In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 16-949V

(to be published)

P.M.,	*	
	*	Special Master Corcoran
Petitioner,	*	
	*	Dated: September 24, 2019
v.	*	
	*	Multiple Sclerosis; Influenza Vaccine; Relapse; Significant Aggravation; *Althen* Prong I; *Loving* Prong Four; Treating Expert
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
	*	
Respondent.	*	
	*	

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

Mallori B. Openchowski, U.S. Dep't of Justice, Washington, DC, for Respondent.

DECISION[1]

On August 5, 2016, P.M. filed a petition seeking compensation under the National Vaccine Injury Compensation Program ("Vaccine Program")[2] alleging that he experienced the significant aggravation of his underlying multiple sclerosis ("MS")—a diagnosis which predated vaccination by three years—as a result of receiving the influenza ("flu") vaccine on October 9, 2014. Petition ("Pet.") (ECF No. 1) at 1. An entitlement hearing was held on June 7, 2018, in Washington, D.C., and the parties subsequently filed post-hearing briefs and supplemental reports, completing that process in late-April of 2019.

[1] This Decision shall be posted on the Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012)). **This means that 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 Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen 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 whole Decision will be available to the public. *Id.*

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3758, codified as amended at 42 U.S.C. §§ 300aa-10 through 34 (2012) [hereinafter "Vaccine Act" or "the Act"]. Individual section references hereafter will be to § 300aa of the Act (but will omit that statutory prefix).

The matter is finally ripe for resolution, and after review of the record and all submissions, I deny an entitlement award in this case. As discussed in greater detail below, although Petitioner succeeded in demonstrating that his preexisting MS became dramatically worse in a purely clinical sense in the immediate weeks after vaccination, and offered a credible opinion from a treating expert to support his claim, the record does not permit the conclusion that the flu vaccine *can* cause MS exacerbations, or that it did so in this case.

I. Factual Background

Pre-Vaccination MS Diagnosis

More than three years prior to the vaccination at issue, in 2011, P.M. was diagnosed with MS. The nature and basis for this diagnosis, along with Petitioner's subsequent disease course, has great significance in resolving this case.

The medical record establishes that Petitioner's symptoms dated back to 2003, when he first noticed pain in the left side of his face, scalp itching, numbness and weakness of the extremities, and ataxia. Ex. 6 at 12, 58. Indeed, a subsequent pain physician noted in a record from January 2012 that P.M. had previously been diagnosed with "unusual, right-sided temporal headaches," in his twenties, even before his MS diagnosis. Ex. 5 at 2. A June 24, 2011 brain MRI showed multiple brain lesions, and then a follow-up MRI of the cervical spine (the upper portion of the spine closest to the brain) performed on June 29, 2011 revealed a "large, expansile" lesion at the C2 level (in addition to what was previously detected in the brain). Ex. 6 at 2, 6, 11. On August 16, 2011, P.M. was first diagnosed with "relapsing/remitting MS" ("RRMS") and prescribed appropriate medication. *Id.* at 57–60.

The following year, on January 18, 2012, Petitioner was treated with a cervical nerve root block for radicular pain that petitioner related to MS. Ex. 16 at 13–14, 27 (Petitioner noting an eight month history of pain "since I discovered I have MS"). He subsequently continued to follow a neurologist for his MS symptoms between 2012 and 2014. Petitioner's pain physician noted in this time period that his symptoms were severe enough to interfere with his work. Ex. 5 at 2. In addition, in June 2013, P.M.'s urologist described his MS as "pretty severe," characterized by a "sudden fairly severe neurological deficit" and weakness and numbness of the left arm, although medication helped to stabilize his condition. Ex. 10 at 4.

On January 30, 2014, P.M. saw neurologist Donna Graves, M.D. at the University of Texas Southwestern Medical Center in Dallas, Texas. At this time he reported "constant" nerve pain in the left face, neck, and chest, with itching and intermittent shock-like sensations in the face and scalp, and that these symptoms did not improve despite medicinal treatment. Pet. Ex. 2 at 10. Dr. Graves specifically noted that a brain MRI performed on October 16, 2012, showed one new,

additional lesion compared with the June 2011 study. *Id.* at 11. Dr. Graves did not perform a physical examination of petitioner, but assessed RRMS and neuropathic pain. *Id.* at 12. She recommended that Petitioner change his medicines a bit, and recommended a repeat MRI and follow-up in six months. *Id.* at 13.

Six months later, on July 25, 2014, Petitioner presented to a new neurologist, Darin Okuda, M.D., also at the UT Southwestern Medical Center. Pet. Ex. 2 at 54–56. (As discussed in great detail below, Dr. Okuda was also Petitioner's sole testifying expert in this case). P.M. reported facial pain and pains radiating to the shoulders. Dr. Okuda did not perform a physical exam, and largely recommended that Petitioner maintain his existing treatments. *Id.* at 57. The next month, on August 26, 2014, P.M. saw his primary care physician ("PCP") J. Shaun Murphy, M.D., reporting a three-week history of severe left groin/testicular pain that radiated to his stomach during an erection. Ex. 4 at 1–2. Dr. Murphy described Petitioner's "MS symptoms" as left-sided neck, face, and arm pain, and diagnosed epididymitis, prescribing an antibiotic.

On September 24, 2014, P.M. went to an orthopedist, Kenneth Dauber, M.D., for evaluation of two-year history of intermittent right hip pain that was occurring more frequently and interfering with exercise. Ex. 9 at 1–2. Petitioner denied numbness and tingling but did report fatigue, and his examination and x-ray were unremarkable. Dr. Dauber diagnosed trochanteric bursitis, and prescribed Mobic (non- steroidal anti-inflammatory drug) and physical therapy. *Id.* at 5.

Vaccination And Subsequent MS Course

P.M. was thirty-two years-old when he received a seasonal flu vaccination on October 9, 2014. Ex. 1 at 1. Seven days later, on October 16, 2014, he contacted Dr. Okuda's office by email and telephone, reporting new onset of numbness in his legs, and feelings of weakness for the last two days (or beginning October 14th—five days after vaccination). Ex. 19 at 226–27, 230. Although Petitioner had then been planning to leave for vacation on October 19, 2014, he was advised to monitor his symptoms and go to an urgent care center if he started to experience burning pain or gait abnormalities. He denied fever, cough, or any signs of infection but agreed to undergo laboratory testing and an MRI. *Id.* An MRI of the thoracic[3] level of the spine was performed on October 16, 2014. It revealed an approximately 1.2cm lesion in the ventral cord around the T6 level, with subtle enhancement (which could support the conclusion that the lesion was new)[4]

[3] The term "thoracic" pertains to the thorax (chest). *Dorland's Illustrated Medical Dictionary* 1920 (32 ed. 2012) (hereinafter "*Dorland's*"). The thoracic spine is the middle portion of the spinal column in the thoracic/chest region. *Id.*

[4] As the experts explained at hearing (and consistent with what has been established in prior decisions), contrast enhancement involves injection of gadolinium into a patient, a substance that is readily detected by an MRI, and which will reveal active/new MS lesions (since it can leak across blood-brain barrier breaches). Tr. at 141–42; *see also*

"suggestive of a focus of transverse myelitis, consistent with history of multiple sclerosis." Ex. 2 at 23. (The results of this MRI, and its significance in light of Petitioner's claim, is a hotly-disputed issue that is explored below in greater detail).

The next week, on October 23, 2014, P.M. saw Dr. Okuda, informing him of his onset on October 15, 2014, describing numbness from his stomach to his feet bilaterally, with weakness in his legs that was greater on the left than right side. Ex. 2 at 5–6, 32–33. He had been placed on steroids "Saturday" [October 18, 2014] and was now "80%" back to baseline, although he still was experiencing numbness at the waist and in the right arm, erectile dysfunction, significant fatigue, cognitive difficulties, imbalance, and weakness that prevented him from running. He denied recent illness but reported his receipt of the flu shot in early October. *Id.*

On examination, P.M. showed muscle weakness of the legs, left greater than right, sensory deficits in both legs, mild difficulty walking on heels and toes, slow foot tapping but normal coordination. His medication was increased and additional MRIs were planned. Dr. Okuda at this time expressed the view that there was "a clear association between his recent vaccination and disease recrudescence." *Id.* at 5–6.

Petitioner continued to treat with Dr. Okuda through 2015 and beyond. Dr. Okuda maintained that petitioner suffered from RRMS, with notations of an aberrant reaction to antigens in the flu vaccine. *See, e.g.*, *Id.* at 1, 45, 52–53; Ex. 19 at 130. A February 2015 MRI (Ex. 2 at 17–18) revealed no further advancement of the October 2014 spinal cord lesion, with brain lesions first seen in 2012 also stable (in terms of size and appearance), suggesting that Petitioner's MS was not progressing. Ex. 2 at 17–18. By the spring of 2015, Dr. Okuda was firmly proposing (relying on his substantial experience treating MS generally and Petitioner specifically) that P.M.'s exacerbation was vaccine-caused. *Id.* at 52–53.

Since mid-2015, P.M.'s condition has fluctuated. Although he experienced some worsening of symptoms in August 2015, MRIs did not reveal the development of any new lesions. Ex. 19 at 72, 169–73. His ambulatory and other residual motor deficits persisted into early 2016, but he otherwise appeared to be coping and keeping up with his treatments. *Id.* at 130. The same was the case six months later, with ongoing weakness, fatigue, and motor difficulties, but no new acute neurological events. Ex. 20 at 36–37. By the winter of 2018, P.M. began experiencing a new symptom impacting his vision and involving eye pain, resulting in a diagnosis of optic neuritis. Ex. 29 at 1–9.

Maciel v. Sec'y of Health & Human Servs., No. 15-362V, 2018 WL 6259230, at *2 n.5 (Fed. Cl. Spec. Mstr. Oct. 12, 2018).

