In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 14-920V
(to be published)

L.Z., Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	Special Master Corcoran Filed: August 24, 2018 Decision; Denial of Entitlement; Multiple Sclerosis ("MS"); Influenza ("flu") Vaccine; Significant Aggravation.

Ronald Craig Homer, Conway, Homer, P.C., Boston, MA, for Petitioner.

Adriana R. Teitel, U.S. Dep't of Justice, Washington, DC, for Respondent.

DECISION DENYING ENTITLEMENT[1]

On September 29, 2014, L.Z. filed a Petition under the National Vaccine Injury Compensation Program (the "Vaccine Program"[2]), alleging that the influenza ("flu") vaccine she received on October 16, 2011, caused her to suffer an unspecified "neurological demyelinating injury." Pet. at 1, ECF No. 1. She later amended her claim, alleging that the flu vaccine either caused transverse myelitis ("TM"), optic neuritis ("ON"), and/or multiple sclerosis ("MS"), or

[1] This Decision will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means the Decision will be available to anyone with access to the internet**. As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the published Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen (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). Otherwise, the entire Decision will be available in its current form. *Id.*

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755 (codified as amended at 42 U.S.C. §§ 300aa-10–34 (2012)) (hereinafter "Vaccine Act" or "the Act"). All subsequent references to sections of the Vaccine Act shall be to the pertinent subparagraph of 42 U.S.C. § 300aa.

significantly aggravated an underlying neurologic condition. Am. Pet. at 2, Nov. 5, 2015, ECF No. 26.

A hearing in this matter was held on November 13, 2017. After consideration of the record and testimony provided at hearing, I find that Petitioner is not entitled to a compensation award. The record best supports the conclusion that Petitioner suffered from MS predating her vaccination, leaving only the claim that the flu vaccine significantly aggravated that illness. But Petitioner has not established a plausible causation theory that the flu vaccine could cause an MS relapse/exacerbation, nor has she offered sufficient preponderant evidence that in her specific case the flu vaccine *was* the cause of any subsequent symptoms she experienced or that it likely worsened her overall expected course.

I. Factual Background

Pre-Vaccination History

L.Z.'s pre-vaccination history strongly suggests that she was already experiencing some kind of neurologic injury at the time she received the flu vaccine in 2011.

For example, on March 5, 2009—over two years prior to the vaccination at issue—Petitioner was seen at the Nicklas Chiropractic practice in Paso Robles, California, for a visual change involving her right eye that she said had begun the previous day. Ex. 4 at 1–3. A week later, on March 11, 2009, she reported persistent visual change affecting distance vision, as well as neck pain. *Id.* at 5–6. The following year, on September 22, 2010, she returned to Nicklas Chiropractic with complaints of left-sided neck stiffness of one-week duration. *Id.* at 12. Two days later, on September 24, 2010, L.Z. underwent a new patient visit with Klyda White, D.O. Ex. 25 at 1. At this time, she complained of bilateral hearing loss, tinnitus, and pain for several days. *Id.* Medical history was positive for neck and back pain, although she was treated only for cerumen impaction. *Id.*

A few months later, in late December 2010, L.Z. returned to Nicklas Chiropractic complaining of tingling at the tip of her right thumb which she reported had been ongoing for the past month. Ex. 4 at 14. She sought additional treatment at Nicklas Chiropractic on January 21, 2011, stating that she had awoken with a stiff neck (which she attributed to lifting a heavy item after moving the prior weekend). *Id.* at 15. She also reported having a resolving headache and numbness of her left thumb pad. *Id.*

The following summer, Petitioner saw her primary care physician, Dr. Donella Jenkins, on August 27, 2011, complaining of right eye redness, photophobia, and decreased vision for one

week. Ex. 18 at 1. Her conjunctiva appeared inflamed and a pterygium[3] was noted laterally. *Id.* Dr. Jenkins's impression was that Petitioner had conjunctivitis, and antibiotic eye drops were prescribed. *Id.* Approximately a month later, on September 28, 2011, L.Z. returned to Nicklas Chiropractic, and was again treated with manual therapy and traction for recurrent neck pain and stiffness. Ex. 4 at 18.

Receipt of Flu Vaccine and Purported Reaction

On October 16, 2011, L.Z. received a flu vaccine in her left deltoid. Ex. 1 at 1–2; Ex. 24 at 3. There is no contemporary record evidence suggesting she experienced any immediate reaction to the vaccination. However, a little over three weeks later, on November 7, 2011, Petitioner was examined by Rex Stevens, D.C. (a chiropractor), at SLO Wellness Center in San Luis Obispo, California, after complaining of chronic lower back pain and random pain mid-back and in her neck. Ex. 17 at 1. She specifically described having experienced bilateral lower extremity numbness with associated weakness, plus right foot tingling and the feeling that her left leg would give out after prolonged standing and walking, reporting that all of the above had lasted a week since receipt of the flu vaccine. *Id.* L.Z. also provided written statements in this case alleging that she began experiencing adverse symptoms approximately two weeks post-vaccination. *See* Aff. filed as Ex. 29 at 3, Mar. 31, 2015, ECF No. 17-1.

Dr. Stevens's exam of Petitioner revealed positive straight leg raising on the right with inability to walk on right heel, 2/5 strength for dorsiflexion, decreased sensation to pinprick along L4-5 and L5-S1 dermatomes, and reduced range of motion of lumbar spine. Ex. 17 at 1–2. Based upon the history Petitioner provided (which included her pre-vaccination experiences), Dr. Stevens noted in the medical history portion of the relevant record that "[p]ast MD suggests patient may have MS." *Id.*

The following week, L.Z. went to see Dr. Jenkins on November 12, 2011, complaining of symptoms comparable to what she had described to Dr. Stevens (e.g., right foot numbness, left foot dragging, and loss of coordination). Ex. 18 at 2. As the visit notes indicate, Petitioner reported at this time that ten years earlier she had experienced vertigo and vision problems, and that in the past she had thrown her back out, suffered urinary incontinence, and had fallen at work resulting in hand numbness. *Id.* She also informed Dr. Jenkins that her current symptoms worsened the longer she was on her feet, but improved with sitting. *Id.* An examination revealed ankle weakness, and based upon Dr. Jenkin's recommendation, L.Z. was referred for a magnetic resonance imaging ("MRI") and consultation with a neurologist, Dr. Mary Amir. *Id.*

[3] A pterygium is an abnormal triangular fold of membrane in the interpalpebral fissure of the eye that extends from the conjunctiva to the cornea. *Dorland's Illustrated Medical Dictionary* 1551 (32nd ed. 2012) (hereinafter "*Dorland's*").

Petitioner's Neurology Work-up

L.Z. was examined by Dr. Amir on November 14, 2011. Ex. 16 at 33. Petitioner reported to Dr. Amir the same general history that she had provided treaters over the prior week, suggesting again that her numbness and leg movement problems began in October. *Id.* However, she also informed Dr. Amir of symptoms predating vaccination. For example, she reported that five weeks before (or immediately prior to her receipt of the flu vaccine), she had experienced the sensation of having a "ball" in the center of her right foot that was accompanied by numbness. *Id.* She also indicated that the frequency and intensity of her recent urinary incontinence had increased over the past three weeks, although it had begun after her children were born. And she complained of exercise intolerance, as well as back and neck sensations that Dr. Amir identified as Lhermitte's sign.[4] *Id.* at 34.

Dr. Amir's exam of L.Z. revealed a normal gait, mild weakness in her right hamstring, mildly increased muscle tone in her left lower extremity, abnormal bilateral Babinski[5] signs, and a bilateral upper extremity tremor (although worse on the left side). Ex. 16 at 34. Based upon the above, Dr. Amir assessed Petitioner's symptoms as evidencing MS. *Id.* She recommended a Solu-Medrol infusion,[6] requested an ophthalmology evaluation, and advised Petitioner to undergo a lumbar puncture. *Id.*

At the same time as her visit to Dr. Amir, Petitioner also had several MRIs performed. The brain MRI revealed white matter changes in her brainstem consistent with MS. Ex. 10 at 1. The treating radiologist did not test for lesion enhancement, however.[7] The lumbar spine MRI showed a disc protrusion at L5-S1 that impinged on the right S1 nerve root. *Id.* at 2. Petitioner's thoracic and cervical spine MRIs showed scattered areas of T2 hyperintensity, most consistent with MS. *Id.* at 3–4.

