflammation in neurodegenerative disorders, with Timothy Cunningham, PhD, at Drexel Medical School in Philadelphia, Pennsylvania. Id. at 1.

Dr. Souayah is currently licensed to practice medicine in the state of New Jersey, and is board-certified in neurology, neuromuscular medicine, and electrodiagnostic medicine. Pet. Ex. 230 at 1-2. He has been an attending physician at University Hospital at Rutgers, University of New Jersey Medical School in Newark, New Jersey, since 2004. Id. at 2. He is also an Associate Professor of Neurology, Neuroscience, Pharmacology, and Physiology at Rutgers. Id. at 2; Tr. 40. Dr. Souayah also directs clinics that see patients with muscular dystrophy, congenital neuropathy, and peripheral neuropathy. Pet. Ex. 230 at 2; Tr. 41. He is a fellow with the American Academy of Neuromuscular and Electrodiagnostic Medicine. Tr. 43.

2. History of Petitioner's Medical Treatment

Dr. Souayah testified that "approximately two weeks" after the vaccination, petitioner "developed pain in the right hip radiating to her foot." Pet. Ex. 70 at 1.[24] In July 2009, approximately four to five weeks after the vaccination, she "woke up feeling lightheadedness and experiencing unusual heavy sensations in all her extremities [. . .] followed by tingling in her right

[24] Citing Pet. Ex. 2 at 3.

foot and leg." Id.[25] By mid-July, these symptoms had progressed to "constant numbness in her right foot." Id.[26]

On August 2, 2009, four weeks later, approximately eight weeks after the vaccination, petitioner experienced a severe headache with slurred speech and loss of peripheral vision. Pet. Ex. 70 at 1, 9. On August 6, 2009, a brain MRI showed (1) an enhancing lesion in the left parietal lobe and (2) a non-enhancing lesion in the left occipital lobe. Id. at 2 (referencing Pet. Ex. 23 at 36-37). Her cerebrospinal fluid was positive for oligoclonal bands. Pet. Ex. 70 at 2 (citing Pet. Ex. 23 at 28).

Dr. Souayah summarized petitioner's subsequent clinical course. Petitioner had additional relapses on October 20, 2009, and March 4, 2010, further MRIs showed progression of white matter disease, she did not respond to steroids, and she had only a limited response to plasmapheresis. Her doctors questioned their initial diagnosis of multiple sclerosis and performed an open brain biopsy on March 11, 2010. Dr. Souayah noted that the biopsy was "not consistent with demyelinating plaque of multiple sclerosis," and that the "distribution of the microglia and astrocytic infiltrates suggest[ed] a more diffuse process within the white matter, possibly inflammatory in nature." Pet. Ex. 70 at 5. CADASIL testing was negative. Id. at 6. Although "[n]o active vasculitis was identified," certain treating physicians offered that diagnosis. Id. at 6, 9. Dr. Souayah noted that in spring 2015, petitioner had another significant relapse and was noted to have irreversible cortical loss. Tr. 84-90.

3. Diagnosis of Petitioner's Condition

Petitioner was found to have white matter disease, which is non-specific but suggestive of vasculitis of the CNS as well as CNS demyelinating disorders including relapsing ADEM and MS. Pet. Ex. 70 at 10. After fully reviewing her clinical history, Dr. Souayah opined that petitioner's course most resembled a CNS demyelinating disorder, most likely MS. Tr. 50.

Dr. Souayah initially thought that petitioner's clinical presentation in August 2009, including a severe headache, could be suggestive of CNS vasculitis,[27] a disease characterized by "otherwise unexplained neurological or psychiatric deficit."[28] Pet. Ex. 115 at 2. The most common presenting symptom is headache, "usually insidious with sub-acute onset." Id. However, petitioner's brain biopsy did not show the "typical" histopathological features of vasculitis. Pet. Ex. 70 at 31.[29] Her brain biopsy also showed "no evidence of vasculitic or neoplastic or infectious

[25] Citing Pet. Ex. 22 at 28.

[26] Citing Pet. Ex. 22 at 29.

[27] CNS vasculitis is "an idiopathic vasculitis affecting small and medium-sized intracranial vessels, marked by headache, progressive intellectual deterioration, and recurrent cerebral infarcts." Dorland's at 83.

[28] Hajj-Ali, R.A. and L.H. Calabrese, "Diagnosis and Classification of Central Nervous System Vasculitis," xx J. AUTOIMMUN. 1-4 (2014) [Pet. Ex. 115].

[29] Gotkine, M. and A. Vaknin-Dembinsky, "Central Nervous System Vasculitis," 15 CURR. TREAT. OPTIONS NEUROL. 367-74, 368 (2014) [Pet. Ex. 111].

process." Tr. 61 (citing Pet. Ex. 21 at 39). Furthermore, vasculitis is diagnosed only after excluding other conditions that can "cause or mimic the angiographic or pathological features of the disease," such as CADASIL, ADEM, and MS. Pet. Ex. 115 at 2. In the present case, genetic testing for CADASIL was negative. Pet. Ex. 70 at 6. However, petitioner's treating physicians kept ADEM and MS in the differential diagnosis. In summary, based on the brain biopsy findings and other more likely diagnoses, Dr. Souayah did not believe that vasculitis was petitioner's diagnosis. Pet. Ex. 70 at 31; Tr. 48-49.

Dr. Souayah opined that petitioner's course was more consistent with a CNS demyelinating disorder. Pet. Ex. 70 at 17. He also stated that there is a "spectrum" of CNS demyelinating disorders, all of which cause disseminated damage to the central nervous system and have similar initial clinical presentations. Pet. Ex. 70 at 17.[30] These include ADEM and MS. Pet. Ex. 70 at 17. One important difference between ADEM and MS is the disease course. ADEM is usually monophasic; however, "in some children a self-limited and transient multiphasic demyelinating phase occurs." Pet. Ex. 137 at 2. "There [is] no consensus as to whether multiphasic ADEM could encompass more than two ADEM episodes." Id. at 3. "Cases with more than two events [are] considered extremely suspicious for MS." Id. Compared to ADEM, MS is a "lifelong disorder characterized by an ongoing demyelinating process." Id.

Dr. Souayah filed an article by Noseworthy et al.[31] listing various symptoms of CNS demyelinating disorders. Onset may include sensory disturbances; limb weakness; clumsiness; gait ataxia; unilateral optic neuritis; and diplopia. Pet. Ex. 160 at 1.

Dr. Souayah opined that petitioner's first symptoms in her right hip, leg, and foot in July 2009 were non-specific, but consistent with CNS demyelination caused by either ADEM or MS. Pet. Ex. 70 at 17; Tr. 52-53. Her subsequent headaches, slurred speech, and left side hemianopsy (loss of visual field) in August 2009 are also consistent with both diseases. Pet. Ex. 70 at 17; Tr. at 52-53. He opined that the lesions revealed on the August 2009 MRI were "highly suggestive" of a demyelinating disease. Tr. at 54-56. The oligoclonal bands found on August 6, 2009, were also consistent with a diagnosis of MS. Tr. at 56-57.

Dr. Souayah opined that the initial time course was also consistent with either ADEM or MS. He stated the symptoms in petitioner's right hip, leg, and foot were manifestations of her first

[30] See Dale R.C. & Branson J.A., "Acute Disseminated Encephalomyelitis or Multiple Sclerosis: Can the Initial Presentation Help in Establishing a Correct Diagnosis?," 90 ARCHIVES OF DISEASES IN CHILDHOOD 636-39 (2005) [Pet. Ex. 99]; see also Karussis D. & P. Petrou, "The Spectrum of Post-Vaccination Inflammatory CNS Demyelinating Syndromes," 13 AUTOIMMUN. REV. 215-24 (2004) [Pet. Ex. 135]; Krupp et al., "Consensus Definitions Proposed for Pediatric Multiple Sclerosis and Related Disorders," 68 NEUROLOGY S7-12 (2007) [Pet. Ex. 137]; Sejvar et al., "Encephalitis, Myelitis, and Acute Disseminated Encephalomyelitis (ADEM): Case Definitions and Guidelines for Collection, Analysis, and Presentation of Immunization Safety Data," 25 VACCINE 5778 (2007) [Pet. Ex. 188]; Noorbaksh et al., "Acute Disseminated Encephalomyelitis: Clinical and Pathogenesis Features," 26 NEUROL. CLIN. 759-80, 771 (2008) [Pet. Ex. 218].

