

# In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 14-1140V

Filed: June 28, 2024

RICHARD GREENSLADE,

Petitioner,

v.

SECRETARY OF HEALTH AND  
HUMAN SERVICES,

Respondent.

Special Master Horner

*Leah V. Durant, Law Offices of Leah V. Durant, PLLC, Washington, DC, for petitioner.  
Debra A. Filteau Begley, U.S. Department of Justice, Washington, DC, for respondent.*

## DECISION<sup>1</sup>

On November 24, 2014, petitioner filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10, *et seq.* (2012),<sup>2</sup> alleging that the influenza (“flu”) vaccine he received on November 23, 2011, caused him to develop transverse myelitis (“TM”). (ECF No. 1.) As of a status conference on October 14, 2015, petitioner’s counsel clarified that petitioner was also pursuing a claim that his flu vaccination significantly aggravated the TM he developed following his earlier Zostavax<sup>3</sup>

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<sup>1</sup> Because this decision contains a reasoned explanation for the special master’s action in this case, it will be posted on the United States Court of Federal Claims’ website in accordance with the E-Government Act of 2002. See 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), petitioner has 14 days to identify and move to redact medical or other information the disclosure of which would constitute an unwarranted invasion of privacy. If the special master, upon review, agrees that the identified material fits within this definition, it will be redacted from public access.

<sup>2</sup> Within this decision, all citations to § 300aa will be the relevant sections of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

<sup>3</sup> Zostavax is the “trademark for a preparation of zoster vaccine live,” a subcutaneously administered live attenuated virus vaccine that is used to renew immunity against herpes zoster in older individuals. *Zostavax*, DORLAND’S MEDICAL DICTIONARY ONLINE, <https://www.dorlandsonline.com/dorland/definition?id=54152> (last visited Jan. 24, 2023); *Zoster Vaccine Live*, DORLAND’S MEDICAL DICTIONARY ONLINE, <https://www.dorlandsonline.com/dorland/definition?id=116591> (last visited Jan. 24, 2024). Throughout this decision, “Zostavax” or “zoster” vaccine will be used to refer to this vaccine. The Zostavax vaccine is not covered by this program. 42 C.F.R. § 100.3. Accordingly, petitioner does not have any claim with

and Prevnar vaccinations on September 21, 2011. (ECF No. 42.) Thus, petitioner now alleges that his condition was caused, or alternatively significantly aggravated, by his flu vaccination. (ECF No. 144, p. 1, 2 n.2.) For the reasons set forth below, I conclude that petitioner is *not* entitled to compensation.

### I. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make several factual demonstrations, including showing that an individual received a vaccination covered by the statute; received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury.

In some cases, the petitioner may simply demonstrate the occurrence of what has been called a “Table Injury.” That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the “Vaccine Injury Table,” corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table. If so, the Table Injury is presumed to have been caused by the vaccination, and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. §§ 300aa-13(a)(1)(A)-(B); § 300aa-11(c)(1)(C)(i); § 300aa-14(a).

In many cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table. In such instances, an alternative means exists to demonstrate entitlement to a Program award. That is, the petitioner may gain an award by showing that the recipient’s injury was “caused-in-fact” by the vaccination in question. § 300aa-13(a)(1)(A); § 300aa-11(c)(1)(C)(ii). In such a situation, of course, the presumptions available under the Vaccine Injury Table are inoperative. The burden is on the petitioner to introduce evidence demonstrating that the vaccination actually caused the injury in question. *Althen v. Sec’y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines ex rel. Sevier v. Sec’y of Health & Human Servs.*, 940 F.2d 1518, 1525 (Fed. Cir. 1991). Because TM is not a Table Injury, 42 C.F.R. § 100.3, petitioner must satisfy this burden of proof.

The showing of “causation-in-fact” must satisfy the “preponderance of the evidence” standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); see also *Althen*, 418 F.3d at 1279; *Hines*, 940 F.2d at 1525. Under that standard, the petitioner must show that it is “more probable than not” that the

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respect to his allegation that the Zostavax vaccine initially caused his TM. See § 300aa-11(c)(A); see also *Scanlon v. Sec’y of Health & Human Servs.*, 114 Fed. Cl. 135 (2013) (concluding that a petitioner must have received a covered vaccine to survive a motion to dismiss and that the zoster vaccine is not so covered).

vaccination was the cause of the injury. *Althen*, 418 F.3d at 1279. The petitioner need not show that the vaccination was the sole cause of the injury or condition, but must demonstrate that the vaccination was at least a “substantial factor” in causing the condition, and was a “but for” cause. *Shyface ex rel. Shyface v. Sec’y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). Thus, the petitioner must supply “proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury;” the logical sequence must be supported by “reputable medical or scientific explanation, i.e., evidence in the form of scientific studies or expert medical testimony.” *Althen*, 418 F.3d at 1278; *Grant ex rel. Grant v. Sec’y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner may not receive a Vaccine Program award based solely on his or her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1).

In what has become the predominant framing of this burden of proof, the *Althen* court described the “causation-in-fact” standard, as follows:

Concisely stated, *Althen*’s burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury. If *Althen* satisfies this burden, she is “entitled to recover unless the [government] shows, also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine.”

*Althen*, 418 F.3d at 1278 (citations omitted). The court also indicated that, in finding causation, a Program fact finder may rely upon “circumstantial evidence,” which the court found to be consistent with the “system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants.” *Id.* at 1280.

Generally, respondent bears the burden of demonstrating the presence of any alternative cause by preponderant evidence only if petitioner satisfies his *prima facie* burden. § 300aa-13(a)(1)(B); *Walther v. Sec’y of Health & Human Servs.*, 485 F.3d 1146, 1150 (Fed. Cir. 2007). Respondent may also present evidence relating to an alternative cause to demonstrate the inadequacy of petitioner’s evidence supporting his case in chief, but petitioner does not bear the burden of eliminating alternative causes where the other evidence on causation is sufficient to establish a *prima facie* case under *Althen*. *de Bazan v. Sec’y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008); *Walther*, 485 F.3d at 1149-50.

Petitioner further alleges that his flu vaccination significantly aggravated the indolent TM he developed following his earlier pneumococcal and zoster vaccinations on September 21, 2011. (ECF Nos. 42, 144.) The Vaccine Act defines a significant aggravation as “any change for the worse in a preexisting condition which results in

markedly greater disability, pain, or illness accompanied by substantial deterioration of health.” § 300aa-33(4). Where a petitioner in an off-Table case is seeking to prove that a vaccination aggravated a preexisting injury, petitioners must establish the three *Althen* prongs along with three additional factors described in the prior *Loving* case. See *Loving ex rel. Loving v. Sec’y of Health & Human Servs.*, 86 Fed. Cl. 135, 144 (2009) (combining the first three *Whitcotton* factors for claims regarding aggravation of a Table injury with the three *Althen* factors for off table injury claims to create a six-part test for off-Table aggravation claims); see also *W.C. v. Sec’y of Health & Human Servs.*, 704 F.3d 1352, 1357 (Fed. Cir. 2013) (applying the six-part *Loving* test). The additional *Loving* factors require petitioners to demonstrate aggravation by showing: (1) the vaccinee’s condition prior to the administration of the vaccine, (2) the vaccinee’s current condition, and (3) whether the vaccinee’s current condition constitutes a “significant aggravation” of the condition prior to the vaccination. *Loving*, 86 Fed. Cl. at 144.

## II. Procedural History

On November 24, 2014, petitioner filed his petition, alleging that approximately two days after he received the flu vaccination, he started experiencing weakness and numbness, and ultimately suffered TM that was caused-in-fact by the flu vaccination he received on November 23, 2011.<sup>4</sup> (See ECF No. 1, p. 2.) Along with the petition, petitioner filed medical records, marked Exhibits 1-2, and an affidavit of petitioner, marked Exhibit 3. (See ECF No.137, p. 1.) Petitioner subsequently filed additional medical records via compact disc. (ECF Nos. 7-8, 10; Exs. 4-5.) This case was first assigned to Special Master Millman. (ECF No. 4.)

During a status conference on August 18, 2022, Special Master Millman advised that the primary issue in the case was whether petitioner’s November 23, 2011 flu vaccination significantly aggravated the TM he developed after receiving the Zostavax and Prevnar vaccinations on September 21, 2011. (ECF No. 41.) In a subsequent status conference on October 14, 2015, petitioner’s counsel confirmed that petitioner was pursuing a claim that his flu vaccination significantly aggravated the TM he developed following his earlier Zostavax and Prevnar vaccinations. (ECF No. 42.)

Petitioner filed additional medical records via compact disc in November and December 2015, followed by a Statement of Completion on December 28, 2015. (ECF Nos. 43, 45, 46; Exs. 6-7.) On January 29, 2016, petitioner filed a status report confirming that he communicated a settlement demand to respondent. (ECF No. 47.) During a status conference on February 8, 2016, respondent’s counsel indicated that respondent is not interested in settlement “because the onset of petitioner’s transverse myelitis came too quickly after receiving [the] influenza vaccine to show causation.” (ECF No. 48.)

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<sup>4</sup> Petitioner was initially represented by Scott Rooney. On May 1, 2015, Mr. Rooney filed a motion to withdraw as attorney, which was granted. (ECF Nos. 18, 28.) On August 10, 2015, petitioner moved to substitute Leah V. Durant as attorney of record. (ECF No. 37.)

On March 24, 2016, respondent filed his Rule 4(c) report, recommending against compensation. (ECF No. 49.) Respondent stated that it was not clear that petitioner suffers from TM and noted that some of petitioner's treating physicians did not believe his testing was consistent with TM. (*Id.* at 6-7.) Respondent further asserted that petitioner exhibited similar symptoms of his alleged condition prior to his flu vaccination. (*Id.* at 7 (citing Ex. 1, pp. 565, 581).) Respondent also pointed out that petitioner was experiencing symptoms of his condition on the day of his flu vaccine and the day after his flu vaccine, raising a question regarding appropriate temporal association. (*Id.* (citing Ex. 1, pp. 569, 572).)

Petitioner then filed an expert opinion by neurologist Lawrence Steinman, M.D. (ECF Nos. 57, 61; Exs. 12, 55.) After petitioner filed additional medical records (ECF Nos. 65, 66, 69; Exs. 56-62), respondent filed responsive expert reports from neurologist Jeffrey Gelfand, M.D., M.A.S., and immunologist Thomas Forsthuber, M.D., Ph.D. (ECF Nos. 70, 71; Ex. A; Ex. B.) The parties then exchanged further reports by their experts. (ECF Nos. 76, 82, 86, 88; Exs. 64, 75, C, D.)

This case was reassigned to my docket on June 5, 2019, but shortly thereafter was assigned to Special Master Corcoran for alternative dispute resolution ("ADR"). (ECF Nos. 89-90, 92-93.) However, on January 23, 2020, the case was removed from the ADR process without any informal resolution and again reassigned to my docket for further proceedings. (ECF Nos. 99, 100.)

A two-day entitlement hearing was set to commence on November 12, 2020. (ECF No. 104.) However, on October 1, 2020, petitioner filed a report from a new expert, Carlo Tornatore, M.D. (Ex. 81), and additional medical records. (ECF No. 108; Exs. 78-80, 82-97.) A status conference was held on October 2, 2020, during which petitioner explained that he was initially unable to confirm Dr. Tornatore's participation in the case and received an expert report from him only recently. (ECF No. 112, p.1.) Respondent requested an opportunity to respond to Dr. Tornatore's expert report. (*Id.* at 2.) Based on my review of the filings and after discussing the issue with the parties, I concluded that the filing of Dr. Tornatore's report rendered the case unripe for hearing. (*Id.* at 1-2.) Thus, the hearing scheduled for November 2020 was cancelled. (*Id.* at 2.)

Respondent filed supplemental reports from Dr. Gelfand and Dr. Forsthuber on December 15, 2020. (ECF Nos. 115, 116; Exs. E; G.) Petitioner then filed supplemental reports from Drs. Tornatore and Steinman. (ECF Nos. 118, 119; Exs. 98, 103.) The expert report stage concluded with respondent's subsequent filing of supplemental reports from Drs. Gelfand and Forsthuber on October 22, 2021. (ECF No. 123; Exs. H, I.)

A two-day entitlement hearing was ultimately scheduled to commence on September 29, 2022. (ECF Nos. 131, 132.) In the interim, petitioner filed updated medical records, as well as a supplemental affidavit signed by petitioner and two additional affidavits signed by Jessica Cushard and Elmer S. Kittle. (ECF No. 136; Exs. 108-09, 123-25.) Both parties filed additional medical literature. (ECF Nos. 136, 138;

Exs. 110-122, H.) The parties filed simultaneous prehearing briefs on September 6, 2022. (ECF Nos. 143, 144.) A two-day hearing was held on September 29 and 30, 2022, by video conference. (See Transcript of Proceedings (“Tr.”), at ECF Nos. 150-51.) Drs. Tornatore and Steinman testified on behalf of petitioner, and Drs. Gelfand and Forsthuber testified on behalf of respondent. (*Id.*)

At the hearing, there were objections to certain testimony. (See *e.g.*, Tr. 441-47.) At the close of the hearing, respondent’s counsel requested an opportunity to address those objections in post-hearing briefs. (*Id.* at 456.) In a post-hearing order, I directed both parties to file updated curricula vitae for Drs. Steinman, Tornatore, and Forsthuber and ordered petitioner to file the medical literature by Talaat et al. that was discussed during Dr. Tornatore’s rebuttal testimony, as well as the handwritten demonstrative that was used by petitioner’s counsel during opening statement. (ECF No. 147.) I further ordered the respondent to file status report upon review of the Talaat article, proposing a filing deadline for a responsive supplemental report by Dr. Forsthuber. (*Id.*) Respondent filed a status report on October 31, 2022, proposing a deadline for filing his responsive expert report. (ECF No. 152.) Respondent subsequently filed Dr. Forsthuber’s supplemental report in response to the Talaat article on January 23, 2023. (ECF No. 153; Ex. J.)

On March 31, 2023, petitioner filed a supplemental report by Dr. Tornatore in response to Dr. Forsthuber’s most recent report. (ECF No. 155; Ex. 130.) Thereafter, petitioner filed a joint status report on behalf of the parties, confirming that the evidentiary record is complete. (ECF No. 156.) However, the parties could not agree with respect to post-hearing briefs. (*Id.*)

In a Scheduling Order, filed April 7, 2023, I acknowledged the parties’ differing proposals with respect to any appropriate briefing schedule; however, I concluded that the parties should have an opportunity to file simultaneous post-hearing briefs. (ECF No. 157.) Petitioner subsequently filed a joint status report on behalf of the parties indicating their agreement that post-hearing briefing should be limited to any new issues raised at the hearing and in the post-hearing filings. (ECF No. 158.) This was later amended to a sequential briefing schedule. (Non-PDF Scheduling Order, filed June 6, 2023.)

On June 5, 2023, petitioner filed his post-hearing brief. (ECF No. 159.) On June 26, 2023, respondent filed his responsive post-hearing brief. (ECF No. 161.) Petitioner thereafter filed his reply brief on August 9, 2023. (ECF No. 164.)

Accordingly, this case is now ripe for resolution.

### III. Factual History

#### a. As Reflected in the Medical Records

Petitioner was a 66-year-old retiree at the time of his alleged injury. (*E.g.*, Ex. 1, p. 587.) His medical history prior to vaccination was significant for a vitamin B12 deficiency and chronic abdominal pain secondary to an abdominal surgery he underwent in the 1960s. (*See, e.g., id.* at 582-83.) On September 21, 2011, petitioner visited his primary care physician, Catherine Foster, M.D., with concerns about stomach pain, his teeth “falling out,” and intermittent right leg pain. (*Id.* at 587-88.) During this visit, petitioner received the pneumococcal and zoster (“Zostavax”) vaccines. (*Id.* at 586-87, 590.) On September 22, 2011, September 23, 2011, September 27, 2011, and October 12, 2011, petitioner called Dr. Foster’s office to discuss concerns related to treatment for his vitamin B12 deficiency. (*Id.* at 584-86.) Petitioner did not report any neurologic symptoms during these telephone encounters.

Petitioner returned to Dr. Foster on November 23, 2011, with complaints of continued stomach pain and a “lack of ability to sense [the] need to defecate.” (Ex. 1, p. 581.) He also reported persistent right leg pain for the last three to four years and “pain in the posterior neck and upper back and shoulders” for the last four weeks. (*Id.*) He denied having any recent injuries that would cause his neck, back, and shoulder pain. (*Id.*) Dr. Foster assessed the shoulder pain as seemingly muscular and improving. (*Id.* at 582.) Petitioner received the flu vaccination at issue during this encounter. (*Id.* at 580, 583.)

On November 28, 2011, five days following his flu vaccination, petitioner called Dr. Foster to discuss concerns about “severe myalgias and associated generalized weakness to the point that he cannot walk.” (Ex. 1, p. 580.) He described weakness in his bilateral extremities, neck, and upper back. (*Id.*) He stated that he could barely lift a coffee cup to his mouth. (*Id.* at 579.) Dr. Foster noted that these symptoms were new since his last visit. (*Id.* at 580.) He reported that his muscle pain began about one month earlier but went away until it returned the previous Friday, three days prior to the telephone encounter and two days post flu vaccination.<sup>5</sup> (*Id.* at 579.) However, he further indicated that “this is the worst it has been.” (*Id.*) Dr. Foster recommended petitioner go to the emergency room (“ER”). (*Id.* at 580.)

Upon arrival to the Veterans Affairs (“VA”) Ann Arbor ER on November 28, 2011, petitioner reported that he had been experiencing weakness, numbness, and pain in his bilateral extremities “for the last [four] days,” which would place onset on the day after his flu vaccination.<sup>6</sup> (Ex. 1, p. 572.) He also reported leg spasms, and although he

<sup>5</sup> The nurse documenting the telephone encounter also noted that petitioner received the flu vaccine on Friday. (Ex. 1, p. 579.) Petitioner received the flu vaccine on Wednesday, November 23, 2011. (*Id.* at 580.)