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[4] Lhermitte's sign refers to "electriclike shocks spreading down the body" occurring when a patient "flexes the head forward." *Dorland's* at 1713. It is seen mainly in MS. *Id.*

[5] Babinksi reflexes or signs are produced by stimulation of the sole of the foot; in adults, the upward flexing of the big toe can be a sign of neurologic dysfunction. *Dorland's* at 1611.

[6] A Solu-Mendrol infusion (or "methylprednisolone injection") is a corticoid steroid used to treat MS flares. *See Methylprednisolone (Injection Route)*, Mayo Clinic (Mar. 1, 2017), https://www mayoclinic.org/drugs-supplements/methylprednisolone-injection-route/description/drg-20075216 (last accessed on July 25, 2018).

[7] Lesion enhancement on MRI occurs after the uptake in the lesion of a gadolinium-based contrast agent injected into a subject's blood. *See W.C. v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 440, 444 (2011). Enhancement reveals a breakdown of the blood-brain barrier (since the contrast agent is able to go into the brain). *Id.* Such a breakdown can trigger neurological injury, by allowing infectious or inflammatory agents into the brain and central nervous system, causing damage. *Id.* In an MS patient, enhancement typically reveals the presence of new lesions (as opposed to old lesions which are considered "non-enhancing"). *See Taylor v. Sec'y of Health & Human Servs.*, No. 13-700V, 2018 WL 2050857, at * 21 & n. 4 (Fed. Cl. Spec. Mstr. Mar. 9, 2018). MRI Enhancement can assist treaters in distinguishing between MS and other neurological diseases such as acute disseminated encephalomyelitis ("ADEM").

The following month, L.Z. was evaluated by an ophthalmologist, Dr. Ahmad Amir,[8] on December 6, 2011, for "possible MS, visual disturbance [right eye]." Ex. 12 at 6. At this time, Petitioner recalled an episode of visual disturbance two weeks earlier that she associated with numbness and an inability to pick up her right foot, although she also repeated earlier statements that most of her symptoms had begun six to eight weeks before (which would be around the same time as, or prior to, her flu vaccine receipt). *Id.* Dr. Amir's exam revealed mild pallor of the optic disc, mild color distortion, and a large afferent pupillary defect involving the right eye. *Id.* Dr. Amir's impression was that Petitioner suffered from ON, and he discussed initiating oral steroids but proposed deferring treatment decisions to a neurologist. *Id.*

Based on the above exams, diagnostic testing, and the MRIs, Dr. Mary Amir prepared a letter to Petitioner's primary care provider, Dr. Jenkins, on December 8, 2011. Ex. 2 at 2. In it, Dr. Amir opined that L.Z. suffered from relapsing/remitting multiple sclerosis. *Id.* at 1. The letter also noted a concern for an elevated Lyme's disease titer. *Id.* According to Dr. Amir, L.Z. was counseled with respect to the MS diagnosis and encouraged to keep records to track her symptoms, and to begin adhering to a strict medical regiment. The letter did not propose any date of onset of L.Z.'s symptoms, however, nor did it mention the flu vaccine. *See id.* By 2012, Petitioner demonstrated overall improvement, although she continued to experience some numbness and other sequelae that suggested ongoing neurologic deficits. Ex. 12 at 1; Ex. 17 at 11.

Subsequent Treatment for MS and Related Symptoms

In the ensuing years since being diagnosed with MS, L.Z. has continued to receive treatment for her condition. She visited an orthopedic surgeon, Dr. James Carr, in 2013, in the hope of confirming whether certain symptoms she continued to experience were connected to her prior MS diagnosis or instead reflected separate back and spine issues. Ex. 5 at 1; Aff. filed as Ex. 29 at 6 (confirming visit). At this time, she informed Dr. Carr of the various neurologic symptoms she had experienced in the past (i.e., gait abnormalities, incontinence, numbness in the right leg, bilateral lower extremity weakness, and sexual dysfunction). Ex. 5 at 1. Dr. Carr's physical examination revealed normal results, however. *Id.* at 2–3. He referred L.Z. for additional brain and cervical spine MRIs (which were reviewed by Dr. Nelson Yamagata, a neurologist, the following April 2014) and prescribed six weeks of physical therapy for mild disc herniation. *Id.* at 4, 12.

Approximately a year later, on March 3, 2014, L.Z. had a follow-up appointment with Dr. Carr, at which time she stated that she had not experienced any "bad" episodes of weakness for about two and one-half years. Ex. 5 at 5. Dr. Carr assessed her with lower back pain, lumbar degenerative disc disease, herniated disc, and radiculopathy, and proposed no surgical

[8] Petitioner's neurologist, Dr. Mary Amir referred her to Dr. Ahmad Amir for an eye exam. *See* Ex. 12 at 2. Treatment notes do not indicate if the two Dr. Amirs were related.

intervention, but also referred her to a neurologist, Dr. Yamagata, for further evaluation. *Id.* at 8, 11.

Petitioner saw Dr. Yamagata on April 16, 2014. Ex. 7 at 3–5. She described her prior history with neurologic problems, noting that although over time the weakness in her feet had improved, she still felt that she had not returned to her baseline level, and stated that she continued to experience exercise intolerance and a sense of bladder urgency. *Id.* at 3. Dr. Yamagata's initial assessment was that L.Z. had likely not experienced "further exacerbations since her initial spells [of TM and ON]," but proposed a follow-up MRI to assess where she was from a neurological standpoint. *Id.* at 4.

Petitioner's May 2, 2014 MRI revealed new, non-enhancing foci of high signal in the bilateral frontal gyri, but no lesions in the brainstem compared to her November 2011 study. Ex. 5 at 16; Ex. 7 at 6. Around this time, L.Z. also experienced "sudden increased weakness and stiffness in her legs and difficulty walking." Ex. 5 at 16. Dr. Yamagata concluded that petitioner had "probable transverse myelitis with an episode of visual change in the past," though "the cause for her initial symptoms [was] not clear." *Id.* MS, neuromyelitis optica, and Lyme disease were included in the differential diagnosis. *Id.* A second opinion obtained from an infectious disease specialist was consistent with Dr. Yamagata's assessment. Ex. 9 at 3.

Since the spring of 2014, L.Z. has continued to monitor her MS with treatment and additional imaging studies. She has experienced what may be additional MS-related episodes that have been responsive to proper treatment. *See, e.g.*, Ex. 23 at 1–2; Ex. 27 at 3; Ex. 35 at 21, 33; Ex. 38 at 1, 3. MRI studies performed in March 2016 and May 2017 revealed further radiologic evidence of lesions and white matter damage that confirms the accuracy of her 2011 initial MS diagnosis. *See, e.g.*, Ex. 35 at 5; Ex. 36 at 1; Ex. 39.

II. Expert Opinions

A. *Dr. Salvatore Napoli*

Dr. Napoli authored two reports and testified at the entitlement hearing on Petitioner's behalf. *See* Expert Report filed as Ex. 31, Oct. 15, 2015, ECF No. 25 ("First Napoli Rep."); Expert Report filed as Ex. 33, July 15, 2016, ECF No. 32 ("Second Napoli Rep."). Dr. Napoli opined that L.Z. suffers from a relapsing/remitting form of MS that was subclinical at the time of vaccination but exacerbated by the flu vaccine. Tr. at 39, 69.