[31] Noseworthy et al., "Multiple Sclerosis," 343 N. ENG. J. MED. 938-952 (2000) [Pet. Ex. 160].

episode. Pet. Ex. 70 at 17. The headaches, slurred speech, and left side hemianopsy constituted a second episode or relapse.[32] Id.

Throughout his expert report filed February 10, 2015, Dr. Souayah states that petitioner could have either relapsing ADEM or an atypical, relapsing-remitting MS. Pet. Ex. 70 at 17, 18, 19, 22, 26, 27, 28, 30, 42. The report was based on only the records he had received at that time and mainly focused on petitioner's initial onset in July 2009 and her relapse in August 2009. Tr. 47-48.

At the entitlement hearing, Dr. Souayah testified that after review of additional and updated records, he believes petitioner has an "aggressive form of relapsing-remitting multiple sclerosis." Tr. at 50. He acknowledged that the CNS lesions' size, location, and progression; the lack of response to steroids; and the partial response to plasmapheresis were all atypical for MS. Id. at 61-62, 65, 67. However, he agreed with three treating neurologists who all believed that MS was the best diagnosis. Dr. John Fink noted in October 2010 that the "exacerbating-remitting course, the multifocal localization… the cerebrospinal fluid showing oligoclonal bands and… the brain white matter abnormality [are all] suggestive of the diagnosis of multiple sclerosis." Tr. at 75 (citing Pet. Ex. 1, 1-2). In the fall of 2011, Dr. Lisak and Dr. Giger-Mateeva both wrote that petitioner's course was consistent with an aggressive form of MS with confluent lesions. Tr. at 79-82 (citing Pet. Ex. 42, pp. 41-43). Petitioner's April 2015 relapse and her most recent MRIs showing irreversible cortical loss further support the diagnosis of a permanent, ongoing demyelinating condition, such as MS. Tr. at 84-90.

4. Medical Theory

Dr. Souayah opined that the HPV vaccine is capable of causing demyelinating disorders such as MS through the mechanism of molecular mimicry. He supports the theory with literature related to the rabies vaccine and subacute encephalomyelitis,[33] and the recombinant hepatitis B vaccine and multiple sclerosis.[34] Petitioner filed two articles reporting VAERS data on Guillain-

[32] Dr. Souayah's opinions as to onset appear to mirror the notes by petitioner's treating physician, Dr. Asbury, in which Dr. Asbury noted that her first episode occurred in July 2009 (awoke feeling "woozy" and limbs felt heavy, transitioned into tingling in right foot and leg), and that her second episode occurred in August 2009 (headache and visual loss). See supra note 7; Pet. Ex. 22 at 28-29.

[33] Uchimura and Shiraki, "A Contribution to the Classification and the Pathogenesis of Demyelinating Encephalomyelitis, with Special Reference to the Central Nervous System Lesions Caused by Preventive Inoculation Against Rabies," 16 J. NEUROPATHOL. EXP. NEUROL. 139-203 (1957) [Pet. Ex. 201].

[34] Comenge & Girard, "Multiple Sclerosis and Hepatitis B Vaccination: Adding the Credibility of Molecular Biology to an Unusual Level of Clinical and Epidemiological Evidence," 66 MED. HYPOTHESES 84-86 (2006) [Pet. Ex. 87]; Faure, "Multiple Sclerosis and Hepatitis B Vaccination: Could Minute Contamination of the Vaccine by Partial Hepatitis B Virus Polymerase Play a Role Through Molecular Mimicry?," 65 MED. HYPOTHESIS 509-20 (2005) [Pet. Ex. 95]. Fourrier et al., "Hepatitis B Vaccine and First Episodes of Central Nervous System Demyelinating Disorders: A Comparison Between Reported and Expected Number of Cases," 51 BR. J. CLIN. PHARMACOL. 489-90 (2001) [Pet. Ex. 99]; Hernan et al., "Recombinant Hepatitis B Vaccine and the Risk of Multiple Sclerosis: A Prospective Study," 63 NEUROLOGY 838-42 (2004) [Pet. Ex. 121];

Barré Syndrome ("GBS") following the influenza[35] and HPV vaccines.[36] Petitioner also filed case reports of the HPV vaccine and ADEM[37] and case reports of the HPV vaccine and MS.[38] Dr. Souayah stated that these reports suggest a causal association between the HPV vaccine and these demyelinating disorders. He emphasized that case reports are the best evidence available, because these disorders are rare and thus, it is difficult to conduct large, controlled epidemiological studies. Tr. 108-10.[39]

Demyelinating disorders are thought to occur in people that are genetically susceptible. These disorders are also "immune-mediated," meaning that they develop when the immune system is somehow activated and then attacks the self, due to the molecular mimicry mechanism. Pet. Ex.

Mikaeloff et al., "Hepatitis B Vaccine and the Risk of CNS Inflammatory Demyelination in Childhood," 72 NEUROLOGY 873-80 (2009) [Pet. Ex.153].

[35] Souayah et al., "Guillain-Barré Syndrome after Influenza Vaccination in the United States, A Report from the CDC/ FDA Vaccine Adverse Event Reporting System (1990-2009)," 29 J. CLIN. NEUROMUSCULAR DISEASE 66-71 (2012) [Pet. Ex. 74].

[36] Souayah et al., "Guillain-Barré Syndrome after Gardasil Vaccination: Data from Vaccine Adverse Event Reporting System 2006-2009," 29 VACCINE 886-89. (2011) [Pet. Ex. 194].

[37] Borja-Hart et al., "Human Papillomavirus Vaccine Safety in Pediatric Patients: An Evaluation of the Vaccine Adverse Event Reporting System," 43 ANN. PHARMACOTHER. 356-59 (2009) [Pet. Ex. 85]; DiMario et al., "A 16-Year-Old Girl with Bilateral Visual Loss and Left Hemiparesis Following an Association Against Human Papillomavirus," 25 J. CHILD NEUROL. 321-27 (2010) [Pet. Ex. 93]; Karussis & Petrou, "The Spectrum of Post-Vaccination Inflammatory CNS Demyelinating Syndromes," 13 AUTOIMMUN. REV. 215-24 (2014) [Pet. Ex. 132]; Mendoza Plasencia et al., "Acute Disseminated Encephalomyelitis with Tumefactive Lesions after Vaccination against Human Papillomavirus," 25 NEUROLGIA 58-59 (2010) [Pet. Ex. 150]; Pellegrino et al., "Acute Disseminated Encephalomyelitis Onset: Evaluation Based on Vaccine Adverse Events Reporting Systems," 8 PLoS ONE e77776 (2013) [Pet. Ex. 174]; Schaffer et al., "HPV Vaccine: A Cornerstone of Female Health, A Possible Cause of ADEM?," 255 J. NEUROL. 1818-20 (2008) [Pet. Ex. 186]; Wildemann et al., "Acute Disseminated Encephalomyelitis Following Vaccination Against Human Papilloma Virus," 72 NEUROLOGY 2132-33 (2009) [Pet. Ex. 206].

