# In the United States Court of Federal Claims

**OFFICE OF SPECIAL MASTERS**

No. 11-77V

Filed: June 17, 2013

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| SHERRIL K. STILLWELL, | * | |
| | * | Influenza (Flu) Vaccine; Acute |
| Petitioner, | * | Demyelinating Encephalomyelitis |
| | * | (ADEM); Record Evidence Does Not |
| v. | * | Support Alleged Injury |
| | * | |
| SECRETARY OF HEALTH | * | |
| AND HUMAN SERVICES, | * | |
| | * | |
| Respondent. | * | |
| ********** | | |

Sol Ajalat, Ajalat & Ajalat, North Hollywood, CA, for petitioner.
Alexis Babcock, U.S. Dep't of Justice, Washington, DC, for respondent.

## DECISION[1]

### I. Introduction

On February 7, 2011, Sherril Stillwell (petitioner) filed a petition for compensation under the National Vaccine Injury Compensation Program (the Program),[2]

[1] Because this published decision contains a reasoned explanation for the action in this case, the undersigned intends to post this decision on the website of the United States Court of Federal Claims, in accordance with the E-Government Act of 2002 § 205, 44 U.S.C. § 3501 (2006). In accordance with the Vaccine Rules, 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). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted decision. If, upon review, the undersigned agrees that the identified material fits within the requirements of that provision, such material will be deleted from public access.

[2] The Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-10 et seq. (hereinafter "Vaccine Act" or "the Act"). Hereafter, individual section references will be to 42 U.S.C. § 300aa of the Act.

alleging that she suffered from acute demyelinating encephalomyelitis (ADEM) as a result of an influenza vaccination she received on February 22, 2008.[3]

Respondent recommended against compensation. Respondent challenged petitioner's claim that she developed ADEM. Resp't's Report at 7. Respondent further challenged the vaccine-relatedness of petitioner's injury. Id.

The parties presented expert opinions in support of their respective positions. Dr. Marcel Kinsbourne testified for petitioner. Dr. Jeffrey Cohen testified for respondent. An entitlement hearing was conducted in Washington, D.C., on March 30, 2012. Thereafter, the parties filed post-hearing briefing. The matter is now ripe for a ruling.

The question here is whether petitioner's condition can be characterized as ADEM. The parties and their respective experts focused on this issue in their written submissions and at hearing. Simply stated, petitioner asserts that she suffers from an atypical case of ADEM. Respondent disputes that. Although respondent agrees with petitioner that ADEM can have wide variability in its presentation, respondent contends that numerous aspects of petitioner's clinical course are too unusual to merit an ADEM diagnosis.

As discussed in detail below, the weight of the evidence does not preponderate in favor of a finding that petitioner suffers from vaccine-related ADEM. Accordingly, petitioner is not entitled to Program compensation.

## II. Factual Background

Petitioner was born on October 25, 1954. Pet'r's Ex. 1 at ¶1. As a child, she had rheumatic fever, but fully recovered. Pet'r's Ex. 4 at 69.[4] Her subsequent medical history was remarkable for smoking, hypothyroidism, gastroesophageal reflux disease, panic and anxiety disorders, and osteoarthritis of the knees. Pet'r's Ex. 3 at 165. Petitioner also suffered from insomnia. Pet'r's Ex. 5 at 25.

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[3] In her petition, petitioner alleged she developed encephalomyelitis as a result of an influenza vaccination. Petition (Pet.) at 3. However, as discussed below, she subsequently defined her injury as acute demyelinating encephalomyelitis (ADEM).

[4] All citations to Exhibits 1-7 refer to the pagination adopted by petitioner at the bottom right hand corner of each page.

On February 22, 2008, petitioner was evaluated for recurrent pain in her right knee, a discomfort that was attributed to degenerative joint disease. Pet'r's Ex. 3 at 165. During this office visit, petitioner was treated with injections of steroids and lidocaine in each knee. Id. at 168. She also received the subject influenza vaccination. Pet'r's Ex. 2 at 2.

Petitioner next sought medical treatment two months later, on April 28, 2008. Pet'r's Ex. 4 at 161. At that time, she presented with dizziness and unsteadiness. Id. She reported that she had suffered for one week with vertigo and nausea, for two weeks with weakness that had worsened, and for three weeks with right ear pain. Id. She further reported that she had "no energy" and that it had been "very difficult to get out of bed in [the morning]." Id. Her treating physician, Chierry Anderson Poyotte, M.D., an internist, diagnosed her with an ear infection (otitis media) and vertigo. Id. at 163.

Two days later, on April 30, 2008, petitioner again presented to Dr. Poyotte complaining of ongoing vertigo, malaise, and fatigue. Id. at 154. She also complained of "buzzing [in her] right ear while [lying] on [her] right side." Id. Dr. Poyotte advised petitioner "to follow up with her [p]sychiatrist for reevaluation." Id. at 155.

Six days later, on May 6, 2008, petitioner saw Natalie Ting, a doctor of osteopathic medicine, with complaints of continuing fatigue and dizziness. Id. at 147. She reported that she felt dizzy "every moment of every day" for the previous three weeks and that her dizziness worsened with movement. Id. She also reported "feeling numb on the right side of her body" during the three week period preceding her office visit. Id. Observing a "[d]epressed mood and affect[,]" Dr. Ting suspected that petitioner's symptoms "[might] have a psych[iatric] origin" because her "[e]xam [was] not [consistent] with her complaints." Id. at 148-49.

Three days thereafter, on May 9, 2008, petitioner presented to Kijung Paul Sung, M.D., an internist, again complaining of ongoing vertigo, dizziness, and fatigue. Id. at 139-40. Petitioner further complained of "partial numbness [on the] right side of her body." Id. at 140. Petitioner indicated that she felt "drunk when [she] walk[ed]." Id. She also demonstrated "decreased sensation to light touch over [the] right [side of her] face, right upper extremities, and right lower extremities." Id. at 141. During this visit, petitioner had a computer tomography (CT) scan and magnetic resonance imaging (MRI) taken of her brain, the results of which were normal. Id. at 142-43.

At the end of May, petitioner presented to the emergency room complaining of vertigo, taste disturbance, ataxia, numbness and weakness on her right side, and an

inability to find words. Pet'r's Ex. 4 at 127. She was hospitalized for three days, from May 27 to May 29, 2008. Id. at 127. She showed "no sign of otitis media." Id. at 128. She had a brain and a cervical spine MRI (with and without contrast), the results of which were normal. Id. at 127. The "etiology of her symptoms [was] unclear," and she was advised to see a neurologist on June 9, 2008, and to follow up with her psychiatrist. Id. at 129.

Petitioner presented to David Shaw, M.D., a neurologist, on June 9, 2008. Id. at 114. She related that she had continuing dizzy spells accompanied by a spinning sensation. Id. She also related that almost two weeks after her hospitalization, she had developed numbness on the right side of her body, fatigue, general weakness, an unsteady gait, nausea, blurred vision, decreased taste sensation, and intermittent neck pain. Id. at 114-15. Dr. Shaw's diagnostic impression was "[p]ossible or probable multiple sclerosis [(MS)]," but he noted that petitioner's MRI did not show the "obvious evidence" of the characteristic lesions that are associated with that condition. Id. at 116. Nonetheless, Dr. Shaw prescribed copaxone to treat petitioner's perceived MS. Id.

The next day, on June 10, 2008, petitioner underwent an EEG and a visual evoked response test, the results of which were normal. Id. at 111, 120. Ten days later, on June 20, 2008, she reported no improvement in her symptoms after a ten-day course of copaxone. Id. at 104.

Later in the day, petitioner presented to William Miller, M.D., another neurologist. Pet'r's Ex. 3 at 155. She complained of "progressive dizziness, imbalance, numbness, and weakness" that had lasted several weeks. Id. Petitioner indicated her symptoms had worsened, she had begun to slur her speech, and her legs felt "extremely heavy." Id. During this office visit, she commented that on further reflection, "she [had] noticed several weeks of feeling that [her] socks seemed too tight on [her] legs . . . prior to the onset of her vertigo." Id. at 159. Dr. Miller saw "no lesion on [her] MRI to explain [her] symptoms" and noted that it would be "hard to localize [a] lesion that would explain all of her symptoms." Id. at 158. Among the diagnoses Dr. Miller considered were "neuronitis or other vestibular dysfunction"[5] and MS. Id. at 161. Dr. Miller discussed with petitioner's family the possibility that petitioner was exhibiting the first demyelinating event of MS, but he observed that it would be unusual "for symptoms to

[5] Neuronitis is "inflammation of one or more neurons." Dorland's Illustrated Medical Dictionary (32d ed. 2012) at 1268 (Dorland's). Vestibular dysfunction consists of "a single attack of severe vertigo, usually accompanied by nausea and vomiting . . . [which] usually improves within a few days." Id.

be so severe without seeing [a] change on [petitioner's] MRI." Id. Although the testing of petitioner's cerebrospinal fluid (CSF) protein levels showed oligoclonal bands, such findings were "nonspecific and [could] be seen with viral infections and other etiologies." Id. Dr. Miller did not recommend treatment for MS, but he did recommend "following up with her psychiatrist to make sure treatment of her anxiety [was] maximized as well." Id.

On July 8, 2008, petitioner returned to Dr. Shaw. Pet'r's Ex. 4 at 90. Dr. Shaw noted that a scheduled MRI of her thoratic spine could potentially confirm a diagnosis of MS, but opined that because some of her "symptoms . . . [could not] be totally explained by" the findings on her MRI, "[s]tress and anxiety . . . [could not] be ruled out." Id. He also noted that petitioner's "[m]uscle strength [was] probably normal on all 4 limbs, although she [could not] stand well and she need[ed] assistance to walk." Id. at 89. Petitioner complained of intermittent dizziness, balance problems, and slurred speech. Id. In addition, she reported numbness on the right side of her face, arm, and leg that had lasted for over a month. Id.