Dr. Napoli obtained his medical degree from Albany Medical College in Albany, New York, where he also completed his residency in neurology. *See* CV filed as Ex. 32, Oct. 8, 2015, ECF No. 24-2 ("Napoli CV"). After medical school, Dr. Napoli went on to complete two

fellowships, one in EMG/neurophysiology/spasticity training at Tufts University St. Elizabeth's Hospital, and one in MS at Harvard Medical School. Tr. at 5; Napoli CV at 2. Following his clinical fellowship years, he served as an associate neurologist at Brigham and Women's Hospital Partners Multiple Sclerosis Center in Boston. Napoli CV at 2. Thereafter, he served as the Medical Director for the Steward Spasticity Service Center at Steward Foxboro and Norwood Hospital in Massachusetts. *Id.* He then joined the Neuro Institute of New England's Multiple Sclerosis Center, where he presently serves as the President and Medical Director. Tr. at 6; Napoli CV at 2. He also continues to serve as the Medical Director for the Steward Multiple Sclerosis Institute at Steward Foxboro and Norwood Hospital. Napoli CV at 2.

Dr. Napoli has ample clinical expertise treating neurologic illnesses like MS—and in particular deep knowledge on the use of imaging technologies and interpretation of their results. Tr. at 5–6, 29. He estimated that he has treated or overseen 1,500 patients with MS (or similar diseases) during his tenure. Tr. at 6. Dr. Napoli acknowledged, however, that he has far less experience with research. *Id.* at 30. He has also had little exposure to immunologic matters beyond a fellowship in which he participated from 2003–05. *Id.* at 5; Napoli CV at 2. Dr. Napoli has published two professional articles and one case study. Napoli CV at 6.

Dr. Napoli's opinion relied on his reading of Petitioner's medical history. He noted that indicia of pre-vaccination symptoms from the medical records were somewhat vague (making it difficult for him to be certain that her MS predated receipt of the flu vaccine), and that it was indisputable that L.Z. was "functioning" in an overall healthy manner before vaccination. Tr. at 9, 12, 18, 19, 39. Dr. Napoli nevertheless acknowledged that Petitioner's illness likely existed (albeit in an arguably subclinical form) *prior* to receiving the flu vaccine. *E.g.*, *id.* at 19 ("she had it to begin with"), 42 ("I think she definitely had some kind of subclinical stuff going on to begin with"), 44, 67. In particular, he agreed that Petitioner's pre-vaccination bilateral thumb numbness, along with her previously-reported bladder problems, could constitute initial presenting symptoms of MS. *Id.* at 39–40.[9]

Dr. Napoli next identified record evidence of MS-related symptoms after vaccination that he deemed significant under Petitioner's causation theory. He characterized her post-vaccination course of symptoms as "fulminant,"[10] beginning with myelitis/spinal cord myelopathy and followed by ON. Tr. at 9, 18, 28. Her initial fall 2011 MRI revealed a thoracic lesion that he opined likely would have shown enhancement had contrast been employed in the imaging process. Tr. at 11, 66–67. She also displayed bilateral, lower-extremity weakness—a symptom distinguishable from what Petitioner had previously experienced before vaccination. *Id.* at 68. And Dr. Napoli

[9] Dr. Napoli did not, however, deem the evidence of a possible pre-vaccination ophthalmologic problem as a likely pre-vaccination MS symptom, arguing that it did not appear to have had a neurologic origin. *Id.* at 42–43, 59, 60–61.

[10] Dr. Napoli defined fulminant to mean "severe and quick or sudden." Tr. at 144.

characterized her ON diagnosis in December 2011 as an unusual occurrence that suggested a susceptibility to autoimmune injury or an environmental cause underlying all of her post-vaccination symptoms. *Id.* at 15–17.

Based upon the above, Dr. Napoli opined that L.Z. "took a hit" after receipt of the flu vaccine, causing "disability" and "residual issues downstream," confirming that she was suffering from MS[11] (whether or not her illness predated vaccination). Tr. at 10, 19, 20. To explain biologically how this occurred, he proposed molecular mimicry between components of the flu vaccine[12] and self protein sequences resulting in autoimmune cross-reactivity, whereby the immune system would mistakenly attack self structures, confusing them with presenting antigens in the vaccine. First Napoli Rep. at 5. He noted that this mechanism had been confirmed as reliable by literature discussing animal models and the wild flu virus (although not the vaccine). Tr. at 22–23, 25, 48–49, 61–62; First Napoli Rep. at 5; Second Napoli Rep. at 4. He admitted that most flu virus peptides had not been shown to have a cross-reaction potential with the myelin basic protein ("MBP") components of nerve cells (found in the central nervous system ("CNS"), where MS would be expected to begin), but stressed that the rarity of a vaccine-caused injury meant that the biologic process he proposed could not be ruled out as implausible (and that in fact there was evidence that flu virus components could instigate an MBP reaction). Tr. at 51–52, 61–62.

Because of his acknowledgement of the strong likelihood that L.Z.'s MS predated vaccination, Dr. Napoli spent some time at hearing testifying about the nature of MS's course. In his experience, MS-associated lesions can be subclinical for a long time while other unaffected parts of brain "pick[] up the slack," with the result that patients do not manifest symptoms. Tr. at 38. Thus (and in keeping with his earlier admissions about Petitioner's pre-vaccination history), Dr. Napoli seemed to accept that the Petitioner's claim actually turned on whether the flu vaccine could have aggravated her underlying disease—and he answered that question in the affirmative.

To do so, Dr. Napoli discussed how MS "flares," or exacerbations (a term which he deemed congruent with an MS relapse), occur. Tr. at 37. Different environmental factors can trigger an MS exacerbation—stress, weather changes, or an infection. *Id.* at 21, 47–48, 70. But such triggers would generally not cause a significant worsening of the patient's condition (nor would they establish a new event akin to the formation of new lesions). *Id.* at 21–22, 70. Because vaccines are intended to elicit an adaptive immune response (so that the body will in the future recognize and fight off wild infections comparable to the vaccine administered), they "create potentially a remote

[11] Dr. Napoli spent some time in his testimony addressing the propriety of MS as a diagnosis applicable to L.Z.'s symptoms—although it is not really a contested issue in light of Dr. Venkatesan's agreement that Petitioner had MS. Tr. at 26–27, 35–36.

[12] Even though the flu vaccine's formula changes year to year, Dr. Napoli proposed that "antigenic similarity" between yearly variations would still be able to spark an autoimmune cross-reaction, and thus an individual previously vaccinated might nevertheless respond to the newer version of the vaccine. Tr. at 62–63.

chance of a cascade" that could have a more significant and dramatic effect on susceptible individuals.[13] *Id.* at 48, 73. Here, there was no evidence of other environmental triggers, like stress—but there was evidence of vaccination before L.Z.'s symptomatic flare in November 2011. *Id.* at 74, 146.

Dr. Napoli offered some scientific and medical evidence to support his assertions that vaccines could trigger a worsening of an individual's preexisting MS. First Napoli Rep. at 5; Second Napoli Rep. at 2–4. However, certain of these articles were less supportive of his opinion than they seemed at first glance. For example, at hearing Dr. Napoli referenced a 1967 article that reviewed nine case reports in which vaccines are alleged to have caused MS exacerbations or relapses—none of which involved the flu vaccine. Tr. at 57–58; *see* H. Miller, et al., *Multiple Sclerosis and Vaccination*, 2 Brit. Med. J. 210, 210–13 (1967), filed as Ex. 31, Tab F, ECF No. 45-6 ("Miller"). Dr. Napoli also acknowledged that case reports generally were not particularly probative of causation, although he stressed that the rarity of a vaccine-induced MS exacerbation had to be taken into account. *Id.* at 48. Overall, Dr. Napoli could not point to any studies demonstrating an association between the flu vaccine and MS exacerbation—and even accepted the legitimacy of articles offered by Respondent establishing *the contrary* (as discussed below)—but again maintained that the rare character of the injury at issue had to be taken into account when weighing such evidence. *Id.* at 57–58 (admitting Respondent's studies show "there's no link" between the flu vaccine and an increased risk of MS exacerbation).