[38] Gold & McIntyre, "Human Papillomavirus Vaccine Safety in Australia: Experience to Date and Issues for Surveillance," 7 SEX HEALTH 320-24 (2010) [Pet. Ex. 109]; Grimaldi-Bensouda et al., "Autoimmune Disorders and Quadrivalent Human Papillomavirus Vaccination of Young Female Subjects," 275 J. INTERN. MED. 398-408 (2014) [Pet. Ex. 112]; Sutton et al., "CNS Demyelination and Quadrivalent HPV Vaccination," 15 MULT. SCLER. 116-19 (2009) [Pet. Ex. 195]; Verstraeten et al., "Analysis of Adverse Events of Potential Autoimmune Etiology in a Large Integrated Safety Database of AS04 Adjuvanted Vaccines," 26 VACCINE 6630-38 (2008) [Pet. Ex. 202].

[39] Citing Evans et al., "'Prepandemic' Immunization for Nova Influenza Viruses, 'Swine Flu' Vaccine, Guillain-Barré Syndrome, and the Detection of Rare Severe Adverse Events," 200 J. INFECTIOUS DISEASES 321-28, 325, Table 3 (2009) [Pet. Ex. 214] (providing the number of subjects required to test the existence of an increased level of risk associated with a vaccine).

70 at 29; Tr. 97-104. Molecular mimicry is the name for the process whereby an infectious antigen has a similar molecular structure as some part of the body; the immune system cannot distinguish the antigen from that part of the body; and the immune system attacks both. Dr. Souayah explained that a properly functioning immune system recognizes when an infectious antigen is present and activates T cells and B cells. The B cells then produce antibodies, and the T cells and antibodies specifically attack the infectious antigen and do not attack the body. Tr. 97-104.

Dr. Souayah opined that either the live HPV (virus) or the HPV vaccine can cause this response. Tr. 98-100. In support of this proposition, he cited an article by Wucherpfenning and Strominger[40] reporting "striking sequence similarity" between one peptide found in the HPV virus and one peptide found in myelin basic protein ("MBP").[41] Id. at 107-09. After discovering this similarity, Wucherpfenning and Strominger successfully used the HPV peptides to stimulate T cells which attacked both the HPV and MBP. Pet. Ex. 215 at 698-99. Wucherpfenning and Strominger also noted that HPV was a "latent, persistent" infection which can remain in the body and trigger repeated immune system attacks against both the HPV and the homologous myelin. Id. at 700. These repeated attacks would be consistent with a chronic, relapsing demyelinating disorder such as MS. Id. at 696; Tr. 108.

Dr. Souayah stated that the Wucherpfennig and Strominger article was significant because it demonstrated molecular mimicry between peptides in live HPV and peptides in myelin. Tr. 108. He stated that there is "no reason why the vaccine for HPV will not cause the same . . . immune reaction." Id. Dr. Souayah suggested that compared to the live virus, the HPV vaccine could produce an even more robust immune reaction. Pet. Ex. 70 at 29-30; Tr. at 100-02. He cited an article by Harro et al.[42] for the proposition that the HPV vaccine is highly immunogenic. Pet. Ex. 70 at 29. He also stated that the immune response continues for "a long time." Tr. 103; see also Pet. Ex. 70 at 20-22. He cited a clinical study by the vaccine's manufacturer, Merck,[43] which found

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[40] Wucherpfenning & Strominger, "Molecular Mimicry in T Cell-Mediated Autoimmunity: Viral Peptides Activate Human T Cell Clones Specific for Myelin Basic Protein," 80 CELL 695-705, 698 (1995) [Pet. Ex. 215]. The researchers discuss the circumstances under which they discovered that the live HPV virus could cause the activation of autoreactive T cells with sequence similarity to MBP. Id. at 695. Although the article does not address this possibility in the context of the HPV vaccine, which does not contain a live viral component, Dr. Souayah opined that "if the [live] virus is able to trigger a[n] immune reaction against HPV, there is no reason why the vaccine from HPV will not cause the same … immune reaction." Tr. 108.

[41] Myelin is "the substance of the cell membrane of Schwann cells that coils to form the myelin sheath," which is made up of proteins and acts as an "electrical insulator." Dorland's at 1218. The process of demyelination occurs when the myelin sheath is destroyed. Id.

[42] Harro et al., "Safety and Immunogenicity Trial in Adult Volunteers of a Human Papillomavirus 16 L1 Virus-Like Particle Vaccine," 93 J. NAT'L CANCER INSTITUTE 284-92, at 91 (2001) [Pet. Ex. 120].

[43] Merck, "GARDASIL®, Merck's Cervical Cancer Vaccine, Demonstrated Efficacy in Preventing HPV-Related Disease in Males in Phase III Study," available at http://www.businesswire.com/news/home/20081113005144/en#.Urc6Sdoo4qQ at 29 (2008) [Pet. Ex. 104].

that anti-HPV antibodies peaked about seven months after the administration of the vaccine, then declined until month 24, and remained detectable at month 36. Pet. Ex. 70 at 22.

5. Logical Sequence of Cause and Effect

Applying this theory to petitioner's specific case, Dr. Souayah opined that the HPV vaccine induced an immune response against petitioner's myelin sheath, thereby causing her injuries. Pet. Ex. 70 at 18, 30, 42; Tr. 92, 110-12. He opined that petitioner's "genetic profile and other biologic factors specific to [her] immune system probably predisposed her to develop central nervous system demyelination." Pet. Ex. 70 at 18. However, he did not see any evidence of this condition in her pre-vaccination history. Before the vaccine, petitioner was a healthy woman without any history of inflammation, infection, or autoimmune disease. Tr. 90, 111.[44] She had no history of trauma that could explain the numbness, weakness, and pain in her right leg shortly after the vaccination. Id. at 115.

After ruling out other possible triggers, Dr. Souayah opined that petitioner's HPV vaccine was the most likely cause of her condition. Tr. 92, 130. Like the HPV discussed in the article by Wucherpfenning and Strominger, the HPV vaccine had some antigenic similarity to the petitoner's myelin sheath. Pet. Ex. 70 at 18. Therefore, petitioner's immune system attacked both.

Dr. Souayah explained that the oligoclonal banding found in petitioner's cerebrospinal fluid on August 6, 2009, suggests "an autoimmune process going on in the brain." Tr. 142. Petitioner's August 6, 2009 MRIs revealed white matter damage that was not "congenital" and "uniform." Id. at 69. Instead, the damage was "acquired." Id. This also suggested that the damage was triggered by something in particular. Dr. Souayah believes that trigger was the vaccine.

Dr. Souayah opined that there was no other alternative etiology for petitioner's immune response. In her later clinical course, petitioner had an upper respiratory infection. Tr. 167-68. Dr. Souayah explained that subsequent triggers can cause relapse in patients with MS, but the subsequent trigger does not suggest etiology. The molecular mimicry here was triggered by vaccination. Id. at 170. In other words, "the fact that … one of [petitioner's] subsequent relapses occurred after an upper respiratory infection… does not take away… from [his] theory" that the vaccine was the initial triggering event. Id. at 172.

6. Timing

Dr. Souayah opined that there was a medically acceptable period of time between petitioner's vaccination, her body's production of antibodies, and her first symptoms. Once an antigen enters the body, the immune system "will start producing [antibodies] within the first few days, reaching a peak within two [to] three weeks ..." Tr. 169. See also id. at 149; Pet. Ex. 70 at 25. He stated that the Gardasil vaccine triggers antibody production very quickly and that

[44] On cross-examination, Dr. Souayah acknowledged that petitioner was diagnosed with molluscum contagiosum on the day she received the Gardasil vaccine. He opined that molluscum contagiosum was a "focal" infection rather than a "systemic" infection. Tr. 121-22. He did not know whether it could trigger an immune response in the body. Id. at 122. Dr. Souayah was not "aware of any association in the medical literature between that infection and MS." Id. at 175.

seroconversion[45] to the Gardasil vaccine would take between two to six weeks. Tr. 115, 142. Once the antibodies are present, they would begin attacking both the vaccine and the myelin sheath. Dr. Souayah stated, "[I]f you have the antibodies, you have the players, so you may say there is some autoimmune reaction that caused molecular mimicry and the damage." Id. at 167. This attack on the myelin sheath would then cause lesions in the brain and the manifestation of symptoms.