A second test of petitioner's CSF was conducted on July 17, 2008, three months after petitioner first sought treatment for her symptoms. Pet'r's Ex. 7 at 14-15. That test revealed five oligoclonal bands, which were suggestive of MS. Id. Subsequently, on August 2, 2008, an MRI (without contrast) of petitioner's brain was performed; it showed "[i]ncreased FLAIR and T2 signal intensity . . . of unclear etiology." Pet'r's Ex. 3 at 123. In the reviewing physician's assessment, petitioner's MRI exhibited an "unusual lesion." Id. The lesion was indicative of a demyelinating disease that was "[p]robably inflammatory, [and] atypical." Id. Petitioner was noted to have non-specific dizziness, gait disorder, anxiety disorder, mild lymphocytic pleocytosis, and oligoclonal bands. Id. at 121-24. Dr. Miller did not find a clear etiology for petitioner's symptoms. Pet'r's Ex. 4 at 72.

On August 20, 2008, petitioner presented to Christopher Di Stasio, M.D., another neurologist. Id. at 69. Petitioner was referred to Dr. Di Stasio for an additional opinion regarding her suspected MS. Id. at 73. She reported that the general weakness in her legs persisted, but her symptoms of vertigo and numbness on the right side of her body were improving. Id. She also described a "cold/tingly feeling of the right lower face [and] jaw with a pulling sensation that radiate[d] down [the] right side of [her] neck into [her] shoulder . . . [with] episodes of her entire body feeling heavy, difficulty speaking, [and] feeling as though she [might] faint." Id. She related that she was using a wheelchair "for in-home mobility." Id. Dr. Di Stasio observed that the result of petitioner's previous MRIs of the thoracic spinal cord and cervical spine revealed no abnormalities. Id. at 71.

He also noted the abnormalities Dr. Miller noted in the results of petitioner's August 2, 2008 MRI of her brain. Id.

Dr. Miller appears to have consulted with Dr. Di Stasio about the unclear etiology of petitioner's condition. Id. at 74. In Dr. Di Stasio's view, petitioner was suffering from ataxia. Id. at 71. He "suspect[ed]" her symptoms "[might] represent a post-infectious immune process." Id. at 71. He noted that her symptoms had begun around April of 2008, but that she seemed to be getting better slowly. Id.

Petitioner continued to see Dr. Miller for her neurologic problems. On September 8, 2008, Dr. Miller diagnosed her with demyelinating disease that was "prob[ably] postinfectious," but was "improving slowly." Pet'r's Ex. 3 at 102.

Nearly eighteen months later,[6] on March 20, 2010, petitioner had another brain MRI. Id. at 61. Compared to her August 2, 2008 brain MRI, this image showed improvement. Id. Dr. Miller reiterated his earlier diagnostic impression that petitioner was suffering from a demyelinating disease, a probable "monophasic demyelinating event." Pet'r's Ex. 7 at 7. Dr. Miller noted that although petitioner was reporting "increased weakness now with multiple symptoms," her "MRI actually look[ed] better." Pet'r's Ex. 3 at 65. He stated that the appearance of new lesions would have been consistent with a diagnosis of MS, but he did not find any. See id.; see also Pet'r's Ex. 7 at 6-7.

On April 14, 2010, petitioner presented again to Dr. Sung, who noted that she was "alert and oriented," and had "normal sensation and normal strength," but exhibited abnormal coordination and an abnormal gait with noticeable shuffling. Pet'r's Ex. 4 at 56-57.

An MRI of petitioner's cervical spine (without contrast) was performed on May 23, 2010, to help evaluate petitioner's worsening gait, as well as the weakness in her arm and left lower extremity. Pet'r's Ex. 7 at 4. Petitioner's problems with speech continued until June 2010. See Pet'r's Ex. 3 at 12. Her problems with coordination, balance, and walking continued through July 2010. See id. at 1.

On July 30, 2010, petitioner returned to Dr. Sung complaining of body pain that lasted nearly six months. Pet'r's Ex. 4 at 22-24. Dr. Sung diagnosed petitioner with,

[6] Petitioner did not submit any medical records from the year 2009, presumably because "[s]he lost her job and then lost her . . . insurance [with Kaiser] for one year," Pet'r's Ex. 4 at 53, and thus, had no appointments with doctors during that time.

among other things, a demyelinating disease of the central nervous system and fibromyalgia. Id. at 25. The pain associated with her apparent fibromyalgia persisted over the next three months, through November 2010. See id. at 4.

A few months later, on February 7, 2011, petitioner filed a vaccine claim. Petitioner did not submit any records thereafter that speak to her current condition.

As reflected in the opinions of the parties' experts, the parties disagree about the nature of petitioner's condition and its vaccine-relatedness. Before evaluating petitioner's claim, the undersigned turns first to summarize the opinions of the experts.

**A. Dr. Marcel Kinsbourne, Petitioner's Offered Expert**

Petitioner filed an expert report from Dr. Marcel Kinsbourne, a neurologist, to support her claim.[7] Pet'r's Ex. 8. Dr. Kinsbourne holds medical licenses in the United Kingdom, Canada, North Carolina, the Commonwealth of Massachusetts, and the Commonwealth of Virginia. ECF Doc. No. 26, filed Mar. 28, 2012, at 1. He has held numerous teaching positions and hospital appointments in various capacities at universities in each of the aforementioned locations. Id. at 1-2. Additionally, he has authored and edited many medical articles, books, and medically-related literature over his lengthy career as a neurologist. Id. at 5-34.

Dr. Kinsbourne is not a currently practicing clinician; he has not had an active clinical neurology practice since 1980. Tr. 61-62. Because his work since 1981 has focused on behavioral disorders, he has not treated a patient with ADEM since 1980. Tr. 62. Before then, he saw "quite a few cases of ADEM." Tr. 62.

Dr. Kinsbourne describes ADEM as "an immune-mediated demyelinating disorder of the central nervous system [(CNS)]" that "commonly presents acutely, with multifocal neurological findings, including motor deficits." Pet'r's Ex. 8 at 6. Dr. Kinsbourne

[7] Petitioner filed the medical literature on which Dr. Kinsbourne relied as attachments to his initial expert report, Pet'r's Ex. 8, on a compact disc. See ECF Doc. No. 12, filed May 10, 2011. The 602 pages of the medical literature were divided into eight separate PDF files, seven of which contained more than one medical article. See id. at 2. Petitioner did not provide exhibit numbers for the PDF files or the separate articles. Thus, all citations to the medical literature referenced in Dr. Kinsbourne's initial expert report correspond to petitioner's "Index of References" found in her "Notice of Filing of CD," see id., and the pinpoint page cites refer to the page numbers adopted by petitioner.

opined that as a result of receiving the influenza vaccine, petitioner developed "a variant of ADEM," marked by "[a] subacute onset." Id.

Dr. Kinsbourne acknowledged that in 2011, the Institute of Medicine (IOM) found the evidence insufficient to establish a causal relationship between receipt of a flu vaccine and the onset of ADEM.[8] Tr. 78. But, he pointed to the findings of the 2009 Lapphra report,[9] which were suggestive of a causal relationship between the administered flu vaccine and the onset of neurologic injuries. Tr. 80-81. Dr. Kinsbourne also pointed to a chapter from the well-regarded textbook of Merritt's Neurology,[10] stating that vaccine-induced ADEM may be a possbility when neurologic signs develop within four to twenty-one days after vaccination. Tr. 86.

Adverting to the mention of a causal association between various vaccinations (including flu) and ADEM in the medical literature, Dr. Kinsbourne insisted that, "although rare, [this causal link] is well recognized." Pet'r's Ex. 8 at 7 (citing Pet'r's Ex. 8-6 at 500, Hiroshi Shoji & Mashahide Kaji, The Influenza Vaccination and Neurological Complications, 42:2 The Japanese Soc'y of Internal Med. 1 (2003)).

He posited that the flu vaccine can cause ADEM by inducing an autoimmune response through molecular mimicry. Id. at 9. He explained that ADEM occurs when "autoreactive cells enter the [central nervous system] during immune surveillance and . . . encounter homologous myelin protein [to] culminat[e] in a destructive autoimmune process in the [central nervous system]." Id. at 10. He added that the flu vaccine can cause ADEM through another immunologic mechanism of "bystander activation of autoreactive immune T cells." Id. This process can occur together with and augment the

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[8] Institute of Medicine, Adverse Effects of Vaccines: Evidence and Causality 308 (Kathleen R. Stratton et al. eds., 2011). Dr. Kinsbourne cited this report in his supplemental expert report, see Pet'r's Ex. 9 at 6, but petitioner did not file it as an exhibit.

[9] Pet'r's Ex. 8-4 at 383, Keswadee Lapphra et al., Adverse Neurologic Reactions After Both Doses of Pandemic H1N1 Influenza Vaccine With Optic Neuritis and Demyelination, 30:1 The Pediatric Infectious Disease J. 84 (2009).

[10] The chapter, Viral Infections, in the textbook Merritt's Neurology (L.P. Rowland ed., 2005), was authored by Burk Jubelt and James R. Miller. See Pet'r's Ex. 8-3 at 310. The parties interchangeably referred to the textbook chapter as either "Jubelt" or "Merritt's."

effect of molecular mimicry. Id. Because there was no evidence of an "event[] . . . capable of causing or triggering ADEM"[11] that occurred within the same time frame, id. at 12, Dr. Kinsbourne opined that petitioner's "ADEM variant was caused by an immune-mediated reaction to [her] influenza vaccine." Id. at 13.

Dr. Kinsbourne averred that the onset of petitioner's ADEM began "[a]pproximately four weeks after" her February 22, 2008 influenza vaccination, and "progressed for several months before it stabilized." Id. at 5. He stated that petitioner's medical records "showed changes compatible with immune activation" in her cerebrospinal fluid and her "[t]reating physicians considered her illness to be inflammatory and postinfectious in nature, but atypical." Id. Dr. Kinsbourne conceded that none of petitioner's physicians treated her specifically for ADEM, but he claimed that their treatment of petitioner nonetheless "implied [that her inflammatory condition] was immune[-]mediated" and would respond to the administration of cortical steroids, a prescriptive course that would have been consistent with a finding of ADEM. Tr. 92.