In addition to the above, Dr. Napoli opined that the timing of onset of L.Z.'s alleged exacerbation—two to three weeks post-vaccination—was medically acceptable based on reliable medical literature. Tr. at 26; First Napoli Rep. at 5; Second Napoli Rep. at 3; *see* L. Schoenberger, et al., *Guillain-Barré Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976–1977*, 110 Am. J. Epid. 105, 105 (1976), filed as Ex. 31, Tab G, ECF No. 45-7; K. Stratton, et al., *Adverse Events Associated with Childhood Vaccines: Evidence on Causality*, Institute Med. 47 (1994), filed as Ex. 31, Tab H, ECF No. 45-8. He acknowledged, however, that some of that literature was distinguishable—for example, because it involved a slightly different mechanism inapplicable to the theory proposed. Tr. at 49–50 (discussing K. Wucherpfennig, et al., *Molecular Mimicry in T Cell-Mediated Autoimmunity: Viral Peptides Activate Human T Cell Clones Specific for Myelin Basic Protein*, 80 Cell 695, 695, 698 (1995), filed as Ex. 31, Tab C, ECF No. 45-3 ("Wucherpfennig")). Dr. Napoli also noted that evidence from the medical record of possible neurologic symptoms (for example, a foot dropping) within days or a week of vaccination might present an unreasonable onset timeframe, given the period he felt the biologic mechanism of molecular mimicry would take to unfold. *Id.* at 32–33. On the other

[13] Dr. Napoli proposed (in somewhat conclusory fashion) that L.Z. likely had some genetic predisposition to suffer from an autoimmune response induced by vaccination. A person's genetics, he opined, can render them susceptible to demyelination caused by an autoimmune process. Tr. at 10, 20–21. He acknowledged, however, that such assertions were suppositions based principally on the fact that Petitioner's MS was diagnosed after receiving the flu vaccine, and not upon actual evidence of L.Z.'s genetic susceptibility. *Id.* at 66.

side of the spectrum, Dr. Napoli proposed that, based on his reading of the relevant literature, a timeframe exceeding two to three months was likely too long—although a vaccine might still be causal even if exacerbation was evident up to nine to twelve weeks later. *Id.* at 34. At all times, Dr. Napoli stressed the relatively brief temporal relationship between vaccination and L.Z.'s initial symptoms as particularly persuasive evidence to him of an association. *Id.* at 11.

Finally, Dr. Napoli's testimony addressed whether any alleged vaccine-caused MS exacerbation could be deemed to have worsened the overall expected course of L.Z.'s MS. He opined that this had occurred—but did so based on the circular logic that because Petitioner experienced an MS relapse post-vaccination, her illness had by definition "worsened." Tr. at 69. He admitted, however, that he could not opine whether she would have experienced a similar "hit" at some time in the future regardless of whether she had received a vaccine. *Id.* At bottom, he placed great weight on the fact that there was nothing else in the record other than the flu vaccine's administration that might explain her exacerbation. *Id.* at 27.

B. *Dr. Arun Venkatesan*

Dr. Venkatesan filed a single report and testified on Respondent's behalf at hearing. *See* Expert Report filed as Ex. A, Mar. 8, 2016, ECF. No. 28-1 ("Venkatesan Rep."). Dr. Venkatesan received his medical degree and a Ph.D. in microbiology and immunology from the University of California, Los Angeles. CV filed as Ex. B, Mar. 8, 2016, ECF No. 28-2 ("Venkatesan CV"). Following medical school, he completed a neurology residency at Johns Hopkins University in Baltimore, Maryland. *Id.* at 1. He also completed a second fellowship in neuroimmunology and neuroinfectious diseases at Johns Hopkins, and later joined the faculty in 2007 as an assistant professor in the neurology department. *Id.*

Since 2009, Dr. Venkatesan has served as the director of the encephalitis center at Johns Hopkins, and frequently sees both adult and pediatric patients with MS and other autoimmune CNS disorders. Tr. at 77. According to Dr. Venkatesan, thirty percent of his time involves a clinical practice seeing patients, with the remainder involving research, teaching, and overseeing neurology residents. *Id.* at 79, 81. Dr. Venkatesan estimates that in his career he has seen more than 1,000 MS patients. *Id.* at 78. He has also published numerous articles related to neuroinflammatory and neuroinfectious diseases. Venkatesan CV at 1–2.

Dr. Venkatesan agreed with Dr. Napoli that L.Z. was properly diagnosed with MS, although he more affirmatively placed its onset as predating her vaccination. Tr. at 114. He also disputed Petitioner's contention that the flu vaccine can (and in this case did) cause exacerbation of MS. *Id.* at 82.

Dr. Venkatesan began his testimony by discussing MS and its relationship to other neuroinflammatory conditions. He defined MS as a chronic demyelinating disease of the CNS, resulting in progressive neurologic dysfunction. Tr. at 83. It often features relapses after an initial event, and thus its course can be characterized by plateaus (with limited or controlled symptoms) and flares. *Id.* Other identified CNS inflammatory conditions, such as TM (inflammation of the spinal cord) or ON (inflammation of the optic nerve) can be symptomatic of MS (and can even constitute an initial presenting symptom), but can also stand on their own as separate illnesses (especially if other indicia for MS have not been established). *Id.* at 78, 83, 88. Dr. Venkatesan characterized such kinds of CNS inflammation as more "eloquent," or indicative of MS, than others. *Id.* at 86–87.

When generally diagnosing MS, Dr. Venkatesan stressed the importance of reviewing radiologic evidence in conjunction with a patient's clinical symptoms. He referred to instances in which a patient's MRI reveals the presence of CNS lesions but where no clinical symptoms are present as "radiologically isolated syndrome" ("RIS"), while he defined evidence of symptoms suggestive of CNS demyelination or inflammation without corroborative MRI evidence as "clinically isolated syndrome" ("CIS"). Tr. at 84–85. Ultimately, an MS diagnosis depends on a finding of dissemination of lesions and symptoms both in *time* (meaning that they are not seen on only a single occasion) and *space* (i.e. across multiple locations in the CNS). *Id.* at 85, 88. In Dr. Venkatesan's view, a lack of radiologic evidence of lesions makes it difficult to confirm an MS diagnosis. *Id.* at 85–86. Symptom relapses could occur in a timeframe of once a year to once every few years, and an individual relapse could last a few weeks or longer. *Id.* at 89–90.

Dr. Venkatesan disputed the sufficiency of Petitioner's evidence supporting her contention that the flu vaccine could cause or exacerbate MS, given its chronic nature. Tr. at 113. He acknowledged the reliability of scientific evidence establishing that direct infection can cause MS and/or contribute to an autoimmune process. *Id.* at 122, 130–31. He also did not contest that other illnesses involving demyelination (for example, the peripheral neuropathy Guillain Barré syndrome ("GBS")) could be vaccine-induced. *Id.* at 124. But in his view, vaccines could not produce an MS relapse. Rather, a vaccine could at most (and indirectly—by, for example, causing a fever leading to an increase in body temperature) only induce transient changes in an individual already suffering from MS—*not* alter an existing course of MS for the worse. *Id.* at 114.

To support his opinion, Dr. Venkatesan (in his report and direct testimony) offered the views of trustworthy members of the relevant scientific community, as well as reliable scientific and medical literature, that he proposed contradicted Petitioner's theory. He noted that the American Academy of Neurology has stated that there is "level A" evidence establishing no risk of post-vaccination MS exacerbation. Tr. at 99–100; Venkatesan Rep. at 3. One article offered by Respondent directly studied the effect of the flu vaccine on MS but found no post-vaccination relapse. Tr. at 91–92; *see* C. Confavreux, et al., *Vaccinations and the Risk of Relapse in Multiple*

Sclerosis, 344 New Engl. J. Med. 319, 319 (2001), filed as Ex. C, ECF No. 49-1 ("Confavreux"). The Confavreux study examined 643 MS patients (fifteen percent of whom reported having been vaccinated during the preceding twelve months) to evaluate the relative risk of a vaccine-related relapse. But Confavreaux determined that a vaccinated individual had a *reduced* chance of relapse—and its authors expressed high confidence in the statistical accuracy of their findings in concluding that vaccinations did not appear to increase the risk of relapse in MS patients. Tr. at 93–94; Confavreaux at 324–25. Dr. Venkatesan admitted, however, that the sample size of the Confavreaux study was relatively small—a factor that suggests its findings should have less probative weight than Respondent urged. Tr. at 125.