II. Expert Testimony

A. Dr. Darin Okuda

Dr. Okuda testified at hearing for Petitioner, and also prepared three expert reports. *See* Report, dated April 6, 2017, filed as Ex. 23 (ECF No. 15-1) ("First Okuda Rep.); Report, dated December 18, 2017, filed as Ex. 26 (ECF No. 27-1) ("Second Okuda Rep."); Report, dated November 28, 2018, filed as Ex. 37 (ECF No. 57-1) ("Third Okuda Rep."). Dr. Okuda was personally familiar with Petitioner's case, having served as Petitioner's primary neurologic treater even before the vaccination in question. Dr. Okuda opined that there was an association between P.M.'s receipt of the flu vaccine and his subsequent clinical experience, and that in fact Petitioner experienced a nerve-demyelinating event that worsened his preexisting MS due to vaccination. Tr. at 29, 36, 58.

Dr. Okuda is a board-certified neurologist currently employed at the Clinical Center for Multiple Sclerosis in Dallas, Texas. Curriculum Vitae of Dr. Okuda, filed as Ex. 24 (ECF No. 15-2) ("Okuda CV"). He is a fellow in the American Neurological Association, and he considers himself a specialist in MS, seeing approximately 2000 patients per year across the Dallas metropolitan area. Tr. at 5–6, 11–12. He received his bachelor's, master's, and medical degrees from the University of Hawaii. Okuda CV at 1. He then completed a fellowship in neuroimmunology at the University of California, San Francisco. *Id.*

At present, Dr. Okuda is a professor of neurology and neurotherapeutics at University of Texas – Southwest in Dallas, where he serves as director of the MS/neuroimmunology imaging program. Tr. at 7. He is also director of the "neuroinnovation" program, which he described as seeking to leverage technology with neuroscience in order to develop new and more effective neurodiagnostic tools (such as better three-dimensional imaging of MS lesions). *Id.* at 7–8. He has performed research into new technologies designed to better predict MS's advancement, specifically looking at the impact of lesion shape and structure, or the construction of more technologically-advanced hardware and software used for imaging and testing generally. *Id.* at 13–14. Dr. Okuda also has been involved in research evaluating the effectiveness of FDA-approved therapies for individuals with "radiologic isolated syndrome," or RIS (a diagnosis applicable to individuals whose central nervous system ("CNS") lesions, which would be indicative of MS, are discovered inadvertently, without the patient experiencing outward, typical MS symptoms).[5] *Id.* at

[5] Dr. Okuda contrasted RIS with "clinically isolated syndrome," or CIS, which presents the opposite set of circumstances (a patient with outward, recognizable MS symptoms who otherwise displays no evidence of imaging of CNS lesions). Tr. at 9–10. Individuals can live long lives without awareness that they possess the kinds of lesions indicative of MS (which can continue to advance without outward clinical symptoms). *Id.* at 11, 25–26, 42. CIS can be identified before the presence of lesions. *Id.* at 68.

10, 12–13. He has published articles on RIS plus his work on 3-D imaging, and has won awards for technologic innovations as well. *Id.* at 15–16.

In forming an opinion in this case, Dr. Okuda emphasized that his thought process did not occur simply in preparing to support Petitioner's claim, but rather in "real time"—beginning in October 2014, when Dr. Okuda was treating Petitioner and witnessed the purported immediate after-effects of the flu vaccine. Tr. at 79. That opinion was in turn based on clinical experience plus background knowledge of the medical and scientific field, although Dr. Okuda noted that he did consider additional literature that he researched as part of the process for preparing an actual written report. *Id.* at 79–80.

Dr. Okuda began his hearing testimony by defining some medical terms relevant to this case. He characterized MS as an autoimmune condition involving immune system-mediated inflammation in the CNS. Tr. at 44. It is the primary cause of neurologic impairment in young people, although it is more common in the female population than male, and also more prevalent with Caucasians. *Id.* at 18, 37. MS most often has a relapsing/remitting course, with it less commonly resolving completely (albeit leaving the person with deficits) or taking a more severe progressive and downward course. *Id.* at 101–02, 106.

Diagnosing MS requires evaluation of a combination of clinical and radiologic signs or symptoms. Clinically, treaters look for symptoms that would suggest the presence of CNS demyelination. Tr. at 19. From an imaging standpoint, MS is established by dissemination of CNS lesions in "space and time," taking into account the location of the lesions, their appearance, and their recurrent development, all of which point to immunologic involvement. *Id.* at 19–20. In addition, MS can be diagnosed via evaluation of the results of paraclinical testing, including lumbar punctures to analyze cerebrospinal fluid, blood tests, and electrophysiologic testing. *Id.* at 20. Although MS was historically associated with fairly severe outcomes (often characterized by motor impairment that necessitated lifelong use of a wheelchair or walker), advancements in treatment have rendered its course more benign (although Dr. Okuda said it was not wholly understood why this was the case, noting that changes in the environmental factors that had caused MS in the past may also be playing a role in making the disease less progressive). *Id.* at 43.

Dr. Okuda deemed MS as "principally driven" by environmental factors, something he maintained had been borne out by twin studies. Tr. at 44–45. In particular, exposure to a direct infection or some other foreign contaminant could instigate the autoimmune process resulting in MS. *Id.* at 46–48. He also allowed, however, that preexisting genetic susceptibility to autoimmunity might also be a factor in who experiences MS. *Id.* at 45. Some of the mechanistic processes that might mediate MS immunologically include molecular mimicry (in which antigens presented to the immune system resemble self protein sequences, causing the antibodies produced in response to those antigens to also attack the self structures) or secondary immune responses (in

which an ongoing immune reaction is worsened or made chronic) like bystander activation. *Id.*

Dr. Okuda also provided a brief overview of a typical course of MS. The most benign course possible would be RIS with no clinical/outward symptoms at all. Tr. at 43. Probably more than half of all MS patients have some symptoms, but usually their overall course is light. *Id.* However, MS is often associated with symptoms relapse, which can be precipitated by a large variety of factors. Things like the failure to maintain medicinal treatments, the changing of kinds of medicine, or social stressors can all trigger MS flares. *Id.* at 30–33. He admitted that a flare trigger could not always be identified, but proposed that, based on his experience, an educated guess was possible 30 to 40 percent of the time given the context in which the flare occurred. *Id.* at 75.

Turning to the facts of this case, Dr. Okuda began with an overview of Petitioner's history. He first started treating P.M. in July 2014. Tr. at 17–18. P.M. had previously been diagnosed in 2011 with RRMS, which Dr. Okuda admitted meant that the Petitioner would be expected to experience later symptoms relapses. *Id.* at 18, 102. Petitioner's symptoms had begun in 2003. Initial MRIs from 2011 revealed "typical" MS lesions and locations, with a clinical presentation also consistent with MS (e.g., weakness in limbs, sensory disturbances). *Id.* at 21; Ex. 6 at 11. By June 2011, Petitioner developed a single lesion located in the upper cervical spinal cord, reflecting that Petitioner's MS largely constituted a "mixed brain and spinal cord disease." Tr. at 60; *see also id.* at 20.

Despite its preexistence and likelihood of recurrence, Dr. Okuda expressed the view that Petitioner's overall MS course before his vaccination in 2014 was mild—and likely to remain so. Tr. at 33. From a radiologic/imaging standpoint, Petitioner's pre-vaccination "overall lesion burden or extent of involvement was generally stable and not substantial," suggesting his future course was not likely to be severe. *Id*. at 21. Dr. Okuda did acknowledge the identification of the new brain lesion in 2012, but deemed it asymptomatic, and possibly attributable to a "technical issue" from the performance of the MRI. *Id.* at 24–25, discussing Ex. 2 at 258 (October 17, 2012 MRI). Clinically, before vaccination P.M. was (in Dr. Okuda's view) doing well, since he was fully active at work and ambulatory, with symptoms that were (at that time) mostly sensory in nature and impact and which were responsive to medicinal treatment. *Id.* at 24, 26. Dr. Okuda deemed especially significant the fact that Petitioner's "expanded disability status scale" ("EDSS")[6] score was zero or close to it. *Id.* at 22–23.

After vaccination, however, Petitioner became much worse in Dr. Okuda's estimate. Tr. at

[6] EDSS is a diagnostic score used in MS to "gauge the clinical well-being of a given individual. Tr. at 22–23. A zero means no impairment, while a seven reflects being confined 50 percent to a wheelchair. Tr. at 23; *see also* J. Kurtzke, *Historical and Clinical Perspectives of the Expanded Disability Status Scale*, 31 Neuroepidemiology 1, 6 (2008), filed as Ex. 26, Tab A (ECF No. 27-1).

36. As noted above, P.M. had contacted Dr. Okuda's office on October 16, 2014, indicating that he had begun to experience new symptoms two days earlier (and thus not even a week from the date of vaccination on October 9th). *Id.* at 66. The imaging that was subsequently performed (*see* Ex. 3 at 3) revealed a lesion at the T6 level of the thoracic spine that Dr. Okuda felt was consistent with P.M.'s symptoms. *Id.* at 27, 67. The lesion was also enhancing, revealing its recent nature. *Id.* at 67. Dr. Okuda did not actually see Petitioner for examination until October 23, 2014, at which time he presented with things Dr. Okuda deemed "referable to the spinal cord"— weakness in both legs and sensory disturbances like numbing and tingling, plus pyramidal muscle weakness. Tr. at 26–28. Thereafter, P.M.'s recovery has been incomplete, with physical symptoms including fatigue, discomfort, low energy levels, lack of bladder control, and other things (along with a corroborating EDSS score of 6, in contrast to his previous zero)—all of which Dr. Okuda attributed to the T6 lesion discovered in October 2014. Tr. at 28–29.