<sup>6</sup> The same medical record also documents that petitioner’s symptoms began three days prior. (Ex. 1, p. 574.) Petitioner also previously reported that his extremity weakness began three days prior, on Friday, November 25, 2011. (*Id.* at 579-80.) However, it appears from the medical records that petitioner’s

reported “problems with his right leg” for the past year, he could not specifically describe his “problems.” (*Id.*) Petitioner further explained that he had noticed that he could feel hot water on his head and shoulders while in the shower, but the water felt cold below his head and shoulders. (*Id.*) A physical examination revealed that petitioner had weakness of his shoulder girdle and was unable to raise his arms against resistance. (*Id.* at 573-74.) The ER doctor also found that petitioner had weakness in his hips, but not in his distal extremities. (*Id.* at 574.) Petitioner was admitted to the hospital with a diagnosis of TM. (*Id.*)

While at the hospital, petitioner reported that his shoulder and neck soreness started on the previous Thursday, which would be the day after his flu vaccination. (Ex. 1, p. 565.) Petitioner explained that the soreness subsequently spread down his arms and legs, and he began feeling numbness and coldness in his extremities. (*Id.*) He described tightness in his shoulders and stated that it felt like there was “sand in them.” (*Id.*) Petitioner also reported feeling a pins and needles sensation in all four extremities. (*Id.* at 565-66.) He stated that he experienced “an identical episode” two months prior and noted that “[t]he onset was identical and the entire symptomatology lasted 3-4 days and then gradually resolved on its own.” (*Id.* at 566.) Additionally, he noted that he had been suffering from painful cramping in his bilateral calves for the last several months, but the cramping occurred more often in his right calf and seemed to be “more frequent during [this] constellation of symptoms.” (*Id.*) Upon physical examination by neurologist Joseph Corey, M.D., Ph.D., petitioner showed reduced reflexes in his legs, inability to stand or walk, and decreased sensation in his upper and lower extremities. (*Id.* at 567.) Given that all four of petitioner’s extremities were impacted and the pain began in his neck and shoulders, Dr. Corey noted that petitioner’s symptoms were likely localized in his cervical spine. (*Id.*) Dr. Corey assessed petitioner with possible myelopathy, polyradiculopathy, or TM and recommended cervical spine imaging. (*Id.*)

Shortly after petitioner was admitted to the hospital, he developed urinary retention and needed a catheter. (Ex. 1, pp. 550-51.) Petitioner underwent a cervical spine MRI on November 29, 2011. (*Id.* at 803-06.) The MRI revealed “moderately advanced degenerated disc disease with the disc osteophyte complexes causing mild central spinal stenosis at C3-C4 and C6-C7.” (*Id.* at 806.) It also showed a “mild” or “faint T2 signal prolongation,” but there was “no contrast enhancement associated with it.” (*Id.* at 805.) The impression included “[m]oderately advanced” and “equivocal findings [for] small area of focal T2 signal prolongation in the ventral aspect of the right hemi cord at C3 vertebral level, suggesting either demyelination or gliosis.” (*Id.* at 806.) Dr. Corey reviewed the MRI findings and opined that the results showed “T2 signal change ~C3-C4 and some hazy enhancement at this level, as well as C6-C7 level.” (*Id.* at 549.) His impression was that the MRI findings were concerning for an intrinsic cord process as the cause of the TM. (*Id.*)

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symptoms of shoulder and neck soreness manifested first and symptoms progressed to include weakness and numbness by the following day. (See *id.* at 565-66.)

Additionally, a cerebrospinal fluid (“CSF”) study showed slightly elevated protein at 61 mg/dL (reference range of 12 to 60 mg/dL) and an elevated myelin basic protein at 4.0 ng/mL (reference range of 0.0 to 1.0 ng/mL) but was otherwise normal. (Ex. 1, pp. 763, 82.) It was noted that petitioner had an elevated antinuclear antibody (“ANA”), prompting consideration of a series of autoimmune disorders. (See *id.* at 709.) Except for a positive MRSA culture, testing for infectious etiologies was negative. (*Id.* at 776-79, 784-85.) Petitioner’s serum was negative for zoster. (*Id.* at 777.) Testing for several central nervous system (“CNS”) antibodies was also negative. (*Id.* at 770-82.) Also on November 29, 2011, a nurse noted that petitioner complained of his bilateral shoulders and knees being “locked up” and that petitioner’s range of motion was more limited than it had been upon arrival. (*Id.* at 550.)

On December 1, 2011, petitioner attended a physical therapy session while at the hospital. (Ex. 1, pp. 527-28.) During the session, petitioner was unable to move his legs, he had significant weakness in his arms, and he had decreased sensation in his arms and legs. (*Id.*) On the same date, petitioner saw Dr. Corey for a neurology evaluation. (*Id.* at 524-26.) Dr. Corey noted decreased strength and sensation on physical examination and a differential diagnosis of TM, MS, or potential brain disease. (*Id.* at 526.) Dr. Corey again noted that petitioner’s MRI was “concerning for an intrinsic cord process” as the cause of the TM; however, the cause was still unknown. (*Id.*) Petitioner began a three-day course of Solu-Medrol<sup>7</sup> and a seven-day course vitamin B12 therapy to address the TM and was given Flexeril for his muscle spasms. (*Id.*) He was also placed on oxygen due to hyperventilation and prescribed Ativan for anxiety. (*Id.*)

The next day, on December 2, 2011, petitioner began showing slight improvement and regained some use of his right arm. (Ex. 1, pp. 519-20.) He remained non-ambulatory due to extensive weakness in his legs. (*Id.* at 520.) Petitioner’s treating neurologist, Dr. Corey, suggested that TM was unlikely as there were no inflammatory changes in CSF and petitioner had a non-enhancing lesion. (*Id.* at 517.) During a neurology consultation on December 3, 2011, Dr. Corey again noted, “Transverse Myelitis and Multiple Sclerosis are on the differential, but the lack of enhancement coupled with his largely normal CSF results (other than protein of 61) would make this very unusual, as does his older age.” (*Id.* at 493.) Dr. Corey recommended an additional two-day course of Solu-Medrol. (*Id.*) Because petitioner’s symptoms had worsened since his initial cervical spine MRI, Dr. Corey recommended an additional MRI of his brain and total spine to evaluate for any changes. (*Id.*) The next day, petitioner was seen by neurology again and he reported his recent flu vaccination. (*Id.* at 476.) It was noted that TM “has been reported after many

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<sup>7</sup> Solu-Medrol is an intramuscular or intravenous injection of synthetic glucocorticoid derived from progesterone that is used as an anti-inflammatory and immunosuppressant in short-term emergency treatment. *Solu-Medrol*, DORLAND’S MEDICAL DICTIONARY ONLINE, <https://www.dorlandsonline.com/dorland/definition?id=46174> (last visited June 5, 2024); *Methylprednisolone*, DORLAND’S MEDICAL DICTIONARY ONLINE, <https://www.dorlandsonline.com/dorland/definition?id=31014> (last visited June 5, 2024); *Methylprednisolone Sodium Succinate*, DORLAND’S MEDICAL DICTIONARY ONLINE, <https://www.dorlandsonline.com/dorland/definition?id=89219> (last visited June 5, 2024).

vaccinations,” but the relationship between his vaccination and his condition was not explored as petitioner’s “work-up has not been consistent with Transverse myelitis.” (*Id.*)

Petitioner underwent a thoracic and cervical spine MRI on December 5, 2011. (Ex. 1, pp. 797-802.) The MRI revealed “[s]table appearance of hyperintensity along the anterior spinal cord at C2-C4 with stable cervical spondylosis” and “[i]ncreased thin tumor flow-void along the posterior aspect of the spinal cord from mid thoracic spinal cord down to L1, could represent a dural AV fistula” but there was “no associated expansion of the spinal cord or T2 hyperintensity on the spinal cord.” (*Id.* at 802.) On December 5, 2011, petitioner was transferred to the University of Michigan (“UofM”) hospital for evaluation of a possible venous malformation in his spinal cord based on his MRI findings from the previous day. (*Id.* at 443; Ex. 8, pp. 6-7.) Radiologists at the UofM hospital reviewed the December 5, 2011 MRI and concluded:

On postcontrast imaging, patchy areas of abnormal contrast enhancement are seen dorsal to the cord at T9-T10 to T12-L1 levels. No convincing evidence for abnormal flow-voids is seen on T2 axial imaging. A venous structure is seen exiting from right L1-L2 neuroforamen and can be traced superiorly up to T11 level posterior to the conus. Between T9-T10 and T11, no significant areas of enhancement are seen. This could represent a mildly dilated venous channels. The possibility of dural AV fistula, even as less likely, cannot be entirely excluded. Clinical correlation is recommended.

Intramedullary high T2 signal area is seen on the left at C7-T1 level, concerning for plaques of demyelination versus transverse myelitis. Smaller similar area is also seen on right C4-C5 level. Intramedullary high T2 signal is seen from C2-C3 to C4-C5 levels.

(Ex. 8, pp. 64.) During a neurology consultation with Larry Junck, M.D., on December 6, 2011, it was noted that petitioner initially reported an identical episode as occurring “about two months ago,” but “when questioned here today at UofM, he states that it might have only been about 1-2 weeks ago.” (*Id.* at 48.) He maintained that “[t]he onset was identical and the entire symptomatology lasted 3-4 days” before gradually resolving on its own without medical intervention or lasting deficits. (*Id.*) Dr. Junck reiterated that petitioner received a flu vaccine prior to the onset of his symptoms and that while TM “has been reported after many vaccinations . . . [petitioner’s] work-up has not been consistent with [TM].” (*Id.* at 50.) During a neurosurgical inpatient consult, it was noted that petitioner’s MRI showed “multiple areas of T2 hyperintensity throughout the cervical and thoracic cord,” “irregular enhancement of the dorsal caudal thoracic spine,” and “mild degenerative disc changes,” but “no active neurosurgical issues at this time.” (*Id.* at 24.) A spinal angiogram performed on December 8, 2011, ruled out a dural venous fistula. (*Id.* at 66-69; Ex. 1, pp. 443, 447-48.)

On December 9, 2011, petitioner was transferred back to the VA Ann Arbor Hospital. (Ex. 1, pp. 443-47.) Upon transfer, petitioner was seen by Dr. Corey with

reports of ongoing weakness. (*Id.*) Dr. Corey noted that “extensive workup to date aside from aforementioned spinal cord lesions and low vitamin B12 (no s/p 2 days IV replenishment) has been negative.” (*Id.* at 443.) Petitioner’s presumed diagnosis was autoimmune myelitis, given his negative workup. (*Id.* at 447.) A brain MRI performed on December 12, 2011, was normal. (*Id.* at 792-93.) By December 13, 2011, petitioner had improved, but his symptoms continued to wax and wane. (*Id.* at 409.) Throughout his hospital course, petitioner’s lack of definitive diagnosis was a persistent point of frustration. (*Id.* at 398, 411, 421, 457, 528-29.)

Petitioner was discharged from VA Ann Arbor ER and transferred to the VA Community Living Center on December 14, 2011. (Ex. 1, pp. 4-8.) Petitioner’s primary diagnosis at discharge was weakness and spinal cord lesion. (*Id.* at 4; Ex. 4, pp. 7-8; Ex. 2, pp. 5-9.) While at the VA Community Living Center, petitioner continued to attend physical therapy sessions. (*E.g.*, Ex. 1, pp. 382-83.) On December 22, 2011, petitioner saw neurologist Ben Segal, M.D., who noted that petitioner “originally presented on 11/28/2011 after his 2nd episode of neck and shoulder pain (in 10 days) that instantaneously radiated down his body into legs and was associated with extreme weakness.” (*Id.* at 316.) Petitioner described how “[e]ach episode left him [bed] bound, the first for 3 days in mid 11/2011 and the second led to pursuit of medical care on 11/28/2011.” (*Id.*) Dr. Segal assessed “myelopathy was most likely due to a demyelinating event.” (*Id.* at 321.) Dr. Segal noted that a “[p]ossible cause is flu vaccine several weeks before [petitioner’s] initial symptoms,” but later qualified that “[t]he relationship between the myelopathy and his recent influenza vaccination is uncertain.” (*Id.* at 320-21.) Petitioner continued to improve with inpatient rehabilitation, and he remained at the VA Community Living Center until January 6, 2012, when he was discharged home. (Ex. 4, pp. 1-3.) At the time of his discharge, petitioner could ambulate with a front-wheeled walker but still needed a wheelchair at times. (*Id.* 3.) He could also perform most of his activities of daily living without assistance. (*Id.*) Petitioner’s discharge diagnosis was TM with unknown etiology. (*Id.* at 1.)

Following his discharge from inpatient rehabilitation, petitioner’s condition again deteriorated. I have reviewed the remaining medical records; however, it is not necessary to discuss petitioner’s subsequent course in detail. Neither the parties nor their experts have asserted that the subsequent course of petitioner’s condition affects their assessment of the alleged causal relationship to vaccination.

During a follow-up neurology visit on June 21, 2012, petitioner reported that he was weak, incontinent, and dependent on his wheelchair, despite continued therapy. (Ex. 1, pp. 140-45.) The attending physician noted that petitioner’s symptoms could be attributed to TM that was resolving upon his initial presentation but it was unclear if petitioner’s vaccinations “played any part [in] his disease process.” (*Id.* at 144-45.) The physician further noted that petitioner’s condition “may have at least partially responded to 5 day course of Solumedrol in early 12/2011.” (*Id.* at 144.) By 2014, petitioner had become completely wheelchair dependent. (*See e.g.*, Ex. 4, p. 50.) Additionally, he developed pain and spasticity (increased tone and reflexes) in his extremities, continued

to suffer constipation, and had difficulty controlling his bladder function. (See e.g., *id.* at 43-44.)

In response to petitioner's inquiry, Dr. Foster noted on October 28, 2023, that she does not confirm that petitioner's shingles vaccine was related to his paralysis, although she noted his history of "presumed autoimmune myelitis with extensive, negative work up in 11/2011." (Ex. 108, pp. 44-45.)

Petitioner continues to suffer from sequela of his injury. He remains wheelchair dependent and continues to suffer paraplegia, neurogenic bowel and bladder, pain, spasticity, and weakness. (See e.g., Ex. 7; Ex. 76, p. 20; Ex. 108, pp. 12-13, 28, 46, 81; Ex. 109, pp. 28-29, 49, 89, 97, 118-244, 258, 271, 295-331.) Petitioner also continues to experience deficiencies in vitamins D and B12. (See e.g., Ex. 108, p. 82.)

## **b. As Reflected in the Affidavits**

### **i. Affidavits of Petitioner**

Petitioner filed two affidavits, marked as Exhibits 3 and 123. (ECF No. 136.) In his affidavit, petitioner states that, prior to receipt of the subject flu vaccine on November 23, 2011, he did not suffer "any signs or symptoms of paralysis," was never diagnosed with TM, was not wheelchair bound, and did not require in-home medical care or physical therapy. (Ex. 3, ¶¶ 3, 8-9.) Following his vaccination, petitioner states that he began to develop tingling and numbness in his lower extremities and was incapable of moving his legs. (*Id.* ¶ 4.) He states that he went to the ER on November 28, 2011, with complaints of continued numbness, tingling, and difficulty moving his lower extremities.<sup>8</sup> (*Id.* ¶ 5.) He explains that a CSF evaluation revealed that he "had a myelin basic protein at 4.0" and he was subsequently diagnosed with TM. (*Id.* ¶¶ 6-7.) As a result, petitioner states that he requires a wheelchair, in-home medical care, and physical therapy. (*Id.* ¶ 10.) He further contends that he continues to suffer emotional distress and physical injury as a result of the subject vaccination. (*Id.* ¶ 13.)

In his supplemental affidavit, petitioner clarifies that he was vaccinated in November of 2011 and "was hospitalized within days." (Ex. 123, ¶ 1.) He described how he "started feeling unwell" after his vaccination and how he was paralyzed from the neck down "shortly after" arriving at the ER. (*Id.*) He states that he remained in the hospital for several months before returning home where he continued to have trouble walking. (*Id.*)

Regarding residual symptoms, petitioner indicates that the cramping in his legs progressed to point of spasticity, which has not abated. (Ex. 123, ¶¶ 1-2.) Petitioner explains that his legs remain folded under him in a cramped position and he cannot use or straighten them. (*Id.* ¶ 2.) Despite taking muscle relaxers on a daily basis, petitioner states that he continues to feel constant pain, making sleep and daily activities difficult. (*Id.*) Petitioner further explains that he is now confined to a wheelchair and struggles

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<sup>8</sup> The affidavit misstates the date as September 28 rather than November 28.

moving and transferring in and out of his wheelchair, compounding his difficulty performing daily activities, such as cooking and cleaning. (*Id.* ¶ 4.) He is also no longer able to drive a car. (*Id.*) Petitioner explains that he could previously “work on all sorts of mechanical and construction projects,” but his spasticity has prevented him from continuing to do so. (*Id.* ¶ 5.) Although he admits that he sustained a military injury prior to vaccination, which resulted in difficulty with bowel movements, petitioner claims that these symptoms have only gotten worse since vaccination. (*Id.* ¶ 3.) He states that he developed an inability to urinate without the assistance of a catheter. (*Id.*) Lastly, he describes the psychological toll of his injury, which he states is “terrible” and “has taken the joy out of everything.” (*Id.* ¶ 5.) He further states that “know[ing] that nothing will take this pain away makes [him] just want to die sometimes.” (*Id.*)

Petitioner states that he experienced some relief with massage therapy, but Veteran’s Affairs has refused to cover such treatment. (Ex. 123, ¶ 6.) He further explains that he must cover the cost of his medication and medical supplies with his own income, “which is minimal at this point.” (*Id.*)

Notably, petitioner claims that he “experienced similar symptoms after receiving different vaccine [a] few months earlier” and that “those symptoms were short lived and resolved on their own.” (Ex. 123, ¶ 1.)