In another article filed by Respondent, a number of vaccines were evaluated to determine if they were associated with demyelinating events like MS or ON, but its authors did not find such an association. Tr. at 94–95; *see* F. DeStefano, et al., *Vaccinations and the Risk of Central Nervous System Demyelinating Diseases in Adults*, 60 Arch. Neuro. 504 (2003), filed as Ex. D, ECF No. 49-2 ("DeStefano"). Although the DeStefano study did not specifically include TM as a separate category, Dr. Venkatesan still maintained that the study would have included persons similarly situated to L.Z., whose MS presented initially as spinal cord inflammation that might first appear to be TM to treaters. *Id.* at 95. DeStafano did, however, include the flu vaccine among the studied vaccines, and found with high statistical confidence that the vaccine was not associated with MS. *Id.* at 96.

Dr. Venkatesan also discussed a third article involving a randomized trial of flu vaccine administration intended to determine whether MS exacerbations occurred at an increased rate. Tr. at 96–97; *see* A. Miller, et al., *A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial of Influenza Immunization in Multiple Sclerosis*, 48 Neuro. 312 (1997), filed as Ex. E, ECF No. 49-3 ("Miller 2"). Although Dr. Napoli proposed in his second report that Miller 2 revealed a risk of exacerbation double those in the non-vaccinated cohort, Second Napoli Rep. at 3, Dr. Venkatesan argued that this finding was not statistically significant (a point supported also by the authors of the study)—and more importantly, that Miller 2 included individuals who had experienced exacerbation or MS flares up to 175 days after vaccine administration, and thus (under Petitioner's own theory) were highly *unlikely* to have experienced a vaccine-induced exacerbation within a medically acceptable timeframe. Tr. at 97, 126–28. [14]

Besides highlighting literature and other evidence tending to rebut any association between the flu vaccine and MS exacerbation, Dr. Venkatesan reviewed the specific elements of

[14] In addressing the Miller 2 MS flare/exacerbation timeframes, Dr. Venkatesan also briefly touched on the scientific reliability of Petitioner's broader argument that her alleged flu vaccine-induced exacerbation occurred in a medically acceptable timeframe. He noted that timeframes of 42 days, or even three months, post-vaccination for flares observed in some of Petitioner's literature applied to non-vaccinated individuals as well, and thus it could not be concluded that these periods were reasonable from a medical standpoint. Tr. at 98–99.

Petitioner's causation theory. He admitted that molecular mimicry as a general matter is a scientifically plausible biologic mechanism to explain how an autoimmune process might unfold. Tr. at 131. However, he questioned its relevance to the pathologic processes of chronic diseases involving a "sustained immune response," such as MS, as opposed to acute diseases that progress rapidly like GBS. *Id.* at 139–40. He noted that certain literature confirmed the fact that MS progresses as a result of an overall failure in the immune system response, and is therefore less likely to be driven simply by cross-reactivity attributable to homology between antigens in a vaccine and self protein sequences. *Id.* at 140–41.

Another article offered by Respondent to establish the lack of association between the flu vaccine and MS exacerbation considered the larger question of whether the flu vaccine could encourage a *nonspecific* T cell autoreactive response in patients with MS—finding that it did not. *See* N. Moriabadi, et al., *Influenza Vaccination in MS: Absence of T-Cell Response Against White Matter Proteins*, 69 Neuro. 938, 942–43 (2001), filed as Ex. G, ECF No. 49-5 ("Moriabadi"). In Dr. Venkatesan's reading, Moriabadi reduced the likelihood that the flu vaccine would produce *any* auto-immune cross-reaction against MBP in the first place. Tr. at 108–09. He later acknowledged, however, that the extremely small sample size of tested individuals greatly reduced Moriabadi's overall probative value. *Id.* at 109, 129.

Dr. Venkatesan otherwise denied knowledge of reliable scientific evidence establishing that MS would occur via molecular mimicry, and endeavored to rebut those items Petitioner offered to link the flu vaccine to MS. *Id.* at 111. Certain items of literature purporting to make such a connection involved TM rather than MS, or involved acute cases of TM rather than MS presenting with TM-like symptoms, and were therefore distinguishable on those grounds, he reasoned. Tr. at 110; *see, e.g.*, F. Pidcock, et al., *Acute Transverse Myelitis in Childhood: Center-Based Analysis of 47 Cases*, 68 Neuro. 1474 (2008), filed as Ex. 31, Tab E, ECF No. 45-5; N. Agmon-Levin, et al., *Transverse Myelitis and Vaccines: A Multi-Analysis*, 18 Lupus 1198 (2009), filed as Ex. 31, Tab D, ECF No. 45-4 ("Agmon-Levin"). Agmon-Levin also was completely based on case reports, reducing its overall scientific reliability. Tr. at 130; Agmon-Levin at 1199. And an article offered by Petitioner to establish molecular mimicry, Wucherpfennig, involved flu virus strains different from the formula relevant to this case, and/or established that an absence of precise homology could result in no cross-reactive potential at all. Tr. at 100-07; Wucherpfennig at 698–99.

Besides questioning the science supporting Petitioner's theory, Dr. Venkatesan looked carefully at L.Z.'s medical history and concluded that Petitioner's MS likely predated her vaccination. In so opining, he acknowledged that the evidence was not iron-clad, but that he found significant certain symptoms she had displayed prior to October 2011, such as incontinence as well as her bilateral thumb numbness, reasonably suggestive of MS (if not fully supportive of the diagnosis). Tr. at 111, 116–17, 133, 136. Based on his own experience, he also proposed that a

pre-vaccination MRI might have produced radiologic findings consistent with MS, although he noted that this was ultimately only informed speculation. *Id.* at 112, 132. Dr. Venkatesan took issue with Dr. Napoli's proposal that Petitioner's MS (to the extent it predated vaccination) may have existed at a "subclinical" level, arguing that the concept had no scientific meaning. Tr. at 86.

By contrast, although Dr. Venkatesan did not dispute that Petitioner displayed significant and concerning MS symptoms post-vaccination, he questioned whether her post-vaccination course reflected an alarming worsening of existing MS. Tr. at 117–18. In so maintaining, Dr. Venkatesan took issue with Petitioner's assertion that her post-vaccination symptoms were "fulminant." *Id.* at 113, 116. In his professional view, "fulminant" would only describe an exacerbation that was characterized by both greater symptomatic severity and evidence of extensive and expanding lesions—not what was reflected in Petitioner's medical history. *Id.* at 119–20, 137. In Dr. Venkatesan's view, Petitioner's course was consistent with what a typical MS patient would likely experience in a relapse, and thus did not reveal anything out of the ordinary. *Id.* at 90–91, 112, 120.

III. Procedural History

As noted above, this case was initiated in September 2014. Petitioner subsequently filed relevant medical records, concluding the process at the end of December 2014 with the Statement of Completion. ECF No. 13. Respondent's Rule 4(c) Report was thereafter filed on February 27, 2015, ECF No. 15, in which Respondent challenged the appropriateness of an entitlement award.

Petitioner's first expert report from Dr. Napoli was filed later that fall, on October 8, 2015. Based upon representations contained therein that seemed to allow for the possibility that L.Z.'s MS predated her October 2011 vaccination, but that the vaccine was nevertheless responsible for her subsequent symptoms, I ordered Petitioner to amend her claim to include significant aggravation as a claim, Min. Order, Oct. 19, 2015, and she did so in early November. Am. Pet. at 2, Nov. 5, 2015, ECF No. 26.

The following spring of 2016, Respondent filed an expert report from Dr. Venkatesan, and Petitioner responded in July 2016 with Dr. Napoli's second expert report. The parties next agreed that the matter was ready for hearing, and I set it down to be tried on November 13, 2017. Prehr'g Order, Aug. 22, 2016, ECF No. 35. The hearing went forward as scheduled, and the parties filed post-hearing briefs in the first quarter of 2018. The matter is now ripe for decision.