Dr. Kinsbourne relied, in part, on the 2007 Sejvar article[12] to support his opinion that petitioner suffered from ADEM. See Tr. 30, 50-55, 156. This article set forth "firm guidelines for the diagnosis of ADEM for the specific purpose of assisting in the evaluation of questions of vaccine injury." Tr. 30. It outlined a number of diagnostic criteria for ADEM that Dr. Kinsbourne posited were applicable in this case, including: (1) a single brain lesion; (2) trouble finding words; (3) cranial nerve abnormalities; (4) motor weakness; (5) sensory abnormalities; (6) ataxia and gait dysfunction; and (7) arm tremors. Tr. 53 (citing Pet'r's Ex. 9-1 at 8, the 2007 Sejvar article). He asserted that petitioner had exhibited five of the nine criteria discussed in the article—"decreased arousability, aphasia, motor weakness, sensory abnormalities, and ataxia," Pet'r's Ex. 9 at 1-2, and he observed that a proper diagnosis of ADEM requires only one of the listed criteria. Tr. 53.

The 2007 Sejvar article also identified MRI findings of diffuse or multifocal white matter lesions as necessary criteria for an ADEM diagnosis. Tr. 75-76. Dr. Kinsbourne

[11] Dr. Kinsbourne opined that petitioner's ear infection had no relation to her vertigo or any of her other symptoms. Tr. 94-95.

[12] Pet'r's Ex. 9-1, James J. 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 5771 (2007). The parties interchangeably referred to this article as the "Sejvar article" and the "Brighton Group" article.

acknowledged that petitioner's lesion was not multifocal, Tr. 75-76, but he asserted that the description of petitioner's MRI findings was consistent with a diffused lesion. Tr. 76.

As further evidence of the vaccine-relatedness of petitioner's injury, Dr. Kinsbourne pointed to: (1) the lesion detected on her brain stem; (2) the subacute onset of her disorder; (3) the presence of oligoclonal bands in her cerebrospinal fluid (CSF) test results; and (4) the medically acceptable four-week interval between her vaccination and the onset of her ADEM. Pet'r's Ex. 8 at 10-11; see also Tr. 22-25. Although Dr. Kinsbourne admitted that "some features of [petitioner's] case are . . . not typical" for ADEM, he urged that "her condition nonetheless fits within the bounds of [an] ADEM diagnosis." Pet'r's Ex. 9 at 1; see also Tr. 38-39 (Dr. Kinsbourne describing petitioner's subacute onset as "unusual").

Dr. Kinsbourne averred that ADEM "'usually occur[s] a few days or weeks following vaccine administration or virus-like disease.'" Pet'r's Ex. 8 at 6 (quoting Pet'r's Ex. 8-6 at 511, Institute of Medicine, Influenza Vaccines and Neurological Complications 36 (Kathleen R. Stratton et al. eds., 1994)). It "is preceded by an infectious event within a medically reasonable timeframe . . . in the majority of cases." Tr. 33. But he denied any such infectious event in this case.

Based on the documented first appearance of petitioner's symptoms, and her later recollection that she had "experienced some tightness and numbness around both ankles and began to have an unaccustomed weakness," Dr. Kinsbourne posited that the onset of petitioner's demyelinating disorder occurred in the third week of March 2008. Tr. 9; see also Tr. 25. Dr. Kinsbourne described petitioner's disorder as "monophasic" and non-progressive; he asserted that her condition was marked by "a rise time, a plateau, and then a decline of symptoms." Tr. 21. In his view, petitioner reached her plateau during her hospitalization at the end of May 2008. Tr. 25.

Citing two articles—the 1999 Singh article and the 2004 Leake article[13]—Dr. Kinsbourne insisted that ADEM can have a subacute onset, such as occurred in this case. Pet'r's Ex. 9 at 4. Quoting an excerpt from the 1994 IOM report stating that "the latencies for . . . ADEM [may extend] . . . from 5 days to 6 weeks," Dr. Kinsbourne took the position that the onset of ADEM can take up to forty-two days, even though the most common time frame for the onset of ADEM is one or two weeks. Tr. 34. Although he

[13] Pet'r's Ex. 8-6 at 503, Surendra Singh et al., Acute Disseminated Encephalomyelitis: MR Imaging Features, 173 AJR 1101 (1999); Pet'r's Ex. 8-4 at 387, John A.D. Leake et al., Acute Disseminated Encephalomyelitis in Childhood: Epidemiologic, Clincal and Laboratory Features, 23:8 Pediatric Infectious Disease J. 756 (2004).

recognized that cases with delayed symptom onset were not typical for ADEM, Dr. Kinsbourne noted that such cases were "clearly mentioned in the literature." Tr. 38. He confessed, however, that he was unaware of any reports in the literature involving the progression of ADEM—as in this case—over the course of multiple months. Tr. 72.

**B. Dr. Jeffrey Allen Cohen, Respondent's Offered Expert**

Respondent filed an expert report from Jeffrey Allen Cohen, M.D., a clinical neurologist, challenging petitioner's claim. Resp't's Ex. A. Dr. Cohen is board certified in neurology, neuromuscular diseases, and clinical neurophysiology. Tr. 104. He has treated patients with ADEM, among other disorders. Tr. 104-05. He is a professor of neurology at Dartmouth Medical School and the chief of the neurology section at Dartmouth Hitchcock Medical Center. Tr. 102. He treats patients and supervises neurology students and fellows about four-and-a-half days per week. Tr. 103.

Based on his review of petitioner's medical records, Dr. Cohen disagreed with Dr. Kinsbourne's opinion that petitioner developed ADEM as a result of the flu vaccine she received. Resp't's Ex. A at 1. Although he agreed that petitioner had "an acquired demyelinating syndrome," he indicated that—like petitioner's own treating doctors—he could not affix a more specific diagnostic label to her condition. Tr. 169-70. He was clear, however, that petitioner's "clinical picture was not consistent with a diagnosis of ADEM." Resp't's Ex. A at 6. He asserted that the medical literature is bereft of "reliable evidence" showing that the flu vaccine can cause ADEM," [14] id.; see also Tr. 111, but he allowed that a vaccination could cause a demyelinating disorder. Tr. 141.

Dr. Cohen outlined the "clinical features of ADEM" with which most subjects present:

> [an] [a]brupt onset; [s]omnolence, confusion, seizures, headache, meningeal signs,[15] fever; [and] 97% [of cases occur in] children and adolescents. Id. [Onset occurs, at most,] four weeks . . . between [the] inciting event and [the] evolution of the neurological picture. Id. [Imaging reveals] confluent diffuse areas of demyelination; a single lesion is not considered to be consistent with the diagnosis of ADEM. Id. [Typically, an afflicted subject is responsive] to steroid therapy.

[14] Dr. Cohen described the causation evidence as "very, very scant." Tr. 111.

[15] Meningeal signs are those exhibited when the meninges have been irritated. See Dorland's at 1132. The meninges are the "three membranes that envelop the brain and spinal cord." Id.

Resp't's Ex. A at 2.

Dr. Cohen explained that there is no "specific marker" for ADEM; rather, the condition requires "a clinical diagnosis . . . supplemented . . . [by] laboratory examinations." Tr. 107. Magnetic resonance imaging can assist in making an ADEM diagnosis because such imaging will show the "predominantly white matter lesions . . . [and] the . . . diffused multifocal white matter changes" that are characteristic of the condition. Tr. 108. Dr. Cohen explained that "it would be very unusual" for a patient with ADEM to show no evidence of diffused, multifocal white matter changes on imaging. Tr. 108.

Dr. Cohen observed that ADEM is "a disease that is severe and swift in its onset, reaches a nadir, and then . . . gets better . . . to a great degree . . . . [T]he total course [between] illness . . . [and] recovery is measured in months, not years." Tr. 178. In his clinical experience, the symptoms of ADEM fully manifest, at most, four weeks after the inciting event. Tr. 155-56.

Dr. Cohen discussed the aspects of petitioner's medical history that he believed militated against a finding that she suffered from ADEM. Tr. 152-53, 155; see also Resp't's Ex. A at 2-3, 5. He argued that Ms. Stillwell's symptoms of "decreased arousability, aphasia, motor weakness, sensory abnormalities and ataxia;" are not dispositive of an ADEM diagnosis because they are not "diagnosis-specific neurologic findings;" such symptoms could occur in patients suffering from, among other injuries, either a stroke, a traumatic brain injury, or MS. Resp't's Ex. C at 1. In Dr. Cohen's view, the primary factor that most disfavors a diagnosis of ADEM is the lack of "a markedly depressed level of consciousness" during the course of petitioner's illness. Id.

Dr. Cohen noted that other common indicators of ADEM were absent in petitioner's case. In particular, he did not see any record of petitioner suffering from facial weakness, a symptom of ADEM readily noticeable to evaluating medical personnel. Tr. 113-14. Nor did he see any evidence of lesions on either petitioner's May 15, 2008 or May 28, 2008 MRIs. Tr. 114. Dr. Cohen observed that the presence of oligoclonal bands on petitioner's imaging were features that "can occur in any demyelinati[ng] disease." Resp't's Ex. A at 5. But "they are more representative of MS than ADEM." Id. Dr. Cohen added that the results of petitioner's June 10, 2008 EEG were normal. Tr. 114. He testified that if petitioner had the symptoms of impaired speech or a depressed level of consciousness, corroborative evidence would have appeared on her MRI or EEG, to confirm an ADEM diagnosis. Tr. 115.

Dr. Cohen elaborated that "the area of demyelination [visible on petitioner's imaging] was limited to the brainstem which is not the usual location for ADEM." Resp't's Ex. A at 2. "[N]or was the area of [detected] demyelination as extensive as [typically occurs] in ADEM." Id.

Petitioner's protracted "course [of illness] is [also] very atypical for ADEM—[which generally] progresses over weeks, not months." Id. at 2. Dr. Cohen asserted that a subacute onset "of over four weeks is very unusual." Id. at 5.

Dr. Cohen explained that as anomalous as petitioner's symptom onset was, so was her lack of any appreciable recovery. Id. at 2, 5. These features of petitioner's condition—when considered together—were strikingly uncharacteristic of ADEM. Id.