Dr. Souayah also reviewed petitioner's clinical course. She received the vaccine on June 4, 2009, and began producing antibodies shortly thereafter. These antibodies could have begun attacking the brain, which manifested in the sensory symptoms in her left leg within a few weeks of the vaccine (July episode). The first clinical tests on August 6, 2009, confirmed that by that time, petitioner had positive oligoclonal bands in her CSF. Tr. 56. As in petitioner's case, when the bands are present only in the CSF, rather than in both the CSF and the blood, this indicates that "the immunoglobulins are produced … in the CNS," and suggests an autoimmune process. Id. at 56, 142. Oligoclonal bands indicate autoimmune or immunologic dysfunction in the body and can indicate a diagnosis of MS. Id. at 57. Dr. Souayah testified that one would expect to see abnormal immunoglobulins within eight to 12 weeks. This is consistent with petitioner's clinical presentation, as she was found to have oligoclonal bands on August 6, 2009, approximately 12 weeks after she received the Gardasil vaccination.

7. Review of the MRIs

Based on his review of the MRIs, Dr. Souayah opined that petitioner's demyelinating injury began after the vaccination, progressed rapidly, and shows lesions consistent with her various symptoms. Petitioner did not have any brain MRIs predating the vaccine, but she had no prior history of illness or injury. Tr. 137; Pet. Ex. 70 at 18. Dr. Souayah testified that petitioner's left parietal lesion and the left occipital lesion developed shortly before the August 5, 2009 MRIs.

Petitioner's initial brain MRI was performed on August 5, 2009, and it shows two lesions. One is an enhancing lesion in the deep white matter of the left parietal area of the brain. This lesion is consistent with the numbness in petitioner's right lower extremity.[46] Tr. 158-59. The second, smaller lesion was seen in the left occipital lobe. Dr. Souayah testified that it was a small lesion, and that it may have been related to petitioner's headaches and visual problems. Id. at 162.

Dr. Souayah opined that these lesions were not present before the vaccination was administered on June 4, 2009, but rather that they developed quickly, were observed on the August 5, 2009 MRIs, and showed even further progression on the October 2009 MRIs. Tr. 137. Indeed, Dr. Souayah stated that the October 2009 MRIs showed "aggressive" progression that he had never seen before in any other patient. Id. at 165. In summary, Dr. Souayah opined that the lesions developed after the vaccine, they were consistent with petitioner's symptoms and clinical course, and they suggested an "aggressive autoimmune reaction" to the vaccine. Id. at 166.

[45] Seroconversion is "the change of a patient's serologic test results from negative to positive, indicating development of antibodies in response to infection or immunization." Dorland's at 1698.

[46] Dr. Souayah further testified that a lesion could be present before it enhances, but that it will enhance once it breaks the blood brain barrier ("BBB"). Tr. 160. Also, an old lesion will not enhance. Id. at 161.

ii. Respondent's Expert, Dr. Thomas Leist

1. Qualifications

Respondent filed two reports and presented testimony from Dr. Thomas P. Leist, a neuroimmunologist and a professor at Thomas Jefferson University in Philadelphia, Pennsylvania. Tr. 176; Resp. Ex. L. He earned a doctoral degree in biochemistry and immunology from the University of Zurich. Tr. 177. Dr. Leist then completed a fellowship in viral immunology at the University of Zurich, followed by a fellowship in viral latency at the University of California Los Angeles. Id. He obtained his medical degree in 1993 from the University of Miami, where he was an internal medicine intern from 1993 to 1994. Id. He was a neurology resident at Cornell Medical Center/ Memorial Sloan-Kettering Cancer Center in New York, New York, from 1994 to 1997. Resp. Ex. L at 1. Afterwards, he held the position of Senior Clinical Staff Associate at the National Institute of Neurological Disorders and Stroke at the National Institutes of Health from 1997 to 2000. Id.

Dr. Leist is licensed to practice medicine in Pennsylvania and Maryland. Resp. Ex. L; Tr. 177-78. He is board-certified in psychiatry and adult neurology and serves as an editor and peer-reviewer for medical journals. Tr. 178. Dr. Leist is an attending physician, professor of neurology, and director of the fellowship program in multiple sclerosis. Id. at 179. He stated that approximately 85 percent of his patients have multiple sclerosis. Id. at 182.

2. Diagnosis of Petitioner's Condition

Dr. Leist opined that petitioner had an atypical presentation and could not be easily diagnosed. Tr. 185. Dr. Leist stated that petitioner's clinical course set forth in the medical records is inconsistent with ADEM. First, the initial MRI in August 2009 suggested the presence of lesions of different ages, which would be more consistent with a longer, chronic disease course. Resp. Ex. C at 8; Resp. Ex. I at 3. The August 2009 CSF analysis findings of oligoclonal bands were also unusual. According to Dr. Leist, oligoclonal bands are only present in about ten percent of ADEM cases. Resp. Ex. C at 8; Resp. Ex. I at 3; Tr. 190.

He also characterized petitioner's presentation as being "very, very atypical" for multiple sclerosis. Tr. 185. Petitioner's lesions did not have the surrounding edema normally observed in multiple sclerosis cases. Id. at 187-88. In addition, when petitioner experienced further symptoms in October 2009 and underwent another MRI, none of the lesions were enhancing, which is also atypical for MS. Id. at 193.

Dr. Leist also stated that the March 2010 brain biopsy showed diffuse distribution of microglial and astrocytic infiltrates, which is inconsistent with demyelinating conditions like ADEM or multiple sclerosis, and is more suggestive of an inflammatory process. Resp. Ex. C at 8; Resp. Ex. I at 3.

Dr. Leist stated that he struggled to arrive at an appropriate diagnosis for petitioner. Tr. 185. He noted his personal acquaintance with and respect for petitioner's treating neurologist, Dr. Lisak, and several of the other treating physicians at the same health system. Id. He eventually deferred to their diagnosis of multiple sclerosis, "[a]s long as we can agree that this is a very atypical form of multiple sclerosis." Id. at 219.

3. Response to Petitioner's Medical Theory

Dr. Leist critiqued several elements of Dr. Souayah's theory that the HPV vaccine caused petitioner's demyelinating condition through the mechanism of molecular mimicry. First, he criticized Dr. Souayah's reliance on case reports about demyelinating conditions following vaccination. He stated that case reports "are not sufficient to establish causation," and stressed the need for further analysis. Resp. Ex. I at 6. Indeed, several articles expressly stated that the authors did not find any increased risk between the HPV vaccine and the diseases. Resp. Ex. I at 5, Tr. 201-02.[47] Dr. Leist also claimed that the Institute of Medicine ("IOM") had "methodological concerns" about the article by Hernan et al. concluding that the recombinant Hepatitis B vaccine was associated with an increased risk of MS. Resp. Ex. I at 6.[48]

Dr. Leist also critiqued Dr. Souayah's articles drawing from VAERS data.[49] Resp. Ex. I at 5-6; Tr. 203-04. Dr. Leist stated that VAERS is a passive reporting system which can identify risk signals. Resp. Ex. I at 6. However, it is not appropriate to draw any conclusions from this data, before determining that it is accurate. Resp. Ex. I at 6; Tr. 205. A proper study should obtain and review each individual's medical records, confirm the diagnosis, and rule out alternative causes, before drawing larger conclusions. Resp. Ex. I at 6. Dr. Leist suggested that Dr. Souayah did not conduct this deeper review of the VAERS data, before drawing his conclusions.