IV. Applicable Law

A. *Petitioner's Overall Burden in Vaccine Program Cases*

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 11(c)(1), 13(a)(1)(A), 14(a); *see also Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[15] In this case, Petitioner does not assert a Table claim.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(a)(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enters. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). 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, a petitioner must demonstrate that the vaccine was "not only [the] 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). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Secretary of Health & Human Services*, 418 F.3d 1274, 1278 (Fed. Cir. 2005): "(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 proximate temporal relationship between vaccination and injury." *Althen*, 418 F.3d at 1278.

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the

[15] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Human Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Human Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. App'x 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Human Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Human Servs.*, 121 Fed. Cl. 230, 245 (2015), *vacated on other grounds*, 844 F.3d 1363 (Fed. Cir. 2017).

In discussing the evidentiary standard applicable to the first *Althen* prong, many decisions of the Court of Federal Claims and Federal Circuit have emphasized that petitioners need only establish a causation theory's biological plausibility (and thus need not do so with preponderant proof). *Tarsell v. United States*, 133 Fed. Cl. 782, 792–93 (2017) (special master committed legal error by requiring petitioner to establish first Althen prong by preponderance; that standard applied only to second prong and petitioner's overall burden); *Contreras*, 121 Fed. Cl. at 245 ("[p]lausibility . . . in many cases *may* be enough to satisfy *Althen* prong one" (emphasis in original)); *see also Andreu*, 569 F.3d at 1375. At the same time, there is contrary authority from the Federal Circuit suggesting that the same preponderance standard used overall in evaluating a claimant's success in a Vaccine Act claim is also applied specifically to the first *Althen* prong. *See, e.g.*, *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1350 (Fed. Cir. 2010) (affirming special master's determination that expert "had not provided a 'reliable medical or scientific explanation' *sufficient to prove by a preponderance of the evidence a medical theory* linking the [relevant vaccine to relevant injury]") (emphasis added). Regardless, one thing remains: petitioners always have the ultimate burden of establishing their Vaccine Act claim *overall* with preponderant evidence. *W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted); *Tarsell*, 133 Fed. Cl. at 793 (noting that *Moberly* "addresses the petitioner's overall burden of proving causation-in-fact under the Vaccine Act" by a preponderance standard).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Human Servs.*, 956

F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party'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 particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs*., 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Caves v. Sec'y of Dept. of Health & Human Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review denied*, 100 Fed. Cl. 344, 356 (2011), *aff'd without op.*, 475 Fed. App'x 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *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 timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 2013 WL 1896173 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review denied* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Standards Applicable to Significant Aggravation Claim*

In this matter, besides arguing that the flu vaccine caused her MS, Petitioner also offers a parallel theory that the vaccine significantly aggravated her neurologic illness by causing an MS relapse or flare. Where a petitioner so alleges, the *Althen* test is expanded, and the petitioner has additional evidentiary burdens to satisfy. *See generally Loving v. Sec'y of Health & Human Servs*., 86 Fed. Cl. 135, 144 (2009). In *Loving*, the Court of Federal Claims combined the *Althen* test with the test from *Whitecotton v. Secretary of Health & Human Services*, 81 F.3d 1099, 1107 (Fed. Cir. 1996), which related to on-Table significant aggravation cases. The resultant "significant aggravation" test has six components, which require establishing:

> (1) the person's condition prior to administration of the vaccine, (2) the person's current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person's current condition constitutes a "significant aggravation" of the person's condition prior to vaccination, (4) a medical theory causally connecting such a significantly worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) a showing of a proximate temporal relationship between the vaccination and the significant aggravation.

Loving, 86 Fed. Cl. at 144; *see also W.C.*, 704 F.3d at 1357 (holding that "the *Loving* case provides the correct framework for evaluating off-table significant aggravation claims"). In effect, the last three prongs of the Loving test correspond to the three *Althen* prongs.

Subsumed within the *Loving* analysis is the requirement to evaluate the likely natural course of an injured party's preexisting disease, in order to determine whether the vaccine made the petitioner worse than he would have been but for the vaccination. *Locane v. Sec'y of Health & Human Servs.*, 685 F.3d 1375, 1381–82 (Fed. Cir. 2012) (upholding special master's determination that petitioner had failed to carry her burden of proof in establishing that her preexisting injury was worsened by the relevant vaccine); *Hennessey v. Sec'y of Health & Human Servs.*, No. 01-190V, 2009 WL 1709053, at *41–42 (Fed. Cl. Spec. Mstr. May 29, 2009), *mot. for review denied*, 91 Fed. Cl 126 (2010). The critical point of examination is thus "whether the change for the worse in [petitioner's] clinical presentation was aggravation or a natural progression" of the underlying condition. *Hennessey*, 2009 WL 1709053, at *42.[16] The Federal Circuit has upheld the

[16] The legislative history of the Vaccine Act strongly supports interpreting "significant aggravation" as requiring a claimant to establish that a vaccine rendered a preexisting condition qualitatively worse than it would have been otherwise—not simply that the affected individual experienced a post-vaccination symptom that contrasts with the individual's comparatively better pre-vaccination health. *See* H.R. Rep. No. 99-908, at 15 (1986) ("This [significant aggravation] provision does not include compensation for conditions which might legitimately be described as pre-existing (e.g., a child with monthly seizures who, after vaccination, has seizures every three and a half weeks), *but is meant to encompass serious deterioration* (e.g., a child with monthly seizures who, after vaccination, has seizures on a daily basis" (emphasis added)).

determinations of special masters that worsening was not demonstrated in connection with establishing a petitioner's overall preponderant burden of proof for a non-Table causation-in-fact claim. *See, e.g., Snyder/Harris v. Sec'y of Health & Human Servs.*, 553 F. App'x 994, 999–1000 (Fed. Cir. 2014); *Locane*, 685 F.3d at 1381–82.[17]

The mere fact a vaccine might "trigger" a transient negative response in an individual with an underlying condition is not proof of worsening if that individual would be expected to experience a similar overall course regardless. *Faoro v. Sec'y of Health &Human Servs.*, No. 10-704V, 2016 WL 675491, at *27 (Fed. Cl. Spec. Mstr. Jan. 29, 2016), *mot. for review denied*, 128 Fed. Cl. 61 (Fed. Cl. Apr. 11, 2016) (finding that "the vaccinations would not have changed her clinical course and thus, the vaccinations did not significantly aggravate her preexisting condition"). This point has been emphasized in a subcategory of Program cases involving the claim that a child's Dravet syndrome (a rare seizure disorder now understood to be caused by the SCN1A gene mutation) was significantly aggravated by vaccination. *Faoro*, 2016 WL 675491, at *1. In such cases, special masters have repeatedly determined that petitioners failed to show that a child's expected outcome would have been different but for the vaccination—even though it was not disputed that the child's first major seizure had been triggered by vaccination. *Id.* at *2 ("[a]lthough H.E.F.'s vaccinations may have caused a low-grade fever or otherwise triggered her first seizure, neither the initial seizure nor her vaccinations caused or significantly aggravated her Dravet syndrome and resulting neurological complications"); *see also Snyder/Harris*, 553 F. App'x at 1003 (special master was not arbitrary in finding that petitioners' expert failed to show that the child's outcome would have been different had he not received the vaccinations at issue).

C. *Law Governing Analysis of Fact Evidence*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Human Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (it is

[17] This is consistent with the fact (well recognized by controlling precedent) that evidence of "worsening" relevant to Respondent's alternative cause burden may reasonably by evaluated by a special master in determining the success of a petitioner's prima facie showing. *Snyder/Harris*, 553 F. App'x at 1000, *quoting Stone*, 676 F.3d at 1380 ("no evidence should be embargoed from the special master's consideration simply because it is also relevant to another inquiry under the statute"); *see also de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("[t]he government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the petitioner's evidence on a requisite element of the petitioner's case-in-chief").

within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

Medical records that are created contemporaneously with the events they describe are presumed to be accurate and "complete" (i.e., presenting all relevant information on a patient's health problems). *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Human Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"); *Rickett v. Sec'y of Health & Human Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). This presumption is based on the linked propositions that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Human Servs.*, No. 11-685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Human Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Human Servs*., No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Human Servs*., 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. denied sub. nom. Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight")).