Dr. Okuda also commented on P.M.'s subsequent course into 2015 and beyond. A February 2015 MRI (Ex. 2 at 17–18) revealed no further advancement of the October 2014 spinal cord lesion, with brain lesions first seen in 2012 also stable (in terms of size and appearance), as well as no other new enhancing lesions. Tr. at 35. At least at this time as revealed by MRI, Petitioner's MS was not progressing. *Id.* at 35–36. By 2018, Petitioner did suffer a new clinical attack, in the form of an episode of optic neuritis. *Id.* at 34. Dr. Okuda admitted, however, that he could not directly link this later relapse to the October 2014 vaccination, although he allowed for the possibility that once the flu vaccine had "let the horse out of the barn," any further relapses could be connected. *Id.* at 64–65.

A significant dispute between the parties in this case is the proper interpretation of the October 16, 2014 thoracic spine MRI, and in particular whether the fact that the new lesion seen at that time was enhancing suggests *when* that lesion first arose. Dr. Okuda admitted that an enhancing lesion is primarily evidence of the existence of an ongoing acute process, the start of which is difficult to ascertain given existing science. Tr. at 67 ("[A]n MS lesion could enhance for up to one year."); *see also id.* at 187–88. The presence of enhancement would typically allow the conclusion that a lesion had arisen weeks to a month before its detection. *Id.* at 22. In addition, Dr. Okuda admitted that (consistent with the CIS/RIS division) "we are able to pick up disease well before a lesion enhances," while at the same time lesions can exist or develop unaccompanied by symptoms. *Id.* at 185–86. He, however, expressed the opinion that a lesion could arise (and hence be detectible on MRI) in as little as one day, and thus maintained the view that the lesion that was observed on October 16, 2014 more likely than not arose post-vaccination. *Id.* at 67–69, 186–87, 189–90.

Dr. Okuda went on to provide his views on vaccine causation specifically. First, he maintained that vaccines can produce MS relapses. He deemed it a rare occurrence generally, but said he had personally encountered a handful of instances in his medical career in which he had

seen a vaccine associated with some kind of other neurologic injury, such as Guillain-Barré syndrome, with only one other instance he could recall involving MS. Tr. at 30, 76–77. To support his contentions, Dr. Okuda offered some items of literature that reveal the relationship between infectious pathogens and MS, thus allowing for the inference that vaccination (which apes the infectious process, albeit on a far more limited scale) could propagate disease in a similar fashion. *See, e.g.*, Tr. at 56 (discussing J. Libbey, et al., *Role of Pathogens in Multiple Sclerosis*, 33 Int'l. Rev. of Immunology 266–83 (2014)), Filed as Ex. 23 Tab C (ECF No. 44-3)). He also referenced one article discussing the known relationship between other autoimmune conditions and vaccination (although it noted a proposed association between MS and the Hepatitis B vaccine had not been confirmed). Tr. at 56 (discussing S. Salemi, et al., *Could Autoimmunity be Induced by Vaccination?*, 29 Int'l Rev. Immunology 247–69 (2010), filed as Ex. 23 Tab E (ECF No. 44-5)). Dr. Okuda acknowledged, however, that he offered no direct proof associating the flu vaccine with MS, allowing that relapse could not always be attributed to a prior vaccination. *Id.* at 87, 92. Nevertheless, Dr. Okuda felt that a vaccine could be causal of a relapse at least on a "one-off" basis, and that at bottom he saw no other explanation for P.M.'s relapse but his prior receipt of the flu vaccine under the circumstances of this case. *Id.* at 29–30, 51–52, 58–59, 87.

As for potential biologic mechanisms explaining how the flu vaccine might produce an MS relapse, Dr. Okuda offered several alternatives. He noted that molecular mimicry—a well-understood autoimmune mechanism often invoked in vaccine injury cases, in which foreign antigens (whether presented by infection or vaccine) resemble, or "mimic," self protein sequences, causing antibodies produced in response to the antigen to also attack the self—was in his view generally helpful in explaining CNS demyelinating events. Tr. at 46, 49. In addition, secondary mechanisms like bystander activation, in which primed immune cells nonspecific to a particular antigen causing a primary immune response are nevertheless stimulated, thereby exacerbating and encouraging the initial response, might also be the engine of a vaccine-caused MS relapse. *Id.* at 46. Dr. Okuda admitted he could not in this case identify the specific target of the proposed autoimmune response, or that there was similarity between flu vaccine antigens and some CNS structure sufficient for molecular mimicry to occur. *Id.* at 86–87. He nevertheless insisted that "some antigen" in the flu vaccine was responsible, and that an autoimmune process could unfold through a combination of mechanisms, which could in turn be the result of the vaccine's specific formulation or design. *Id.* at 86; *see also id.* at 48.

To support the above, Dr. Okuda offered some literature that he maintained demonstrated how these potential mechanisms might initiate an autoimmune process resulting in an MS relapse. Tr. at 56–57 (discussing R. Fujinami, et al., *Molecular Mimicry, Bystander Activation, or Viral Persistence: Infections and Autoimmune Disease*, 19 Clinical Microbiology Rev. 80 (Jan. 2006), filed as Ex. 23 Tab D (ECF No. 44-4); A. Bar-Or, et al., *Abnormal B-Cell Cytokine Responses a Trigger of T-Cell-Mediated Disease in MS?* 67 Annals Neurology 452 (2010), filed as Ex. 23 Tab F (ECF No. 44-6) (excited chemokine response can mediate bystander activation of

proinflammatory T cells, leading to MS relapse) ("Bar-Or"). Importantly, however, Dr. Okuda also admitted that these articles did not link vaccination to the proposed biologic processes. *See, e.g.*, Bar-Or, *supra*, at 458 (addressing only the propensity of wild infection to trigger new MS disease activity via the evaluated process). Dr. Okuda acknowledged that it remained unclear whether the same mechanisms for how MS might initiate could equally be applied to exacerbation cases. Tr. at 50. But he stressed his belief that, given that the "underpinning" of MS's pathogenesis is likely autoimmune, there is no reason not to expect that exacerbation of an existing case of MS would proceed in the same mechanistic manner. *Id.*

Second, Dr. Okuda emphasized his determination that the flu vaccine did in fact produce P.M.'s MS relapse, beginning within a week of vaccination. He deemed the onset of symptoms close in time to vaccination a "clear inflection point," making it difficult for him not to associate the two. Tr. at 54. There was no question that Petitioner's overall health, motor skills, and mood took a turn for the worse after the vaccination. *Id.* at 34. He also noted there appeared to be no other explanations for the relapse, like some unexpected social stressors. *Id.* at 75.

In the course of discussing Petitioner's immediate post-vaccination change in health, Dr. Okuda was asked about record evidence suggesting the existence of related symptoms before vaccination (some of which Dr. Okuda might not have factored into his opinion). For example, Respondent asked him about Petitioner's August 2014 claim of testicular pain when visiting his PCP—something that was not referenced in the history Dr. Okuda prepared in October 2014. Tr. at 83–84. Dr. Okuda allowed that the event might have some significance, although he also pointed out that the effects of a demyelinating lesion in the thoracic region of the spinal cord would not likely locate to the testes in terms of pain or other symptoms. *Id.* at 83. He also admitted that his consideration of P.M.'s history as of October 2014 might (due to his own hospital's electronic records gathering system) have not taken into account Petitioner's visit to the orthopedist for treatment of hip pain, although he again distinguished it from the kind of symptoms he would associate with a CNS injury to the brain or spine. *Id.* at 73, 81–82, 99–100. Although a sudden onset of hip pain might, in Dr. Okuda's estimation, be attributable to a CNS issue, in this case Petitioner's hip problems have reportedly existed for some time, reducing the likelihood that they were associated with his October symptoms. *Id.* at 101.

Dr. Okuda also addressed the timing of P.M.'s post-vaccination symptoms onset, which he agreed (based on Petitioner's symptoms complaint and date of MRI detection of the T6 lesion) had occurred within five days of vaccination. Tr. at 51. Dr. Okuda deemed anything within a month of a trigger as medically reasonable, especially since (in his understanding) symptoms could take up to several months to manifest. *Id.* He did, however, also maintain that where a vaccine was the trigger for an MS relapse, he would only be comfortable with a timeframe of no more than a month. *Id.* at 84. He added that even a reaction within 24 hours was in his view medically acceptable, based on the innate immune response to vaccination (which could cause an

increase in body temperature), but added that this sort of reaction was akin to an MS "pseudo-exacerbation," which can also occur after a common infection, and is distinguishable from a true MS relapse of the kind Petitioner experienced. *Id.* at 84–86. He ultimately proposed that P.M.'s lesion most likely formed between one day to a week after vaccination. *Id.* at 86.

Dr. Okuda's testimony next touched on the larger question of whether Petitioner's MS course had been worsened by vaccination, answering that question in the affirmative. Tr. at 99, 102. He began with a discussion of "Kurtzke's Rule of Five"—a scale employed in the treatment of MS that rests on the assumption that a patient's first five years of clinical status "may provide great insights" into what the patient will experience with the disease in later years. *Id.* at 37; J. Kurtzke, *Historical and Clinical Perspectives of the Expanded Disability Status Scale*, 31 Neuroepidemiology 1, 1, 7 (2008), filed as Ex. 26, Tab A (ECF No. 27-1). Thus, a patient who does not experience significant motor or cerebellar involvement in his disease course is unlikely to experience symptoms related to either later on. *Id.* In this case, P.M. did have motor impairment as of 2011 (although he recovered), but did not have cerebellar involvement. *Id.* at 38. Overall, Dr. Okuda deemed Petitioner's pre-vaccination course milder than post. First Okuda Rep. at 2–4.