Dr. Leist stated that the IOM has evaluated the studies published to date on the possible associations between HPV and ADEM, MS, TM, and neuromyelitis optica. Certain articles provide evidence of temporality between HPV and these diseases. Resp. Ex. C at 7. However, the IOM found no epidemiologic evidence that HPV is associated with an increased risk of any of these diseases. Id. He also filed a statement from the Global Advisory Committee on Vaccine Safety, ("GACVS") which acknowledged the case reports, but concluded, "multiple epidemiological studies have not demonstrated any increased risk of autoimmune diseases, including MS," in association with the HPV vaccine.[50] He also emphasized that the HPV vaccine is given to a population group that already has a higher incidence rate of demyelinating disorders, suggesting that the vaccine was not necessarily the cause. Resp. Ex. I at 5;[51] Tr. 197, 201-02.

Dr. Leist, however, did not challenge Dr. Souayah's general explanation of molecular mimicry. Resp. Ex. I at 5. He agreed that demyelinating disorders are believed to be immune-mediated. He stated that "infections can activate the immune system," and that "[i]nfections have been reported to trigger MS relapses." Tr. 205. He also stated that the "[i]mmune system plays a very significant role in multiple sclerosis." Id. at 226. He acknowledged that "molecular mimicry

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[47] Referencing Gold et al. [Pet. Ex. 109].; Grimaldi-Bensouda et al. [Pet. Ex. 112]; Sutton et al. [Pet. Ex. 195]; Verstraeten et al. [Pet. Ex. 202].

[48] Citing Hernan et al. [Pet. Ex. 121].

[49] Citing Souayah et al. [Pet. Ex. 74]; Souayah et al. [Pet. Ex. 194].

[50] Citing Global Advisory Committee on Vaccine Safety, Statement on the Continued Safety of HPV Vaccination (Mar. 12, 2014) at 1-2 [Resp. Ex. I, Tab 2].

[51] Citing Sutton et al. [Pet. Ex. 195].

has been shown to play a role in certain autoimmune disorders – or certain demyelinating disorders, particularly of the peripheral nervous system." Id. at 226-27. Dr. Leist noted that there is a "very good model" of molecular mimicry, campylobacter jejuni and GBS. Id. at 227. He generally admitted that "[a]utoantibodies, T cells, and molecular mimicry may contribute to the symptoms of ADEM, transverse myelitis, neuromyelitis optica, or [MS]." Resp. Ex. C at 7-8.

He opined there was no evidence linking demyelinating conditions to HPV. Resp. Ex. C at 8. Dr. Leist stated, "Wild type human papilloma virus isolates are not generally recognized as being associated with post infectious immune mediated conditions of the central or peripheral nervous system." Resp. Ex. C at 7. However, he did not address or refute the findings of Wucherpfenning and Strominger regarding homology between a peptide present in wild HPV and a peptide present in myelin basic protein. Pet. Ex. 215.

Dr. Leist opined that even if a live virus can cause a particular illness, it is much less likely that a vaccine containing non-live particles of that virus, like the HPV vaccine, will cause the same illness. He stated that unlike a live virus, a vaccine containing viral peptides (like HPV) does not replicate within the body. Tr. 228. Therefore, Dr. Leist testified that a vaccine can stimulate an immune response, but it will be relatively short-lived. Id. at 198; 228.

Dr. Leist opined that "if petitioner's disease was caused by an aberrant immune response," that response was unlikely to have been triggered by the "non-live" HPV vaccine. Resp. Ex. C at 10. Instead, he opined, it was more likely to have been caused by a live viral infection which was present at the same time. Id. Specifically, petitioner was diagnosed with molluscum contagiosum on June 4, 2009, the day she received the vaccine. Id. at 1. Dr. Leist stated that molluscum contagiosum is a "viral infection" that is present in "the skin and occasionally [the] mucous membranes," and is "contagious until the bumps are gone, which may last up to [six] months or longer." Resp. Ex. C at 7; Tr. 205. Dr. Leist opined that an infection, such as molluscum contagiosum, could potentially be a trigger for MS. Tr. 205. He stated that MS can be developing for some time before symptoms manifest and the patient becomes aware. Id. at 225. He further stated that oligoclonal bands take at least six weeks and are indicative of a "more chronic presence of an immune response within the central nervous system." Id. at 226. And as noted above, Dr. Leist stated that unlike a vaccine, a live infection replicates within the body and stimulates a greater immune response. Id. at 228.

However, on cross-examination, Dr. Leist admitted that he was not aware of any serious complications from molluscum contagiosum. Tr. 235-36. He was unaware of any medical literature or other information showing that molluscum contagiosum causes CNS demyelination or neurologic manifestations. Id. at 236.

Dr. Leist was asked about Dr. Souayah's statements that compared to wild HPV, the HPV vaccine is more immunogenic and triggers greater production of antibodies. Tr. 229. Dr. Leist responded that "the vaccine is geared towards inducing a protective immunity in the individual. And, so, the vaccine, by itself, obviously is [going] to do exactly that." Id.

4. Response to Petitioner's Argument Regarding A Logical Sequence of Cause and Effect

Dr. Leist opined that petitioner's HPV vaccination administered on June 4, 2009, did not contribute to a new condition or exacerbate a preexisting condition. Tr. 186; see also Resp. Ex. C at

10; Resp. Ex. I at 6. He stated that there was no evidence that petitioner had "any immediate or delayed side effect from the vaccination in the hours and days following the vaccination." Resp. Ex. C at 6.

Like Dr. Souayah, Dr. Leist opined that oligoclonal banding is indicative of an immunological response. Resp. Ex. C at 8. Specifically, it reveals that B cells have been producing antibodies within the CNS. Tr. 189. However, Dr. Leist opined that oligoclonal banding is not diagnostic for a particular condition and can be present in a broad range of neurological diseases, including cerebrovascular disease, seizure disorders, amyotrophic lateral sclerosis ("ALS"),[52] polyneuropathy, and glioma. Resp. Ex. C at 8. Dr. Leist, did not, however testify that petitioner had any of those other diseases.

Dr. Leist noted that none of petitioner's treating physicians opined that the vaccine caused her injuries. Resp. Ex. C at 10, Tr. 205. He noted that on January 18, 2012, Dr. Lisak recorded that petitioner's mother blamed the vaccine but that petitioner "clearly had her second episode quite remote from that." Resp. Ex. C at 6; Tr. 205 (citing Pet. Ex 32 at 2).

As noted above, Dr. Leist believes that case reports are insufficient to support an association between the HPV vaccine and demyelinating conditions. He stated that even if the vaccine can cause some demyelinating conditions, it did not cause petitioner's very atypical, devastating course. Tr. at 199. He referenced Sutton et al., a case report provided by Dr. Souayah, which reported on five individuals who experienced a demyelinating event within 21 days of receiving the HPV vaccine. Pet. Ex. 195 at 2. Dr. Leist noted that "complete or near-complete clinical recovery was observed in all [five] patients … following the administration of intravenous methylprednisone." Tr. at 199 (referencing Pet. Ex. 195 at 2). In contrast, petitioner experienced repeated relapses and has not recovered. In other words, Dr. Leist's opinion is that even if these case reports are supportive of a relationship between HPV and demyelinating conditions, they do not support a logical sequence of cause and effect in petitioner's case.

5. Response to Petitioner's Timing Argument

Dr. Leist opined that the time frame from vaccine to onset in this case was not medically acceptable. First, he did not believe that onset was close enough to the vaccination. In support of this proposition, he cited an article by Rowhani-Rahbar et al.,[53] who formulated clinically acceptable time frames for onset of two specific adverse events following immunization ("AEFIs"): febrile seizures and ADEM. Resp. Ex. I at 3-4; Tr. 216-18. Rowhani-Rahbar et al. propose a "primary short interval of [five to] 28 days," "for epidemiologic assessments of causality between a particular vaccine and ADEM." Resp. Ex. I at 274. This interval "incorporates time periods best substantiated by available biological and epidemiologic data." Id. A secondary time interval of two to 42 days was also proposed, which was "biologically plausible but associated with greater uncertainty." Id.