However, there are situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Human Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such

testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Human Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Human Servs*., No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *La Londe v. Sec'y of Health & Human Servs*., 110 Fed. Cl. 184, 203–04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

D. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Human Servs*., 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594–96 (1993). *See Cedillo v. Sec'y of Health & Human Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (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).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Human Servs*., 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of

expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts of his own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 (1997)); *see also Isaac v. Sec'y of Health & Human Servs*., No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review denied*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 Fed. App'x 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). 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").

E. *Consideration of Medical Literature*

Both parties filed medical and scientific literature in this case, but not every filed item factors into the outcome of this decision. While I have reviewed all of the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case—just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Human Servs.*, No. 2015-5072, 2016 WL 1358616, at *5 (Fed. Cir. Apr. 6, 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Human Servs.*, 527 F. App'x 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

ANALYSIS

I. Overview of Medical Terms and Relevant Prior Decisions

The parties' experts agreed largely on the proper definition of MS and what kind of clinical or radiologic evidence establishes its existence. As Program case law recognizes, MS is categorized as a demyelinating central nervous system disease. *See Taylor v. Sec'y of Health & Human Servs.*, No. 13-700V, 2018 WL 2050857, at *21 (Fed. Cl. Spec. Mstr. Mar. 9, 2018). Patients diagnosed with MS typically experience multiple episodes of CNS demyelination separated in time and space, evidencing a more progressive decline in their overall health course. *Id.* An MRI can be used to corroborate the dissemination in space and time requirement, and often reveals old lesions as well as enhancing/new lesions. *Id.* Evidence of oligoclonal bands in cerebrospinal fluid testing, which reveal brain inflammation, is also frequently seen in patients with MS. *Id.* Symptoms can include numbness or weakness in the body, loss of vision, tremors, unsteady gait, slurred speech, and dizziness. *Id.*

Other Program claimants have attempted to argue that a vaccine (including the flu vaccine) significantly aggravated a person's preexisting MS, to varying degrees of success. *See, e.g.*, *Quackenbush-Baker v. Sec'y of Health & Human Servs.*, No. 14-1000V, 2018 WL 1704523 (Fed. Cl. Spec. Mstr. Mar. 14, 2018) (flu vaccine significantly aggravated the petitioner's preexisting MS); *W.C. v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 440 (2011) (upholding special master's determination that flu vaccine did not significantly aggravate preexisting MS); *Bubb v. Sec'y of Health & Human Servs.*, No. 01-721V, 2005 WL 1025707 (Fed. Cl. Spec. Mstr. Apr. 29, 2005) (tetanus toxoid vaccine did not significantly aggravate preexisting MS). None of these decisions are completely on point (and some are actually distinguishable), but they nevertheless provide guidance in addressing the claim at hand.

In *W.C.*, the claimant (as here) alleged that the flu vaccine aggravated his previously-asymptomatic MS (with onset about 12 days after vaccination), but the special master responsible for the case denied entitlement. Upon review, in discussing the fourth *Loving* prong (the "can cause" element under the direct *Althen* test), the Court of Federal Claims noted that Respondent had offered much of the same medical literature used in this case to attack the association between the flu vaccine and exacerbation of MS—Moriabadi, Confavreaux, DeStefano, and Miller 2. *W.C.*, 100 Fed. Cl. at 455–56. The Court upheld the special master's determination, but in doing so was careful to note that factually and scientifically, the case presented some close calls that could have been decided by a different special master with the opposite result, and thus the underlying decision was upheld mainly as a function of the proper application of the review standards. *Id.* at 456 (noting that although that the evidence was "so closely balanced that the decision could have gone either way," nevertheless "the court cannot say that the special master's findings were arbitrary").

Bubb does not involve the flu vaccine, but is a stronger endorsement of the case against an association between vaccines and MS exacerbation than *W.C.* There, it was undisputed that the petitioner suffered from MS before vaccination. *Bubb,* 2005 WL 1025707, at *2. In addition, the record supported the conclusion that not only had the petitioner experienced a relapse post-vaccination, but that the relapse overall resulted in a sufficiently severe worsening of her condition to constitute a "significant aggravation" under the Act. *Id.* at *22. Nevertheless, the special master decided the claim against the petitioner, largely due to her inability to connect the tetanus vaccination to her MS worsening. *Id.* at *24. Like the present case and *W.C.*, the respondent offered Confavreaux and DeStefano to rebut any purported association between vaccination and MS exacerbation, *id.* at *20–21—evidence the special master found persuasive in "significantly undercut[ting]" the case study evidence offered by the petitioner. *Id.* at *24. This in addition to the lack of other probative evidence relating exacerbation to the vaccine (such as the views of contemporaneous treaters) resulted in the denial of entitlement.

In *Quackenbush-Baker*, by contrast, a petitioner succeeded in establishing that the flu vaccine significantly aggravated her MS. However, the petitioner's MS was wholly asymptomatic prior to vaccination, and thus deemed to have preexisted solely on the basis of MRI evidence (unlike the present case). *Quackenbush-Baker*, 2018 WL 1704523, at *8. The asymptomatic, RIS nature of petitioner's MS seems to have factored heavily in the special master's finding in petitioner's favor. *Id.* at *14–15. It also appears that the scientific evidence deemed so persuasive in *W.C.* or *Bubb* on the question of a vaccine's capacity to exacerbate MS was not offered by the experts in *Quackenbush-Baker* either. *Id.* at *15–17.

II. Petitioner Has Not Established Her Significant Aggravation Claim with Sufficient Preponderant Evidence

Although Dr. Napoli made some attempt to hedge his opinion, he ultimately acknowledged several times that it was reasonable to conclude from the medical record that L.Z.'s MS predated her receipt of the flu vaccine. *See, e.g.*, Tr. at 19, 39–40, 42, 44, 67; First Napoli Rep. at 4. Dr. Venkatesan was not so equivocal on this point. Tr. at 111, 116–17, 133, 136. Both views were based on record evidence of pre-vaccination neurologic symptoms.

After consideration of the same evidence plus expert testimony, I find as well that it is more likely than not the case that Petitioner's MS began *before* vaccination. The radiologic evidence bulwarks this conclusion. Although the MRIs performed on L.Z. were not "enhanced," and therefore could not help treaters determine whether any lesions viewed were old or more recent, they were performed within a month of vaccination, and revealed sufficient amounts of lesions to corroborate (with Petitioner's clinical presentation) an MS diagnosis. As has been recognized in other Program cases, lesions can preexist an MRI by weeks or even months. *See, e.g., Borrero v. Sec'y of Health & Human Servs.*, No. 01-417V, 2008 WL 4527837, at *21 (Fed. Cl. Spec. Mstr. Sept. 24, 2008); *Stevens v. Sec'y of Health & Human Servs.*, No. 99-594V, 2006 WL 659525, at

*23 (Fed. Cl. Spec. Mstr. Feb. 24, 2006). Accordingly, it is more likely that these lesions predated vaccination (especially when considered in the context of the medical record evidence suggesting L.Z. had been experiencing neurologic symptoms for some time before vaccination).

Based on this initial determination, Petitioner's direct causation claim cannot succeed, as she cannot demonstrate a vaccine "caused" an illness predating vaccination. *See, e.g.*, *Locane v. Sec'y of Health & Human Servs.*, 99 Fed. Cl. 715 (2011) (petitioner's alleged vaccine-induced injury began prior to her vaccinations and therefore vaccine causation could not be established), *aff'd*, 685 F.3d 1375 (Fed. Cir. 2012); *W.C.*, 100 Fed. Cl. at 453 (upholding special master's denial of direct causation claim where petitioner's medical records suggested lesions developed pre-vaccination). I therefore will not engage in an *Althen* review of her direct causation claim. Instead, I turn to Petitioner's alternative claim: that the flu vaccine significantly aggravated her MS. I address the most relevant *Loving* factors in order of their importance to my overall determination.[18]

A. *Petitioner Has Not Established a Plausible Causation Theory*

Having heard the experts and reviewed each side's medical literature, I find that Petitioner has not presented a plausible theory, supported by sufficient reliable evidence, that the flu vaccine could exacerbate an existing course of MS. At best, Dr. Napoli offered persuasive evidence that the flu virus or vaccine could *initiate* MS. He certainly proposed a mechanism, molecular mimicry, that has been deemed reliable in this context in past Program cases, and I do not consider the argument to lack a scientific foundation. *See, e.g.*, *Quackenbush-Baker*, 2018 WL 1704523, at *16–17.