#### ii. Affidavit of Jessica Cushard

Petitioner filed an affidavit of Jessica Cushard, marked as Exhibit 124. (ECF No. 136.) In her affidavit, Ms. Cushard states that she is a friend of petitioner’s and that “it has been very disturbing to see what has happened to him since being vaccinated.” (Ex. 124, ¶ 1.) She explains that she transported petitioner to the ER when he began experiencing difficulty walking and breathing following vaccination. (*Id.*) “During the rest of that day and evening, [she] watched as he went from mostly functional to being completely paralyzed from the neck down.” (*Id.*) Ms. Cushard describes how petitioner remained in the hospital for several months and underwent “test after test with no conclusions.” (*Id.*) She further describes how he could eventually walk with the assistance of a walker and was discharged from the hospital. (*Id.*)

Ms. Cushard explains that, rather than improving upon discharge, petitioner’s legs started cramping to the point that they were spastic and painful. (Ex. 124, ¶ 2.) She states that he sought further testing, “but no solution was found for the problem” and “[t]he best they could do was to prescribe a large amount of daily muscle relaxers to try to help ease the cramping.” (*Id.*) Ms. Cushard describes how petitioner’s legs are always folded together as if “he has constant charley horses in all of his leg muscles.” (*Id.*) As a result, she explains that he is confined to a wheelchair, making “any normal daily activities like cooking, cleaning, bathing, etc.” difficult. (*Id.*) She states that petitioner experiences spasms on top of the cramping “if he moves just the wrong way.” (*Id.*) His pain makes getting comfortable and sleeping difficult. (*Id.*)

Ms. Cushard goes on to describe how, “[a]round the same time that all of this happened,” petitioner started to experience difficulty urinating and required the assistance of a catheter. (Ex. 124, ¶ 3.) She further describes how petitioner’s difficult with bowel movements caused him to lose about 65 pounds because he was afraid to eat. (*Id.*) However, Ms. Cushard indicates that she is unsure of whether these symptoms are “a result of the original problem or a side effect of so many muscle relaxers.” (*Id.*)

Ms Cushard explains that, prior to vaccination, petitioner was a very active person. (Ex. 124, ¶ 4.) She states that petitioner walked a lot and drove a car, but he can no longer do either of these activities. (*Id.*) She suggests that petitioner spends most of his time inside of his apartment because the battery power on his mobile wheelchair dictates how far he can travel. (*Id.*) Ms. Cushard also states that petitioner does not often go outside in the winter because the cold weather causes his legs to spasm. (*Id.*) Ms. Cushard states that she can see why petitioner seems to be very depressed most of the time. (*Id.*)

Finally, Ms. Cushard states that does not believe that there could have been any other cause for petitioner’s condition as “[n]othing else notable happened around that time.” (Ex. 124, ¶ 5.)

iii. Affidavit of Elmer S. Kittle, Jr.

Petitioner filed an affidavit of Elmer S. Kittle, Jr., marked as Exhibit 125. (ECF No. 136.) In his affidavit, Mr. Kittle states that he has known petitioner “for many years.” (Ex. 125, ¶ 1.) He explains that he would be devastated if he had to go through what petitioner has gone through. (*Id.*) Mr. Kittle describes how petitioner “used to walk everywhere” prior to the vaccinations. (*Id.* at ¶ 2.) Mr. Kittle explains that petitioner’s condition “left him discouraged and in a wheelchair without hope of every walking again.” (*Id.*)

## IV. Expert Opinions

### a. Petitioner's Experts

#### i. Carlo Tornatore, M.D.<sup>9</sup>

In support of his claim, petitioner presented the expert opinion of Carlo Tornatore, M.D. Dr. Tornatore authored three expert reports in support of petitioner's claim. (Exs. 81, 98, 130.) Additionally, at the hearing, he was proffered without objection as an expert in neurology with a special expertise in demyelinating diseases of the CNS, including MS and TM. (Tr. 29, 32.)

Regarding the onset of petitioner's condition, Dr. Tornatore opined that petitioner experienced the first manifestations of his TM "several weeks prior to the 11/23/2011 influenza vaccination and that the vaccination profoundly aggravated the TM resulting in the precipitous onset of quadriparesis." (Ex. 81, p. 15; Tr. 33-34; see *also* Tr. 106-07 (opining that onset was "sometime in that three- to four-week period prior to the influenza vaccination" and that the end of October to the beginning of November 2011 time frame "makes the most sense . . . from a historical standpoint").) Dr. Tornatore explained that, prior to the pneumococcal and zoster vaccinations, petitioner's medical condition was significant for gastrointestinal issues, as well as right posterior thigh and calf pain and an apparent vitamin B12 deficiency; however, there was no record of significant neurologic symptoms. (Tr. 34-36 (citing Ex. 1, pp. 597-600).) Nonetheless, he noted that during a visit with Dr. Foster on November 23, 2011, petitioner reported experiencing pain in the posterior neck and upper back and shoulders for the past four weeks. (Tr. 36-38; Ex. 81, p. 16; see *also* Ex. 98, p. 3 (emphasizing that petitioner's neck and shoulder pain was present before he received the flu vaccine).) Dr. Tornatore associated petitioner's reports of neck, back, and shoulder pain with his TM. (Ex. 81, pp. 17-18; Ex. 98, p. 3; see *also* Tr. 39, 112.) He stressed that a primary care physician may not necessarily tease out neurologic symptoms (Tr. 119), and that "pain described as musculoskeletal symptoms can have an origin in the central nervous system demyelination." (Ex. 81, pp. 17-18). He further noted that petitioner's November 23, 2011 encounter included a new symptom – the lack of ability to sense the need to

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<sup>9</sup> Dr. Tornatore received his medical degree from Georgetown University School of Medicine before completing an internship in internal medicine at Providence Hospital, his residency in neurology at Georgetown University Hospital, and a fellowship in molecular virology at National Institutes of Health. (Ex. 82, p. 2; Ex. 81, p. 2.) He is board certified in neurology and specializes in demyelinating conditions of the CNS. (Ex. 82, p. 1, Tr. 30-31.) Dr. Tornatore currently works a professor and the Chair of the Department of Neurology at Georgetown University Medical Center, as well as the Chair and Neurologist-in-Chief of the Department of Neurology at Medstar Georgetown University Hospital. (Ex. 82, p. 3; Ex. 81, pp. 1-2; Tr. 29-30.) Additionally, he is the Director of Georgetown University Hospital's Neurology Clerkship Program, Multiple Sclerosis Clinic, and Spasticity Clinic. (Ex. 82, pp. 3-4; Ex. 81, pp. 1-2.) At the hearing, Dr. Tornatore explained that he has been in practice for thirty years with most of his time spent treating patients with "the whole spectrum" of neuroinflammatory disorders of the nervous system, including transverse myelitis. (Tr. 30.) He further explained that he has over thirty years of experience reading MRIs and spent around seventeen years teaching neurology residents and medical students how to read MRIs. (*Id.* at 31.) Dr. Tornatore has published several articles on cell biology and pathology of demyelinating disorders and diseases of the CNS. (Ex. 81, pp. 8-13.)

defecate, which he explained is a sign of sensory abnormalities in the spinal cord. (Tr. 36-38 (citing Ex. 1, pp. 591-93).)

On cross-examination, Dr. Tornatore acknowledged that petitioner had a longstanding history of gastrointestinal issues (Tr. 112-14); however, he opined that the significance of the new symptom became apparent after petitioner developed pain, motor symptoms, and bowel and urinary incontinence as “evidence that there might be something already indolent in the cervical spinal cord.” (Tr. 40-41, 115-16). Dr. Tornatore also acknowledged that the degenerative disc disease seen on MRI could potentially account for petitioner’s neck and shoulder pain, but he maintained that petitioner’s neurologic symptoms suggest that his pain originated from “within the spinal cord and not from nerve root impingement.” (Tr. 164-65.) Citing petitioner’s age, Dr. Tornatore opined that the degree of degenerative changes would be expected and that he did not believe that the two conditions could be acting synergistically. (Tr. 165.) Dr. Tornatore noted that “inflammatory conditions of the spinal cord can be brief in duration with remission back to baseline,” similar to what petitioner described to his treating physicians. (Ex. 98, p. 3.) Dr. Tornatore concluded that in the weeks prior to petitioner’s flu vaccination, “there were multiple references to transient as well as ongoing symptoms referable to the cervical spinal cord.” (*Id.*)

Addressing petitioner’s MRIs of the cervical spine, Dr. Tornatore opined that petitioner’s presentation on November 23, 2011, was consistent with the cervical spine lesions seen on subsequent MRI. (Ex. 81, p. 18.) He explained that, once there is an injury to the spinal cord, the presence of enhancement on MRI simply “tells us about the timing, but it doesn’t really tell us anything about the symptoms themselves.” (Tr. 65.) He explained that it is significant that the cervical spine lesions did not enhance with contrast as a non-enhancing lesion on T2-weighted imaging indicates that the lesion is generally at least 2-3 weeks old. (Ex. 81, pp. 18-19 (citing M. Lai et al., *A Preliminary Study into the Sensitivity of Disease Activity Detection by Serial Weekly Magnetic Resonance Imaging in Multiple Sclerosis*, 60 J. NEUROLOGY, NEUROSURGERY, & PSYCHIATRY 339 (1996) (Ex. 96); Francois Cotton et al., *MRI Contrast Uptake in New Lesions in Relapsing-Remitting MS Followed at Weekly Intervals*, 60 NEUROLOGY 640 (2003) (Ex. 97)); Tr. 56-59, 132-33.) Dr. Tornatore explained that a paper cited by Dr. Gelfand, Bulut et al. (*infra* at Ex. E, Tab 3), also bolstered his opinion as that study confirmed that an MRI within 10 days of symptom onset is more likely than not to have gadolinium enhancement. (Ex. 98, p. 4; Tr. 82-84, 151-52.) Thus, Dr. Tornatore opined that the MRI findings from November 29, 2011, indicate that the lesions likely developed between November 7, 2011, and November 14, 2011, which overlaps with the onset of petitioner’s cervical and shoulder symptoms. (Ex. 81, p. 18.) He added that petitioner’s MRIs “revealed partial myelitis, not full thickness myelitis.” (Ex. 98, pp. 3-4; Tr. 76-79.) He explained that partial myelitis involves an inflammatory process and “can result in transient spinal cord symptoms,” which is consistent with petitioner’s reports to his treating doctors. (Ex. 98, pp. 3-4; Tr. 76-79.) Dr. Tornatore further explained that the pathology and kinetics of partial myelitis is comparable to multiple sclerosis (“MS”) as partial myelitis is seen in over 60 percent of MS patients, and MS patients often

experience “a flare of transverse myelitis” that “can be absolutely identical to what [petitioner] experienced.” (Tr. 86, 139, 176-77.)

Dr. Tornatore explained that, although there are some instances when clinicians can parse out symptoms as being caused by one lesion or another, petitioner’s case is “a little muddier.” (Tr. 59-61.) However, he opined that the inability to pinpoint a specific lesion as causing a specific symptom “is less important than the fact that it’s all referable to the cervical spinal cord.” (Tr. 61, 65.) Dr. Tornatore explained that “MRI findings for transverse myelitis are nonspecific.” (Ex. 81, p. 20 (citing Rohit Bakshi & John C. Mazziotta, *Acute Transverse Myelitis After Influenza Vaccination: Magnetic Resonance Imaging Findings*, 6 J. NEUROIMAGING 248 (1996) (Ex. 88)).) Here, however, Dr. Tornatore found it significant that there were two non-enhancing lesions on MRI.<sup>10</sup> (Tr. 67, 72-73.) Based on his clinical experience, Dr. Tornatore opined that it is highly improbable for someone to develop two lesions at the same time and for both of the lesions to lose their enhancement within less than 5 days. (*Id.* at 67, 81, 84, 137-38.) He suggested that it could be argued petitioner had a “recurrent disease” due to there being “two different lesions” and “two different episodes.” (*Id.* at 84, 107-08; *see also* Tr. 140-42 (explaining that the location of petitioner’s lesions lends support for his opinion that the lesions are distinct, given what we know about the kinetics of blood-brain barrier breakdown).) When I asked why it would be the case that the second lesion was unlikely to progress in the absence of the flu vaccination, Dr. Tornatore relied on “the tempo” of petitioner’s reported symptoms. (*Id.* at 68, 170-72; *see also* Tr. 144 (explaining that the significance of the MRI studies showing non-enhancement is informed by petitioner’s symptom course).) He explained that older patients experience immunosenescence, and that petitioner’s advanced age, in combination with the lack of enhancement and normal CSF, suggests that his neck pain likely would have resolved on its own but for the flu vaccination. (Tr. 170-73.) Dr. Tornatore opined that “there’s no question that the inflammation is in one area and is starting to spread to other areas in the spinal cord, causing these other symptoms” (*Id.* at 70-71), and that petitioner’s “clinical course is by far the most important” sign of augmented inflammation (*Id.* at 158). He explained that there need not be a robust amount of inflammation to cause significant symptoms, given the relatively small size of the spinal cord, and that the location of the inflammation can have an impact on the severity of the symptoms. (*Id.* at 71-72, 77-78, 93, 162-63.) He agreed that the clinical progression of the symptoms itself “can demonstrate that the inflammatory process is progressing.” (*Id.* at 71.)

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<sup>10</sup> When asked about the December 5, 2011 MRI results, Dr. Tornatore explained that the results were reviewed and determined to show “irregular areas of enhancement dorsal to the lower cord.” (Tr. 73-74 (citing Ex. 8, pp. 63-65).) He clarified that these results demonstrate that the “hazy enhancement” was in the thoracic spine, rather than the cervical spine. (*Id.* at 74.) Either way, Dr. Tornatore explained that the “patchy areas of abnormal contrast enhancement” referred to “blood vessels that were outside of the spinal cord” and suggestive of mildly prominent venous channels; however, a subsequent angiogram ruled out dural fistula. (*Id.* 74-75 (citing Ex. 8, p. 7).) Dr. Tornatore explained that the lesions seen on subsequent MRI studies were “all there from the 29th onward,” and “[n]one of the lesions [were] enhanced.” (*Id.* at 72.) In response to my question regarding whether his opinion would change if I were to accept the initial impression of hazy enhancement, Dr. Tornatore explained that his opinion would not change because the faintness of the enhancement would indicate that the “it’s starting to resolve” and CSF analysis confirmed that there was no “bona fide enhancement.” (Tr. 167-68.)

Following the flu vaccination on November 23, 2011, petitioner reported “a progression of the symptoms,” including worsening muscle aches, weakness, sensory loss, and bowel and bladder issues. (Tr. 41-46 (citing Ex. 1, pp. 575-78, 588-90), 79; Ex. 81, p. 16.) Dr. Tornatore opined that these symptoms are referable to the cervical spinal cord as “part of a larger continuum of pain that becomes more diffuse.” (Tr. 43-44 (citing Ex. 1, p. 590), 69-70 (citing Ex. 1, p. 577).) Although he acknowledges that petitioner may not be an accurate historian, Dr. Tornatore emphasized petitioner’s report of a prior “identical episode” and suggested that it is difficult to tease out whether petitioner’s pre-vaccination symptoms had resolved or whether his post-vaccination symptoms were part of the same continuum.<sup>11</sup> (*Id.* at 46-48, 75, 122.) Dr. Tornatore acknowledged that petitioner’s affidavit includes a statement that he had not experienced paralysis, numbness, or tingling prior to his flu vaccination; however, Dr. Tornatore found the contemporaneous medical records to be more compelling than an affidavit that was authored at least three years after the events. (*Id.* at 123-25, 177-78.) He explained that the medical records confirm that, on four separate occasions, petitioner told four different medical providers about his prior episode. (*Id.* at 124-25.) Moreover, Dr. Tornatore submitted that the affidavit and the medical records were not inherently inconsistent because petitioner did not report paralysis when describing his prior episode to his providers and it is not entirely clear what petitioner meant when he used the word “paralysis” in his affidavit. (*Id.* at 124, 178.)

Dr. Tornatore explained that petitioner’s CSF, which did not reveal any inflammatory cells, indicates that the inflammatory process was not acute. (Tr. 50-52, 158-59.) The presence of elevated myelin basic protein, in combination with the lack of elevated white blood cell count, further bolstered Dr. Tornatore’s belief that the inflammatory injury was not new. (*Id.* at 50-52.) Dr. Tornatore explained that a study by Talaat et al. demonstrates that there are “immune hyper-responders” that may experience constitutional symptoms, despite lower absolute levels of the measured serum factors. (Ex. 130, pp. 1-4 (citing Kawsar R. Talaat et al., *Rapid Changes in Serum Cytokines and Chemokines in Response to Inactivated Influenza Vaccination*, 12 *INFLUENZA & OTHER RESPIRATORY VIRUSES* 202 (2018) (Ex. 127)); Tr. 442-43.) He opined that “the absolute level of a measured soluble factor is less important than the fact that there is a measurable clinical response to an antigenic challenge.” (Ex. 130, p. 5.) Dr. Tornatore further testified that non-enhancement on MRI suggests that the blood-brain barrier has been reestablished; however, this does not mean that the inflammation has subsided as the presence of a T2 lesion indicates that the inflammation has gotten into the spinal cord and the reestablished blood-brain barrier has sealed it in. (Tr. 153.) Because the spinal fluid is outside of the blood-brain barrier, inflammation in the spinal cord will no longer be reflected in the CSF once the blood-brain barrier has been reestablished. (*Id.* at 158-59.) Thus, petitioner “continues to

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<sup>11</sup> Dr. Tornatore evaluated Dr. Foster’s November 28, 2011 addendum, where she stated that petitioner had developed symptoms including generalized weakness and myalgias since his visit the week before, as her recognition of new symptomology since the November 23, 2011 encounter. (Tr. 43-44 (citing Ex. 1, p. 590).) Additionally, Dr. Tornatore references a notation by petitioner’s treaters from the initial hospitalization that petitioner had a previous identical episode as recognition that his subsequent symptoms were a continuum. (*Id.* at 69-70 (citing Ex. 1, p. 577).)

have very significant neurologic issues” as the inflammation remains, despite unremarkable CSF. (*Id.* at 78, 153-54.) Moreover, Dr. Tornatore opined that, while an initial immune response may result in an increase in cytokines or chemokines, “the subsequent triggering of the cellular and other portions of the humoral arm of the immune system can result in downstream CNS inflammatory effects long after the serum cytokine/chemokine levels have dropped to normal.” (Ex. 130, p. 4.)

Dr. Tornatore agreed with Dr. Steinman’s assessment that the flu vaccine can cause a significant aggravation of TM. (Ex. 81, p. 19.) He added that TM has been reported following flu vaccination and cited several case reports linking the flu vaccine with TM. (*Id.* at 19-21 (citing Bakshi & Mazziotta, *supra*, at Ex. 88; Isabelle Korn-Lubetzki et al., *H1N1 Vaccine-Related Acute Transverse Myelitis*, 13 *ISR. MED. ASS’N J.* 249 (2011) (Ex. 92); Wafa Akkad et al., *Longitudinally Extensive Transverse Myelitis Following Vaccination with Nasal Attenuated Novel Influenza A(H1N1) Vaccine*, 67 *ARCHIVES NEUROLOGY* 1018 (2010) (Ex. 86); Naoko Nakamura et al., *Neurologic Complications Associated with Influenza Vaccination: Two Adult Cases*, 42 *INTERNAL MED.* 191 (2003) (Ex. 93)).) He explained that a person’s response to a vaccine, which is initially produced to create protective immunity, is comparable to a person’s response to infectious antigens, and therefore, the recombinant or live attenuated antigens used in vaccines can similarly produce autoimmunity. (*Id.* at 21.) Dr. Tornatore identified multiple mechanisms by which an infectious antigen may induce autoimmunity but noted that molecular mimicry is the most common. (*Id.* at 21-22.) In addition to molecular mimicry, Dr. Tornatore identified the potential mechanisms of epitope spreading and polyclonal activation. (*Id.* at 22.)