Dr. Okuda also talked about "lesion burden," i.e. the number of lesions an MS patient has and what that predicts about his likely prognosis. In support, he cited an item of literature. L. Fisniku, et al., *Disability and T_2 MRI Lesions: a 20-Year Follow-Up of Patients with Relapse Onset of Multiple Sclerosis,* 131 Brain 808 (2008), filed as Ex. 26, Tab B (ECF No. 27-1) (the "Queen Square" Study). The Queen Square Study, Dr. Okuda maintained, established that the number of MS lesions an individual had was associated with their long-term outcome—and in particular the likelihood that their disease course would be progressive rather than of lesser risk of future attack and impairment. Tr. at 38–39. Here, he proposed that the relatively small number of lesions P.M. had before vaccination did not predict a notably adverse outcome. *Id.* at 29, 36, 38. Dr. Okuda acknowledged that the Queen Square Study involved a relatively small patient sample, and also did not take into account the impact of spinal cord impairment (a factor more directly linked to poor outcomes—especially in this case), but still deemed it overall a reasonable study given the difficulties in obtaining good data relevant to the subject. *Id.* at 38–39.

Complementing the above, Dr. Okuda discussed a different item of literature he co-authored that suggested cervical lesions in an MS patient predicted thoracic lesion involvement. Tr. at 39–42; L. Hua, et al., *Thoracic Spinal Cord Lesions are Influenced by the Degree of Cervical Spine Involvement in Multiple Sclerosis,* 53 Spinal Cord 520 (2015), filed as Ex. 26, Tab C (ECF No. 45-6) ("Hua"). Hua evaluated 126 MS patients, most of whom suffered from RRMS, and all of whom had MRI scans performed in the brain, cervical, and thoracic spine regions (although the scan evidence reviewed came from a single scanning session rather than from scans performed over the course of the patient's illness history). Hua, *supra*, at 522. Hua's authors specifically observed that thoracic lesions were more likely in patients with two or more cervical lesions, as

opposed to brain-located lesions—although they also concluded that the risk of a thoracic lesion existed simply with the presence of a single cervical lesion (which Petitioner unquestionably had). *Id.* at 523–24. Dr. Okuda, however, interpreted Hua's findings as suggesting that "the chance of [Petitioner] having further disease within the thoracic spinal cord [was] low" based on the single cervical lesion (even though Hua does not expressly make this association). Second Okuda Rep. at 2.

Dr. Okuda also commented on certain articles, some of which Respondent offered (like large-scale epidemiologic studies), that arguably undermine Petitioner's claim that the flu vaccine exacerbated his MS. In so doing, he agreed that available epidemiologic evidence largely confirms the overall safety of vaccination for MS patients, as reflected in the recommendations of the National MS Society Tr. at 92, 104. Indeed, he allowed not only that receiving the flu vaccine may be especially important for MS patients (whose treatment therapies might weaken their immune systems and thus make them susceptible to certain infections that vaccination could help prevent), but also that vaccines might in fact *protect* against future symptom flares. *Id.* at 93, 105. He maintained, however, that these kinds of studies were not sufficiently powered to detect the rare occurrence of a post-vaccination adverse event or possibility of aggravation, and also have their own biases. Tr. at 52–54, 57, 94–95.

One such article goes directly to Petitioner's contention—that the flu vaccine caused his relapse—but concludes the *opposite*. C. Confavreux, et al., *Vaccinations and the Risk of Relapse in Multiple Sclerosis*, 344 New Eng. J. Med. 319, 319, 324 (2001), filed as Ex. F (ECF No. 30-2) ("Confavreux"). Confavreux 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, determining 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. *Id.* at 324–25. Another article, published around the same time as Confavreux, performed a general literature search of studies looking into the purported association between vaccination and MS, finding "strong evidence" that the flu vaccine did not result in MS exacerbation. O. Rutschmann, et al., *Immunization and MS: A Summary of Published Evidence and Recommendations,* 59 Neurology 1837, 1837 (2002), filed as Ex. J (ECF No. 30-6) ("Rutschmann").

Dr. Okuda, however, disputed the application of such literature in this case, arguing that (despite Confavreux's overall large cohort sample size) the evaluated patient sample would likely not have included P.M., due to his purported genetic susceptibility (although Dr. Okuda tacitly acknowledged that Petitioner's ethnic heritage and gender did not completely set him aside as an outlier under the circumstances). Tr. at 89–91. He also later observed that only 135 patients of the total cohort could be confirmed to have had a vaccine in the 12 months prior to relapse— with only 15 patients receiving a vaccine within one to two months of relapse (precisely the

relevant time period herein), thereby greatly reducing the statistical strength of the study's overall findings when applied to this case. Tr. at 94, *citing* Confavreux, *supra*, at 324 Table 2. Dr. Okuda later pointed out that Rutschmann specifically stated that it could not "definitely exclude a slight risk of increase of exacerbation after [flu vaccine] immunization" (although it also concludes in the next paragraph that "there is definitive evidence against a *substantial* increased risk of MS exacerbation after influenza vaccine"). Tr. at 96, *citing* Rutschmann, *supra*, at 1840 (emphasis added).

B. Dr. Timothy Vartanian

Dr. Vartanian filed three reports for Respondent and testified at hearing. Report, dated June 9, 2017, filed as Ex. C (ECF No. 19-1) ("First Vartanian Rep."); Report, dated April 20, 2018, filed as Ex. K (ECF No. 43-1) ("Second Vartanian Rep."); Report, dated April 22, 2019, filed as Ex. L (ECF No. 70-1) ("Third Vartanian Rep."). He opined that P.M.'s pre-vaccination MS was not exacerbated by the flu vaccine, and specifically that the newly-discovered October 2014 thoracic lesion most likely predated vaccination by weeks. Tr. at 115–16, 145.

Dr. Vartanian received his Ph.D. and medical degree from the University of Chicago after obtaining his bachelor's degree from Oakland University. Curriculum Vitae of Dr. Vartanian, dated Oct. 16, 2013, filed as Ex. D (ECF No. 19) ("Vartanian CV"). He then completed an internship at Brigham and Women's Hospital, a residency in neurology at Massachusetts General Hospital, and fellowships at Beth Israel Hospital and Harvard Medical School. Vartanian CV at 2. Dr. Vartanian is board certified in adult neurology and is a member of the American Society of Neuroscientists. *Id.* at 3. He has published numerous articles on neurologic matters. *Id.* at 15–21.

Dr. Vartanian is a professor of neurology at Weill Cornell Medical College, and the director of the MS and demyelinating diseases unit at New York Presbyterian Hospital. Tr. at 109. Consistent with his certifications, he is a specialist in MS as well as other autoimmune diseases implicating or involving the CNS. *Id.* at 110. His practice includes a mix of research, teaching, and clinical work, and he estimates he presently is overseeing the cases of 500 to 600 patients. *Id.* at 111–12. He has performed research aimed at understanding CNS lesion formation and myelin repair, and has been published often. *Id.* at 112–14.

Much like Dr. Okuda, Dr. Vartanian devoted some time at hearing to defining medical terms and concepts relevant to Petitioner's claim. He stated that the common, relapsing/remitting form of MS that P.M. was diagnosed with is characterized by unpredictable swings that can vary in severity and length. Tr. at 116–17, 157, 183. He also echoed Dr. Okuda's statements about RIS versus CIS, agreeing that MRI evidence of a disease process can advance without corresponding symptoms, and that lesion location was highly relevant to symptoms presentation. *Id.* at 117 (explaining that "[n]ot all lesions are clinically apparent."); *see also id.* at 142–43. He

also noted, however, that in his experience newly-formed lesions tended not to be immediately symptomatic. *Id.* at 143.

Dr. Vartanian agreed that environmental factors can trigger MS relapses, although he stressed that medical science cannot identify the precise "agent" for relapse, and disputed Dr. Okuda's contention that a triggering factor can be identified even a third of the time. Tr. at 121–22, 130, 161. On the contrary, he stated that medical science typically could *not* explain what caused a new lesion or symptoms flare (consistent with the fact that patients can have numerous new lesions with no symptoms at all). *Id.* at 147. He denied, however, that the medical community considers vaccines to be a plausible causal factor, pointing out the consensus among medical professionals and MS-oriented professional societies of the safety of vaccination for MS patients (although he agreed vaccination was still a relevant fact to take into account in assessing a patient's medical history). Tr. at 121, 123. At best, he proposed that the only trustworthy identifiable explanations for relapses are the "rebound effect" if a patient is taken off certain MS drug treatments, or the results of stress. *Id.* at 122. He also observed that, regardless of a flare's proposed etiology, it would be treated in the same manner. *Id.*

Dr. Vartanian discussed the general utility of MRIs, and he specifically explained the use of enhancement in identifying active brain or spinal lesions. Tr. at 141–42. He maintained that a lesion that enhances in imaging is evidence of "massive destruction" sufficient to breach the blood-brain barrier, such as after a stroke or the effects of a brain tumor. *Id.* at 142, 180. But, because enhancement "marks the apex of lesion," it is likely that a lesion that is observed via enhancement has been forming for some time before its observation on MRI. *Id.* at 144. As a result, the medical community (in Dr. Vartanian's estimation) deems lesions to have likely formed weeks to even months prior to the time they enhance. *Id.* at 142, 145. This is true regardless of whether the lesion is located on the spine or in the brain. *Id.* at 144.

Dr. Vartanian's opinion accepted the accuracy of P.M.'s RRMS diagnosis (Tr. at 131– 32), but he considered certain evidence from Petitioner's pre-vaccination medical history as *consistent* with his later disease course. The initial brain MRI (performed on Petitioner on June 24, 2011—a few days after he reported symptoms) revealed brain and medulla lesions that were not initially deemed enhancing (thus suggesting that they were fairly old). Tr. at 132; Ex. 6 at 11.[7] Stressing the importance of "neuroanatomical localization" in neurology (i.e., the concept that different areas of the CNS control or impact different nerve systems in various parts of the body), Dr. Vartanian found it unsurprising that these lesions were primarily affecting "sensory pathways." Tr. at 134.

[7] Dr. Vartanian stressed at hearing that his MRI comments were based not on direct review of the images themselves but the medical record history notations of the radiologists and neurologists who performed or analyzed them. Tr. at 137. I later ordered both parties to have their experts review the original images and file post-trial supplemental reports. Those reports are discussed below.