Dr. Cohen disagreed with petitioner's assertion that her symptoms plateaued during her hospitalization at the end of May 2008. Tr. 116. He pointed to the decision by petitioner's treating physicians to begin a course of steroid therapy as an indication "that they thought . . . she was getting worse." Tr. 117. He observed that the steroids had "no clear benefit" to petitioner. See Pet'r's Ex. 4 at 73. As further evidence of her worsening condition, Dr. Cohen noted that petitioner required a wheelchair in August 2008, but she had not needed one previously. Tr. 117. Dr. Cohen explained that the record evidence of petitioner's ongoing and unrelenting problems did not support a finding that she suffered from ADEM because symptoms in "the majority of [ADEM] patients . . . tend[] to resolve over a period of . . . two, three, four months. [This] doesn't mean that they get totally back, but they don't have [a negative] progression" of their symptoms. Tr. 119.

Dr. Cohen took notice that none of petitioner's treating physicians, including Dr. Miller, the neurologist who treated petitioner for months, considered her demyelination to be vaccine-related. Resp't's Ex. A at 3. He took further notice that "[n]one of [petitioner's] treating neurologists ever suggested a possible diagnosis of ADEM nor did they specifically treat her for ADEM." Id. at 1; see Tr. 119.

Dr. Cohen remarked that "ADEM is a disease [that appears] almost exclusively . . . [in] children and adolescents." Resp't's Ex. A at 3. Petitioner was an adult at the time of her onset, and her records indicate that two months after receiving the flu vaccine, she was diagnosed with an ear infection. Tr. 135. According to Dr. Cohen, that ear infection could have caused her early symptom of vertigo. Tr. 135.

Dr. Cohen criticized Dr. Kinsbourne's reliance on certain medical articles and the conclusions he drew from them, Resp't's Ex. A at 4, principally because the subjects

presented with a different clinical picture than did petitioner. Id. at 3 (citing the 2003 Shoji article[16]; see also Resp't's Ex. C at 1 (challenging Dr. Kinsbourne's reliance on the 2007 Sejvar article).

Dr. Cohen allowed that the clinical manifestations of ADEM may vary, but insisted that the condition's onset is almost always acute, involving the "sudden fulminant" appearance of certain symptoms that were notably absent during petitioner's course of illness.[17] Tr. 141-42; see also Pet'r's Ex. 9 at 2 (defining ADEM "as a first acute fulminant demyelinating episode without any previous neurologic history."). In his experience, the claim that petitioner experienced a "sub-acute" onset of neurologic symptoms at nearly four weeks (or longer) after vaccination exceeded "the spectrum of [presentation for] ADEM," particularly when the other distinguishing features of ADEM were missing. Tr. 145. Dr. Cohen opined that petitioner improperly sought to characterize her case as one of atypical ADEM. Tr. 122, 160, 164.

## III. Discussion

### A. The Applicable Legal Standard

To prevail on a non-Table vaccine claim such as petitioner has asserted here,[18] petitioner must show that the vaccine was "'not only a but-for cause of the injury but also a substantial factor in bringing about the injury.'" Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1321 (Fed. Cir. 2010) (quoting Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)). Petitioner must prove her

[16] Pet'r's Ex. 8-6 at 500.

[17] Pet'r's Ex. 9-1 at 2 ("histological confirmation of inflammation of the brain, encephalopathy, decreased or absent response to the environment, decreased or absent eye contact, inconsistent or absent response to external stimuli, decreased arousability, seizure associated with loss of consciousness, visual field defects, fever, EEG findings consistent with encephalitis, neuroimaging consistent with encephalitis.").

[18] If petitioner alleges an injury listed on the Vaccine Injury Table (Table) that occurred within the correlative time frame set forth in the Table, petitioner's vaccine claim is deemed a Table claim, and a presumption of causation attaches. See § 300aa-14; see also 42 C.F.R. § 100.3. If petitioner alleges an injury that is not listed on the Table, such as the ADEM injury alleged in this case, the vaccine claim is deemed a non-Table case and no presumption of causation attaches. Id. Petitioner must therefore satisfy her burden of proof by proving that her injuries were caused-in-fact by her vaccination. See § 300aa-13(a)(1)(A).

vaccine claim by a preponderance of the evidence. Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005).

The preponderant evidence standard under the Vaccine Act requires proof that a vaccine more likely than not caused the vaccinee's injury. Id. at 1279; see also In re Winship, 397 U.S. 358, 371–72 (1970) (Harlan, J., concurring) (quoting F. James, Civil Procedure, 250–51 (1965)) (a preponderance of the evidence standard requires the trier of fact to "believe that the existence of a fact is more probable than its nonexistence before the [special master] may find in favor of the party who has the burden to persuade the [special master] of the fact's existence."). But, this evidentiary standard "allows a finding of causation in a field bereft of complete and direct proof of how vaccines affect the human body." Capizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1324 (Fed. Cir. 2006). Mere conjecture or speculation will not establish a probability. See Snowbank Enter., Inc. v. United States, 6 Cl. Ct. 476, 486 (1984).

Petitioner satisfies her burden of showing that the received vaccination brought about her injury by providing (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a proximate temporal relationship between vaccination and injury. Althen, 418 F.3d at 1278.

Proof of vaccine causation must be supported by a sound and reliable "medical or scientific explanation that pertains specifically to the petitioner's case, although the explanation need only be 'legally probable, not medically or scientifically certain.'" Moberly, 592 F.3d at 1322 (quoting Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994)); see also Grant v. Sec'y of Health & Human Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992) (requiring that the medical theory must support actual cause).

Petitioner may use circumstantial evidence to prove her case, and "close calls" regarding causation may be resolved in favor of petitioner. Althen, 418 F.3d at 1280. Causation can be supported by a treating physician's opinion that a vaccination was causally linked to the vaccinee's injury if the special master finds the opinion to be both reliable and persuasive. Moberly, 592 F.3d at 1324-25; see also Capizzano, 440 F.3d at 1326. Mere temporal association is not sufficient to prove causation. Grant, 956 F.2d at 1148.

Because the parties dispute the nature of petitioner's injury here, the undersigned first applies the analytical framework endorsed in Broekelschen v. Sec'y of Health &

Human Servs., 618 F.3d 1339 (Fed. Cir. 2010) and Lombardi v. Sec'y of Health & Human Servs., 656 F.3d 1343 (Fed. Cir. 2011).

### B. The Weight of the Record Evidence Does Not Preponderate in Favor of a Finding that Petitioner Suffers From ADEM

Petitioner alleges that she suffers from ADEM. See Pet'r's Ex. 8 at 6. Petitioner's own expert, Dr. Kinsbourne, concedes that this case is an "unusual" and "atypical" one for ADEM. The parties do not dispute that petitioner does suffer from some sort of neurologic illness, but they disagree on what her illness is. Respondent contends that petitioner's condition cannot be characterized as ADEM—or an atypical variant thereof, as petitioner and Dr. Kinsbourne propose. See Resp't's Exs. A, C.

Special masters are required to evaluate the record as a whole. 42 U.S.C. § 300aa-13. The record here reveals many extraordinary characteristics of petitioner's presentation that call into question the appropriateness of a diagnosis of an atypical ADEM variant. The undersigned is persuaded, on this record, that petitioner's onset, symptoms, and the course of her illness diverge in too many respects and by too great a degree from the presentation of ADEM to even be deemed an atypical form of ADEM. Yet, petitioner does appear to suffer from another, unspecified illness that has bewildered her physicians.

Six factors, in particular, weigh against a finding that petitioner has ADEM. The factors are: (1) the statistical improbability that petitioner has ADEM; (2) the absence of an ADEM diagnosis from her treaters; (3) the appearance of her brain lesion; (4) the timing of her symptom onset; (5) the nature and severity of her symptoms; and (6) the protracted course of her illness and her limited recovery. The undersigned addresses these factors in turn.

#### i. The Statistical Improbability That Petitioner Suffers From ADEM

Both Dr. Kinsbourne and Dr. Cohen testified that ADEM primarily afflicts children and adolescents. See Tr. 29; see also Tr. 38 (Dr. Kinsbourne explaining that "most of the cases [of ADEM]" occur in children and adolescents); Tr. 175 (Dr. Cohen agreeing that the vast majority of ADEM cases occur in adolescents or children). The condition is much less common in adults, but "has been reported in young and elderly adults." Pet'r's Ex. 8-4 at 410.

The statistical likelihood that children, rather than adults, would be afflicted by ADEM is well-supported by the literature the experts cited. See, e.g., Pet'r's Ex. 8-2 at

195; Pet'r's Ex. 8-4 at 410; Pet'r's Ex. 8-3 at 301; Resp't's Ex. A-6[19]; Resp't's Ex. A-9 at 6. At the time petitioner developed her symptoms, she was nearly 54 years old. This statistical factor merits consideration, although it is not dispositive. The undersigned turns now to consider the other factors that inform the likelihood of petitioner's alleged ADEM diagnosis.

**ii. The Absence of an ADEM Diagnosis From Petitioner's Treaters**

The parties do not dispute, and a review of petitioner's medical records confirms, that none of petitioner's treating physicians diagnosed her with ADEM. See Tr. 69, 177. Dr. Miller, petitioner's treating neurologist over the course of several months, did not once suggest ADEM as a possible diagnosis for her various neurologic symptoms in his differential diagnoses. Instead, petitioner's various treating physicians considered MS as a possible diagnosis, but apparently concluded she did not suffer from it. See Pet'r's Ex. 3 at 16 (petitioner advised during an office visit dated June 15, 2010, that she had been "told her symptoms are not [MS] but a demyelinating brain disorder").