Dr. Tornatore explained the concept of the “fertile field” model, in which an antigen with sequence homology to self-proteins may prime autoreactive T-cells but not initiate an adverse immune reaction on its own; however, later stimulation by a vaccine – even one without cross-reactive antigens or sequence homology – can initiate an autoimmune reaction in a susceptible person and lead to inflammatory demyelination. (Ex. 81, p. 22 (citing William Huynh et al., *Post-Vaccination Encephalomyelitis: Literature Review and Illustrative Case*, 15 *J. CLINICAL NEUROSCIENCE* 1315 (2008) (Ex. 90)).) He elaborated that a subsequent flu vaccination can induce a rapid increase of cytokines and chemokines, resulting in augmented inflammation in hyper-responders, (Tr. 442-43 (citing Talaat et al., *supra*, at Ex. 127)), and the fertile field concept can explain why petitioner was experiencing constitutional symptoms despite a lack of pleocytosis in the CSF. (*Id.* at 155-57.) He also pointed out that the National Multiple Sclerosis Society recommends delaying vaccination of persons who are experiencing ongoing CNS inflammation, out of concern that vaccination could aggravate the underlying inflammatory condition. (Ex. 98, p. 5.)

Dr. Tornatore offered 1-63 days (with a mean of 16.5 days) as the appropriate time frame for TM to be caused by flu vaccination. (Ex. 81, p. 23 (citing Bakshi & Mazziotta, *supra*, at Ex. 88, p. 248).) However, the Institute of Medicine (“IOM”) has recognized that the latency between subsequent exposure to the antigen and development of the immune response will likely be shorter due to recognition of memory

B and T cells during the primary immune response. (Ex. 98, p. 8.) He pointed to a study by Langer-Gould et al., in which researchers concluded that a vaccine can act as a “proinflammatory cofactor in individuals with subclinical autoimmunity,” such that vaccination may “hasten symptom[s] onset but not change the long-term risk of developing MS.” (Tr. 89-92 (quoting Annette Langer-Gould et al., *Vaccines and the Risk of Multiple Sclerosis and Other Central Nervous System Demyelinating Diseases*, 71 J. AM. MED. ASS’N NEUROLOGY 1506 (2014) (Ex. 102)).) He elaborated that the role of adjuvants in triggering an immune response “affirms the concept that muscle tissue is capable of mounting a rapid immune response, with antigen bearing cells quickly evident in draining lymph nodes shortly after vaccination.” (Ex. 98, pp. 9-10 (citing Frank Liang & Karin Loré, *Local Innate Immune Responses in the Vaccine Adjuvant-Injected Muscle*, 5 CLINICAL & TRANSLAT’L IMMUNOLOGY e74 (2016) (Ex. 101)); Tr. 100-03.) Dr. Tornatore further opined that vaccine-induced inflammation can aggravate underlying CNS inflammation rapidly due to the kinetics and anatomy of “draining lymph nodes and their proximity to the spinal cord.” (Ex. 98, pp. 8-11 (citing Laurent Jacob et al., *Anatomy and Function of the Vertebral Column Lymphatic Network in Mice*, 10 NATURE COMM’NS, no. 4594, 2019, at 1 (Ex. 99)); Tr. 96-100.) Thus, Dr. Tornatore asserted that Dr. Forsthuber’s conclusion that it is improbable that the flu vaccine could aggravate symptoms of TM within one or two days overlooks that petitioner had preexisting CNS inflammation prior to receiving the flu vaccine and that aggravation of CNS inflammation is “hastened” when the flu vaccine is a “pro-inflammatory cofactor,” rather than the first induction to autoimmunity. (Ex. 98, pp. 7-8; Ex. 130, p. 3.)

Regarding his reliance on case reports, Dr. Tornatore submitted that “[c]ase reports are exceedingly important teaching tools in clinical medicine given that the bedside approach to every patient is essentially a case report.” (Ex. 98, p. 6.) To demonstrate the importance of case reports, Dr. Tornatore noted that the criterion in Johns Hopkins Transverse Myelitis Center’s model diagnostic approach, which directs the consideration of recent vaccination or systemic illness, was based on the clinical experience of practitioners at Johns Hopkins that noticed a clinical history of prior vaccination within a month of presentation in around 30% of TM patients. (*Id.* (citing Chitra Krishnan et al., *Transverse Myelitis: Pathogenesis, Diagnosis and Treatment*, 9 FRONTIERS BIOSCIENCE 1483 (2004) (Ex. 100)).) He further noted that the case studies he relied upon went beyond simply recognizing a temporal relationship and further recognized “a logical sequence of cause and effect which was biologically based.” (*Id.*) Dr. Tornatore asserted that, by contrast, “epidemiology cannot disprove the presence of a rare event” and that petitioner’s case is exceptionally rare. (*Id.* at 7.) Even so, Dr. Tornatore asserted that Langer-Gould et al. provides epidemiologic evidence by noting that a vaccine can act as a “pro-inflammatory cofactor” in susceptible individuals. (*Id.* (citing Langer-Gould et al., *supra*, at Ex. 102).)

ii. Lawrence Steinman, M.D.<sup>12</sup>

Petitioner also relied on the expert opinion of Lawrence Steinman, M.D. Dr. Steinman authored five expert reports in support of petitioner's claim. (See Exs. 12, 55, 64, 75, 103.) He also testified at the entitlement hearing, during which he was proffered without objection as an expert in the fields of neurology and neuroimmunology. (Tr. 182.)

Regarding diagnosis, Dr. Steinman concurred with Dr. Tornatore's analysis and opined that petitioner most likely has TM. (Ex. 12, p. 9; Tr. 183.) He noted that petitioner's treating physicians explored several alternative diagnoses, and petitioner's testing was negative for infection, mass lesion, and vascular malformation. (Ex. 12, p. 9.) He noted that petitioner's spinal angiography was negative, meaning petitioner did not have a dural venous fistula malformation. (Ex. 55, pp. 2-3 (citing Ex. 8, p. 7).) He explained that petitioner's history of pain in his neck, upper back, and shoulders four weeks before his flu vaccination is consistent with TM. (Ex. 12, p. 9 (citing Ex. 1, p. 581).) At the hearing, Dr. Steinman clarified that "the whole picture emerged" with petitioner's difficulty walking and sensory issues around the time he was first hospitalized. (Tr. 218-19.) He added that petitioner's Solu-Medrol therapy on December 1, 2011, "might have masked the evolution of more pronounced inflammation on subsequent MRI and on any subsequent examination of the spinal fluid." (Ex. 12, p. 9; Tr. 206.) He further suggested that treaters may have performed the spinal tap too soon to reveal pleocytosis in the spinal fluid. (Tr. 207.) Thus, Dr. Steinman contended that petitioner's TM was not idiopathic as Dr. Forsthuber and Dr. Gelfand suggested. (Ex. 64, pp. 4, 8; Tr. 185, 207.)

Dr. Steinman opined that petitioner had "smoldering" myelitis as evidenced by earlier episodes of symptoms that were identical to petitioner's symptoms following his flu vaccination. (Tr. 183; Ex. 12, p. 27.) To support his opinion, he pointed to a medical history of "pain in the posterior neck and upper back and shoulders" for approximately 4 weeks prior to flu vaccination (Ex. 55, p. 2 (citing Ex. 1, p. 581); Ex. 12, p. 27) and petitioner's reports of an earlier "identical episode" (Ex. 12, p. 27 (citing Ex. 1, pp. 16, 326)). He claimed that petitioner's "earlier episodes indicate that the transverse myelitis was brewing and that his immune system was primed." (Ex. 12, p. 27.) Dr. Steinman clarified that, in using the descriptor "smoldering," he was referring to a condition that

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<sup>12</sup> Dr. Steinman received his medical degree from Harvard University in 1973. (Ex. 65, p. 1.) He is board-certified in neurology and has practiced adult and pediatric neurology at Stanford University. (Ex. 12, p. 7; Ex. 65, p. 2; Tr. 180.) For the first twenty years of his career, Dr. Steinman "saw all sorts of patients." (Tr. 180.) He specifically treated both adults and children who suffered from various forms of inflammatory neuropathy, including TM, acute disseminated encephalomyelitis, neuromyelitis optica, MS, and others. (Ex. 12, p. 7.) Although he still treats patients while attending a couple weeks per year, Dr. Steinman mostly does referrals on patients with probable neuroinflammatory diseases. (Tr. 180.) He is currently a professor of neurology at Stanford University. (Ex. 12, p. 7; Ex. 65, p. 1; Tr. 180.) Dr. Steinman's research focuses on how the immune system attacks the nervous system, and he has published on various topics involving vaccines and neurological disorders, including molecular mimicry. (Ex. 12, pp. 7-8; Ex. 65, pp. 5-45; Tr. 181-82.) He holds numerous American and European patents, including several U.S. patents relating to vaccines. (Ex. 12, p. 8; Ex. 65, pp. 2-3.)

was neither fully developed nor subclinical. (Tr. 215-16.) He also opined that petitioner's "smoldering" myelitis had been initially triggered by his prior zoster vaccination. (*Id.*; Ex. 12, p. 27.) Petitioner's November 29, 2011 antibody test was negative for zoster (Ex. 1, p. 777); however, Dr. Steinman opined that this is not dispositive. (Tr. 217.) Dr. Steinman suggested that petitioner likely had immunity to varicella-zoster due to his age. (*Id.* at 216.)

Dr. Steinman opined that it is biologically plausible that the flu vaccine can cause or significantly aggravate TM by triggering immunity to myelin lipids and proteins via molecular mimicry.<sup>13</sup> (Ex. 12, p. 10.) According to Dr. Steinman, the specific components of the 2011-12 flu vaccine, which included an H1N1 virus, can trigger an immune response to myelin proteins and various complex sugars called gangliosides.<sup>14</sup> (*Id.*; Tr. 184.) He noted that "[g]angliosides are key structures associated with the pathogenesis of inflammatory polyneuropathy," and described molecular mimicry

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<sup>13</sup> Dr. Steinman explained that molecular mimicry occurs when the same protein fragment (*i.e.*, peptide epitope) is recognized by T cell receptors that bind to slightly different portion of the self-antigen (*e.g.*, myelin basic protein). (Ex. 12, pp. 14-15.) Dr. Steinman used a computer program and bioinformatic search tool, known as BLAST, to compare a vaccine protein and a protein that is known to be targeted in a disease with the goal of determining whether there is sufficient similarity. (Ex. 75, pp. 6, 9-14, Tr. 184, 209-12.) He used a "three-step filtration system" to identify molecular mimics between the subject vaccines and antigens that are targeted in TM. (Ex. 103, pp. 5-8.) In the first step, Dr. Steinman explained that a viral peptide with homology at five amino acids within a stretch of twelve amino acids can induce clinical signs of experimental autoimmune encephalomyelitis ("EAE") in mice. (Ex. 12, p. 14 (citing Anand M. Gautam et al., *A Viral Peptide with Limited Homology to a Self Peptide Can Induce Clinical Signs of Experimental Autoimmune Encephalomyelitis*, 161 J. IMMUNOLOGY 60 (1998) (Ex. 35); Anand M. Gautam et al., *Minimum Structural Requirements for Peptide Presentation by Major Histocompatibility Complex Class II Molecules: Implications in Induction of Autoimmunity*, 91 PROCEEDINGS NAT'L ACAD. SCI. USA 767 (1994) (Ex. 36)); *see also* Ex. 64, p. 6; Tr. 210-12.) He explained that the identical amino acids need not be consecutive and that certain amino acid substitutions will have no effect on activation of a response if such variation is within a certain degree of degeneracy. (Ex. 12, pp. 14, 18-19 (citing Kai W. Wucherpfennig et al., *Structure of Human T-Cell Receptors Specific for an Immunodominant Myelin Basic Protein Peptide: Positioning of T-Cell Receptors on HLA-DR2/Peptide Complexes*, 92 PROCEEDINGS NAT'L ACAD. SCI. USA 8896 (1995) (Ex. 38); Stefan Hausmann et al., *Structural Features of Autoreactive TCR that Determine the Degree of Degeneracy in Peptide Recognition*, 162 J. IMMUNOLOGY 338 (1999) (Ex. 40)).) Dr. Steinman explained that "[d]egeneracy refers to how structurally similar amino acids can still be recognized by an auto immunogenic T cell receptor." (Ex. 12, p. 18.) He noted that Wucherpfennig et al. found that "various substitutions at key residues" did not interfere with T cell recognition of myelin basic protein." (*Id.* at 19 (citing Wucherpfennig et al., *supra*, at Ex. 38).) In the second step, the areas of alignment are filtered based on three peer reviewed papers. (Ex. 103, p. 5 (citing Anand M. Gautam et al., *supra*, at Ex. 35; Anand M. Gautam et al., *supra*, at Ex. 36; Robert Root-Bernstein, *Rethinking Molecular Mimicry in Rheumatic Heart Disease and Autoimmune Myocarditis: Laminin, Collagen IV, CAR, and B1AR as Initial Targets of Disease*, 2 FRONTIERS PEDIATRICS, Aug. 2014, at 1 (Ex. 107)).) He explained that this filtration eliminates homologies that are below the threshold for inducing clinical symptoms of neuroinflammation. (*Id.* at 5-6.) In the last step, the peptide sequences are further filtered so that only those that have been identified by the Immune Epitope Database or the Influenza Research Database remain. (*Id.*)

<sup>14</sup> In particular, Dr. Steinman relied on the fact that the vaccine petitioner received contained A/California/7/09 (H1N1)-like virus, A/Perth/16/2009 (H3N2)-like virus, and B/Brisbane/60/2008. (Ex. 12, p. 10 (citing U.S. FOOD & DRUG ADMIN., NEWS RELEASE: FDA APPROVES VACCINES FOR 2011-2012 INFLUENZA SEASON (July 18, 2011) (Ex. 23)).)

between gangliosides and *Campylobacter jejuni* (“*C. jejuni*”) as one of the best examples of molecular mimicry. (Ex. 12, p. 11 (citing C.W. Ang et al., *Structure of Campylobacter jejuni Lipopolysaccharides Determines Antiganglioside Specificity and Clinical Features of Guillain-Barré and Miller Fisher Patients*, 70 INFECTION & IMMUNITY 1202 (2002) (Ex. 26); Y. Fukami et al., *Anti-GQ1b Antibody Syndrome: Anti-Ganglioside Complex Reactivity Determines Clinical Spectrum*, EUR. J. NEUROLOGY, 2015, at 1 (Ex. 27); Lawrence Steinman, *Autoimmune Disease: Misguided Assaults on the Self Produce Multiple Sclerosis, Juvenile Diabetes and Other Chronic Illnesses. Promising Therapies are Emerging*, SCI. AM., Sept. 1993, at 107 (Ex. 28).) He cited a study by Wucherffpenig et al. that found that the flu virus shares molecular similarities with myelin basic protein and that antibodies to myelin basic protein cross-react with flu virus. (*Id.* at 14-15 (citing Wucherppfenig, *supra*, at Ex. 38).) This is important because it has been shown that immunity to myelin basic protein is related to TM (*Id.* at 14 (citing Oded Abramsky & Dvora Teitelbaum, *The Autoimmune Features of Acute Transverse Myelitis*, 2 ANNALS NEUROLOGY 36 (1977) (Ex. 33)) and immune responses to gangliosides are associated with neuroinflammation (*Id.* at 20 (citing Jennifer L. Kanter et al., *Lipid Microarrays Identify Key Mediators of Autoimmune Brain Inflammation*, 12 NATURE MED. 138 (2006) (Ex. 41); Peggy P. Ho et al., *Identification of Naturally Occurring Fatty Acids of the Myelin Sheath That Resolve Neuroinflammation*, 4 SCI. TRANSLAT’L MED., June 6, 2012, at 1 (Ex. 42)).) Dr. Steinman identified molecular mimics between the components of the 2011-12 influenza vaccine and myelin basic protein that he opined are sufficient to trigger neuroinflammation. (Ex. 75, pp. 11-12; Tr. 214.) Comparing the hemagglutinin of A/California/7/09 H1N1 and myelin basic protein, Dr. Steinman identified the sequence GTCYPGDFIDY with five of eleven identical amino acids.<sup>15</sup> (Ex. 75, pp. 11-13; Tr. 214.)

Further to this, Dr. Steinman asserted that “the zoster vaccine contains a molecular mimic to the same myelin protein that has molecular mimics in the 2011-12 vaccine.” (Ex. 12, p. 10; Tr. 184.) Specifically, Dr. Steinman found several potential

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<sup>15</sup> Following critique from respondent’s experts, Dr. Steinman defended his criteria for determining whether there is sequence homology between a protein and a self-antigen in his supplemental reports and testimony. He explained that a BLAST search is the preferred search tool of Silvanovich et al., who derided the “sliding window” approach for finding rungs of consecutive amino acids in a protein that may have immunogenicity. (Ex. 75, p. 6, 15 (citing Andre Silvanovich et al., *The Value of Short Amino Acid Sequence Matches for Prediction of Protein Allergenicity*, 90 TOXICOLOGICAL SCIS. 252 (2006) (Ex. 116)).) He further explained that he applied two peer reviewed papers, which were both published in the official journal of the American Association of Immunologists and studied the effects of a molecular mimic of five of twelve identical amino acids and required that the amino acids in the sequence be identical, but not consecutive. (Ex. 64, pp. 6-7 (citing Gautam et al., *supra*, at Ex. 35; Gautam et al., *supra*, at Ex. 36); Tr. 427.) Even under this criteria, researchers found that 40% of mice displayed clinical signs of EAE, such as paralysis, after injection with a viral peptide that had 5 of 11 identical and 3 consecutive amino acids between the virus and myelin basic protein. (Ex. 64, pp. 6-7; see Ex. 12, p. 14.) Dr. Steinman further defended his reliance on Wucherppfenig et al. by citing a paper by Ahmed et al., which found that the vaccine contain hemagglutinin, as well as “a diversity of other influenza viral antigens and egg proteins,” such as nucleoprotein. (Ex. 64, p. 7 (citing Syed Sohail Ahmed et al., *Antibodies to Influenza Nucleoprotein Cross-React with Human Hypocretin Receptor 2*, 7 SCI. TRANSLAT’L MED., July 1, 2015, at 1 (Ex. 22)); Ex. 75, pp. 15-16.) Dr. Steinman also disputed the relevance of E values beyond determining whether proteins are in a similar family. (Tr. 430.)

molecular mimics between components of the zoster vaccine and myelin basic protein, which he opined are also sufficient to induce neuroinflammation. (Ex. 12, pp. 20-23.) Specifically, Dr. Steinman identified a five of ten match and an eight of ten match with similar and identical amino acids between myelin basic protein and Zoster ORF 47, and a five of eight match between myelin basic protein and Zoster ORF 56. (Ex. 12, pp. 20-23; see *also* Ex. 75, pp. 8-11; Tr. 213-14.) He further identified the following homologies between the zoster vaccine and myelin basic protein: TKTGLPQR with a five out of ten match and SLFLLKHGLTRD with a six out of twelve match. (Ex. 75, p. 8; Tr. 214.) Dr. Steinman suggests that epitope spreading<sup>16</sup> can therefore result in a recall response, despite two different vaccines being involved. He explained that “[t]hey both have mimics of myelin basic protein and therefore by this molecular spreading, determinant spreading, you get a recall response when [petitioner] gets the influenza [vaccine].” (Tr. 195.) He explained that “epitope spreading[] can certainly explain how one myelin basic protein region on zoster could spread via this mechanism to a different region of myelin basic protein, and cause a recall response.” (Tr. 434.) Thus, based on the components contained in the zoster vaccine and flu vaccine, Dr. Steinman opined that the flu vaccine can trigger a “recall response” to myelin basic protein induced by an earlier zoster or flu vaccination.<sup>17</sup> (Ex. 12, pp. 10, 23, 27; Tr. 195, 214-16.) Dr. Steinman concluded that homology with myelin basic protein and both the zoster vaccine and the flu vaccine was sufficient to possibly provoke TM (Tr. 184, 189-90) and that petitioner’s flu vaccination likely “aggravated the smoldering symptoms initially triggered by” petitioner’s zoster vaccine approximately two months earlier (*Id.* at 215-16; Ex. 12, p. 27.).<sup>18</sup>

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<sup>16</sup> Dr. Steinman explains “epitope spreading” as a concept by which a break in tolerance to a myelin protein for one epitope precedes a break in tolerance to other components of the same myelin molecule. (Ex. 12, p. 21 (citing Eli E. Sercarz, *Arraying Autoimmunity Treatment*, 21 NATURE 1017 (2003) (Ex. 44)); see *also* Ex. 75, p. 8.) He notes that the process of epitope spreading generally takes “a few weeks” and that the “approximately two, two-and-a-half months [between receipt of the zoster and flu vaccines] . . . would have been more than enough time for a recall response to have been mustered.” (Tr. 195.)