However, the second MRI, performed on June 29, 2011 (which revealed a nonenhancing, "expansile"[8] cervical spinal cord lesion close to the brain's base), prompted the radiologist to look again at the earlier MRI, and in so doing noticed "some minimal patchy enhancement" for the previously-discovered brain lesions. Tr. at 133–35; Ex. 6 at 7. Although the radiologist proposed that the lack of enhancement seen in the second MRI could be "due to the limitations of the study," Dr. Vartanian found the enhancing now identified on a second review "interesting," because it suggested to him that the observed lesions likely *predated* the symptoms that prompted Petitioner to seek medical intervention at this time (and which led to performance of the MRI in the first place). Tr. at 135. Dr. Vartanian based this assertion on the view that "most contrast-enhancing lesions last for a few weeks." *Id.* at 136–37.

Petitioner's course in the subsequent three-plus year period prior to vaccination was, in Dr. Vartanian's estimation, best characterized as "active" rather than "clinically silent." Tr. at 137. He noted that an October 2012 MRI revealed a new non-enhancing brain lesion, for example. *Id.* at 138; Ex. 2 at 67. He admitted that Petitioner was asymptomatic from a clinical standpoint for much of this time. *Id.* at 139, 153. Dr. Vartanian, however, deemed that not uncommon for someone with overall ongoing MS, especially given the radiologic evidence of additional lesions. *Id.* at 139–40 ("[T]he disease is never gone.").

In addition, and contrary to Dr. Okuda, Dr. Vartanian expressed the opinion that P.M. was experiencing "a fairly significant lesion burden" before October 2014. Tr. at 137. He later acknowledged (as stated in one of his reports) that even a total number of 4-9 lesions was in fact not a significant sum (Tr. at 155–56; Second Vartanian Rep. at 2). But, Dr. Vartanian stressed that lesion burden should also be deemed a function of volume and severity in addition to pure number, and when those factors were taken into account, the record allowed for the conclusion that Petitioner's burden was actually "moderate to heavy." *Id.* at 155. To support this contention, Dr. Vartanian noted that pre-vaccination records described several "hyperintense" lesions, which to him meant significant axon damage. *Id.*; Ex. 2 at 67. He also stressed the size of the cervical lesion observed in 2011 as establishing evidence of a somewhat severe pre-vaccination course. Tr. at 136.

Moving on to the post-vaccination period, Dr. Vartanian considered what the October 2014 MRI established. He agreed it revealed the existence of the T6 thoracic lesion (which he proposed was located around the lower part of the sternum), but maintained that despite enhancement, the lesion's date of formation could not be pinpointed. Tr. at 144–45. He suggested, however, that it most likely "formed weeks before" its discovery (and hence before the October 9, 2014 vaccination). *Id.* He based this opinion in part on research he claimed establishes that lesion genesis typically predates enhancement by weeks to months, as well as the concept that enhancement does

[8] Dr. Vartanian defined expansile to mean "it's occupying space." Tr. at 136.

not shed light on the date a lesion came into existence, although he admitted he had not set forth this aspect of his opinion in his reports, nor could he offer literature substantiating this proposition. *Id.* at 146, 173, 180. He also discounted the importance of the lesion's location as suggestive of its etiology, noting that thoracic spinal cord lesions were not uncommon in MS, and that the existence of a single spinal cord lesion (here, the cervical lesion observed in June 2011) suggested more were possible—even in different parts of the spinal cord, as observed in Hua. *Id.* at 147–48.[9]

Besides commenting on the medical record, Dr. Vartanian opined that the flu vaccine could not likely produce MS relapses or symptoms flares. Tr. at 168. Although he accepted that vaccines have been credibly associated with certain adverse events (for example, the rabies vaccine with acute demyelinating encephalomyelitis, or earlier versions of the flu vaccine and Guillain-Barré syndrome), he denied that there was sufficient reliable scientific or medical evidence to link the flu vaccine to CNS demyelinating events common to MS. *Id.* at 167–68, 170. In so testifying, he noted that even if certain biologic mechanisms proposed by Dr. Okuda, like molecular mimicry, were reasonably associated with autoimmune processes resulting in other neurologic diseases, there was inadequate medical or scientific evidence to link them to the process that resulted in CNS demyelination. *Id.* at 169–70, 174. He deemed other environmental factors (for example, genetic variants among different ethnic or nationality groups) as more likely to contribute to the pathogenesis of MS. *Id.* at 162 (discussing MS epidemic in Faroe Islands after British began occupation, when merely by the presence of British individuals, native islanders were exposed to uncommon viral infections to which they were susceptible, having not been exposed before).

Dr. Vartanian rejected the proposition that vaccination and wild virus infection were analytically interchangeable for purposes of establishing causation. Tr. at 130. In so opining, he allowed that some kinds of infections (mycoplasma or pneumonia) might credibly be associated with MS exacerbation, but denied that the influenza virus could also be included in that group. *Id.* at 129. He also noted that the manner in which infection propagates in the body, via "multiple epitopes" that elicit more immune responses than vaccination, and through direct tissue damage as well, "sets up a nidus for colonization and infection" and "also provides a more robust environment for the immune response," making it a "much more dramatic immune stimulator than a vaccine." *Id.* at 131, 163, 165–66 (direct infection can cause "multifocal inflammatory demyelination"). He opined that unlike vaccination, infection can directly cause breach of the blood-brain barrier "in the absence of an immune response," leading to a secondary inflammatory immune response (which he did allow could be autoimmune in nature). Tr. at 163, 166. The same is true, he maintained, for lesion formation itself, which can be associated with initial blood-brain barrier openings (although they may not be initially detectable via enhancement). *Id.* at 163–64 (MS may

[9] Dr. Vartanian also discussed some of Petitioner's more recent medical records. He noted that P.M. experienced an MS flare in his optic nerve in 2018, resulting in neuritis symptoms in the ocular region for the first time. Tr. at 149–50. He characterized this location as not uncommon for an MS flare, however, and denied that it was the natural result of, or otherwise associated with, the 2014 thoracic lesion. *Id.* at 150.

directly begin with "some insult to the blood-brain barrier," rather than through an immune response).

To support his contention that the flu vaccine could not likely produce MS relapses, Dr. Vartanian offered several items of scientific and medical literature, like Confavreux. Confavreux was a 2001 clinical study aimed at evaluating whether there was a link between vaccination of any kind and MS flares. Confavreux, *supra*, at 319. In Dr Vartanian's view, the fact that it was a "crossover" study (in which patients served as their own control)[10] made it sufficiently powered to be reliable even if the overall sample size pertinent to the present case was not particularly large. *Id.* at 319–20; Tr.at 123–24. Confavreux evaluated over a year-long period the medical histories of MS patients with no relapse who had one thereafter, evaluating their relapses in two-month periods from vaccination, in comparison with two-months periods without prior vaccination, and found no higher incidence of relapse. Confavreux, *supra*, at 320, 324; Tr. at 124–25. Dr. Vartanian emphasized that the eight-week risk interval used in Confavreux to look for post-vaccination relapse was particularly "liberal," as it would have caught almost any adverse event that could arguably be vaccine-caused. Tr. at 125.

In addition to Confavreux, Dr. Vartanian offered another clinical study that sought to directly evaluate the relationship between vaccines and MS relapse. B. Michielsens, et al., *Serial Magnetic Resonance Imaging Studies With Paramagnetic Contrast Medium: Assessment of Disease Activity in Patients with Multiple Sclerosis Before and After Influenza Vaccination*, 30 Eur. Neurology 258 (1990), filed as Ex. H (ECF No. 30-4) ("Michielsens"). Michielsens looked at MRIs for 11 patients with relapsing-remitting MS within three weeks of vaccination both before and after (a period of time consistent with the alleged timeframe in this case), to assess the presence of post-vaccination flares. Tr. at 126–27, Michielsens, *supra*, at 258. The study found no higher interval of new/contrast-enhancing lesions post-vaccination. Tr. at 127, Michielsens, *supra*, at 259. Dr. Vartanian accepted, however, that an 11-patient sample size was likely too small to deem the study's conclusions statistically significant. Tr. at 172–73.

Dr. Vartanian also cited literature review articles summarizing the state of medical literature on the association between vaccination and MS relapse, none of which supported Petitioner's claim. *See generally* Rutschmann, *supra*, 1837; M. Mailand, et al., *Vaccines and Multiple Sclerosis: A Systematic Review*, 264 J. Neurology 1035 (2017), filed as Ex. G (ECF No. 30-3) ("Mailand"). Mailand, published just over 15 years after Confavreux, confirmed that no studies since that time had demonstrated a plausible association between vaccination and MS flares. Tr. at 126; Mailand, *supra*, at 1036. Rutschmann was published in 2002, but had the same focus and reached the same conclusions (albeit based on fewer items of literature than Mailand).

[10] A crossover, or cross-sectional, analysis is a statistical tool for understanding the relationship between two or more variables in which each data point is associated with a different unit of observation measured at a specific point in time. *Reference Manual on Scientific Evidence* 352, 354 (3d ed. 2011).

Rutschmann, *supra*, at 1840. Dr. Vartanian deemed such review articles a persuasive response to criticism focused on the scope of reliability of individual clinical studies, like Confavreux, given that the review articles took into account so many individual pieces of literature (while noting the absence of subsequent studies that would negate earlier determinations about the absence of a vaccine-MS exacerbation relationship). Tr. at 128. He acknowledged, however, that some of these articles referenced studies that were somewhat supportive of Petitioner's position. *See, e.g.*, Tr. at 171 (citing Rutschmann, *supra*, at 1841, Table 2) (citing study finding that five percent of 80 MS patients who experienced relapse did so within six weeks of receipt of flu vaccine)).