The parties' experts also considered the treatment petitioner received from her attending doctors during the course of her emerging illness. Dr. Kinsbourne and Dr. Cohen agreed that the three days of steroid treatment she received was strongly suggestive of her physicians' suspicion that she had MS. Dr. Kinsbourne testified, however, that three days of administered steroids was not long enough to treat MS. See Tr. 74-75, 177-78. He maintained that the treatment "is classically used for ADEM" as well, but confessed that he was "not sure what the [treating physicians'] thought process was" because they never documented a diagnosis of ADEM for petitioner. Tr. 74. Dr. Cohen countered Dr. Kinsbourne's testimony, insisting that a three-day course of steroids was insufficient to treat the onset of ADEM, Tr. 109, but was appropriate for the treatment of an acute MS attack. Tr. 109. In Dr. Cohen's view, petitioner's symptom presentation—that is, the onset, type, duration, severity, and course of her symptoms—was too atypical for a diagnosis of, and treatment for, ADEM. Tr. 154. That none of the physicians who regularly examined and treated her contemplated the illness that petitioner now claims she has does not support a finding in her favor.

[19] Respondent did not file the medical articles on which Dr. Cohen relied as separate exhibits. Rather, she filed nine separate PDF files as part of an "Appendix" to his expert opinion. See ECF Dkt. No. 14, July 19, 2011. All citations to the medical literature referenced in Dr. Cohen's report refer to these filings.

### iii. The Appearance of Petitioner's Brain Lesion

The parties agree that petitioner's brain imaging shows demyelination has occurred in her brainstem and has created a single lesion in the area of her pons. The lesion was first detected on an MRI conducted in August 2008. See Pet'r's Ex. 3 at 123-24; Tr. 72, 117, 164-165.

What the parties dispute is the nature of the lesion. The parties disagree on whether the lesion is diffuse or focal and whether the appearance of the lesion is supportive of a finding of ADEM. See Resp't's Ex. A at 2.

Dr. Kinsbourne argued that diffuse or multifocal lesions are a necessary criterion to diagnose ADEM. Tr. 75. He described the lesion detected in petitioner as "single" and "diffused," Tr. 22, which—he asserts—would comport with the "classical descriptions of ADEM" lesions. Pet'r's Ex. 8 at 10. Dr. Kinsbourne cited six sources to support this proposition,[20] three of which described "ADEM [lesions that were] confined to the brainstem" only.[21] But, he acknowledged that multiple lesions throughout the central nervous system are a much more common finding in cases of ADEM than is a solitary lesion located in the brainstem, such as presented in petitioner's case. Tr. 69. Nonetheless, Dr. Kinsbourne asserted that petitioner's presenting symptoms and the finding of a single diffused lesion in petitioner's brainstem were sufficient to support a diagnosis of ADEM. See Tr. 21, 23-24, 37-38, 53-58, 71, 75, 89.

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[20] Pet'r's Ex. 8-1 at 1, Helga Almeida Silva et al., Magnetic resonance imaging in five patients with a tumefactive demyelinating lesion in the central nervous system, 57 Arq. Neuropsychiatric 921 (1999); Pet'r's Ex. 8-2 at 194, Jin Hwan Cheong et al., Acute disseminated encephalomyelitis associated with influenza vaccination, 35 J. Korean Neurosurgical Soc'y 223 (2004); Pet'r's Ex. 8-5 at 442, J. I. O'Riordan et al., Long term MRI follow-up of patients with post infectious encephalomyelitis: evidence for a monophasic disease, 167 J. Neurological Sciences 132 (1999); Singh et al., supra note 13; Pet'r's Ex. 8-2 at 594, A.J. Barkovich, Pediatric Neuroimaging (4th ed. 2005); Pet'r's Ex. 8-8 at 592, Recai Turkoglu & Erdem Tuzun, Brainstem encephalitis following influenza vaccination: Favorable response to steroid treatment, 27 Vaccine 7252 (2009).

[21] K. Tateishi et al., Acute disseminated Encephalomyelitis Confined to Brainstem, 12 J. Neuroimaging 67 (2002); Zhengqi Lu et al., Comparative Brain Stem Lesions on MRI of Acute Disseminated Encephalomyelitis, Neuromyelitis Optica, and Multiple Sclerosis, PLoS ONE 6(8) (2011); Singh et al., supra note 13.

Dr. Cohen cited the 2009 Callen article[22] to support his claim that the confinement of petitioner's demyelination to the brainstem was notably unusual for ADEM subjects, who more generally present with extensive lesions on brain imaging. Resp't's Ex. A at 2; see also Tr. 117-118, 161, 164-165 (Dr. Cohen testifying that a solitary lesion located in the brainstem was atypical for an ADEM subject). The 2009 Callen article provided MRI "diagnostic criteria . . . that [might] be useful in differentiating children experiencing the first attack of [MS] from those with monophasic [ADEM]." Resp't's Ex. A-2 at 1. The authors compared and analyzed MRI data from subjects suffering from MS with those suffering from ADEM and found that the "[d]iffuse, bilateral lesions [more prevalent in ADEM subjects]. . . emerged as an important differentiating feature between the . . . groups." Id. at 6.

Dr. Cohen also cited the 2006 Wingerchuk article,[23] id. at 5, which described the MRI results in ADEM subjects as "typically reveal[ing] multifocal, bilateral, often large white matter lesions." But, the article's authors did recognize the reporting of "[a] wide spectrum of exceptional findings . . . including [the detection of a] normal initial brain scan, lesion development only during the clinical recovery stage, [and] a solitary lesion restricted to an area such as the brain stem." Id.

In the 2000 Dale article,[24] the authors discussed the MRI findings performed in thirty-five individuals with ADEM. The imaging uniformly showed "disseminated [central nervous system] lesions," the majority of which were large. Pet'r's Ex. 8-2 at 205. In another study of forty-two ADEM patients, the imaging showed demyelination, with "[l]esions typically number[ing] 3-8," but only "rarely" did a "solitary" lesion appear. Pet'r's Ex. 8-4 at 391. Although ADEM can present with a solitary diffused lesion, see Pet'r's Ex. 8-8 at 596, the medical literature on which the parties relied consistently reported that individuals suffering from ADEM generally have multiple lesions in their CNS. See, e.g., Pet'r's Ex. 8-3 at 305 ("Cerebral lesions are usually disseminated but solitary lesions [do] occur in about 10% and 30% of cases. Lesion

[22] Resp't's Ex. A-2 at 1, D.J.A. Callen et al., Role of MRI in the differentiation of ADEM from MS in children, 72:11 Neurology 968 (2009).

[23] Resp't's Ex. A-9 at 2, Dean M. Wingerchuk, The clinical course of acute disseminated encephalomyelitis, 28 Neurological Research 341 (2006).

[24] Pet'r's Ex. 8-2 at 198, R.C. Dale et al., Acute disseminated encephalomyelitis, multiphasic disseminated encephalomyelitis and multiple sclerosis in children, 123 Brain 2407 (2000).

patterns often seen in ADEM includ[e] widespread, multifocal or extensive white matter lesions . . . [that] may evolve over several weeks."); Pet'r's Ex. 8-8 at 596 ("ADEM is characterized [by] multiple lesions distributed all over the CNS."); see also Resp't's Ex. A-1 ("[W]idespread MRI lesion pattern[s] [are] characteristic of ADEM.").

The parties' experts admitted that interpreting petitioner's MRIs here was difficult because neither expert had the opportunity to review the imaging results personally. See Tr. 76, 117. Instead, they relied on the description of the imaging results documented in the notes of petitioner's treating neurologist, Dr. Miller. See Pet'r's Ex. 3 at 123. Dr. Kinsbourne construed Dr. Miller's notations to describe a diffused lesion because Dr. Miller wrote that it "cover[ed] a fair amount of territory" in petitioner's brain. Tr. 76 (discussing Pet'r's Ex. 3 at 123-24). Dr. Cohen disagreed with Dr. Kinsbourne's interpretation, pointing out Dr. Miller did not describe the lesion using either of the terms "diffuse" or "multifocal." Tr. 117-18.

Whether petitioner's brain lesion bore the appearance of the type of lesion usually seen in ADEM subjects is not clear from the record. The medical records do not indicate whether her detected lesion was either diffuse or multifocal, the characteristic presentations for ADEM lesions. None of her treating physicians—who did have the opportunity to review the results of her MRIs—described her discovered lesion using those terms. But her treating neurologist, Dr. Miller, did describe her lesion in plain language that indicated that the lesion was spread over a moderate space in her brain. Notwithstanding this recorded description, the undersigned is not persuaded by Dr. Kinsbourne's assertions that petitioner's lesion was sufficiently diffuse to be suggestive of an ADEM lesion because petitioner's own treating physicians were not persuaded of an ADEM diagnosis based on her radiologic evidence. See Perreira v. Sec'y of Health & Human Servs., 33 F.3d 1375, 1376 n. 6 (Fed. Cir. 1993) ("An expert opinion is no better than the soundness of the reasons supporting it."); Burns v. Sec'y of Health & Human Servs., 3 F.3d 415, 417 (Fed. Cir. 1993) ("The special master concluded that the expert based his opinion on facts not substantiated by the record. As a result, the special master properly rejected the testimony of petitioner's medical expert."). Moreover, the weight of the medical literature on which the parties' respective experts relied supports a finding that the pattern of petitioner's observed demyelination was not representative of ADEM cases.

Petitioner's presenting symptoms also militate against a finding that she suffered from ADEM. Her symptom onset was too protracted, she did not present with the kind of symptoms that are characteristic of ADEM, and the duration of her clinical course and the lack of improvement of her neurologic condition would be unusual for ADEM.

### iv. The Timing of Her Symptom Onset

Petitioner received the subject flu vaccine on February 22, 2008. Pet'r's Ex. 2 at 1. Dr. Kinsbourne opines petitioner's symptom onset began "[a]pproximately four weeks after [her] influenza vaccination." Pet'r's Ex. 8 at 5. Dr. Kinsbourne based this calculation on petitioner's comment to Dr. Miller on June 20, 2008, that "on reflection . . . she [had] noticed several weeks of feeling that socks seemed too tight on [her] legs or that [there] was numbness in her leg prior to the onset of her vertigo." Pet'r's Ex. 3 at 159; see also Pet'r's Ex. 4 at 73 (petitioner reported to Dr. Di Stasio on August 20, 2008, that her initial symptoms included a "feeling that socks or underwear were too tight (mainly on left side)").