<sup>17</sup> In his reports, Dr. Steinman suggested that petitioner may have also received the 2010-11 flu vaccine, which contained an H1N1-like virus, or otherwise had significant immunity to flu due to viral exposure, prior vaccination, or both. (Ex. 12 p. 10.) Although noting petitioner likely had immunity to flu and to hemagglutinin due to his age, his tenure in the armed forces, and Dr. Steinman’s belief that he had previously received a flu vaccine, Dr. Steinman clarified at the hearing that he was not relying on a prior flu vaccination to support his opinion regarding a recall response. (Tr. 188-89; Ex. 12, p. 24.)

<sup>18</sup> There was significant discussion in the reports regarding Dr. Steinman’s initial claim surrounding a dominant peptide in the influenza A hemagglutinin: YVKQNTLKL, which Markovic-Plese et al. found to be cross-reactive with human T cell clone, and a sequence in a component of the flu vaccine that petitioner received (A/perth/16/2009 (H3N2)): YVKQNTLKL. (Ex. 12, pp. 12-13 (citing Silva Markovic-Plese et al., *High Level of Cross-Reactivity in Influenza Virus Hemagglutinin-Specific CD4+ T-Cell Response: Implications for the Initiation of Autoimmune Response in Multiple Sclerosis*, 169 J. NEUROIMMUNOLOGY 31 (2005) (Ex. 29)).) He asserted that “this immune response triggers a cross-reactive immune response” to two myelin mimics of myelin oligodendroglia glycoprotein (“MOG”) and a myelin mimic of 2,3 cyclic nucleotide phosphodiesterase (“2,3 CNPase”). (*Id.* at 13.) In response, Dr. Forsthuber criticized Dr. Steinman’s comparison between the sequence YVKQNTLKL from the Influenza Texas/77 hemagglutinin with the YVKQNTLKL sequence from the Influenza A/perth/16/2009 virus as the “degree of similarity is completely expected” given the fact that these are the same hemagglutinin protein in two flu viruses. (Ex. B, p. 6.) He further noted that Dr. Steinman had mistaken MOG for oligodendrocyte myelin glycoprotein

Dr. Steinman opined that the time frame of symptom onset in less than 72 hours of vaccination is “consistent with what is seen in a recall response to a common antigen.” (Ex. 12, p. 2.) He explained that once a “recall response to myelin basic protein induced by earlier immunization with earlier wild-type influenza virus or wild-type zoster virus, and/or an earlier vaccine to either influenza or zoster” has mounted, “such a response could occur in as short as a day.” (*Id.*; see also Ex. 12, pp. 24-25 (citing Tiroumourougane V. Serane & Bhuvaneswari Kothendaraman, *Tuberculin Test Can Be Read After 24 Hours in Adolescent Children*, 60 J. TROPICAL PEDIATRICS 157 (2014) (Ex. 47); Lin Fan et al., *Variation of Mycobacterium Tuberculosis Antigen-Specific IFN- $\gamma$  Responses in Healthy Tuberculin Skin Test (TST)-Positive Human Subjects*, 7 PUB. LIBR. SCI. ONE e42716 (2012) (Ex. 48); T. Kardjito & J.M. Grange, *Immunological and Clinical Features of Smear-Positive Pulmonary Tuberculosis in East Java*, 61 TUBERCLE 231 (1980) (Ex. 49)) (discussing tuberculin responses that peaked within 24 hours after injection).) He cited an animal study, in which researchers found that myelin reactive lymphocytes can penetrate the CNS “within hours” and were “deep in the ‘parenchyma’ or brain substance” within 60 hours. (Ex. 12, pp. 4-6 (citing Ingo Bartholomäus et al., *Supplementary Information, Effector T Cell Interactions with Meningeal Vascular Structures in Nascent Autoimmune CNS Lesions*, 462 NATURE, at 1 (2009) (Ex. 16)); Tr. 432 (quoting Ingo Bartholomäus et al., *Effector T Cell Interactions with Meningeal Vascular Structures in Nascent Autoimmune CNS Lesions*, 462 NATURE 94, 94 (2009) (Ex. 17, p. 1)) (emphasizing that the 1-2.5 day time frame in Bartholomäus et al. was based on clinical signs of neurologic issues, but “an experimental animal is unable to tell

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(“OMGP”), which “are two completely unrelated proteins, with essentially no sequence homology, despite the similar sounding names.” (*Id.* at 7 (emphasis omitted); Ex. C, p. 8.) Although Dr. Steinman subsequently acknowledged that the sequence referenced by Markovic-Plese et al. was OMGP, not MOG, he asserted that an immune attack on OMGP, triggered by cross-reaction between the flu virus and OMGP, could worsen neuroinflammation. (Ex. 64, p. 5 (citing Xinhua Lee et al., *Oligodendrocyte Differentiation and Myelination Defects in OMGp Null Mice*, 46 MOLECULAR & CELLULAR NEUROSCIENCE 752 (2011) (Ex. 68)); see also Ex. 75, p. 5; Tr. 208-09.) However, Dr. Forsthuber asserted that Dr. Steinman’s reliance on Markovic-Plese et al. is misplaced as neither OMGP nor 2, 3 CNPase have been associated with TM. (Ex. B, p. 7; Ex. C, p. 8; Ex. D, pp. 6-7 (explaining that Lee et al. does not support Dr. Steinman position because the study specifically looked at how the absence of OMGP affected oligodendrocytes and remyelination).)

Dr. Steinman ultimately asserted that “discussion of OMGP is largely irrelevant” as he has provided “numerous molecular mimics between [myelin basic protein] and MOG and the components of the influenza vaccine and zoster vaccines.” (Ex. 75, p. 6.) At the hearing, he further disclaimed any intention of relying on MOG, instead choosing to rely on molecular mimics between myelin basic protein and the zoster and flu vaccines. (Tr. 209 (“So the good news is I’m not pushing either MOG or OMGP. We can just stick to myelin basic protein . . .”); see also Tr. 215 (“There’s also a lot of discussion . . . about MOG, but because of the error in the Markovic-Plese paper, I’m not even -- we don’t have to rely on MOG. We should just stick to the myelin basic protein mimicry between zoster and influenza.”); Tr. 214 (Dr. Steinman indicating that “we should focus on” zoster and the hemagglutinin of influenza as “myelin basic protein determinants”).) Based on his testimony, Dr. Steinman has abandoned his arguments regarding MOG, OMGP, and 2, 3 CNPase, including his suggestion of molecular mimics between the zoster vaccine and MOG. (See Ex. 12, p. 23.) Although Dr. Steinman decided to abandon these arguments at the hearing, I have still reviewed all of the arguments and evidence presented in his prior reports. However, in the interest of brevity, I will not herein address the specific arguments that Dr. Steinman subsequently disclaimed.

you whether they're having subtle neurologic signs").) As another example of how quickly the immune system responds in a recall response, Dr. Steinman cited a study by Odoardi et al., that found exposure to myelin basic protein affected T<sub>MBP-GFP</sub> cells throughout the spinal cord within about 1 hour. (Ex. 12, p. 7 (citing F. Odoardi et al., *Blood-Borne Soluble Protein Antigen Intensifies T Cell Activation in Autoimmune CNS Lesions and Exacerbates Clinical Disease*, 47 PROCEEDINGS NAT'L SCIS. 18625 (2007) (Ex. 18)).) He further cited a series of studies showing that a recall response to self-antigens can manifest "within minutes." (*Id.* at 26 (citing Rosetta Pedotti et al., *An Unexpected Version of Horror Autotoxicus: Anaphylactic Shock to a Self-Peptide*, 2 NATURE IMMUNOLOGY 216 (2001) (Ex. 51); Rosetta Pedotti et al., *Involvement of Both 'Allergic' and 'Autoimmune' Mechanisms in EAE, MS and Other Autoimmune Diseases*, 24 TRENDS IMMUNOLOGY 479 (2003) (Ex. 52); Howard L. Weiner, *The Fine Line Between Autoimmune and Allergic Encephalomyelitis*, 2 NATURE IMMUNOLOGY 193 (2001) (Ex. 53); Edwin Liu et al., *Anti-Peptide Autoantibodies and Fatal Anaphylaxis in NOD Mice in Response to Insulin Self-Peptides B:9-23 and B:13-23*, 110 J. CLINICAL INVESTIGATION 1021 (2002) (Ex. 54)).)

In further support of a proximate temporal relationship, Dr. Steinman pointed to a study by Schonberger et al., which found increased incidence of GBS within 0-1 days of vaccination when compared to later intervals. (Ex. 12, pp. 2-3, 26 (citing Lawrence B. Schonberger et al., *Guillain-Barre Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976-1977*, 110 AM. J. EPIDEMIOLOGY 105 (1979) (Ex. 13)); Ex. 64, p. 8.) He asserted that, despite exploring the relationship between GBS and the flu vaccine, Schonberger is relevant to petitioner's case. (See Ex. 75, pp. 1-2.) Dr. Steinman suggests that the blood-brain barrier of the CNS is similar to the blood-nerve barrier of the peripheral nervous system and, thus, analogy to the time frame for breakdown of the blood-nerve barrier in GBS is instructive of a reasonable time frame for breakdown of the blood-brain barrier in TM. (Ex. 12, p. 3 (citing Takashi Kanda, *Biology of the Blood-Nerve Barrier and Its Alteration in Immune Mediated Neuropathies*, 84 J. NEUROLOGY NEUROSURGERY PSYCHIATRY 208 (2012) (Ex. 14)); Ex. 75, pp. 1-2.)

In supplemental reports, Dr. Steinman defended his theory of causation against criticism from Drs. Forsthuber and Gelfand. (Ex. 64; Ex. 75.) Given that petitioner was 66 years old when he received the flu vaccine at issue, Dr. Steinman explained that he likely possessed anti-ganglioside antibodies, and the flu vaccine therefore could have triggered a recall response to these antibodies. (Ex. 64, p. 2; Ex. 75 pp. 2-3.) Dr. Steinman further stated that Dr. Forsthuber overlooked that flu hemagglutinins are "heavily glycosylated" and that the glycosylation "plays a significant role in the antigenic drift and immunogenicity." (Ex. 64, p. 3 (citing Athanasios Kossyvakis et al., *Challenges in Antigenic Characterization of Circulating Influenza A(H3N2) Viruses during the 2011-2012 Influenza Season: An Ongoing Problem?*, 53 J. CLINICAL MICROBIOLOGY 1493 (2015) (Ex. 66)).) Dr. Steinman cited an article by Tate et al. to show the importance of glycosylation of flu vaccine proteins. (*Id.* at 3-4 (citing Michelle D. Tate et al., *Playing Hide and Seek: How Glycosylation of the Influenza Virus Hemagglutinin Can Modulate the Immune Response to Infection*, 6 VIRUSES 1294 (2014) (Ex. 67)).)

## b. Respondent's Experts

### i. Jeffrey Gelfand, M.D., M.A.S.<sup>19</sup>

To defend against the claim, respondent offered an expert opinion of neurologist Jeffrey Gelfand, M.D., M.A.S. Dr. Gelfand authored three expert reports on behalf of respondent. (See Exs. A, E, I.) He also testified as the entitlement hearing, during which, he was proffered without objection as an expert in the field of neuroimmunology.<sup>20</sup> (Tr. 239, 243.)

Although he does not dispute petitioner's diagnosis of TM (Ex. A, p. 11), Dr. Gelfand opined that petitioner's flu vaccination "did not cause or aggravate his transverse myelitis to a more likely than not standard" (Tr. 244; see also Ex. E, p. 8), and that petitioner instead suffered from an acute, idiopathic TM (Ex. A, pp. 11, 20). He stated that petitioner's history of evolving cervical spinal cord syndrome, neurological examinations showing spinal cord localization, and MRI showing multifocal enhancement and a T2 hypersensitivity in the cervical cord all support a diagnosis of TM.<sup>21</sup> (*Id.* at 11.) Dr. Gelfand opined that petitioner experienced sensory dysfunction that was attributable to the spinal cord, bilateral symptoms, and sensory impairment that

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<sup>19</sup> Dr. Gelfand received his medical degree from Harvard Medical School. (Ex. A, Tab 1, p. 1; Ex. F, p. 1; Tr. 240.) He went on to complete an internship in Internal Medicine, a residency in Neurology, and a fellowship in MS and Neuroimmunology at the University of California, San Francisco ("UCSF"). (Ex. A, Tab 1, p. 1; Ex. F, p. 1; Tr. 240.) He also received a Master's in Advanced Study in Clinical Research from UCSF. (Ex. A, Tab 1, p. 1; Ex. F, p. 1; Tr. 240-41.) He is board-certified in neurology and maintains an active medical license in California. (Ex. A, Tab 1, p. 1; Ex. A, p. 2; Ex. F, p. 1; Tr. 241.) He currently works as an associate professor of clinical neurology and regularly sees patients at UCSF, and the Zuckerberg San Francisco General Hospital. (Ex. A, Tab 1, p. 2; Ex. F, p. 2; Tr. 241.) Dr. Gelfand regularly treats patients with myelitis of various causes, including TM. (Tr. 241-42.) He also works as the Director of the Clinical Fellowship Program and the Assistant Medical Director at UCSF MS and Neuroinflammation Center. (Ex. A Tab 1, p. 2; Ex. F, p. 2; Tr. 241.) Finally, Dr. Gelfand conducts clinical research that is focused on neuroinflammatory disorders. (Ex. A, p. 3; Ex. A, Tab 1, pp. 13-14; Ex. F, p. 14; Tr. 242-43.) He has published 69 peer-reviewed publications, 30 review articles, and 7 books and chapters on this subject. (Ex. F, pp. 16-24; Ex. A, Tab 1, pp. 15-20.)

<sup>20</sup> Although Dr. Gelfand was offered as an expert in neuroimmunology, he deferred to Dr. Forsthuber's more in-depth immunology opinion. (Ex. A, p. 18; see also Tr. 318-20.)

<sup>21</sup> More specifically, he explained that petitioner's presentation "are consistent with accepted diagnostic criteria" for TM, which includes (1) development of sensory, motor, or autonomic dysfunction attributable to the spinal cord; (2) bilateral symptoms; (3) sensory impairment below a certain level; (4) exclusion of extra-axial compressive etiology by neuroimaging; (5) inflammation within the spinal cord as demonstrated by pleocytosis in the CSF, elevated IgG index, or gadolinium enhancement on MRI; and/or (6) progression to nadir between 4 hours and 21 days following onset of symptoms. (Ex. A, p. 11-13; Tr. 244-78 (citing Transverse Myelitis Consortium Working Group, *Proposed Diagnostic Criteria and Nosology of Acute Transverse Myelitis*, 59 NEUROLOGY 499 (2002) (Ex. A, Tab 2)).) Although the MRI showed cervical spinal stenosis, the stenosis was not believed to be significant enough to merit surgical decompression or explain his symptoms, and a spinal dural arterio-venous fistula or other spinal vascular malformation was ruled out. (Ex. A, p. 12; Tr. 262.) Further, Dr. Gelfand opined that petitioner's B12 deficiency did not fully explain his spinal cord syndrome, although it could have magnified some of petitioner's neurologic symptoms. (Ex. A, p. 12; Tr. 262.)

progressed in a manner consistent with what is expected of an evolving spinal cord syndrome. (Tr. 247-48, 258.) That is, Dr. Gelfand submitted that petitioner's clinical syndrome evolved over several days before reaching a nadir over the course of a couple weeks, fitting the standard for what would be expected of an acute TM. (*Id.* at 278.) Regarding inflammation of the spinal cord, Dr. Gelfand explained that, while the CSF analysis revealed a mild protein elevation, there were no other CSF markers of inflammation. (*Id.* at 263; Ex. A, pp. 11-12.) Dr. Gelfand explained that elevated myelin basic protein is a nonspecific marker of an acute injury that is consistent with spinal cord injury, and the fact that it was only mildly elevated does not suggest that it was resolving. (Tr. 268-69.) He also noted that it is common for patients with monophasic conditions, such as acute, idiopathic TM, to have multifocal lesions, and "that a non-enhancing lesion could still be and often is the causative acute [TM] lesion when the rest of the pieces fit." (*Id.* at 274-76.) The monophasic characteristic of acute TM suggests that the multifocal lesions are part of the same process.<sup>22</sup> (*Id.* at 274, 287; see also Tr. 309.) Thus, Dr. Gelfand concluded that petitioner's presentation and testing supported an inflammatory cause of his symptoms and that the most appropriate diagnosis of his condition is acute, idiopathic TM with an autoimmune origin. (Ex. A, p. 13; Tr. 263, 266-67.)