[52] ALS is more commonly known as Lou Gehrig's disease.

[53] Rowhani-Rahbar et al., "Biologically Plausible and Evidence-Based Risk Intervals in Immunization Safety Research," 31 VACCINE 271-77 (2012) [Resp. Ex. I, Tab 1].

Dr. Leist opined that because the mechanisms causing ADEM and multiple sclerosis are very similar, the onset time courses would also be similar. Tr. 198-99; 216. He opined that petitioner's neurological symptoms were outside of both models. Petitioner received the vaccine on June 4, 2009, and Dr. Leist opined that her neurological symptoms began on or about August 1, 2009, a period of 58 days. Resp. Ex. I at 4; Tr. 217, 221. This is outside of both time intervals presented by Rowhani-Rahbar. Resp. Ex. I at 4; Tr. 217-18, 221. Dr. Leist opined that this "speak[s] against an association" between the vaccine and petitioner's injuries. Tr. 218.

On cross-examination, Dr. Leist conceded, however, that the symptoms of multiple sclerosis are not apparent as soon as the disease process begins. Tr. 225. Indeed, he agreed that "it is possible that a disease process is present for an extended period of time before a patient becomes aware." Id.

Dr. Leist was also cross-examined about the timing of petitioner's symptoms. First, in her affidavit, petitioner stated that her right hip pain began within two weeks of the vaccination. Dr. Leist said that this would be within the clinically acceptable five to 28 day interval set forth by Rowhani-Rahbar et al. Tr. 221. Second, petitioner reported experiencing "wooziness" as well as "heavy limbs" and numbness," around July 14, 2009. Dr. Leist agreed that if these symptoms are attributed to petitioner's condition, they would be within the more conservative two to 42 day time interval presented by Rowhani-Rahbar et al. Id. at 222-25.

Dr. Leist's second argument about timing was that the vaccine could not have caused oligoclonal banding and an elevated IgG index by August 6, 2009. He stated that the presence of oligoclonal bands and an IgG index requires expansion of clonal B cell populations in the CNS. Resp. Ex. C at 8; Resp. Ex. I at 3. Dr. Leist cited a study in which "a clear stimulus is given at a clear point in time" to induce allergic encephalitis in rat cells. Resp. Ex. C at 8. Oligoclonal banding could be demonstrated six weeks after the stimulus was introduced. Resp. Ex. C at 8.[54]

There was a period of nine weeks between petitioner's vaccine and the lumbar puncture which revealed oligoclonal bands. Tr. 226. Dr. Leist suggested that the rat model was able to produce oligoclonal banding within six weeks because the stimulus was strong and the all other conditions were controlled. Id. 190, 226. He suggested that it would take longer for a vaccine to generate oligoclonal banding in human cells, *in vivo*. Id. He also opined that the human immune system may be slower, based on observations that the "great majority" (90 percent) of patients with ADEM are not found to have oligoclonal banding. Id. at 190.

6. Review of the MRIs

Dr. Leist opined that the MRIs challenged the working diagnosis of MS. In contrast to most cases of MS involving "focal" demyelinating plaque, petitioner has significant, diffuse white matter disease throughout her brain. Tr. 208.

[54] Dr. Leist does not identify this article in his reports or in his testimony, but a review of the filed medical literature reveals one article which appears to match Dr. Leist's description as Resp. Ex. J, Roström et al., "Oligoclonal IgG Bands Synthesized in the Central Nervous System are Present in Rats with Experimental Autoimmune Encephalitis," 109 ACTA NEUROLOGICA SCANDINAVICA 4106-12 (2004) [Resp. Ex. J].

Dr. Leist was equivocal when asked whether the lesion in petitioner's left parietal area explained the symptoms in her leg. First, he couldn't say "with significant certainty" that this lesion caused the early symptoms in her leg. Tr. 215, 219, 222. But, he agreed that it was possible that the leg "heaviness" came from the brain pathology. Id. at 219. Dr. Leist noted that the symptoms in petitioner's leg began "much earlier" than the August 2009 MRI showing that this lesion was enhancing. Id. at 216. Dr. Leist then opined, "it's not that easy to relate that lesion to [the] symptoms." Id.

Dr. Leist stated that it was very difficult to say how old the left occipital lesion was because it was non-enhancing at the August 2009 MRI. Tr. 188. Dr. Souayah opined that this lesion was consistent with petitioner's headache and visual problems. Dr. Leist did not specifically say whether this was possible or probable. Instead, Dr. Leist suggested that visual difficulties would be linked to a "right-sided brain lesion," which was never found in petitioner's case. Id. at 193, 230-31. He stated that petitioner reported "visual field deficits" when she presented to the hospital in August 2009. Id. at 187. But "that lesion that is contributing very significantly to her overall symptomatology, at least by report, … is not showing on the MRI." Id. Dr. Leist said this right-sided brain lesion is "still not visible on the traditional MRIs," and that this was "concerning." Id. He also said that petitioner had "left homonymous hemianopsia that wasn't supported by a lesion." Id. at 230.

C. Analysis of the Causation Claim

i. Issues Pertaining to Nature of Petitioner's Diagnosis

The parties stipulate that petitioner "has suffered from a CNS inflammatory demyelinating condition." Joint Submission at 1. They ask the undersigned to determine petitioner's "precise diagnosis." Id. The undersigned finds that petitioner does indeed suffer from a CNS inflammatory demyelinating condition. However, a precise diagnosis is not necessary to determine that petitioner is entitled to compensation.

The Federal Circuit has made clear that "identifying [the petitioner's] injury is a prerequisite" to the Althen analysis. Broekelschen, 618 F.3d at 1346. However, it is not necessary to diagnose an exact condition. In Lombardi, the Federal Circuit explained: "[t]he function of a special master is not to 'diagnose' vaccine-related injuries, but instead to determine 'based on the record evidence as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the petitioner's injury." Lombardi v. Sec'y of Health & Human Servs., 656 F.3d 1343, 1351 (Fed. Cir. 2011) (citing Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1382 (Fed. Cir. 2009)). Furthermore, neither the Vaccine Act nor Althen burdens petitioner with establishing a specific diagnosis. See Kelley v. Sec'y of Health & Human Servs., 68 Fed. Cl. 84, 100 (2005) ("The Vaccine Act does not require petitioners coming under the non-Table injury provision to categorize their injury; they are merely required to show that the vaccine in question caused them injury – regardless of the ultimate diagnosis.")

In determining the petitioner's injury, the undersigned considered the record as a whole. § 13(a)(1). She reviewed and relied on statements in the medical records, as medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras v. Sec'y of Health & Human Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). In addition, the treating physicians' opinions are "quite probative," as treating physicians are in the "best position" to evaluate the vaccinee's condition. Capizzano v. Sec'y of

Health & Human Servs., 440 F.3d 1317, 1326 (Fed. Cir. 2006). However, no treating physician's views bind the special master, per se; rather, their views should be carefully considered and evaluated. § 300aa-13(b)(1); Snyder, 88 Fed. Cl. at 745 n. 67. Each opinion from a treating physician should be weighed against other, contrary evidence present in the record – including conflicting opinions from other treating physicians. Hibbard v. Sec'y of Health & Human Servs., 100 Fed. Cl. 742, 749 (Fed. Cl. 2011), aff'd, 698 F.3d 1355 (Fed. Cir. 2012); Caves v. Sec'y of Health & Human Servs., 100 Fed. Cl. 119, 136 (Fed. Cl. 2011), aff'd, 463 Fed. Appx. 932 (Fed. Cir. 2012); Veryzer v. Sec'y of Health & Human Servs., No. 06-522V, 2011 WL 1935813 at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), aff'd, 100 Fed. Cl. 344 (2011).