Finally, regarding Petitioner's comparative state both pre- and post-vaccination, Dr. Vartanian admitted that the October 2014 thoracic lesion was directly connected to Petitioner's "permanent residual symptoms," and had contributed to his disabled state and risk of future disability simply due to the associated scarring. Tr. at 156–57. But he maintained that Petitioner's overall disease course was nevertheless not outside what would be expected in many MS cases. Tr. at 151.[11] He also did not give the same importance to the EDSS score Petitioner had received before vaccination (which Dr. Okuda felt predicted a mild overall disease course), deeming the scale not a "great tool" for measuring the "functional capabilities" of a patient, especially since it was weighted for assessing motor function/ambulation. Tr. at 118–19, 149 (noting that EDSS "fell out of favor" because it did not take into account the impact of cognitive dysfunction attributable to brain lesions); *see also id.* at 179. He similarly discounted the value of the Kurtzke "five year rule" for predicting MS course, terming it only a "partial indicator" that did not preclude relapse even for patients doing well. *Id.* at 148. Ultimately, the disease course that an MS patient would experience is primarily the product of where a new lesion "lands," i.e. whether it locates in an important place neurologically. *Id.* at 149.

III. Post-Hearing Expert Reports

As noted above, neither expert had the opportunity to review the actual MRI images in formulating their opinions, relying instead on contemporaneous medical record notations or observations (and thus secondary sources). I therefore ordered the parties to have their experts directly evaluate the relevant MRI images (since both were competent to do so), and then comment on them in supplemental post-trial reports.

Petitioner filed Dr. Okuda's supplemental report in late November 2018. *See generally* Third Okuda Rep. He agreed with the 2011 MRI findings, but maintained that when compared with the 2014 MRI, "a reduction in the size and conspicuity of previously observed lesions around the [brain] ventricles was present." Third Okuda Rep. at 2. He also opined that the cervical lesion

[11] Dr. Vartanian did, however, also acknowledge that certain of Petitioner's literature, like Queen Square, credibly suggested that a large percentage of MS patients could expect an overall mild disease course. Tr. at 159–60 (citing Queen Square study, *supra*, at 814).

observed in June 2011 had shown improvement over time. *Id.* He thus believed that pre-vaccination, the "overall burden of disease" based solely on the "number and volume of T2 lesions" in the brain and spinal cord, was modest and stable. *Id.*

Dr. Okuda also took the opportunity to comment again on the question of MRI enhancement and what it says about the lesion's likely age. He allowed that "enhancement may persist for up to a month"—a statement that would support the conclusion that Petitioner's enhancing thoracic lesion, first observed on October 16, 2014, began *before* vaccination. But he also maintained that "new contrast enhancing lesions may develop or resolve over a short period of time," offering a nonpublished case study example of a male patient at his own hospital who displayed enhancing lesions within ten days of repeat brain MRIs. Third Okuda Rep. at 5, Fig. 2.[12] He thus argued that "contrast enhancement in humans may occur at the time of lesion onset," supporting the conclusion that P.M.'s 2014 lesion arose in the short timeframe after vaccination.

Dr. Vartanian's supplemental report was filed in April 2019. *See generally* Third Vartanian Rep. Focusing on the October 2014 MRIs (including a follow-up of the brain and spine imagining done at the end of October 2014), Dr. Vartanian questioned whether the thoracic lesion was in fact enhancing as of October 16th, despite what the radiologic record seemed to indicate. Third Vartanian Rep. at 2. He also noted the presence of a cervical lesion on an October 31, 2014 MRI that was non-enhancing, along with multiple lesions on the brain MRI performed at that time. *Id.* Comparing the 2011 to 2014 findings, he characterized the 2011 cervical lesion as "large and expansile," in comparison to the 2014 thoracic lesion. *Id.* He deemed contrast enhancement "not so informative," however, noting that while the prior cervical lesion had unquestionably been enhancing, the 2014 thoracic lesion, in his opinion, showed only "leptomeningeal" enhancement (meaning it revealed inflammation or blood-brain barrier breach of the CNS membranes covering the spinal cord)[13] as opposed to enhancement in the *lesion itself*—thus diminishing the likelihood that the lesion had developed in the brief post-vaccination timeframe. *Id.* at 3.

If "the most conservative estimate" is that lesions enhance for at least one to two weeks after detection, then, Dr. Vartanian opined (based on his determination from review of the MRIs that the thoracic lesion was actually non-enhancing), it was "extremely unlikely" the October 2014 thoracic lesion came into being post-vaccination. Third Vartanian Rep. at 4. His other primary conclusion from review of the MRI images was that Petitioner had already experienced aggressive lesion formation in the three years prior to vaccination (as evidenced by the large cervical lesion

[12] Although Dr. Okuda filed literature to support the contentions in this supplemental report, this part of his opinion was not attributed to some other publication. I will nevertheless consider it valid, albeit only worthy of the weight given any single-patient case study.

[13] *Dorland's* at 123, 1445.

observed in 2011), thus undermining the contention that the overall course of Petitioner's MS was more severe post-vaccination (even if clinical symptoms did worsen due to the impact of the thoracic lesion). *Id.*

IV. Procedural History

After filing the Petition, Petitioner gathered and submitted medical records and final statement of completion on October 18, 2016 (ECF No. 11). Respondent's Rule 4(c) Report was thereafter filed on December 19, 2016 (ECF No. 12). Additional medical records were filed in June 2017 (ECF No. 17), and January through April 2018 (ECF Nos. 31, 33, 38, and 40).

Petitioner thereafter filed an expert report on April 12, 2017, after obtaining one extension of time. Respondent filed Dr. Vartanian's report on June 22, 2017. Petitioner then filed a rebuttal expert report from Dr. Okuda on December 20, 2017 (ECF No. 27), and Respondent filed his supplemental report from Dr. Vartanian on April 26, 2018. (ECF No. 43). In the interim, I set the matter for an entitlement hearing to be held on June 7–8, 2018 (ECF No. 23). The entitlement hearing was held on June 7, 2018, and a post-hearing briefing schedule was also set (in which I included deadlines for filing supplemental expert reports and post-hearing briefs addressing unresolved issues at hearing). The matter is now ripe for resolution.

V. 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).[14] 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.

[14] 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).

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 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 ("Plausibility . . . 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; *see also 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 ("[M]edical 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).

Medical records and/or statements of a treating physician's views, however, 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) ("[T]here 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) (finding that it is not arbitrary or capricious for special masters 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.*; *see also 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, Petitioner maintains that the flu vaccine significantly aggravated his previously-diagnosed MS. Where a petitioner so alleges, the *Althen* test is expanded, and the petitioner has additional evidentiary burdens to satisfy. *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. Sec'y of Health & Human Servs.*, 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.[15] The Federal Circuit has upheld the 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.[16]

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 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

[15] 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)).

[16] 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 ("'[N]o evidence should be embargoed from the special master's consideration simply because it is also relevant to another inquiry under the statute.'" (*quoting Stone*, 676 F.3d at 1380)); *see also de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("The 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.").

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; *see also Doe/70 v. Sec'y of Health & Human Servs.*, 95 Fed. Cl. 598, 608 (2010) ("Given 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) ("It has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.") (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1948)).

There are, however, 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) ("[L]ike 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 ("Written 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) ("[U]niquely 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). But 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 ("Assessments 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) ("[T]his 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. *See Moriarty v. Sec'y of Health & Human Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We 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) ("Finding 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

Although the parties' experts agreed on the proper definition of MS and the kind of clinical or radiologic evidence that establishes its existence, some additional comment is warranted. As Program case law recognizes, MS is a demyelinating CNS 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). It likely has an autoimmune pathogenesis. *W.C. v. Sec'y of Health & Human Servs.,* No. 07-456V, 2011 WL 4537877, at *3 (Fed. Cl. Spec. Mstr. Feb. 22, 2011), *mot. for review den'd*, 100 Fed. Cl. 440 (2011), *aff'd,* 704 F.3d 1352 (Fed. Cir. 2013). Patients diagnosed with MS typically experience multiple episodes of CNS demyelination separated in time and space (meaning throughout the CNS), concurrent with a progressive, if remitting and relapsing, decline in their overall health course. *Taylor*, 2018 WL 2050857, at *21. 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.* Symptoms can include numbness or weakness in the body, loss of vision, tremors, unsteady gait, slurred speech, and dizziness. *Id.*

Other Program claimants have argued 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); *but see 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), *aff'd,* 704 F.3d 1352 (Fed. Cir. 2013), *and 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); *see also Maciel v. Sec'y of Health & Human Servs*., No. 15-362V, 2018 WL 6259230 (Fed. Cl. Spec. Mstr. Oct. 12, 2018) (HPV vaccine did not significantly aggravate existing MS). None of these decisions are completely on point (and some are actually distinguishable), and they do not control the outcome herein, but they nevertheless provide guidance in addressing the claim at hand.

In *W.C.*, the petitioner 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. *W.C.,* 100 Fed. Cl. at 446–47. 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, like Confavreux. *Id.* 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 medical/scientific case against an association between *any* vaccines and MS exacerbation. There, as here, it was undisputed that the petitioner suffered from MS prior to 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.*, Respondent offered Confavreux and similar studies to rebut any purported association between any vaccination and MS exacerbation. *Id.* at *20–21. The special master found this evidence 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.

Quackenbush-Baker, by contrast, stands as an outlier. There, a petitioner succeeded in establishing that the flu vaccine significantly aggravated her MS. However (and unlike the present case), the petitioner's MS was wholly asymptomatic prior to vaccination, and thus deemed to have been preexisting solely on the basis of MRI evidence—essentially RIS. *Quackenbush-Baker*, 2018 WL 1704523, at *8. The asymptomatic, subclinical nature of petitioner's MS seems to have factored heavily in the special master's finding in petitioner's favor, when compared to the post-vaccination record of medical decline. *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* (or given low weight based on the special master's estimation that epidemiologic evidence could never completely eliminate the possibility of the rare occurrence of a vaccine injury). *Id.* at *15–17.