Regarding timing, Dr. Gelfand indicated that the medical records suggest that petitioner first exhibited symptoms of TM on November 24, 2011, the day after his flu vaccination. (Ex. A, pp.14-16; Tr. 247-48, 291-92.) He noted that petitioner did not report any shoulder or back pain when he received his pneumococcal and zoster vaccinations on September 21, 2011. (Ex. A, p. 14 (citing Ex. 1, pp. 586-88); Ex. E, p. 3 (citing Ex. 1, pp. 587-90.) Additionally, he cited telephone encounters with petitioner's primary care clinic on September 22, 2011, September 23, 2011, September 27, 2011, and October 12, 2011, which do not document any symptoms suggestive of TM. (Ex. A, p. 14 (citing Ex. 1, p. 584); Ex. E, p. 3 (citing Ex. 1, pp. 584-85.)

While Dr. Gelfand acknowledged that, on November 28, 2011, petitioner reported an "identical" episode of neck and shoulder pain two months prior, he asserted that the information contained in the medical records does not establish that these symptoms were consistent with TM. (Ex. A, pp. 14-15; Ex. E, p. 5 (stating that "[t]here is no additional documentation provided about what symptoms made the episode 'identical'"); see also Tr. 280-81.) Specifically, he noted that there was no detail as to "the character and pattern" of the symptoms or whether petitioner experienced additional symptoms such as "sensory changes or bowel or bladder involvement to support a spinal cord

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<sup>22</sup> Dr. Gelfand explained that some of petitioner's treating neurologists were concerned about some enhancement in the cervical spine, "but on official neuroradiology final reads, there was no definite enhancement called." (Tr. 288.) However, "there was definite enhancement called overlying the parts of the thoracic cord." (*Id.*) Dr. Gelfand explained that "[t]here's nothing intrinsic that says only one part of the nervous system can be affected at a time," and concurred with Dr. Tornatore's opinion that the definite enhancement was "overlying the dorsal, the back part of the spinal cord, as opposed to being within the spinal cord itself." (*Id.* at 287-89.) Because dural arterio-venous fistula was ruled out by conventional angiogram, Dr. Gelfand opined that the definite enhancement is either prominent vessels or a component of focal inflammation, but "without follow-up imaging, I don't think we can say more." (*Id.* at 289.)

localization for those symptoms.” (Ex. A, pp. 14-15.) Dr. Gelfand also submitted that petitioner’s episode of “identical” symptoms was not typical of acute TM, explaining that “[t]he most common clinical presentation of acute transverse myelitis is an acute neurological syndrome with continued progression to nadir followed either by gradual recovery or stasis persistence of neurological deficits.” (Ex. E, p. 7; see *also* Ex. I, p. 2; Tr. 277.) He further explained that “[s]ymptoms of myelitis can sometimes appear to stutter or manifest subtly,” but this typically occurs in the context of persistent symptom progression “without rapid intervening complete remissions.” (Ex. E, p. 7.) Dr. Gelfand explained that it would be “remarkable clinically” for a patient with such significant neurologic dysfunction to not seek medical care, to not report these symptoms to any provider, and for the symptoms to spontaneously resolve without medical intervention. (Tr. 279-82, 311.) However, assuming that the court accepted petitioner’s claims of experiencing a prior episode of “identical” symptoms, Dr. Gelfand conceded that those reports “could be interpreted as consistent with myelitis.” (Tr. 304-05.) He explained that the one- to two-week time frame “would likely be attributable to a single event of TM;” however, a one- to two-month time frame “would fall far outside the expected onset to nadir time frame typical of acute TM.” (Ex. E, p. 8; Tr. 279-80.) The latter point is important because there is no evidence that petitioner had recurrent TM. (Ex. E, pp. 7-8.) Thus, Dr. Gelfand ultimately disagreed that petitioner had a preexisting smoldering myelitis. (Ex. A, p. 19; Tr. 278.) However, Dr. Gelfand acknowledged that, if the court credits petitioner’s reports of a prior episode, regardless of what time frame was believed, then onset of petitioner’s TM would have predated his flu vaccine. (Tr. 306-07.)

Although Dr. Gelfand initially described neck and shoulder pain as a new symptom as of November 23, 2011 (Tr. 293-95 (citing Ex. 1, pp. 591, 597)), and as “clearly consistent” with TM (Ex. A, p. 15), he later qualified that “[n]eck and back pain are also very common complaints that can be ascribed to many different etiologies, and those symptoms are not specific for any one etiology.” (Ex. E, p. 7; Tr. 296). He elaborated that it is possible for neck and shoulder pain to have a cervical spinal localization, but “in the absence of other features, [he did] not believe that that was reflective of an active myelitis to a more likely than not standard.” (Tr. 248-49, 296; Ex. E, p. 7.) Although he provided, by way of example, descriptions of pain that would allow a clinician to distinguish between neuropathic symptoms and musculoskeletal pain, Dr. Gelfand testified that “[p]ain is an inherently subjective human experience,” and opined that it was reasonable for petitioner’s primary care physician to conclude that petitioner’s neck and shoulder pain on November 23, 2011, had a musculoskeletal etiology. (Tr. 249-51; see *also* Tr. 296 (“Soreness is a relatively nonspecific or vague term, so it really depends on what is meant by soreness.”); Tr. 326-28 (discussing certain records of shoulder pain that demonstrate the clinical complexity of distinguishing between new symptoms and comorbidities).) He explained that “one of the challenges with interpretation [of the medical records] is the limited clinical description that is available.” (Tr. 297.) Dr. Gelfand testified that, even “with the benefit of hindsight and review of the record, I think that the description is -- what we have of it is relatively nonspecific to invoke a neuropathic cause . . . given the available medical record.” (*Id.* at 251.) Additionally, the physical examination on November 23, 2011,

revealed tenderness in the neck and back muscles. (Ex. A, p. 15. (citing Ex. 1, pp. 581-83).) Although he acknowledged that soreness is generally accepted as “within the spectrum of pain and discomfort” (Tr. 292), Dr. Gelfand opined that the soreness/tenderness documented was more suggestive of a muscular cause and noted that no other neurological symptoms were reported. (Ex. A, p. 15. (citing Ex. 1, pp. 581-83); see also Ex. E, p. 4 (concluding that “[p]etitioner’s symptoms at that time were muscular in nature”); Tr. 335-36 (citing Ex. 1, pp. 591-92).) However, he also concurred with the radiology report that assessed petitioner as having degenerative disc disease, rather than compressive myelopathy. (Tr. 259.) Ultimately, Dr. Gelfand admitted that there is “no other explanation in the record for shoulder pain in late November . . . beyond the myelitis.” (*Id.* at 298.)

Regarding petitioner’s inability to sense the need to defecate, Dr. Gelfand opined that, based on the medical record as a whole, this symptom was more likely than not a chronic symptom that predated the onset of petitioner’s TM. (Tr. 252-53, 257.) He referenced a September 21, 2011 encounter, during which it was noted that petitioner “felt the urge for bowel movement” had been “impaired” since his earlier surgery. (*Id.* at 254-55 (citing Ex. 1, pp. 597-99).) He cited another encounter from April 2012, in which it was noted that this symptom predated onset of petitioner’s TM. (*Id.* at 256-57 (citing Ex. 1, p. 174).) However, Dr. Gelfand admitted that the lack of ability to sense the need to defecate could be a precursor to a later incontinence as a symptom of a spinal cord dysfunction in the correct time frame and clinical context. (*Id.* at 254, 257-58.) He further acknowledged that petitioner’s symptom worsened and eventually evolved to include prominent neurogenic bowel symptoms. (Tr. 256-57 (citing Ex. 1, p. 174).)

Dr. Gelfand opined that petitioner’s TM “is most convincingly and compellingly documented with the rapid onset and progression of severe shoulder pains with sand-like sensory change (a neuropathic quality) and weakness with rapidly progressive symptoms localizable to the cervical spinal cord on or around November 24, 2011.” (Ex. E, p. 8.) Dr. Gelfand emphasized that the description of sand in the shoulders “sounds different from the much vaguer descriptions of pain documented previously.” (Ex. A, p. 15.) He stated that petitioner’s reported symptoms on November 25 and 28, 2011, confirm that he was experiencing symptoms of TM at that time. (*Id.* at 15-16 (citing Ex. 1, pp. 565, 572, 579).) He opined that the non-enhancing lesions seen on MRI further confirm myelitis. (Tr. 308.) Thus, based on his review of the medical records, Dr. Gelfand placed the onset of petitioner’s TM at one day post-vaccination on November 24, 2011. (*Id.* at 247-48; Ex. A, p. 15.) However, Dr. Gelfand conceded that petitioner was not seen by a doctor at any point between when he received the flu vaccine on November 23, 2011, and when he presented to the ER on November 28, 2011. (Tr. 300-01.) He explained that, despite the lack of medical records during that time frame, he credited the history provided by petitioner on November 28, 2011, which correlated with physical examination findings. (*Id.*) Thus, Dr. Gelfand opined that onset of petitioner’s TM was likely November 24, 2011, but his symptoms in the following days confirm that petitioner’s documented neck and shoulder pain on November 24, 2011, was associated with an evolving neuropathic syndrome. (*Id.* at 297-98.)

In response to Dr. Tornatore's report, Dr. Gelfand challenged the proposition that the non-enhancing T2 lesions seen on petitioner's MRI indicates that the lesion was at least two- to three-weeks old (Ex. E, pp. 9-10), and instead opined that the lesions likely started no earlier than November 24, 2023, or five days before the MRI (Tr. 307). Dr. Gelfand disputed the relevance of the literature Dr. Tornatore relied on to support his opinion. (Ex. E, pp. 9-10.) He explained that neither the Lai study nor the Cotton study analyzed spinal cord MRIs or spinal cord lesions. (*Id.* at 9 (citing Lai et al., *supra*, at Ex. 96; Francois Cotton et al., *supra*, at Ex. 97).) Additionally, he noted both studies examined patients with MS, not acute TM. (*Id.*) Dr. Gelfand noted that studies focused on spine imaging in acute TM cases have found "varied patterns of gadolinium enhancement on baseline MRI." (*Id.* at 10 (citing E. Bulut et al., *MRI Predictors of Recurrence and Outcome After Acute Transverse Myelitis of Unidentified Etiology*, 40 AM. J. NEURORADIOLOGY 1427 (2019) (Ex. E, Tab 3); J. de Seze et al., *Idiopathic Acute Transverse Myelitis: Application of the Recent Diagnostic Criteria*, 65 NEUROLOGY 1950 (2005) (Ex. E, Tab 4)).) He opined that the non-enhancing lesions cannot be dated with any precision, given this variability. (Tr. 275, 314-15.) Although Dr. Gelfand explained that the Transverse Myelitis Consortium Working Group's proposed diagnostic criteria was developed to aid in identifying the etiology of a condition, rather than to understand the timing (*Id.* at 266-67), he further noted that the criteria for TM do not require contrast enhancement on spinal MRI (*Id.* at 260; see also Ex. E, p. 10). He explained that "enhancement is not always present when a patient has a bona fide acute transverse myelitis" (Tr. 272-73 (citing Bulut et al, *supra*, at Ex. E, Tab 3)), and that, in the case of monophasic acute TM, non-enhancement can mean that the lesion is older or that the MRI is not uncovering a break in the blood-brain barrier due to the limitations of MRI technology (*Id.* at 275-76, 285-86). However, he explained that it is generally understood that an autoimmune myelitis "takes time to build" and an immune process was likely evolving "for some time." (*Id.* at 317-18, 321-22.) He further acknowledged that, if the lesions were present on November 23, 2011, the date of vaccination, then petitioner likely had TM at that time. (*Id.* at 307-08.)

Concerning the lack of inflammatory markers in the CSF, Dr. Gelfand acknowledged that there are some clinical contexts in which a lumbar puncture can be performed too early in an inflammatory syndrome to reveal the true extent of the inflammation. (Tr. 267.) However, he disagreed with Dr. Tornatore's suggestion that the blood-brain barrier healed, trapping the inflammation inside and resulting in the absence of other clinical signs of inflammation. (*Id.* at 283.) In response to my question regarding whether there would typically be a correlation between symptom progression and lesion enhancement, Dr. Gelfand opined that, in the context of an acute inflammatory process, it is counterintuitive for someone to experience a dramatically worsening condition that is temporally associated with non-enhancing lesions. (*Id.* at 283-85.) And, although he testified that clinicians assume that lesions were enhanced at some point in their course, he qualified his opinion by again acknowledging that, in the case of an acute TM, there may not be enhancing lesions on MRI for a number of reasons, including that the lesion is too small or too subtle, or that the MRI is not sensitive enough to detect enhancement. (*Id.* at 284-86.)

Dr. Gelfand disagreed with Dr. Steinman's causal theory and opinion regarding an appropriate time frame for onset of TM following vaccination. (Ex. A, pp. 13-20.) Given Dr. Gelfand's opinion that petitioner's TM first manifested on November 24, 2011, he stated that a one-day interval between vaccination and onset "would be too soon to invoke a post-influenza vaccination myelitis based purely on a molecular mimicry theory." (*Id.* at 17.) He referenced a review that described the minimum time interval between flu vaccination and onset as being seven days. (*Id.* (citing N. Agmon-Levin et al., *Transverse Myelitis and Vaccines: A Multi-Analysis*, 18 LUPUS 1198 (2009) (Ex. A, Tab 5)).) Dr. Gelfand also disputed the applicability of the Schonberger article (*supra*, at Ex. 13), noting that the article explored the flu vaccine's relationship to GBS, an inflammatory polyneuropathy/radiculopathy, not TM, which is an inflammatory spinal cord syndrome with a distinct disease process from GBS. (*Id.* at 18-19.) Instead, Dr. Gelfand pointed to two studies, which found that the measurable risk myelitis following flu vaccination was "extremely low." (*Id.* at 19 (citing Langer-Gould et al., *supra*, at Ex. 102; James D. Nordin et al., *Maternal Safety of Trivalent Inactivated Influenza Vaccine in Pregnant Women*, 121 OBSTETRICS & GYNECOLOGY 519 (2013) (Ex. A, Tab 9)).) Although he conceded that it is possible for myelitis to be aggravated, he explained that "it depends on the specifics of the theory being proposed." (Tr. 324.) Dr. Gelfand ultimately opined that the evidence is insufficient to support that the flu vaccine more likely than not aggravated petitioner's TM.<sup>23</sup> (*Id.*; see also Ex. E, p. 12.)

ii. Thomas Forsthuber, M.D., Ph.D.<sup>24</sup>

Dr. Forsthuber authored six expert reports in support of respondent's position in this case. (See Exs. B-D, G-H, J.) He also testified at the entitlement hearing during which he was proffered without objection as an expert in the field of immunology. (Tr. 339, 345.) A significant portion of Dr. Forsthuber's opinion includes his disagreement that molecular mimicry is a plausible causal theory. However, because I did not find it necessary to reach that question in order to resolve this case, it is not necessary to summarize Dr. Forsthuber's more detailed rebuttal to that proposed mechanism of injury.

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<sup>23</sup> In his second supplemental report, Dr. Gelfand suggested that there were two possible scenarios in this case. In his opinion, the "most likely scenario" places onset at one-day following vaccination. (Ex. I, p. 3.) However, he suggested that there is another "possible scenario, which requires some degree of speculation given the available clinical record." (*Id.*) In this second scenario, Dr. Gelfand suggested that "petitioner's TM began approximately two weeks prior to his flu vaccination, and worsened one day after his flu vaccination." (*Id.*) Dr. Gelfand ultimately maintained that petitioner's flu vaccination did not aggravate his TM to a more likely than not standard. (*Id.*)

<sup>24</sup> Dr. Forsthuber received his medical degree from the University of Tübingen. (Ex. B, Tab. 1, p. 1.) He is board-certified in anatomical and clinical pathology. (Ex. B, p. 1; Tr. 340.) He specializes in immunology, specifically autoimmune disease research and T cell immunology. (Ex. B, p. 1.) He spends about sixty percent of his time conducting medical research. (Tr. 343.) He has published "a little over a hundred" peer-reviewed publications and "a couple of book chapters." (*Id.* at 343; Ex. K, pp. 24-35.) He is currently employed as a professor of immunology and endowed chair of biotechnology at the University of Texas at San Antonio as well as an adjunct professor of pathology, microbiology, and immunology at the University of Texas Health Sciences Center, San Antonio. (Ex. B, p. 1; Tr. 339.)

Dr. Forsthuber explained that MS and TM are comparable neuroinflammatory conditions. (Ex. G, p. 4.) He noted that researchers have studied whether the flu vaccine can induce T cell responses to myelin basic protein in MS patients and found that flu-vaccinated MS patients can mount immune responses against flu but not against myelin basic protein. (Ex. H, p. 17 (citing N.F. Moriabadi et al., *Influenza Vaccination in MS: Absence of T-Cell Response Against White Matter Proteins*, 56 NEUROLOGY 938 (2001) (Ex. H, Tab 15)).) That said, Dr. Forsthuber explained that “there is no reliable evidence that a vaccine given during a flare induces MS or makes MS flares worse, and the advice to delay vaccination is given out of abundance of caution.” (*Id.* at 20.) He disagreed with Dr. Tornatore’s reliance on Langer-Gould et al. (*supra*, at Ex. 102), noting that researchers found the flu vaccine neither increased the risk of MS (or any other CNS demyelinating syndrome) nor accelerated or aggravated relapses. (*Id.*) Further refuting Dr. Tornatore’s claims, Dr. Forsthuber cited a study by Michielsens et al., in which researcher observed MRI studies of MS patients before and after flu vaccination. (*Id.* (citing 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) (Ex. H, Tab 16)).) The study concluded that vaccination had no short-term clinical or subclinical effect on MS activity. (*Id.*)

Regarding the timeframe, Dr. Forsthuber opined that it was highly unlikely for an individual to manifest disease within a one-day time interval after vaccination. (Ex. B, p. 20.) Dr. Forsthuber noted that the Bartholomäus study (*supra*, at Ex. 17) does not demonstrate onset of disease before three days post-vaccination. (*Id.* at 18-20; Tr. 411-13.) He explained that Dr. Steinman relied on studies that looked at T cells in “passive” EAE, but this model creates an immune response that is “completely unlike” the immune response that follows vaccination. (Ex. B, p. 18; Tr. 413.) He described his own study, in which autoimmune demyelinating disease was induced by immunization and onset of clinical signs of EAE coincided with an increase in inflammatory cells in the CNS “approximately 10-11 days after active immunization” with disease peak “approximately one week later, i.e. by 15-21 days.” (Ex. B, pp. 18-19 (citing Rebecca A. Sosa et al., *The Kinetics of Myelin Antigen Uptake by Myeloid Cells in the Central Nervous System during Experimental Autoimmune Encephalitis*, 191 J. IMMUNOLOGY 5848 (2013) (Ex. B, Tab 13).) Additionally, Dr. Forsthuber challenged the relevance of the Schonberger article (*supra*, at Ex. 13) to this case, noting that the article focused on GBS, which is different from TM in clinical features, pathogenesis, diagnostic features, and efficacy of treatments. (Ex. B, p. 18 (citing Chitra Krishnan et al., *Transverse Myelitis: Pathogenesis, Diagnosis and Treatment*, 9 FRONTIERS BIOSCIENCE 1483 (2004) (Ex. B, Tab 2)); see also Ex. C, p. 1.)