Upon careful examination of petitioner's medical records, the undersigned notes that petitioner's treating physicians did not reach a consensus about her condition. However, the medical records, as well as both experts' testimony and medical literature, suggest that petitioner more likely than not suffers from a CNS demyelinating disorder, such as an atypical form of MS.

It is helpful to note that MS is a complex condition with an "enormous" range of differential diagnoses.[55] An international task force on differential diagnosis in MS recommended (1) ruling out non-demyelinating syndromes, based on demographics, specific symptoms and signs, clinical course, radiology, and laboratory tests; (2) determining that those findings were consistent with a demyelinating disease; and then (3) narrowing down the "spectrum" of demyelinating diseases, which can have a shorter course (i.e., monophasic ADEM) or a longer course (e.g., MS). Pet. Ex. 154 at 1159. The key diagnostic criteria for MS is the "dissemination of disease in space and time." Id. at 1158. In other words, the individual should have multiple lesions, which appear to be of different ages.

In this case, the treating physicians considered various differential diagnoses, including vasculitis, before concluding that petitioner has a CNS demyelinating condition such as MS. The undersigned finds the opinion of Dr. Lisak to be particularly probative. More than two years after the onset of petitioner's condition, on September 20, 2011, Dr. Lisak wrote a thorough report discussing petitioner's case, including her personal and family history, symptoms, treatment, MRIs, lumbar puncture, and brain biopsy. Pet. Ex. 32 at 9-11. Dr. Lisak noted that petitioner's white matter disease would be consistent with vasculitis, MS, or Schilder's disease. Id. at 12. By January 18, 2012, Dr. Lisak had reviewed the MRI images and had developed "significant doubts" that they could represent "even longstanding CNS vasculitis." Id. at 1. The director of neuroradiology at Dr. Lisak's clinic agreed that the MRI images were inconsistent with vasculitis. Id. at 1. While Dr. Lisak did not fully rule out vasculitis, he concluded that the most likely diagnosis was "some peculiar variant of MS." Id. at 3. He recommended treatment for multiple sclerosis, including increased doses of baclofen. Id. Dr. John Fink and Dr. Giger-Mateeva concurred with Dr. Lisak's conclusions. Pet. Ex. 42 at 41-43.

Both parties' experts, as well, agreed with Dr. Lisak. Petitioner's expert Dr. Souayah allowed that petitioner's condition is "atypical," but found that Dr. Lisak conducted a "very thorough exam and assessment," and his conclusions were sound. Tr. 80. Respondent's expert Dr. Leist noted his professional acquaintance with and his respect for Dr. Lisak. Id. at 185. Dr. Leist agreed with Dr. Lisak's decision to treat petitioner for multiple sclerosis, "[a]s long as we can agree that this is a very atypical case of multiple sclerosis." Id. at 219.

[55] Miller et al., "Differential Diagnosis of Suspected Multiple Sclerosis: A Consensus Approach," 14 J. MULT. SCLER. 1157-74 (2008) [Pet. Ex. 154].

The undersigned agrees with Dr. Lisak and both experts that petitioner has a CNS demyelinating condition, most likely an atypical form of multiple sclerosis.

ii. Dispute Regarding Onset of Petitioner's Condition

The parties also stipulate that "petitioner has suffered from a CNS inflammatory demyelinating condition since at least early August 2009." Joint Submission at 1. They ask the undersigned to determine more precisely "when the onset of petitioner's condition occurred." Id. The undersigned finds that petitioner's condition began within a few weeks of the vaccine administered on June 4, 2009, when she began experiencing pain and other sensory symptoms in her right leg in mid-July 2009. There is no other clear explanation for these symptoms; such symptoms are non-specific but are associated with demyelinating conditions, and they are consistent with one of the lesions shown on the August 2009 MRI.

In her affidavit, petitioner stated that "a few days or a week or two" after the vaccine was administered on June 4, 2009, she "had pain shooting from [her] right hip down into [her] foot." Pet. Aff. at 1; Tr. 10-12. "A couple of weeks after that, sometime around mid-July of 2009, [petitioner's] hip stopped hurting," but she "began experiencing numbness in [her] right foot." Pet. Aff. at 1. During her initial hospitalization, petitioner reported that one morning in mid to late July 2009, she woke up feeling lightheaded. Pet. Ex. 22 at 28. For most of that day, she felt that her limbs were heavy. Id. at 29. The heaviness "transitioned to tingling in her right foot and leg, then to numbness over the dorsum of her foot and her [second] and [third] toes." Id.

The undersigned accepts petitioner's account of her July symptoms, which are corroborated by the history documented in her medical records by Dr. Asbury. In her affidavit, petitioner reports in mid-July, she began experiencing numbness in her right foot. Dr. Asbury documented that approximately three weeks prior to her admission (on or about July 14, 2009), petitioner's limbs felt heavy, and she began having tingling in her right lower extremity. Thus, the undersigned finds that petitioner's onset was no later than July 14, 2009, 40 days from the date of vaccination.

Dr. Souayah persuasively argued that petitioner's sensory symptoms such as the pain, weakness, tingling, and numbness in her right leg were due to her CNS demyelinating condition. Pet. Ex. 70 at 17; Tr. 52-53. He also filed supportive medical literature.[56] Dr. Souayah further opined that these symptoms would be consistent with the enhancing lesion in the left parietal area. Id. at 158-61. Dr. Leist suggested that the symptoms may have predated the lesion. Id. at 216. However, Dr. Leist did not present a more likely cause.[57] He opined that these symptoms were

[56] Noseworthy et al., "Multiple Sclerosis," 343 N. ENG. J. MED. 938-52 (2000) [Pet. Ex. 160].

[57] Dr. Leist suggested that petitioner's symptoms could be due to a vascular condition caused by petitioner's "longstanding" drug use. Id.[57] He opined that cannabis use can cause vascular and acute onset neurologic dysfunction, including cerebral vasospasm, cerebral ischemia, and arteritis. Resp. Ex. C at 9.[57] Dr. Leist also stated that "vasoconstrictive events have been associated with thunderclap headaches." Resp. Ex. C at 9.

He provided several articles for the proposition that cannabis use can cause vascular and acute onset neurologic dysfunction, including cerebral vasospasm, cerebral ischemia, and arteritis. Resp. Ex. C at 9. However, he conceded that petitioner's drug use was not as excessive as that discussed in the medical literature. Tr. 234. Petitioner began consuming cannabis at age 14, and did so

more likely to have been caused by a lesion in the spinal cord, but this was never found.[58] Id. at 215-25. He also suggested that a vascular event could have caused the hip pain. However, he did not present any evidence of a vascular event and did not claim that would cause the other sensory symptoms. Id. at 234.

Based on the evidence presented, the undersigned finds that it is more likely than not that the onset of petitioner's CNS demyelinating condition was when she began experiencing numbness in her leg, approximately July 14, 2009. The undersigned now analyzes whether petitioner has established entitlement for these injuries, under the test set forth in Althen.

VI. Application of Althen Prongs

a. Althen Prong One: Can the HPV Vaccine Cause CNS Demyelinating Conditions?

Under Althen Prong One, petitioner must provide a "reputable medical theory" demonstrating that the vaccine can cause the type of injury alleged. Pafford, 451 F.3d at 1355-56 (citations omitted). To satisfy this prong, petitioner's theory must be based on a "sound and reliable medical or scientific explanation." Knudsen, 35 F.3d at 548. The medical theory need be "legally probable, not medically or scientifically certain." Id. at 549. A petitioner may satisfy Althen Prong One without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a theory that has general acceptance in the medical or scientific community. Andreu, 569 F.3d at 1378-79 (citing Capizzano, 440 F.3d at 1325-26).