I have previously decided cases in which MS was alleged to have been exacerbated by a vaccine. *See, e.g.*, *L.Z. v. Sec'y of Health & Human Servs.,* No. 14-920V, 2018 WL 5784525 (Fed. Cl. Spec. Mstr. Aug. 24, 2018). In *L.Z.,* I rejected a claim that the flu vaccine significantly aggravated a petitioner's pre-vaccination MS (pled in the alternative to a claim that the vaccine caused it directly). Because MRIs performed about a month after vaccination revealed evidence of lesions, it could not be concluded that the lesions had not predated vaccination. This, plus the fact that the petitioner had displayed some pre-vaccination neurologic symptoms, led me to determine that her MS more likely than not predated vaccination. I also found that Petitioner's expert had failed to preponderantly establish that vaccination *could* aggravate MS, noting the existence of

literature like Confavreux, in comparison to Petitioner's over-reliance on evidence suggesting vaccines could directly cause MS, but not offering anything relating to a vaccine's capacity to promote MS flares. *L.Z.,* 2018 WL 5784525, at *18–19.

II. Petitioner Has Not Established His Significant Aggravation Claim with Sufficient Preponderant Evidence[17]

A. *Petitioner Has Not Offered a Persuasive and Reliable Causation Theory* (*Loving Prong Four*)

As discussed above, there is ample persuasive evidence filed in this action that the flu vaccine is *not* likely to exacerbate an individual's preexisting MS. *See*, *e.g.*, Confavreux; Rutschmann; Mailand; Michielsen. This kind of evidence has also repeatedly been deemed reliable and persuasive in other Program cases involving claims of vaccine-caused MS exacerbation. *See W.C.,* 100 Fed. Cl. at 455–56; *Bubb,* 2005 WL 1025707, at *20–21, 24. While many of these articles are broad reviews of other published literature, all involve direct studies or other epidemiologic analyses, and the review articles written in the ten-plus years since Confavreux's publication identify no subsequent studies suggesting the contrary.

This scientific/medical evidence was ineffectively rebutted by Petitioner. The general argument against it—that epidemiologic studies, no matter how individually trustworthy or scientifically reliable, can *never* preclude the possibility that a particular individual was in fact harmed by a vaccine, given the overall rareness of such injuries—has been unpersuasively maintained in other Program cases. *See, e.g., McCollum v. Sec'y of Health & Human Servs.,* No. 14-790V, 2017 WL 5386613, at *18 (Fed. Cl. Spec. Mstr. Sept. 15, 2017), *mot. for review den'd,* 135 Fed. Cl. 735 (2017), *aff'd,* 760 Fed. App'x 1003 (Fed. Cir. 2019) (discussing *Crutchfield v. Sec'y of Health & Human Servs.,* No. 09-0039V, 2014 WL 1665227 (Fed. Cl. Spec. Mstr. Apr. 7, 2014), *mot. for review den'd*, 125 Fed. Cl. 251 (2014)). As former Special Master Hastings observed in *Crutchfield,* "it is not the Respondent's burden in [a] case to prove that it is *impossible* that [the relevant vaccine] can cause [the alleged injury]. It is, rather, the *Petitioner's burden* to [show the vaccine can cause the injury]." *Crutchfield,* 2014 WL 1665227, at *15 (emphasis in original).

Nor is it convincing to propose that because a claimant need not *offer* such direct epidemiologic evidence to prevail, such evidence should (or must) be disregarded entirely. *D'Toile v. Sec'y of Health & Human Servs.*, 726 Fed. App'x 809, 811–12 (Fed. Cir. Apr. 12, 2018) (special master may consider negative epidemiologic evidence, even though petitioners are not obligated in the first instance to offer positive epidemiologic studies to meet their preponderant burden);

[17] I address the relevant *Loving* prongs in order of their importance to this Decision, and only those prongs upon which the Decision turns.

Grant, 956 F.2d at 1144. Here, the evidence exists and directly undercuts Petitioner's claim, making it appropriate under *Daubert* to consider it in weighing the scientific reliability of Dr. Okuda's contrary assertions.

Petitioner's other efforts to pick apart the studies filed in this case—either by trying to show that P.M. himself might not have been included in some of the studies, the sample sizes were too small, the studies were overall "underpowered," or that alleged genetic variability and susceptibility possessed by Petitioner distinguished his reaction from what was measured in the studies referenced by Respondent—were unsuccessful. At most, arguments about deficiencies in certain items of literature or medical studies might cause me to reduce the weight they should be afforded (and I do not disregard Petitioner's points out of hand; the literature filed in this case does not establish with *medical certainty* that the flu vaccine could not exacerbate MS).[18] But the overall thrust of all of these items remains—and Petitioner did not offer medical or scientific literature suggesting the propensity of vaccination to *produce* MS flares.

Petitioner did somewhat better in establishing a plausible biologic process by which the flu vaccine could theoretically produce an MS exacerbation. Program law firmly does not require proof of mechanism—but in a case like this, where direct proof supporting the claim is lacking, a petitioner can bulwark his case with a variety of circumstantial evidence including persuasive and reliable proof establishing how the vaccine in question might precipitate a reaction resulting in the relevant injury. P.M. certainly proposed a mechanism, molecular mimicry, that has been deemed reliable in this context in past Program cases involving *other* kinds of related CNS injuries, and it could explain how the flu vaccine biologically might initiate a demyelinating process. *See, e.g.*, *Quackenbush-Baker*, 2018 WL 1704523, at *16–17. Similar mechanisms have also been found plausible in the context of the direct causation of CNS injuries like transverse myelitis ("TM") or acute disseminated encephalomyelitis ("ADEM"). *See, e.g.*, *Taylor*, 2018 WL 2050857, at *23 (discussing credibility of theories involving ADEM); *Bender v. Sec'y of Health & Human Servs.,* No. 11-693V, 2018 WL 3679637, at *25 (Fed. Cl. Spec. Mstr. July 2, 2018) (discussing theories involving TM), *mot. for review den'd,* 141 Fed. Cl. 262 (2019). It is hardly unreasonable for Petitioner to have maintained that the same processes might bear on new lesion formation in an *existing* case of MS as well (even if the contextual differences are meaningful).

This, however, reveals a core deficiency of Petitioner's causation theory. The alleged exacerbation in this case began with the new thoracic lesion (rather than just an increase in brain lesions). It would have been greatly helpful to Petitioner's case to highlight evidence supporting an association between the flu vaccine (or flu wild virus) and (for individuals already suffering from MS) the initiations of lesions in *specific parts* of the CNS—especially a location not

[18] Of course, the preponderance evidentiary test (which *petitioners* must satisfy) means that *no* party to a Vaccine Act case is required to establish their points with that degree of certainty. Just as petitioners are not required to conclusively establish that a vaccine caused an injury, but rather that it is "more likely than not" that it did, Respondent can offer evidence of varying weights and probative value to shift the preponderant balance in the other direction.

previously featuring lesions. The science supporting existing Program decisions involving direct CNS injury (like TM) by the flu vaccine to persons not previously suffering from MS had some value in this effort. But (as pointed out by Dr. Vartanian (*see* Second Vartanian Rep. at 5)), Petitioner *has not* attempted to make such a showing.

In fact, the literature filed in this case does not elide a distinction between brain and spinal lesions in terms of overall MS disease process (beyond immediate clinical expression of symptoms). Articles like Hua (upon which Petitioner relied) actually suggest that in a person already suffering from MS, development of thoracic lesions is likely a function of whether lesions *already exist* on the spine (albeit closer to the brain). Hua, *supra*, at 523.[19] And Dr. Okuda's reading of Hua to mean that only an MS patient with *several* cervical lesions has the chance of a thoracic lesion is undercut by Hua's own language, which allows that even a single cervical lesion can be associated with the later development of thoracic lesions. *Id.* ("Our results suggest an increase in risk for the presence of thoracic spinal lesions when *one or more* lesions are present within the cervical spinal cord.") (emphasis added).

The strength of Petitioner's expert showing somewhat counterbalanced the above. Dr. Okuda was a well-qualified and competent neurology expert, whose opinion was reasonable and worthy of weight. Although he does not have a demonstrated expertise in immunology (and hence could not establish, based on his own expertise, what it is about vaccination that would stimulate the immune system of a person suffering from MS sufficient to develop a relapse), his opinion that a vaccine could produce a damaging relapse through some general, immune-stimulation process, and/or via mechanisms associated with other kinds of direct CNS injury, must still be taken seriously—and I do so. His primary role as a treating expert does not mean that I cannot consider his testimony in evaluating the strength of Petitioner's causation theory under the first *Althen* prong. *Capizzano*, 440 F.3d at 1326.

Nevertheless, Dr. Okuda's testimony was far more probative of the "did cause" *Althen* prong, and was not enough to carry Petitioner across the preponderant line in resolving the "can cause" prong. His reports and testimony did not preponderantly establish that the flu vaccine would be expected to produce *any* MS relapse, let alone a focal thoracic lesion. His assertions about an association between the flu vaccine and the biologic processes that might theoretically produce new lesions were also too general, as they pertained more to instances of new CNS injury rather than exacerbation. And his challenges to the studies that negate an association between vaccination and MS relapse were not persuasive. In a case in which there were few on-point studies or items of literature pertaining to the vaccine or claimed injury, Dr. Okuda's strong testimony might carry the day. Not here. Nothing in Program precedent says a special master must give more weight to

[19] I am also aware of no prior decision involving the flu vaccine causing an isolated occurrence of TM or ADEM in an individual already diagnosed with MS. And such a theory, even if formally articulated, would run into the brick wall of evidence (discussed above) suggesting that vaccines *do not exacerbate* existing cases of MS.

the testimony of a testifying treating expert over directly relevant medical or scientific literature. As good and reliable as Dr. Okuda's individual testimony was, he did not overcome the literature.