In response to Dr. Steinman’s recall response theory, Dr. Forsthuber opined that the flu vaccine cannot activate a recall response against an earlier zoster vaccine. (Ex. B, pp. 17-19.) Dr. Forsthuber explained that Dr. Steinman’s causal theory turns on a meaningful relationship between the zoster vaccine and the flu vaccine because, without such relationship, there is no way for the flu vaccine to have activated zoster

specific T cells. (Tr. 400-01.) He explained that, in order for the flu vaccine to induce memory T cells from the prior zoster vaccination, the flu vaccine would need “to contain a peptide that is pretty much identical” to the peptide in the zoster vaccine that induced a T cell response against myelin basic protein. (*Id.* at 401.) Dr. Forsthuber noted that, although Dr. Steinman provided peptides in the zoster vaccine and in the flu vaccine that could have sequence homology to myelin basic protein, he did not compare those peptides to each other. (*Id.*) Dr. Forsthuber compared the peptides from the zoster and flu vaccines and found that those peptides “have essentially no similarity.” (*Id.*) Dr. Forsthuber stressed that there is no evidence that the flu vaccine can recall varicella-zoster immunity as the flu vaccine “does not provide protection against a varicella-zoster virus infection and vice versa,” and as such, “there is no significant sequence homology between these unrelated viruses.” (Ex. B, p. 19 (emphasis omitted).) Dr. Forsthuber emphasized that Dr. Steinman suggests the concept of epitope spreading to explain how the flu vaccine could have reacted to additional epitopes that were spread as a result of the zoster vaccine, even if the flu vaccine does not cross-react with an epitope from the zoster vaccine; however, Dr. Forsthuber opined that it is “very difficult to prove epitope spreading in humans” and that Dr. Steinman has not substantiated this theory. (Tr. 403-05, 409.) He explained that epitope spreading requires “substantial autoimmune disease” to release enough antigens that they will “become immunogenic targets for a new set of autoimmune T cells.” (*Id.* at 405.) He further explained that, in humans, this process can take months. (See *id.* at 410-11.) Dr. Forsthuber also challenged Dr. Steinman’s claims that the zoster vaccine induced a “smoldering myelitis.” (Ex. H, p. 2.) He explained that two doses of the varicella-zoster vaccine are necessary to provide adequate immunity, and it is questionable whether petitioner’s single dose was sufficient to produce a meaningful antibody and/or immune response, especially in light of his negative varicella-zoster antibody titer. (*Id.* (citing J Breuer, *Vaccination to Prevent Varicella and Shingles*, 54 J. CLINICAL PATHOLOGY 743 (2001) (Ex. H, Tab 1)).)

Even if there was a recall response, Dr. Forsthuber suggested that it could not result in an immune response in 24 hours. Dr. Forsthuber provided a detailed explanation of the development of a recall response following vaccination and concluded that it takes approximately 4-5 days for an antibody recall response to form. (Ex. H, pp. 2-5 (citing Jens Wrammert et al., *Rapid Cloning of High-Affinity Human Monoclonal Antibodies Against Influenza Virus*, 453 NATURE 667 (2008) (Ex. H, Tab 3); Rebecca J. Cox et al., *An Early Humoral Immune Response in Peripheral Blood Following Parenteral Inactivated Influenza Vaccination*, 12 VACCINE 993 (1994) (Ex. H, Tab 4); Christopher D. Scharer et al., *Plasma Cell Differentiation is Controlled by Multiple Cell Division-Coupled Epigenetic Programs*, 9 NATURE COMM’NS 1698 (2018) (Ex. H, Tab 5); Stuart G. Tangye et al., *Intrinsic Difference in the Proliferation of Naive and Memory Human B Cells as a Mechanism for Enhanced Secondary Immune Responses*, 170 J. IMMUNOLOGY 686 (2003) (Ex. H, Tab 6)).) He explained that, in line with the time frame for antibody response after re-vaccination with the flu vaccine, it takes about 5-8 days “after boosting of memory B cells from the previous exposure until antibody titers in the blood show a significant rise.” (*Id.* at 5 (citing Scharer et al., *supra*, at Ex. H, Tab 5; Florian Krammer et al., *Antibody Responses in Seropositive Persons*

*After a Single Dose of SARS-CoV-2 mRNA Vaccine*, 384 NEW ENG. J. MED. 1372 (2021) (Ex. H, Tab 7)).) He explained that, even in the case of cell-mediated skin reaction to tuberculin injection, the infiltration of skin with inflammatory T cells still takes about 1-2 days. (Ex. B, p. 19; see also Ex. C, pp. 14-15.) Even assuming that epitope spreading was underway, Dr. Forsthuber opined that this process does not support an onset within 24 hours either. (Tr. 410-11.)

Dr. Forsthuber criticized Dr. Tornatore's reliance on case reports and reviews of case reports that observed TM following vaccination with various vaccines. (Ex. G, p. 1; Ex. H, p. 21.) Dr. Forsthuber explained that the information provided by these sources is limited to a temporal relationship and that they overlooked critical confounding factors. (Ex. G, p. 1.) For instance, the claims of the Akkad study were later called into question when it was suggested that the patient may have had mycoplasma infection prior to onset of TM. (*Id.* at 1-2 (citing Akkad, *supra*, at Ex. 86); Christopher S. Ambrose et al., *A Case Report of Transverse Myelitis Following Influenza Vaccination*, 68 ARCHIVES NEUROLOGY 1085 (2011) (Ex. 87)).) Similarly, onset of the Korn-Lubetzki patient's TM was preceded by a two-day history of fever, suggesting an infectious condition temporally related to the patient's TM. (*Id.* at 2 (citing Korn-Lubetzki et al., *supra*, at Ex. 92).) Dr. Forsthuber pointed out that the IOM has concluded that the "epidemiologic evidence was insufficient or absent to assess an association between influenza vaccine and TM," and that studies reporting onset of TM following vaccination, including Bakshi & Mazziotta (*supra*, at Ex. 88) and Nakamura et al. (*supra*, at Ex. 93), do not provide evidence beyond a temporal association. (*Id.*) Dr. Forsthuber cited two large studies that he indicated found no association between the flu vaccine and TM. (*Id.* (citing James D. Nordin et al., *Maternal Safety of Trivalent Inactivated Influenza Vaccine in Pregnant Women*, 121 OBSTETRICS & GYNECOLOGY 519 (2013) (Ex. G, Tab 4); Roger Baxter et al., *Acute Demyelinating Events Following Vaccines: A Case-Centered Analysis*, 63 CLINICAL INFECTIOUS DISEASES 1456 (2016) (Ex. G, Tab 5)).) Dr. Forsthuber further asserted that the flu vaccine has not been associated with MS, a condition that is related to TM, explained that the National Multiple Sclerosis Society recommend annual vaccination of MS patients with the inactivated seasonal flu vaccine. (*Id.*) The French MS society concurred, concluding that "the available data on seasonal influenza vaccination does not support an increased risk of relapse and disability in MS patients." (*Id.* at 2-3 (citing Christine Lebrun et al., *Immunization and Multiple Sclerosis: Recommendations from the French Multiple Sclerosis Society*, 31 MULTIPLE SCLEROSIS & RELATED DISORDERS 173 (2019) (Ex. G, Tab 6)).)

Regarding Dr. Tornatore's fertile field theory and reliance on Talaat et al. (*supra*, at Ex. 127), Dr. Forsthuber explained that the study was not reliable due to faulty methodology. He opined that the authors did not perform scientifically reliable and generally accepted calculations and instead used standard deviations that were too high to properly determine statistical significance. (Ex. J, p. 3.) He further criticized the lack of unvaccinated control group, which is necessary to control for random variations in cytokine/chemokine levels in the subjects, as "even minimal changes may seemingly appear statistically significant in lieu of proper groups sizes based on power calculations." (*Id.* at 3-4.) This failure is significant because the study observed

cytokine and chemokine levels that were similar to or lower than what can be observed in healthy individuals. (*Id.*) Finally, Dr. Forsthuber noted that there was no way of knowing whether the cytokine and chemokine levels were the result of the vaccine, given that there were significant differences in injection site pain/myalgia before the vaccination and at least one subject may have had concomitant conditions. (*Id.* at 4.) Even if reliable, “the slight changes in the levels of serum cytokines reported by Talaat et al. are irrelevant for the fertile field concept.” (*Id.* at 2.) Dr. Forsthuber explained that the study observed cytokine and chemokine levels that were similar to or lower than what would be observed in healthy individuals, and much lower than what would be observed in autoimmune diseases or required for activation of immune cells. (*Id.* at 3, 7-11.) Some cytokine levels actually decreased post-vaccination, while there was “a significant increase in the powerful anti-inflammatory cytokine IL-10 in the serum, which would counter-regulate the effects of proinflammatory cytokines on immune cells.” (*Id.* at 2.) Moreover, the results showed that cytokines thought to be important in TM are either unaffected or decreased after vaccination. (*Id.* at 11 (citing Puneet Dixit et al., *Cytokines and Matrix Metalloproteinases in the Cerebrospinal Fluid of Patients with Acute Transverse Myelitis: An Outcome Analysis*, 65 INFLAMMATION RESEARCH 125 (2016) (Ex. J, Tab 3)).) Dr. Forsthuber further explained that it took 10 days to develop an autoimmune disease when testing the fertile field concept by immunizing animals with a “strong adjuvant” that has a “highly inflammatory nature,” “severe adverse effects,” and “cannot be used in humans.” (*Id.* at 13-15 (citing Diethilde J. Theil et al., *Viruses Can Silently Prime for and Trigger Central Nervous System Autoimmune Disease*, 7 J. NEUROVIROLOGY 220 (2001) (Ex. J, Tab 11); Matthias G. von Herrath et al., *Microorganisms and Autoimmunity: Making the Barren Field Fertile?*, 1 NATURE REVS.: MICROBIOLOGY 151 (2003) (Ex. J, Tab 12)).)

Moreover, Dr. Forsthuber disputed Dr. Tornatore’s comparison of natural flu infection and vaccines using live attenuated flu virus with the inactivated flu vaccine received by petitioner as vaccines use live attenuated virus, not “live attenuated antigens.” (Ex. G, p. 3 (emphasis omitted).) Dr. Forsthuber further disputed Dr. Tornatore’s assertion that the response to vaccination is similar to the response to infection because it overlooks fundamental differences between the two. (*Id.* at 3-4.) For instance, the flu infection enters through the upper respiratory tract and induces local and systemic protective immunity by generating CD+8 cytotoxic T cells, CD4+ T cells, and antibodies directed against the flu virus, resulting in profound effects on the immune cells in the lungs. (*Id.* at 3.) On the contrary, the inactivated flu vaccine induces a systemic immune response primarily via protective antibodies; however, the inactivated flu vaccine antigens “do not replicate and are poor at inducing cellular immune responses, including CD+8 T cells response.” (*Id.* (citing Daniel F. Hoft et al., *Live and Inactivated Influenza Vaccines Induce Similar Humoral Responses, but Only Live Vaccines Induce Diverse T-Cell Responses in Young Children*, 204 J. INFECTIOUS DISEASES 845 (2011) (Ex. G, Tab 7)).)

Finally, Dr. Forsthuber challenged Dr. Tornatore’s claims regarding a proximate temporal relationship between petitioner’s vaccination and onset of his TM. (Ex. G, pp. 4-8.) He began by noting that most case reports on the association between TM and flu

vaccination have reported an onset of 7 days post-vaccination, at the earliest. (*Id.* at 4 (citing N Agmon-Levin et al., *supra*, at Ex. A, Tab 5).) Dr. Forsthuber acknowledged that the case report by Akkad et al. (*supra*, at Ex. 86) reported an onset that was outside of this time frame but asserted that the report “is not a reliable case report.” (*Id.* at n. 4.) He pointed to a study finding onset of clinical signs of EAE approximately 10-11 days following immunization with autoantigens, with a disease peak approximately 15-21 days post-immunization. (*Id.* at 4-5 (citing Stefan Bittner et al., *Myelin Oligodendrocyte Glycoprotein (MOG<sub>35-55</sub>) Induced Experimental Autoimmune Encephalomyelitis (EAE) in C57BL/6 Mice*, 86 J. VISUALIZED EXPERIMENTS e51275 (2014) (Ex. G, Tab 13); Niannian Ji et al., *Anaphylaxis and Mortality Induced by Treatment of Mice with Anti-VLA-4 Antibody and Pertussis Toxin*, 186 J. IMMUNOLOGY 2750 (2011) (Ex. G, Tab 14)).) Dr. Forsthuber provided a detailed explanation of the time frame for a primary immune response. (*Id.* at 5-7; Tr. 346-50.) He asserted that, following vaccination, it takes approximately 24-36 hours for the first antigen-specific T cells to become activated in the lymph nodes. (Ex. G, p. 6.) It takes a further 3 days for T cell immune responses to become detectable in the regional lymph nodes. (*Id.* at 6-7.) Similarly, it takes about 2-3 days for B cells to become activated and produce detectable levels of IgM antibodies, with peak levels after about 4-7 days and a decline to minimal levels after about 2 weeks. (*Id.* at 7.) IgG antibodies, which have stronger binding to target antigens, “peak approximately 2 weeks after infection/antigen counter.” (*Id.*) This extensive adaptive immune response upon initial encounter creates a secondary (memory) immune response that is accelerated and less severe when the pathogen is re-encountered. (*Id.*) However, Dr. Forsthuber noted that “it will still take a few days for a notable immune response to develop” because that memory T and B cells must become activated and expand before they can generate an effective immune response. (*Id.* at 7-8; Tr. 416-18 (suggesting a time frame of at least five days to mount a memory B cell response).) He further noted that the time frame for immune response is different from the time frame for onset of TM as it takes times for the autoimmune T cells to proliferate and migrate to the CNS/spinal cord, damaging nerve and other cells and inducing clinical symptoms of TM. (Ex. G, p. 8.) Dr. Forsthuber suggested that this additional time frame “is probably best estimated at several days and up to a few weeks” after an autoimmune response has formed on a cellular level. (*Id.*) He noted that Liang & Loré (*supra*, at Ex. 101) “fully support” his proposed time frame. (Ex. H, pp. 22-24.) Thus, Dr. Forsthuber opined that onset of petitioner’s TM was too soon to be associated with an immune response to his flu vaccination. (Ex. G, p. 8.)

## V. Analysis

Petitioner contends that his flu vaccination significantly aggravated his TM. (ECF No. 144, pp. 1, 13.) He argues in the alternative that his TM was caused-in-fact by the subject flu vaccination. (*Id.*) I will first address his significant aggravation claim under the six part *Loving* test. Specifically, under *Loving* prongs one through three, I first address the parties’ factual contentions and find that petitioner suffered a monophasic acute TM with an onset that predated his vaccination. Taking *Loving* prong five out of order, I further explain why there is no evidence to demonstrate that the vaccine affected this condition. Turning to *Loving* prongs four and six, I assume for argument’s

sake that petitioner's theories of causation are viable and turn directly to *Loving* prong six, under which analysis I conclude that petitioner's theories of causation cannot be reliably invoked to explain a significant aggravation of TM occurring within 24 hours of vaccination. Finding that petitioner has not met his burden of proof for a significant aggravation claim, I then briefly confirm that his alternative cause-in-fact claim likewise fails for some of the same reasons, especially the timing of onset. This case is complex insofar as petitioner had an atypical presentation and the expert opinions were premised on many differing factual assumptions in need of resolution. However, the complete analysis below finds that, regardless of whether petitioner's TM initially predated the flu vaccine at issue, the one-day onset of post-vaccination symptoms remains dispositive under either a *Loving* or *Althen* analysis.

#### a. *Loving* Prong One

The first *Loving* prong involves an examination of petitioner's pre-vaccination condition. *Loving*, 86 Fed. Cl. at 144. Although the parties agree petitioner ultimately suffered TM, the parties dispute whether petitioner suffered TM prior to the subject flu vaccination on November 23, 2011. (ECF No. 144, pp. 15-23; ECF No. 143, pp. 9-10.) Petitioner asserts that his TM pre-dated his November 23, 2011 flu vaccination in a "smoldering" form and that the initial onset of that condition occurred "in late October-early November 2011." (ECF No. 144, pp. 15-23.) Respondent disagrees, contending that onset of petitioner's TM occurred the day after his vaccination on November 24, 2011. (ECF No. 143, pp. 11-12.)

Resolving this difference requires an examination of four factual questions: (i) whether petitioner's November 23 report of neck, upper back, and shoulder pain is a symptom of TM or a musculoskeletal complaint; (ii) whether petitioner's November 23 report of an impaired ability to sense the need to defecate is a symptom of TM or of pre-existing gastrointestinal issues; (iii) what, if any, significance should be placed on petitioner's later reports of a prior episode of identical symptoms; and (iv) how likely, if at all, is it that petitioner's later discovered non-enhancing spinal lesions pre-dated his vaccination. After addressing each of these points in turn, it is necessary to briefly discuss (v) in conclusion how they are interrelated.

##### i. Neck, upper back, and shoulder pain

On November 23, 2011, the date petitioner received his flu vaccination, he reported a four-week history of pain in the posterior neck, back, and shoulders. (Ex. 1, pp. 581-83.) He denied any preceding injury and reported that his symptoms were improving without specific treatment. (*Id.* at 581.) This was noted to be a new problem. (*Id.*) Although his primary care physician determined this pain "seems" to be musculoskeletal in etiology (*Id.* at 582-83), she did not at that time have the benefit of knowing what petitioner's subsequent clinical course would entail. Additionally, while a neurologic exam was documented relative to petitioner's lower extremities, physical exam of the neck and back was limited to noting tenderness over the trapezius and

cervical paraspinal muscles. (*Id.* at 582.) Therefore, little if anything confirms any musculoskeletal explanation for these symptoms.