But, as noted above, Petitioner's claim required establishing that the flu vaccine could be associated with flares/exacerbations of an *existing* case of MS, *and* that those vaccine-induced flares could produce a worsened overall course. As Respondent and Dr. Venkatesan established, the evidence offered herein preponderates against this conclusion. The literature filed by Respondent on this point—e.g., Confavreux and DeStefano—is particularly reliable and persuasive, as other decisions have recognized. *See W.C.*, 100 Fed. Cl. at 455–56; *Bubb*, 2005 WL 1025707, at *20–21. Petitioner's arguments that I should not give such evidence much weight because it cannot conclusively disprove a connection between the vaccine and MS flare/exacerbation miss the mark, and reflect an attempt to evade evidence that undercuts

[18] I do not address *all* of the *Loving* prongs, however, for the simple reason that Petitioner's failure to establish linchpin elements of her claim (in particular, that the vaccine could, or did, exacerbate her MS) renders a rote determination of Petitioner's success in establishing each individualized prong unnecessary. *See, e.g.*, *Bigbee v. Sec'y of Health & Human Servs.*, No. 06-663V, 2012 WL 1237759, at *36 (Fed. Cl. Spec. Mstr. Mar. 22, 2012) (citing *Althen*, 418 F.3d at 1278). I do note, however, that Petitioner's evidentiary showing regarding the timing prong is similarly deficient based on the scientific literature submitted (which involves diseases distinguishable from MS). *See* First Napoli Rep. at 5 (relying on the Schonberger study relating to GBS).

Petitioner's case without addressing its substantive merits.[19] Indeed, as noted above, Dr. Napoli effectively conceded that this literature was reliable. *See* Tr. at 57–58.

In response, Petitioner relied heavily on case reports or articles involving different demyelinating conditions like GBS (a peripheral neuropathy) that are distinguishable from CNS conditions. Dr. Napoli otherwise could not imbue Petitioner's theory with reliability that the literature did not support; although I found him to be a competent, credible expert with more than sufficient expertise on the topic of MS and interpretation of the radiologic evidence relevant to it, he lacked the immunologic expertise needed to fill in evidentiary holes in Petitioner's case not otherwise adequately served by the written scientific evidence filed in the case.

Most significantly, there is an absence of reliable scientific proof in this case establishing a central component of Petitioner's significant aggravation claim: that the flu vaccine can cause a preexisting case of MS to worsen beyond what would be expected based on its expected normal course. Petitioner offered no literature discussing this particular concept directly, Tr. at 57, and Dr. Napoli did not relate in his testimony particularized observations from his own medical experience that would render this contention plausible. Respondent, by contrast, offered reliable scientific evidence suggesting that the flu vaccine does *not* worsen MS (and indeed that the vaccine *should* be administered to MS patients given the greater risks that intervening wild virus infections pose such individuals). *See, e.g.*, Moriabadi at 943. Respondent also offered credible and reliable literature suggesting that the flu vaccine might not be able to encourage the chronic autoinflammatory process that characterizes MS. *Id.* at 942–43.

B. *Petitioner Has Not Established Her MS Course Was Worsened by Vaccination*

As noted above, I am cognizant of the fact that in a few situations claimants have successfully established the "can cause" fourth *Loving* prong with respect to the flu vaccine (*e.g.*, *Quackenbush-Baker*, 2018 WL 1704523)—and that resolution of the issue can turn on the quality

[19] While I also take note of Petitioner's argument that epidemiologic evidence cannot conclusively refute a causation theory that is otherwise reliable and/or scientifically plausible, this argument does not diminish the value such evidence can have in appropriate cases. *See Harris v. Sec'y of Health & Human Servs.*, No. 10–322V, 2014 WL 3159377, at *11 (Fed. Cl. Spec. Mstr. June 10, 2014) (epidemiologic studies cannot absolutely refute causal connections, because it is possible that a larger study could always detect an increased risk); *Crutchfield v. Sec'y of Health & Human Servs.*, No. 09-0039V, 2014 WL 1665227, at *15 (Fed. Cl. Spec. Mstr. Apr. 7, 2014) ("[i]t is, in fact, always true that epidemiologic studies can never prove definitively that Factor A never causes Condition B . . . [b]ut it is not the Respondent's burden in this case to prove that it is impossible that [the relevant vaccine] can cause [the alleged injury]"). However, that does not mean such evidence has no value at all. *See, e.g.*, *Johnson v. Sec'y of Health & Human Servs.*, No. 14-113V, 2017 WL 772534, at *19 (Fed. Cl. Spec. Mstr. Jan. 6, 2017) ("I generally find that such [epidemiologic] evidence can be relevant in rebutting a petitioner's arguments about the causal natures of different vaccines").

of expert opinions offered in a specific case, or extent of scientific and medical proof bulwarking the theory. *W.C.*, 100 Fed. Cl. at 455–56.[20] As a result, I allow that a different outcome would be reasonable, if different facts (bulwarked by a stronger causation theory) were offered to establish that a claimant's MS was greatly worsened by receipt of a flu vaccine.

However, even if I deem plausible, for sake of argument, the theory that the flu vaccine *could* worsen a person's MS course, I do not find on this record that Petitioner's MS *was* worsened by the vaccine.

Contrary to Dr. Napoli's argument, the medical record does not suggest that L.Z.'s MS was sufficiently worse post-vaccination to be deemed "fulminant." Rather, it appears that although after receiving the flu vaccine she did experience a transient MS relapse sufficiently debilitating to seek medical intervention, her symptoms were echoes of the milder symptoms she had experienced pre-vaccination over a lengthy period of time. They did not dramatically spike, and therefore did not appear to Dr. Venkatesan, an expert with substantial experience in MS, to reflect an alarming course distinguishable in severity from what other MS patients he has treated would experience. Indeed, after the neurologic consult that Petitioner received in the fall of 2011 resulted in her formal MS diagnosis, it does not appear she had *any* related medical issues at all for an entire year, and did not even have another formally-diagnosed flare until the spring of 2014. *See* Ex. 5 at 16; Ex. 7 at 6. This clinical record does not reflect an individual whose MS was set onto a more destructive and debilitating course than would have been anticipated but for vaccination.

Beyond the above, there is no contemporaneous treater support for the contention that L.Z.'s post-vaccination symptoms were vaccine-caused, or for the larger proposition that the vaccine made her MS worse than it would have been. There is also no medical record evidence suggesting an immediate reaction to vaccination, independent of the symptoms she unquestionably experienced. I cannot conclude from this record that the flu vaccine had anything more than a temporal relationship to Petitioner's MS flare—and such a relationship is well understood in the Program to have little evidentiary bearing when determining entitlement. *See, e.g.*, *LaLonde v. Sec'y of Health & Human Servs.*, 746 F.3d 1334, 1341 (Fed. Cir. 2014) ("[a] temporal correlation alone is not enough to demonstrate causation").

CONCLUSION

Based upon the aforementioned analysis, I conclude that L.Z. has not carried her burden of proof, and therefore I must DENY entitlement in this case.

[20] The literature filed in the present matter does provide reliable support for the contention that a flu vaccine (or wild virus exposure) could cause MS *directly*, as opposed to significantly aggravate a preexisting MS condition. *See, e.g.*, Wucherpfennig at 702; First Napoli Rep. at 5.

In the absence of a timely-filed motion for review (see Appendix B to the Rules of the Court), the Clerk shall enter judgment in accord with this decision.[21]

IT IS SO ORDERED.

/s/ Brian H. Corcoran
Brian H. Corcoran
Special Master

[21] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by filing a joint notice renouncing their right to seek review.