Because of the foregoing, my weighing process did not produce a finding in Petitioner's favor on the first *Althen* prong, despite the fact that the Petitioner offered some reliable evidence. In another case, with more medical or scientific evidence of how the flu vaccine affects MS patients, or how the vaccine (or even wild flu virus) can impact specific parts of the CNS, the outcome could easily be favorable to a petitioner. As science advances, and/or the issue is subject to further (or updated) study, more evidence may be developed that supports the kind of claim asserted herein. But it does not exist *today.* Under the legal standards I must apply, the evidence in this case does not support a finding that the flu vaccine can likely produce MS exacerbations.

B. Petitioner has Not Established that the Short Timeframe in Which His Thoracic Lesion Developed and Resulted in Symptoms was Medically Reasonable (*Loving Prong Six)*

There is no dispute that Petitioner began experiencing clinical symptoms reflecting his subsequently-diagnosed MS relapse on October 14, 2014—five days after vaccination. Ex. 19 at 226–27, 230. Just two days later (now a week from the date of vaccination), an MRI revealed the presence of the thoracic lesion, and the fact of its enhancement established that the lesion was "new." But *how* new? And is this overall timeframe medically reasonable for a vaccine-induced MS flare?

Were I solely relying on the reasoning of prior decisions, I might conclude that a new lesion would take several weeks to a month to form at the soonest—precluding a finding that the lesion in question in this case could have formed in so short a time, and/or that it more likely predated vaccination (even if it was only discovered after the fact). *See, e.g.*, *L.Z.,* 2018 WL 5784525, at *17–18. However, I am not bound in this case by such prior decisions (even my own), and both experts offered reliable opinions on this topic, so further discussion is in order.

Dr. Okuda made a number of persuasive points in favor of the conclusion that the lesion could have arisen post-vaccination. His third report in particular offered some direct evidence of studies demonstrating the short timeframes in which contrast-enhancing lesions can develop. Third Okuda Rep. at 4. He also reasonably relied on his extensive expertise in radiologic matters to offer this opinion, and although the evidence he cited specific to thoracic lesions (as discussed above) was less probative in Petitioner's favor, his assertions still deserved weight. Dr. Vartanian argued the contrary, but did not substantiate his position with reliable literature of his own. Tr. at 146, 173, 180. The evidence thus preponderates, if barely, in favor of Petitioner's contention that a new MS-associated lesion (without taking into account its location) could develop in a week's timeframe.

But could a thoracic lesion *both* appear *and* cause the degree of symptoms Petitioner experienced in that same narrow timeframe? When the question is so expanded (as it should be - since the symptoms not only predated lesion discovery, but are an element of Petitioner's claim that his symptoms worsened after vaccination), the evidence is no longer preponderantly in Petitioner's favor.

Both experts concurred (particularly when discussing the differences between RIS and CIS, but also in commenting on the import of radiologic evidence of MS progression generally) that lesions are very frequently *unaccompanied* by symptoms and can *predate* symptoms by a lengthy time period as well. *See, e.g.*, Tr. at 22, 43, 67, 185–88 (Dr. Okuda) and 142, 144-46, 173 (Dr. Vartanian). The fact that an individual can have "subclinical MS" (in effect, RIS) for a long period thus suggests that lesions and clinical symptoms do not automatically go hand-in-hand. As a result, even if a lesion can develop in such an acute manner, as alleged herein (and as supported by some reliable scientific evidence), it has not been preponderantly established that such a new lesion would *also* more likely than not be immediately accompanied by obvious and severe symptoms. Rather, a lesion more likely might take a longer time to develop and cause symptoms. This weakens the conclusion that the lesion Petitioner experienced more likely than not post-dated vaccination, and reverses preponderance in Respondent's favor.

This is so even if it is correct that P.M.'s immediate post-vaccination symptomatic complications, and associated sequelae, were directly attributable to the new lesion's location in the thoracic spinal region. The record in fact unquestionably supports that conclusion, and both experts concurred Petitioner's new symptoms arose from the location of the new lesion. But, given what is known about the relationship between lesion development and clinical presentation of symptoms, it cannot be determined that the very short timeframe in which P.M. experienced *both* still supports the conclusion that the lesion more likely than not post-dated vaccination. Rather, because the symptoms presented so rapidly, it becomes more likely than not that the lesion already existed, and may have even been enhancing, prior to vaccination.[20] The literature relied upon by Dr. Okuda to establish the speed at which lesions can develop not only says nothing specific about thoracic lesions, but also does not discuss the temporal relationship between lesions and clinical symptoms.

[20] In other words, had an MRI been performed on Petitioner's thoracic spine a week to a month prior to vaccination, it likely would have shown enhancement, even in the absence of the symptoms he later manifested.

C. Even If Petitioner Established That His Symptoms Worsened After Vaccination, He Could Not Show that the Flu Vaccine Caused that Worsening (Loving Prongs Three and Five)

Both sides accept that Petitioner's MS course generally took a turn for the worse after his receipt of the flu vaccine, as he began experiencing symptoms that were of a different nature and severity than before. Their experts also allowed that not all of Petitioner's subsequent experiences (such as his recent optic neuritis) could be vaccine-attributed, or even connected to the October 2014 events. The experts do not, however, concur that Petitioner's overall *course* was worse, with Dr. Vartanian disputing the characterization of P.M.'s MS before vaccination as mild, and proposing that his symptoms were not uncommon for what a person with relapsing/remitting MS would experience, whereas Dr. Okuda maintained that Petitioner was likely to experience a mild outcome before vaccination.

The evidence regarding Petitioner's likely disease course, based on what was known before his October 2014 vaccination, is ultimately inconclusive. I found credible Dr. Okuda's arguments about Petitioner's overall mild lesion burden pre-vaccination, along with his observation that certain common clinical rules-of-thumb used in MS (like the "five-year rule," or Petitioner's EDSS score) suggested that Petitioner's MS would not likely be severe. At the same time, Dr. Vartanian also established persuasively that individuals with RRMS are *always* susceptible to downward symptoms progression at any time. And while Petitioner's pre-vaccination status may not have featured significantly debilitating symptoms (especially when compared to thereafter), it is not wholly accurate to conclude that his earlier condition was notably or uniquely free of burdensome symptoms. *See, e.g.*, Ex. 5 at 2 (Petitioner diagnosed with "unusual" headaches in the years prior to his MS diagnosis), Ex. 10 at 5 (treater characterization of Petitioner's MS as "pretty severe").

In addition, although P.M.'s post-vaccination course may have featured some symptoms that he had not previously experienced and which were of a more severe degree (in particular because of their impact on motor function), his *overall* clinical presentation, from the time he was diagnosed to the present date, does not appear uniquely devastating (as much as it unquestionably has negatively impacted his health and life). I also find that the course of Petitioner's post-vaccination disease was not completely progressive, and both sides agreed that certain of Petitioner's more recent relapses (such as the optic neuritis he experienced) cannot necessarily be attributed to the new thoracic lesion purportedly caused by vaccination.

Based on the above, the record and other evidence is ultimately more supportive of the conclusion that *overall* Petitioner's course, even if immediately worse than what he had experienced pre-vaccination, was not so much more distinctive in severity thereafter to conclude that it was truly "worse" for purposes of the present analysis. Yet even if I focused solely on the impact of the thoracic lesion, allowing it to characterize the totality of Petitioner's post-vaccination

disease process, I would still be unable to find that such worsening was *due to* vaccination. Rather, the record only supports the conclusion that the change in quality of Petitioner's symptoms (and in particular the impact they had on his motor function) was attributable *specifically* to the thoracic lesion—*not* that the flu vaccine *itself* "more likely than not" caused that lesion to come about in the first place. This is partially due to the fact, as noted above, that there is thin evidence suggesting the flu vaccine can produce MS flares of any kind, let alone exacerbations specifically targeting a particular spinal region, and also that it is unlikely a new lesion developing within the space of a week would also immediately be associated with significant symptoms.

The weaknesses of Petitioner's showing on these related prongs of the *Loving* test are best exemplified by his overreliance on the temporal relationship between vaccination and Petitioner's mid-October new symptoms onset. Although Dr. Okuda was a particularly effective treating expert, he ultimately depended too much on the fact that the Petitioner had just received the flu vaccine—and hence relied on the temporal association to the vaccine. *See, e.g.*, Tr. at 29–30, 51–52, 58–59. While the causal propensity of a prior vaccination may be heightened by the views of a knowledgeable treating expert, and therefore worthy of some deference, it remains a slim reed upon which to base a causation determination if the temporal association is *primarily* what the expert finds compelling, as opposed to the propensity of the relevant vaccine to injure, or some other medical development post-vaccination that implicates the vaccine. *Moberly*, 592 F.3d at 1323–24. Not all adverse post-vaccination events are caused by vaccination (since, were that the case, all a claimant would need to do to prevail in *any* Vaccine Act case would be to show onset of injury after vaccination).

Accordingly, even if Petitioner had preponderantly established that his overall MS course worsened post-vaccination (a conclusion I lean strongly against, although it finds some support in the record), he has not *also* shown such worsening could be vaccine-attributed. Petitioner relies too much on the obvious temporal relationship between vaccination and his subsequent symptoms plus discovery of new radiologic evidence of disease process advancement. This is an insufficient basis for the conclusion that the flu vaccine caused Petitioner's MS exacerbation.

Conclusion

This was a *difficult* case. I take P.M.'s injury seriously and the negative impact it has had on his life. His good faith arguments were backed by many solid items of proof, along with a credible treating expert opinion. But on a fundamental point (the capacity of the flu vaccine to theoretically cause an MS flare close-in-time to vaccination, in a particular location, sufficient to constitute a significant aggravation of the underlying disease process) it was not a *close* case. The evidence in the record did not ultimately preponderate in a favorable ruling.

Accordingly, and for the aforementioned reasons, I DENY entitlement in this case. In the absence of a motion for review filed pursuant to RCFC Appendix B, the clerk of the court **SHALL ENTER JUDGMENT** in accordance with the terms of 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 if (jointly or separately) they file notices renouncing their right to seek review.