Petitioner first complained of her vertigo during an office visit in April 2008, nearly eight weeks after she received the flu vaccine. She reported during that office visit in the third week of April that she had developed vertigo "several weeks" earlier, had begun to feel abnormally fatigued, and had developed numbness in her lower legs (primarily around her ankles) that ascended over the ensuing weeks. Pet'r's Ex. 3 at 159-60. By the end of April 2008, petitioner was afflicted by increasingly worsening vertigo, which significantly affected her performance at work. Id. at 118-19; Pet'r's Ex. 1 at 2. When she presented to the hospital on April 28, 2008, she reported a one-week history of vertigo and a two-week history of progressive weakness and loss of energy. Pet'r's Ex. 4 at 162.

Petitioner's own accounts of her symptom onset were inconsistent. Based on her related complaints to her doctors, her symptom onset appears to have begun between the end of March 2008 and the second week of April 2008.[25] As discussed in further detail below, even assuming petitioner's neurologic symptoms did, in fact, begin around the third week of March of 2008, such a symptom onset is toward the tail end of the recognized time frame for the onset of post-vaccinal ADEM.

In the months after her symptom onset, petitioner's neurologic problems persisted and appeared to worsen. Pet'r's Ex. 3 at 112. In August 2008, she reported some

[25] Petitioner saw her treating physicians on numerous occasions between April and June of 2008, and did not mention the sensations she apparently felt in her legs in March of 2008 until she did so "on reflection" during her June 20, 2008 visit to Dr. Miller. The undersigned finds it unlikely that petitioner would have failed to mention these noteworthy symptoms during her late April and early May visits to her treating physicians during which she reported numerous other neurologic complications she had been experiencing in the weeks prior.

improvement in her symptoms, although her gait and balance problems were ongoing. Id.

Dr. Kinsbourne conceded that the subacute presentation of petitioner's symptoms (that is, over the course of a number of weeks after her vaccination—without overt expression) was "unusual" for ADEM. See Tr. 38. He described ADEM as a "monophasic [condition] in almost every case." Tr. 40. He explained "that it came[,] . . . reached a peak[,] . . . reached a plateau, and then . . . got to some extent better." Tr. 39. Yet, he added that "ADEM has an unusually wide variability of presentation," Tr. 28, and there is "a subacute variant [of ADEM]," which has a "more gradual beginning . . . [with] a more prolonged course," Tr. 39. But neither Dr. Kinsbourne nor the literature he filed specifically addressed how subacute the presentation of ADEM could be. Tr. 38.

Dr. Cohen provided important perspective on this issue. Observing that petitioner's symptom onset—as described in her contemporaneous medical records—reflected an irregular case of ADEM, Tr. 164, he explained that, in his experience, ADEM is "a sudden fulminant . . . illness" that presents with "an abrupt onset," Tr. 141, and the entire course of the illness "progresses over [a period of] weeks, not months"--as in petitioner's case. Resp't's Ex. A at 2. Although he agreed that cases of ADEM do occur where the symptom presentation might be described as "subacute," he explained that onset in such cases would occur over--"at most[--]weeks, [but] not months." Tr. 145. Here, he asserted, the onset of petitioner's symptoms after vaccination was beyond the "spectrum" of onset for ADEM. Id.

A review of the parties' submitted medical literature also indicates that petitioner's course was, in the best but unlikely case, an atypical form of ADEM.

In the 2004 Cheong article,[26] the authors explained that "[p]atients with ADEM usually have a monophasic clinical course [that is marked by an] abrupt onset, [and that] last[s] . . . 2 to 4 weeks." Pet'r's Ex. 8-2 at 195. Similarly, in the 2000 Dale article, the authors reported in their study of twenty-eight children with ADEM that the "presentation [of symptoms] varied from an acute explosive onset, with a maximum neurological deficit attained within 1 day, to a more indolent progression with maximum deficit at 31 days (mean 7.1 days)." Id. at 202. "The mean latency between predemyelinating illness

[26] Pet'r's Ex. 8-2 at 195, Jin Hwan Cheong et al., Acute disseminated encephalomyelitis associated with influenza vaccination, 35 J. Korean Neurosurgical Soc'y 223 (2004).

and the onset of neurological signs [for the children] was 13.0 days (range 2-31 days)." Id. at 201.

Dr. Kinsbourne referred to a case report of four individuals with ADEM,[27] in which the authors found that "[a] common feature for all the patients . . . was a rapid deterioration in their condition within a few days after being admitted to the hospital." Pet'r's Ex. 8-3 at 293. "During the . . . weeks [following their admission], the conditions of [three of the individuals] gradually improved," and the fourth patient died seven weeks later. Id. at 292.

Dr. Kinsbourne pointed to the 2008 Huynh study[28] to support his theory that vaccines—and not just illnesses—can cause ADEM. Pet'r's Ex. 8 at 8. The authors of the Huynh study found that in cases of alleged vaccine-related ADEM, "the onset of symptoms may vary slightly: from 1 to 14 days . . . less than one week . . . [or] 1 to 3 weeks . . . after vaccination . . . [with] [s]ymptom onset [that] is usually rapid with progression over hours to a peak in days . . . ." Pet'r's 8-3 at 305 (emphasis added).

Then citing the 1994 IOM report—apparently for its comment on the timing of ADEM onset—Dr. Kinsbourne drew attention to the statement that "ADEM is characterized by acute depression of consciousness and multifocal neurological findings that usually occur a few days or weeks following vaccine administration . . . ." Pet'r's Ex. 8-6 at 511;[29] see also Pet'r's Ex. 8-8 at 575, Olafa Stuv & Scott Zamvil, Pathogenesis, diagnosis, and treatment of acute disseminated encephalomyelitis, 12:4 Current Opinion in Neurology 395 (1999) ("Neurologic symptoms [of ADEM] usually follow between 1 and 20 days [after the inciting event]"); Pet'r's Ex. 8-5 at 474, Louis Reik, Immune-Mediated Central Nervous System Disorders in Childhood Viral Infections, 2:2 Seminars in Neurology 106 (1982) ("Symptoms [of ADEM] usually begin 4 to 21 days after the inciting event").

[27] Pet'r's Ex. 8-3 at 291, Jari Honkaniemi et al., Delayed MR Imaging Changes in Acute Disseminated Encephalomyelitis, 22 Am. J. Neuroradiology 1117 (2001).

[28] Pet'r's 8-3 at 301, William Huynh et al., Post-vaccination encephalomyelitis: Literature review and illustrative case, 15 J. Clinical Neuroscience 1315 (2008).

[29] Institute of Medicine, Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality (Kathleen R. Stratton et al. eds., 1994).

Respondent filed the 1985 Murphy article[30] in which the authors found that ADEM manifests abruptly. Resp't's Ex. A-6 at 1. As reported in the article, the authors studied 805 vaccinated subjects and found that the probability of developing post-vaccinal ADEM in 28 days (or more) was less than one percent (0.6%). Id. at 5-6.

The medical literature the parties' referenced makes clear that ADEM most commonly manifests abruptly, although several of the articles Dr. Kinsbourne cited furnished the barest of support for his proposition that petitioner's subacute onset was an appropriate—even if aberrant—presentation for ADEM. Pet'r's Ex. 8 at 11 (citing Pet'r's Ex. 8-4 at 374). In the 2005 Khurana study, the authors reported that of the 13 individuals they studied, "7 . . . evolved subacutely over 5 to 10 days," but "[s]ix of 13 . . . had rapid progression of symptoms that required prolonged care in the ICU." Pet'r's Ex. 8-4 at 376. Similarly, in the 2007 Menge study,[31] the authors described reports of ADEM where the afflicted patients "developed [symptoms] subacutely over a period of days, . . . [that] led to hospitalization within a week." Pet'r's Ex. 8-4 at 412; see also Pet'r's Ex. 8-4 at 419 ("Neurologic manifestations [of ADEM] begin 3 days to 4 weeks (mean 12 days) following a precipitating event"); Pet'r's Ex. 8-5 at 474 ("Symptoms [of ADEM] usually begin 4 to 21 days after the inciting event."). In the 2001 Schwarz article,[32] the authors studied forty individuals with ADEM and found that "[t]he duration of symptoms before admission was shorter in patients with ADEM [than those with MS and they exhibited] . . . a more abrupt onset of symptoms." Pet'r's Ex. 8-5 at 490. In addition, a number of the case studies Dr. Kinsbourne cited reported an onset of neurologic symptoms in subjects with ADEM within two days to one week of the precipitating event. Id. at 479 (subjects' neurologic injuries manifested five and seven days after a flu vaccine); Pet'r's Ex. 8-5 at 484 (subject's neurologic symptoms manifested four days after a flu vaccine); Pet'r's Ex. 8-8 at 600 (symptom onset five days after a flu vaccine); Pet'r's Ex. 8-2 at 194 (injury manifested two days after a flu vaccine).

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[30] Resp't's Ex. A-6 at 1, James Murphy & James Austin, Spontaneous Infection or Vaccination as Cause of Acute Disseminated Encephlomyelitis, 4 Neuroepidemiology 138 (1985).

[31] Til Menge et al., Acute disseminated encephalomyelitis: an acute hit against the brain, 20 Current Opinion of Neurology 247 (2007).

[32] Pet'r's Ex. 8-5 at 487, S. Schwarz et al., Acute disseminated encephalomyelitis: A follow-up study of 40 adult patients, 56 Neurology 1314 (2001).

The weight of the record evidence before the undersigned establishes that the symptoms of ADEM appear abruptly—that is, between one and two weeks after the triggering event—in the overwhelming majority of cases. The timing of petitioner's symptom onset was unusually protracted. Petitioner's symptom onset occurred slowly and well beyond the typical time frame for the vast majority of subjects afflicted with ADEM. Petitioner's symptom onset—even if it occurred approximately four weeks after her flu vaccine, as she and Dr. Kinsbourne assert—does not fit within the recognized time frame for most cases of ADEM. At best, petitioner's symptom onset occurred at the outer reaches of the recognized time frame for the onset of post-vaccinal ADEM. This factor provides only meager support for petitioner's claim.