As described above, petitioner contends that the HPV vaccine can cause CNS demyelinating conditions. Dr. Souayah stated that such conditions are immune-mediated and could be caused by an aberrant immune response. Tr. 108-10. He provided an article by Wucherpfenning and Strominger, who found sequence similarity between proteins in wild HPV and proteins in the myelin sheath, and who used wild HPV to activate an immune response against the myelin sheath.[59] Dr. Souayah opined that this article demonstrated molecular mimicry between HPV and the self. Id. at 107-09. Dr. Souayah stated that there was no reason why the immune response to the HPV vaccine would be any different. Tr. at 108. Indeed, he provided medical articles which suggest that

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approximately once per month. Id. at 233 (citing Pet. Ex. 22 at 30). This was admittedly less than the subject who smoked up to eight cannabis cigarettes per day and subsequently developed arteritis, reported by Combemale et al.[57] Id. at 234. Dr. Leist's testimony as to drug use and alternative cause was not persuasive and did not meet the evidentiary standards required.

[58] Dr. Leist opined that "symptoms that are significantly related to the lower extremity would certainly suggest or not exclude a lesion within the spinal cord," which has not been found. Tr. 215, 219-20. But he admitted that "deep into the disease process that [petitioner] experienced, the spinal cord didn't show any focal lesions." Id. at 215. MRIs of the cervical and thoracic spine on October 28, 2010, did not reveal any lesions. Resp. Ex. C at 5. Another MRI of the cervical spine on September 20, 2011, also failed to find any lesions. Id. at 6; Resp. Ex. I at 2.

[59] Citing Wucherpfenning & Strominger [Pet. Ex. 215].

compared to live HPV, the HPV vaccine triggers the immune system to produce more antibodies,[60] which remain in the body for a longer period of time.[61]

Dr. Leist did not challenge Dr. Souayah's general explanation of molecular mimicry. Resp. Ex. I at 5. He agreed that CNS demyelinating conditions are immune-mediated. Tr. 205, 226. He also agreed that molecular mimicry is believed to "play a role" in certain demyelinating conditions. Id. at 226-27. Dr. Leist claimed that there was no evidence of molecular mimicry specifically between HPV and myelin. Resp. Ex. C at 8. However, he failed to address the article by Wucherpfenning and Strominger, which does offer some evidence of homology and of an immune response against myelin after the introduction of wild HPV.

For these reasons, the undersigned finds that petitioner has provided preponderant evidence that the HPV vaccine can cause CNS demyelinating conditions through the mechanism of molecular mimicry. Accordingly, petitioner has satisfied Althen Prong One.

b. Althen Prong Two: Did Petitioner's HPV Vaccine Cause Her to Develop This CNS Demyelinating Condition?

Althen Prong Two requires proof of a logical sequence of cause and effect, usually supported by facts derived from the vaccinee's medical records. Althen, 418 F.3d at 1278; Andreu, 569 F.3d at 1375-77; Capizzano, 440 F.3d at 1326; Grant, 956 F.2d at 1148. In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting Althen, 418 F.3d at 1280). Medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528. The petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

Petitioner's clinical course, the MRI findings on August 5, 2009, and the oligoclonal banding present on August 6, 2009, all support petitioner's claim that the vaccination caused an autoimmune reaction consistent with the time course of molecular mimicry.

Petitioner's initial symptoms occurred within the two to forty-two day window in which the mechanism of molecular mimicry has been shown to occur post-vaccination. Petitioner testified that she began experiencing pain in her right hip within "a few days or a week or two," after her June 4, 2009 Gardasil vaccination. Tr. 10; Pet. Ex. 39 at ¶ 4. As the pain gradually subsided,

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[60] Citing Harro et al. [Pet. Ex. 120] (reporting that the immune system produces 40 times more antibodies in response to the HPV vaccine than to the live virus).

[61] Citing Merck [Pet. Ex. 104] (stating that the level of antibodies in the body peak about seven months after the administration of the vaccine, and remain at detectable levels for about 36 months).

petitioner began experiencing numbness in her right foot. Tr. 10; Pet. Ex. 39 at ¶ 5. Approximately four two six weeks after the vaccination, within the two to forty-two day window, petitioner had headaches, loss of vision, hemianopsia, and slurred speech. Tr. 91. Dr. Souayah noted that there was no other explanation for these symptoms, and petitioner did not experience any trauma that could have caused them. Id. at 115.

Further, the August 5, 2009 MRI showed two lesions, one enhancing and the other non-enhancing. Pet. Ex. 23 at 36-37. Dr. Souayah explained that the second, non-enhancing lesion in the occipital lobe was consistent with the headache and visual problems petitioner experienced in mid-July and early August. Tr. 55; Pet. Ex. 23 at 36.

The August 6, 2009 finding of oligoclonal bands in petitioner's CSF indicates an autoimmune disease. Dr. Souayah opined that oligoclonal bands could be present as soon as two weeks, or up to eight to twelve weeks, after a triggering infection, such as a vaccine. Tr. 142-43.

The undersigned finds that the facts of the case, in conjunction with petitioner's mechanism of causation, demonstrate a logical sequence of cause and effect sufficient to satisfy petitioner's burden under Althen Prong II.

c. Althen Prong Three: Is There a Medically Acceptable Temporal Relationship?

Althen Prong Three requires petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That term has been equated to mean a "medically acceptable temporal relationship." Id. The petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disease's etiology, it is medically acceptable to infer causation-in-fact." De Bazan v. Sec'y of Health & Human Servs., 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen Prong One). Id.; Koehn v. Sec'y of Health & Human Servs. 773 F.3d 1239, 1243 (Fed. Cir. 2014); Shapiro v. Sec'y of Health & Human Servs., 101 Fed. Cl. 532, 542 (2011), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 2013 WL 1896173 (Fed. Cir. 2013).

As discussed above, petitioner's condition first manifested as sensory symptoms in her right lower extremity. After reviewing all of the medical records and expert testimony, the undersigned finds that the onset of petitioner's condition was no later than July 14, 2009, which was no later than 40 days after she received the HPV vaccine. Petitioner stated that "sometime around mid-July of 2009," her hip stopped hurting but she began experiencing numbness in her right foot. Pet. Aff. at 1. Dr. Leist agreed that this symptom was well within the more "conservative" time frame of two to 42 days for adverse events following vaccination. Tr. 221-25.[62] In other words, although Dr. Leist challenges the significance of these symptoms, he does not challenge that they have a temporal relationship to the vaccination which is viewed as medically acceptable.

Dr. Souayah opined that the onset of petitioner's condition was medically appropriate for vaccine causation. Shortly after petitioner received the vaccine on June 4, 2009, she began producing antibodies, which could have started attacking the brain. This manifested in the sensory symptoms in her left leg within a few weeks of the vaccine (July episode). Clinical tests performed

[62] Citing Resp. Ex. I, Tab 1.

on August 6, 2017, showed that petitioner had positive oligoclonal bands in her CSF. Tr. 56. As in petitioner's case, when the bands are present only in the CSF, rather than in both the CSF and the blood, this is suggestive of an autoimmune process. Id. at 56, 142. Dr. Souayah testified that one would expect to see abnormal immunoglobulins within eight to 12 weeks. This is consistent with petitioner's clinical presentation, as she was found to have oligoclonal bands on August 6, 2009, approximately 12 weeks after she received the Gardasil vaccination. Dr. Souayah further testified that the lesions seen on petitioner's initial MRI were consistent with the onset of petitioner's symptoms. Thus, there is factual evidence of a medically acceptable temporal relationship (within 40 days).

In accordance with the foregoing, the undersigned finds that petitioner has satisfied Althen Prong Three.

VII. Conclusion

After the undersigned's review of the entire record, see § 300aa-13(a)(1), and in light of the foregoing reasons, the undersigned finds that petitioner is entitled to compensation for an injury that was caused-in-fact by a covered vaccine. 42 C.F.R. § 100.3(a)(XIV); Althen, 418 F.3d 1274. A separate damages order will issue.

IT IS SO ORDERED.

s/ Nora Beth Dorsey
Nora Beth Dorsey
Chief Special Master