**v. The Nature and Severity of Petitioner's Symptoms**

The parties' experts agreed that certain symptoms are characteristic of ADEM, and petitioner's expert conceded that petitioner's presentation "deviated" from the usual presentation of most cases of ADEM. Pet'r's Ex. 9 at 1. Nonetheless, Dr. Kinsbourne asserted that petitioner's condition could be regarded as an atypical variant of ADEM because the condition "has . . . unusually wide variability . . . [in] presentation." Tr. 28. A review of the medical literature filed by the parties, however, persuades the undersigned that petitioner did not exhibit symptoms that were suggestive of ADEM—even an atypical variant—either in nature or in severity.

ADEM "is an uncommon inflammatory demyelinating disease of the central nervous system." Pet'r's Ex. 8-2 at 192. The disease "is believed to be a manifestation of an autoimmune attack on the myelin of the [CNS]." Dorland's at 613. Because the "symptoms and signs of [the condition] . . . are related to the portion of the nervous system that is most severely damaged[,] . . . variable clinical syndromes may occur." Resp't's Ex. A-4 at 4. Thus, "ADEM has no [defined] diagnostic criteria." Pet'r's Ex. 8-2 at 209. But, the main symptom of ADEM is a noticeably decreased level of consciousness, "varying from lethargy to coma." Pet'r's Ex. 8-3 at 291; see also Pet'r's Ex. 8-2 at 202 (69% of subjects with ADEM in one study experienced an "[a]lteration in mental state and level of consciousness"); Pet'r's Ex. 8-4 at 375 ("The typical presentation is that of multifocal neurologic disturbance accompanied by change in mental status."). Symptoms suggestive of meningeal involvement, such as headaches and neck stiffness, also "are common early in the course of all types [of ADEM]." Resp't's Ex. A-4 at 4.

Both Dr. Kinsbourne and Dr. Cohen agreed that individuals afflicted with ADEM typically suffer from a significantly lowered level of consciousness and, in some cases,

coma. See Tr. 28, 52. The parties also agree that petitioner did not exhibit any clear signs of impaired consciousness.[33]

Other symptoms of ADEM include "fever . . . and vomiting; sometimes tremor, seizures, and paralysis." Dorland's at 613; see also Pet'r's Ex. 8-2 at 209 (signs of meningism, which include headache, fever, stiff neck, light sensitivity, disorientation, and—occasionally seizures—are common in ADEM patients). Other neurologic signs or symptoms typically associated with ADEM are "weakness, sensory changes, [and] ataxia." Resp't's Ex. A-9 at 5; see also Pet'r's Ex. 8-2 at 209 (ADEM subjects usually present "with multifocal neurologic disturbance such as ataxia, hemiparesis, cranial nerve palsies, and altered conscious state."); Pet'r's Ex. 8-8 at 578 (The "neurologic signs and symptoms [of ADEM] include parathesias, pain, motor weakness, spasticity, incoordination, dysarthia and dysphagia."). Individuals with ADEM also typically develop complications with their vision. See Pet'r's Ex. 8-2 at 202. Moreover, "[s]ystemic symptoms [of ADEM] including fever, malaise . . . headache, [and] nausea [with] vomiting often precede neurological symptoms." Pet'r's Ex. 8-8 at 578.

The parties disputed whether petitioner's symptoms were sufficiently "severe" to merit an ADEM diagnosis. See, e.g., Tr. 146, 153. The views of the parties' experts are inconclusive on this issue because neither had the opportunity to observe petitioner and thus, to properly evaluate the severity of her symptoms. The undersigned is informed, however, by the silence of petitioner's treaters—who did observe her—on the matter of her symptom severity. Although they noted a worsening of her symptoms of discomfort, the symptoms did not appear to have been sufficiently severe to provoke any concern that petitioner might have ADEM.

In the view of the undersigned, petitioner did not present with the most characteristic of ADEM symptoms. Nor did her symptoms appear with the type of severity and abruptness that generally occurs in cases of ADEM. Although petitioner exhibited some symptoms associated with ADEM, she did not exhibit the particular

[33] Dr. Kinsbourne stated that petitioner's feelings of confusion when she awakened could have been a sign of depressed consciousness, but he acknowledged that this was not a clear sign of diminished consciousness. See Tr. 52, 70. Dr. Kinsbourne further asserted that symptoms involving consciousness were more common in children afflicted with ADEM whereas adults afflicted with ADEM more commonly exhibited symptoms involving sensory and motor problems. Tr. 28. However, none of the medical literature either party submitted speaks to this proposition.

symptoms that the parties agreed are most commonly associated with ADEM, such as a markedly decreased state of consciousness, fever, and headache. This factor does not militate in petitioner's favor.

### vi. The Protracted Course of Petitioner's Illness and Her Limited Recovery

The extended duration of petitioner's clinical course would be unusual for a case of ADEM, further suggesting that petitioner did not suffer from that condition. As Dr. Cohen explained, a typical clinical course of ADEM includes a "severe and swift . . . onset," a "nadir," and then improvement over the course of a period of months. Tr. 178. Dr. Kinsbourne agreed that the onset of ADEM generally does not present over the course of multiple months, Tr. 72, although the course of recovery might require a period of months.

A review of the medical literature submitted by the parties corroborates Dr. Cohen's description of the clinical course of ADEM. The disease manifests in an abrupt, fulminant manner; the symptoms are severe, and then reach a plateau. Shortly thereafter, the individual begins a gradual recovery. See Pet'r's Ex. 9-1 at 3 (a study of seventeen ADEM patients finding the range of disease duration to fall between one and ten months, with an average length of disease duration of four months); Pet'r's Ex. 8-4 at 378 ("All 4 patients in [an] adult [case] series . . . ha[d] rapid deterioration followed by gradual improvement."); Pet'r's Ex. 8-2 at 195 ("Recent studies suggest a more favorable prognosis with rapid recovery."). Moreover, "[r]ecovery is often . . . complete among those who survive," Pet'r's Ex. 8-5 at 474, and individuals afflicted with ADEM generally recover within months of onset. Pet'r's Ex. 8-2 at 198 ("The outcome in the ADEM patients was mixed; 57% of patients made a complete recovery."); Pet'r's Ex. 8-4 at 377 ("Seven of 13 children [with ADEM] had complete recovery."); see also Pet'r's Ex 8-2 at 207 ("Despite the often dramatic presentation [of subjects with ADEM], the[ir] outcome was surprisingly good, with recovery completed between 0.25 and 6 months[.] 57% had no impairments on follow-up . . . [while 17%] had motor disability.").

The parties agree that petitioner's clinical course did not follow the expected clinical course for subjects afflicted with ADEM. Tr. 98, 130. In July of 2008, more than four months after her symptom onset, petitioner reported that her symptoms had worsened; she reported again one month later, in August of 2008, that her symptoms had continued to worsen. Pet'r's Ex. 3 at 121. Petitioner's physical therapist noted that her symptoms—particularly her feelings of weakness—had continued on a downward slope for a four-month period. Pet'r's Ex. 3 at 115. Toward the end of August 2008—nearly five months after her symptoms first appeared—petitioner reported that she was

beginning to feel better with some slow improvement in her condition. Pet'r's Ex. 3 at 109-10. While some of her symptoms began to abate over the ensuing months, her symptoms of dizziness, imbalance, numbness, and weakness persisted through March of 2009—seven months after she first showed signs that her symptoms were improving. Pet'r's Ex. 3 at 81, 86-87; see also id. at 63 (Petitioner "last seen on 3/09, at that time [she had] . . . some improvement . . . [but] over last 2-3 months has had worsening of gait, feels weak all over, feels like knees will give out. Feels more fatigued.") In April of 2010, petitioner returned to her neurologist, Dr. Miller, and reported a "significant[ly] worsening gait and [left extremity] weakness, [and] arm weakness," which led Dr. Miller to evaluate petitioner for a potential cervical cord lesion. Pet'r's Ex. 7 at 5.

The record indicates that petitioner's condition did not plateau and then gradually improve—as would be expected with a case of ADEM. Instead, petitioner struggled—after the gradual onset of her symptoms—with a protracted clinical course marked by many periods of exacerbation. The course of petitioner's illness strongly suggests that she did not suffer from ADEM. The lack of appreciable recovery within a year after her symptom onset further suggests that she did not suffer from ADEM.

Petitioner's overall clinical course was inconsistent with the well-recognized course of ADEM. Although petitioner and her expert, Dr. Kinsbourne, relied heavily on case reports discussing the wide variability of symptom presentation in subjects with ADEM, none of the cases involved subjects with the extraordinary combination of atypical features present in petitioner's case. The undersigned cannot credit petitioner's position on the assertions of her expert alone, Snyder ex rel. Snyder v. Sec'y of Health & Human Servs., 88 Fed. Cl. 706, 742-43 (2009) (special masters are not required to accept the ipse dixit of an expert) (citing Gen. Elec. Co. v. Joiner, 522 U.S. 136, 146 (1997)), and must decline petitioner's urging that she do so.

### C. Petitioner did not suffer from the injury for which she seeks a Program award

In conformance with the statute's direction to evaluate the record as a whole, 42 U.S.C. § 300aa-13, the undersigned finds on the record here—that includes the contemporaneous medical records, petitioner's undiagnosed condition, and the testimony of Drs. Kinsbourne and Cohen—that petitioner has failed to prove by preponderant evidence that she developed ADEM.

This determination precludes a finding of causation in petitioner's favor because the evidence does not support a finding that the vaccinee suffered from the injury for

which petitioner she seeks Program compensation. In such a circumstance, an Althen causation analysis may not be required. See Lombardi, 656 F.3d at 1356 (affirming the special master's decision to forego an Althen analysis after determining that petitioner did not suffer from any of his alleged injuries). Out of an abundance of caution, however, the undersigned evaluates petitioner's theory under the Althen standard.

Because petitioner's injury is yet undefined, it cannot be identified on the Vaccine Injury Table, see 42 C.F.R. § 100.3. Thus, petitioner cannot establish a Table injury. Instead, she must establish that the vaccine she received caused her neurologic complications. See Cedillo v. Sec'y of Health & Human Servs., 617 F.3d 1328, 1335 (Fed. Cir. 2010). To do so, petitioner must show by preponderant evidence that the vaccines brought about her injury by providing: (1) a medical theory causally connecting the vaccination and her injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for her injury; and (3) a showing of a proximate temporal relationship between the vaccination and her injury. Althen, 418 F.3d at 1278.

### 1. Althen Prong One: Petitioner's Medical Theory

Under Althen Prong 1, petitioner must put forth a biologically plausible theory explaining how the received vaccines could have caused the sustained injury. Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1375 (Fed. Cir. 2009). Under this prong, petitioner must make a showing that the received vaccines "can" cause the alleged injury. Pafford, 451 F.3d at 1355-56.

The offered medical theory must be supported by either the vaccinee's medical records or the opinion of a competent physician. Grant v. Sec'y of Health & Human Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992). Support for the offered medical theory must also include an explanation that "pertains specifically to the [claim made in] petitioner's case." Moberly, 592 F.3d at 1322. See Veryzer v. Sec'y of Health & Human Servs., No. 06-0522V, 2010 WL 2507791, at * 24 (Fed. Cl. Spec. Mstr. 2010) (noting that the relevant inquiry is whether, based on facts known to medical science and logical inferences drawn by a qualified expert, the vaccine at issue is more than likely to have caused the alleged injury), aff'd, 100 Fed. Cl. 349 (2011), aff'd, 475 F. App'x 765 (Fed. Cir. 2012).

Petitioner's theory of causation need not be medically or scientifically certain, Knudsen, 35 F.3d at 548-49, but it must be informed by "sound and reliable medical or scientific explanation," id. at 548; see also Veryzer v. Sec'y of Health & Human Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both 42 U.S.C.

§ 300aa-13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioner relies upon a medical opinion to support her theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen, 618 F. 3d at 1347 ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Human Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980)) ("An expert opinion is no better than the soundness of the reasons supporting it.").

Petitioner's medical records do not support her theory that the vaccine she received on February 22, 2008, caused her neurologic condition. There is no indication from her treating physicians that they considered her problems to be vaccine-related. Thus, petitioner must rely on Dr. Kinsbourne's expert opinion to prevail on her claim.

Because Dr. Kinsbourne has failed to persuade the undersigned that petitioner suffers from an ADEM variant, the undersigned does not evaluate whether petitioner put forth a biologically plausible theory explaining how the received flu vaccine could have caused ADEM. Petitioner's claim that she developed ADEM as a result of the receipt of a flu vaccine necessarily fails on Prong One.

An Althen analysis for petitioner's undefined neurologic condition, however, is attempted. The record establishes that Dr. Sung affirmatively diagnosed petitioner with fibromyalgia. See Pet'r's Ex. 4 at 25. But Dr. Kinsbourne did not mention petitioner's fibromyalgia in either of his reports. Nor did the parties address the relevance of this diagnosis,[34] and petitioner has not put forth any evidence that the flu vaccine could have caused her fibromyalgia. To the extent that petitioner claims that the received flu vaccine caused her fibromyalgia, the claim fails for lack of proof.

The medical professionals who examined petitioner during the course of her protracted illness have yet to define or diagnose her neurologic condition. Although her treating neurologist initially considered a diagnosis of MS, no such formal diagnosis was made, and petitioner does not allege she suffers from MS.

The parties do not dispute that petitioner has a lesion in her brain that appears to have resulted from a demyelinating process and is responsible for a measure of her neurologic symptoms. Because the potential spectrum of injuries that petitioner's

[34] Dr. Cohen mentioned this diagnosis once in his testimony, but he declined to discuss whether it had any relevance to petitioner's vaccine claim. See Tr. 181.

symptoms suggest is too broad to evaluate for a vaccine-related injury, the undersigned cannot assess Dr. Kinsbourne's theory of causation adequately.

Petitioner has not satisfied Prong One.

### 2. Althen Prong Two: Logical Sequence of Cause and Effect

Under Althen Prong Two, petitioner must establish "a logical sequence of cause and effect showing that the vaccination was the reason for the injury." Althen, 418 F.3d at 1278. Under this prong, petitioner must show that the received vaccine "did" cause the alleged injury. Pafford, 451 F.3d at 1354.

Petitioner need not make a specific type of evidentiary showing. That is, petitioner is not required to offer "epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, 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 opinion. See id. at 1325-26.

Here, the entirety of Dr. Kinsbourne's opinion regarding the causal relationship between petitioner's flu vaccine and her injuries turned on a finding that petitioner suffers from ADEM. But the evidence does not preponderate in favor of a finding that petitioner suffers from ADEM, the undersigned cannot evaluate whether petitioner's illness is vaccine-related in the manner proposed by Dr. Kinsbourne.

Petitioner does not prevail on Prong Two.

### 3. Althen Prong Three: Timing

Under Althen prong three, petitioner must establish that her injury occurred within a time frame that is medically appropriate for the alleged mechanism of harm. See Pafford, 451 F.3d at 1358 ("Evidence demonstrating petitioner's injury occurred within a medically acceptable time frame bolsters a link between the injury alleged and the vaccination at issue under the 'but-for' prong of the causation analysis."). Petitioner may satisfy this prong by producing "preponderant proof that the onset of symptoms occurred within a time frame for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352.

Petitioner may discharge her burden by showing: (1) when the condition for which she seeks compensation first appeared after vaccination and (2) whether the period

of symptom onset is "medically acceptable to infer causation." Shapiro v. Sec'y of Health & Human Servs., No. 99-552V, 2011 WL 1897650, at *13 (Fed. Cl. Spec. Mstr. Apr. 27, 2011), aff'd in relevant part, vacated in non-relevant part, 101 Fed. Cl. 532, 536 (2011), aff'd 503 F. App'x 952 (2013). The appropriate temporal association will vary according to the particular medical theory advanced in the case. See Pafford, 451 F.3d at 1358.

Dr. Kinsbourne opined that petitioner's symptoms first appeared approximately four weeks after her flu vaccine, and he asserted that this timing was appropriate based on his theory of causation. Pet'r's Ex. 8 at 11.

In particular, Dr. Kinsbourne advanced the theory that petitioner suffered from immune-mediated neurologic injuries that were caused by the biological mechanism of molecular mimicry, and that mechanism was augmented by bystander activation. Pet'r's Ex. 8 at 9-10. In his initial report, Dr. Kinsbourne averred that

> [t]he accepted temporal relationship between influenza vaccination and the onset of immune-mediated neurological disorders is generally accepted as extending to at least 42 days, and there is evidence for even longer latencies between vaccination and disease onset. So the [four week] temporal interval between Ms. Stillwell's vaccination and her first neurological symptoms fits comfortably into this time frame.

Pet'r's Ex. 8 at 11. Dr. Kinsbourne provided no medical literature to support this assertion. None of the articles he referenced in his initial report speak to the timeframe of symptom onset associated with immune-mediated neurologic injuries induced by molecular mimicry and/or bystander activation.

To support his postulate that petitioner's symptom onset occurred within an appropriate temporal interval, Dr. Kinsbourne quoted the 1994 IOM report in his supplemental expert report. Pet'r's Ex. 9 at 4. He claimed that the 1994 IOM report "summarized the range of latencies as follows 'a conservative estimate of the limits of the latencies for both GBS and ADEM is considered to be from 5 days to 6 weeks.'" Id.[35]

[35] Dr. Kinsbourne quotes from Institute of Medicine, Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Casuality 45 (Kathleen R. Stratton et al. eds., 1994) (emphasis added). Although petitioner filed another excerpt of this report, see Pet'r's Ex. 8-6 at 511, petitioner did not file this quoted portion of this report as an exhibit. However, it is available in full online at http://www.nap.edu/catalog.php?record_ id=2138.

Dr. Kinsbourne again relied on this excerpted passage during his testimony at hearing. See Tr. 85. What Dr. Kinsbourne failed to address, however, is the preceding part of the excerpted paragraph, which states:

> . . . the expected latency between an antecedent event . . . and the first symptoms of [Guillain-Barré Syndrome (GBS)] is mainly between 7 and 21 days. Occasional cases appear to have latencies of between 22 and 42 days . . . [this] allow[s] a range of latencies to be stated for GBS, that is, 5 days to 6 weeks. Similarly, ADEM is widely believed to be the human counterpart of experimental allergic encephalomyelitis [(EAE)], and EAE has an observed latency of about 10 to 20 days. ADEM has a similar clinical latency.[36]

The full excerpt from the 1994 IOM report suggests that ADEM has a much shorter latency period than GBS, and this shorter period of latency undercuts Dr. Kinsbourne's assertion that petitioner's symptom onset was medically appropriate for ADEM. This IOM reference provides support for the proposition that petitioner's neurologic complications occurred within the six-week time frame that may be appropriate for the onset of immune-mediated condition of GBS. But that is not the condition that petitioner here has developed.

Petitioner has not offered preponderant evidence that her injuries occurred in a timeframe consistent with the proposed theory of causation. Snyder, 88 Fed. Cl. at 742-43 (special masters are not required to accept the ipse dixit of an expert) (citing Gen. Elec. Co. v. Joiner, 522 U.S. 136, 146 (1997)).

Because petitioner has failed to meet her burden under the Althen prongs, she is not entitled to compensation, and her petition must be dismissed. de Bazan, 539 F.3d at 1354.

## IV. Conclusion

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[36] Institute of Medicine, Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Casuality at 45, available at http://www.nap.edu/openbook.php?record_id=2138&page=45.

For the foregoing reasons, petitioner's claim for Program Compensation fails. The petition **SHALL BE DISMISSED**, and the Clerk of Court shall enter judgment consistent with this decision.[37]

**IT IS SO ORDERED.**

s/ Patricia E. Campbell-Smith
Patricia E. Campbell-Smith
Chief Special Master

[37] Pursuant to Vaccine Rule 11(a), entry of judgment is expedited by the parties' joint filing of notice renouncing the right to seek review.