On petitioner's behalf, both Drs. Tornatore and Steinman persuasively opine that this new symptom was associated with petitioner's TM, given his overall subsequent history. (Tr. 33-34, 230.) Dr. Tornatore in particular explained that neurologic symptoms are sometimes misdescribed as musculoskeletal pain (Ex. 81, pp. 17-18) and that petitioner's neck and upper back pain were otherwise a feature of his post-vaccination condition, which is undisputed as a presentation of TM (Tr. 114). On behalf of respondent, Dr. Gelfand attempts to tease out a musculoskeletal etiology of petitioner's reported shoulder and neck symptoms based on the specific descriptors utilized by petitioner's primary care physician. (Ex. A, p. 15; Tr. 249-50, 300.) However, Dr. Gelfand concedes that neck and shoulder pain can have a cervical spine localization, even if he would not diagnose an active myelitis based on this symptom alone. (Ex. E, p. 7; Tr. 248-49.) Notably, when petitioner later presented for care of what was ultimately determined to be TM, he reported that his symptoms began with increased neck and shoulder soreness. (Ex. 1, p. 565.)

ii. Impaired ability to sense the need to defecate

Petitioner's November 23, 2011 encounter record indicates, *inter alia*, that he was experiencing a "lack of ability to sense the need to defecate," which his experts interpret as a sensory symptom referable to the spinal cord. (Ex. 1, p. 581; Tr. 36-37.) Importantly, however, this history was in follow up for petitioner's chronic abdominal pain and early satiety in contrast to the neck and shoulder pain that was noted to be "new since [last office visit]." (Ex. 1, p. 581.) During petitioner's immediately preceding office visit of September 21, 2011, it was specifically recorded that petitioner "since surgery has felt that urge for BM impaired." (*Id.* at 589.) The surgery in question was a much earlier in life bowel resection (*Id.* at 588), meaning the impaired sense of the need to defecate was chronic. Accordingly, while this symptom could potentially be consistent with an evolving spinal injury (Tr. 36-38, 253-54), there is not preponderant evidence that it is related to petitioner's TM. (See *id.* at 254-55.) Much later, in April of 2012, petitioner's primary care provider recorded that, despite predating his TM, his inability to sense the urge to defecate did worsen following his injury. (Ex. 1, p. 164.) However, when reviewing the records holistically, and, in particular, comparing the encounter records for September 21 and November 23, 2011, there is not preponderant evidence that petitioner reported this symptom as a new or acute symptom occurring at that time.

iii. Reported prior episode of identical symptoms

On four separate occasions while being evaluated for possible TM, petitioner reported an "identical" episode as occurring prior to his flu vaccination. (Ex. 1, pp. 316, 566, 579; Ex. 8, p. 48.) However, he was an inconsistent historian with respect to timing. Specifically:

- A nurse triage note of November 28, 2011, indicates that petitioner “had these muscle aches about one month ago and it went away.” (Ex. 1, p. 579.)
- On November 28, 2011, petitioner reported symptoms that began with shoulder and neck soreness and progressed down his arms and legs to then include sensory abnormalities and weakness. (Ex. 1, pp. 565-66.) He indicated that he experienced “an identical episode” lasting 3-4 days about two months prior, for which he did not seek medical attention. (*Id.* at 566.)
- On December 6, 2011, petitioner had an encounter with Dr. Junck. Dr. Junck reviewed the course of the symptoms that brought him to medical attention on November 28, 2011, and then indicated, “Per report, he did have an identical episode about two months ago.” (Ex. 8, p. 48.) However, Dr. Junck further explained that “when questioned here today at UofM, he states that it might have been only about 1-2 weeks ago. The onset was identical and the entire symptomatology lasted 3-4 days and then gradually resolved on its own. He did not seek medical attention at that time, and he returned to his baseline without any lasting deficits.”<sup>25</sup> (*Id.*)
- On December 22, 2011, petitioner reported that his November 28 hospitalization represented his second episode of neck and shoulder pain within a ten-day time span. (Ex. 1, p. 316.) This would place the onset of the first episode around November 14. In that regard, the record further specifies that the first episode occurred “in mid 11/2011” and left him bed-bound for three days. (*Id.*) In both instances the pain “instantaneously radiated down his body into legs and was associated with extreme weakness.” (*Id.*)

Considering each of these notations and the record as a whole, I find that the evidence preponderates in favor of a finding that petitioner did suffer an episode of symptoms lasting 3-4 days that consisted of neck and extremity pain, weakness, and sensory symptoms. Because Dr. Junck’s record explicitly reflects a conversation intended to clarify this history, I find that it is more likely that the later December 6 and

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<sup>25</sup> Although Dr. Junck wrote that the prior episode occurred 1-2 weeks “ago,” potentially implying one to two weeks prior to the encounter date of December 6, a holistic reading of his note suggests he more likely meant 1-2 weeks prior to the second episode, which had begun on November 24. (See Ex. 8, p. 48.) Two weeks prior to December 6 would have been November 22, just two days prior to the beginning of the second episode. However, Dr. Junck’s record makes clear that he understood there to be two distinct episodes and that the first episode lasted 3-4 days before gradually resolving. (*Id.*) Given that Dr. Junck was specifically seeking to clarify the report of a prior episode, it is unlikely that he would have recorded a history incompatible with the presence of two episodes without remarking on that fact. Thus, Dr. Junck was most likely indicating that petitioner had reported onset of his first episode occurring sometime in mid-November, between about the 10th or 17th.

December 22 records are more accurate in placing this episode sometime in mid-November, rather than one or two months prior. At a minimum, Dr. Junck clarified with petitioner that the time course was more condensed than originally indicated. Especially given that understanding, petitioner's subsequent report that the two episodes occurred ten days apart gives the clearest indication of the temporal relationship between the two episodes. The December 22 history is also more detailed in recording that petitioner specifically recalled being bed-ridden in mid-November, rather than merely estimating how long ago the episode occurred. Further, if one interprets Dr. Junck's record as placing onset of the first episode in mid-November (see *supra* note 25), the two records are entirely consistent whereas the other two records are not (placing onset at one or two months prior respectively). Additionally, petitioner's telephone encounters of September 22, September 23, September 27, and October 12, make it somewhat less likely this episode happened during that period. (Ex. 1, pp. 584-86.)

Although petitioner's deficits may have resolved such that he returned to a functional baseline, his November 23, 2011 report of ongoing neck and shoulder pain prevents a finding that his condition completely resolved. (Ex. 1, p. 581-83.) Moreover, because petitioner was clear and consistent in providing a history wherein the neck and shoulder pain heralded the onset of symptoms in both episodes, I find that it is most likely that the neck and shoulder pain reported on November 23, 2011, began at around the time of this first episode, rather than four weeks prior. This is consistent with petitioner's representation on November 23, 2011, that his symptoms were improving, yet ongoing. (*Id.*)

Dr. Gelfand's hesitation in crediting these reports as consistent with TM are understandable, given that the prior episode was not discussed in detail but rather only in overarching terms. (Ex. A, pp. 14-15; Ex. E, p. 5; Tr. 280-81.) However, he has not persuaded me that the report can be disregarded.

[F]or many medical symptoms or events – such as a headache or other pain, dizziness, nausea, vomiting – the patient's or a parent's testimony may be the best, or only, direct evidence of their occurrence. Medical records related to those symptoms would likely be based on the statements of those who experienced them.

*James-Cornelius ex rel. E.J. v. Sec'y of Health & Human Servs.*, 984 F.3d 1374, 1380 (Fed. Cir. 2021). "Medical records, in general, warrant consideration as trustworthy evidence. The records contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium. These records are also generally contemporaneous to the medical events." *Cucuras ex rel. Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed Cir. 1993). Petitioner's persistence in reporting this prior episode at a critical juncture in his diagnosis and treatment counsels against disregarding the provided history.

Dr. Gelfand also finds it improbable that petitioner's prior episode, being as profound as it must have been, would have not come to medical attention and would have had such a quick recovery. (Tr. 281-82.) This is based on an understanding that what petitioner had described was coextensive with his ultimate inability to walk and inability to use his arms to hold things. (*Id.* at 281.) However, that was not petitioner's presentation at the time he first reported his prior similar symptoms. As of November 28, when petitioner first characterized the prior episode as similar to his present condition, he was still able to stand and ambulate, albeit unsteadily. (Ex. 1, p. 566.) Moreover, though reporting the presence of the same symptoms, he also specified that what he was experiencing beginning after his vaccination "is the worst it has been." (*Id.* at 579.) Although petitioner did report having previously been temporarily bed-bound, it was not until after his hospitalization that his weakness became so profound as to cause him to be unable to walk or perform any activities of daily living. (*Id.* at 316.) In that regard, petitioner additionally denied in his affidavit that he experienced paralysis prior to his flu vaccination. (Ex. 3, ¶ 2.) Dr. Gelfand agreed that paralysis would be on a spectrum with weakness, *i.e.*, weakness is a less severe form of impairment to the motor pathways as compared to paralysis. (Tr. 336.) Thus, the evidence does not favor the conclusion that petitioner's initial episode, though including the same symptoms, was as severe as his later presentation ultimately became.

#### iv. Presence of lesions pre-vaccination

On November 29, 2011, petitioner underwent an MRI study that revealed a "small area of focal T2 signal prolongation in the ventral aspect of right hemi cord at C3 vertebral level, suggesting either demyelination or gliosis." (Ex. 1, p. 806.) Repeat study as of December 5 revealed stable findings. (*Id.* at 799, 801-02; Ex. 8, pp. 64-65.) Ultimately, the experts agree that petitioner had two non-enhancing lesions consistent with TM. Moreover, petitioner asserts that the MRI findings "link" his reported pre-vaccination history of neck and shoulder pain and the T2 lesions. (ECF No. 144, pp. 17-18.) While Dr. Tornatore notes that the duration of lesion enhancement varies, he opines that the lack of enhancement suggests that the lesions were at least 2-3 weeks old when the first MRI study was performed on November 29, 2011. (Ex. 81, pp. 18-19 (citing Lai et al., *supra*, at Ex. 96; Cotton et al., *supra*, at Ex. 97); Tr. 133.) Although Dr. Steinman is hesitant to associate a specific date with the non-enhancing lesions (Ex. 55, p. 3), Dr. Tornatore sought to reconcile their opinions by explaining that both experts agree "that we don't know how old they are, but we know that they're not acute in onset" (Tr. 128-29). Although Dr. Gelfand disagrees that non-enhancing lesions can be dated with precision, he likewise acknowledges that non-enhancing lesions are generally assumed to have been enhancing at some point in their course. (*Id.* at 275, 285.) He stresses, however, that in this case there is no clinical association between petitioner's symptom presentation and any period of known florid lesion enhancement. (*Id.* at 284.)

The evidence is inadequate to definitively age petitioner's lesions. However, all the experts generally agree that non-enhancing lesions were likely enhancing at some point and that enhancing lesions are a marker of inflammation that may be associated with TM. (Ex. 81, pp. 18-19; Ex. 55, pp. 2-4; Ex. A, p. 11-12; Tr. 275-76, 285-86.)

Moreover, Dr. Tornatore is persuasive in placing at least some weight on the notion that lesions typically enhance for about 2-3 weeks. (Cotton et al., *supra*, at Ex. 97, p. 3.) Accordingly, given that the first MRI was performed only about six days post-vaccination, I credit Dr. Tornatore's opinion that it is more likely than not that the lesions predated petitioner's flu vaccination. *Accord W.C.*, 704 F.3d at 1358-59 (accepting the special master's finding based on the unlikelihood that lesions would enhance for a short duration). Notably, Dr. Tornatore's approximation also potentially correlates the likely lesion enhancement to petitioner's reported first episode of symptoms. Dr. Tornatore did testify based on his clinical experience that it is improbable that the two lesions occurred simultaneously (Tr. 67); however, he was nonetheless clear and explicit in opining that both lesions pre-dated petitioner's flu vaccination. (*Id.* at 66.) For his part, Dr. Gelfand opined that it is common for monophasic acute TM to have multifocal lesions. (*Id.* at 274, 276.) Thus, there is preponderant evidence that both of the spinal lesions associated with petitioner's TM predated his flu vaccination.

#### v. Conclusion as to *Loving* prong one

In light of all of the above, I find that there is preponderant evidence that petitioner suffered onset of his TM prior to administration of his November 23, 2011 flu vaccination. The onset of petitioner's TM likely occurred in mid-November and was heralded by a more severe 3-4 day episode of neck and extremity pain, weakness, and sensory symptoms. Although petitioner's function returned to baseline, the TM did not completely resolve, as evidenced by petitioner's report of ongoing neck and shoulder pain at the time of his flu vaccination. Petitioner's spinal lesions more likely than not (though not definitively) pre-dated his flu vaccination. In sum, petitioner was suffering TM for approximately one to two weeks prior to the subject vaccination and was continuing to suffer the attack at the time of the vaccination.

#### b. *Loving* Prong Two

The second *Loving* prong examines petitioner's condition following vaccination. *Loving*, 86 Fed. Cl. at 144. As noted above, at the time of vaccination, petitioner was already suffering TM, which was manifesting at that time with ongoing neck and shoulder pain. However, it is also undisputed that petitioner experienced a second progression of more concerning symptoms consistent with TM following his flu vaccination. (Ex. 81, p. 15; Ex. 12, p. 9; see *also* Ex. A, p. 11.)

The medical records reflect that petitioner first noticed increased shoulder and neck soreness on November 24, 2011, one day post-vaccination. (See Ex. 1, pp. 565, 579.) At this time, petitioner also reported a new sensation of feeling as though he had sand in his shoulders, which Dr. Tornatore interpreted as a sensory symptom. (Tr. 45-46.) Petitioner described soreness spreading down his arms and legs over the next 24 hours or so and progressing to numbness and coldness in his extremities. (Ex. 1, p. 565.) Petitioner presented to the emergency department on November 28, 2011, five days post-vaccination. By that time, petitioner was reporting sensory issues, including an inability to feel changes in temperature below his head and neck and a "pins and

needles” feeling in his extremities. (*Id.* at 565-66.) He had also developed urinary retention, requiring use of a catheter. (*Id.* at 550.) At some point during the five-day interval between his vaccination on November 23, 2011, and when he presented to the emergency department on November 28, 2011, petitioner experienced weakness and difficulty standing, walking, and gripping. (*Id.* at 566, 578-80.) Although petitioner’s clinical course confounded his treaters at times, he was ultimately diagnosed with TM. (*Id.* at 1, 144-45, 199, 320, 445-46; 526, 549.) Drs. Tornatore and Gelfand agree that this was the correct diagnosis. (Tr. 48, 263, 266-67; Ex. A, pp. 11, 13; Ex. 81, p. 23.)

At a follow-up neurology evaluation on December 1, 2011, it was noted that petitioner’s symptoms, namely, his sensory changes and weakness, were progressing. (Ex. 1, pp. 524-26.) Petitioner was administered IVIg Solu-Medrol with some improvement. (*Id.* at 515, 519-20, 526.) However, by December 2, 2011, petitioner was non-ambulatory due to extensive bilateral lower extremity weakness and suffering from impaired sensation, decreased respiratory strength, and weakness in all extremities. (*Id.* at 519-20; *see also* Ex. 1, p. 546 (mentioning a new symptom of shortness of breath on November 30, 2011).) This represents the likely nadir of petitioner’s TM, from which he ultimately never recovered despite a clinical course that continued to fluctuate. (Ex. E, p. 9; Tr. 277-78.) Dr. Gelfand explained that “[t]he most common clinical presentation of acute transverse myelitis is an acute neurological syndrome with continued progression to nadir followed either by gradual recovery or stasis persistence of neurological deficits.”<sup>26</sup> (Ex. E, p. 7; Ex. I, p. 2; Tr. 277.)

“During his 16 day hospital course, his symptoms waxed and waned but he continue[d] to have significant weakness . . . .” (Ex. 1, p. 7.) Repeated MRI studies revealed stable findings (Ex. 1, pp. 797-802, 803-06; Ex. 8, pp. 63-65; *see also* Ex. 1, pp. 1, 144.) After several weeks of physical therapy, petitioner was eventually able to ambulate with the assistance of a front-wheeled walker and to perform most of his activities of daily living without assistance. (Ex. 1, p. 235.) However, by mid-January 2012, petitioner was again reporting weakness and incontinence, and he was dependent on a wheelchair. (*Id.* at 140-45.) And by 2014, petitioner was completely wheelchair bound and reporting pain, weakness, spasticity, neurologic bowel and bladder, and paraplegia. (Exs, 7, 76, 108-09.)

In sum, petitioner experienced a worsening of his symptoms of TM the day following his vaccination. His condition continued to progress for approximately one week post-vaccination. Once he reached his nadir, he continued to suffer a fluctuating course and never recovered.

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<sup>26</sup> In his testimony, Dr. Gelfand indicated that petitioner’s clinical course continued to evolve “over several days” after November 24. (Tr. 278.) In testimony, he suggested that the clinical nadir may then have occurred “over a couple of weeks.” (*Id.*) This testimony is a bit unclear as a nadir would reflect a distinct point in time. However, in his report at Exhibit E, Dr. Gelfand more clearly opined that a prior episode occurring 1-2 weeks prior to his November 24, 2011 symptoms would constitute a single episode of TM with a progression from onset to nadir occurring within the 21-day timeframe set by the diagnostic criteria. (Ex. E, p. 8; *see also* Tr. 279-80.) This is consistent with the nadir occurring around December 2.

### c. *Loving* Prong Three

The third *Loving* prong requires a showing that petitioner's post-vaccination condition constitutes a "significant aggravation" of his pre-vaccination condition. *Loving*, 86 Fed. Cl. at 144. The Vaccine Act defines "significant aggravation" as "any change for the worse in a preexisting condition which results in markedly greater disability, pain, or illness accompanied by substantial deterioration of health." § 300aa-33(4). *Loving* prong three only requires a comparison of petitioner's pre- and post-vaccination conditions. *Loving*, 86 Fed. Cl. at 143; *Sharpe ex rel. L.M. v. Sec'y of Health & Human Servs.*, 964 F.3d 1072, 1082 (Fed. Cir. 2020). Although he need not prove the expected outcome of his pre-vaccination condition or that his post-vaccination condition is worse than the expected outcome, *Sharpe*, 964 F.3d at 1082, petitioner still must show that his post-vaccination condition was affected by his vaccination. *Locane v. Sec'y of Health & Human Servs.*, 685 F.3d 1375, 1381-82 (Fed. Cir. 2012).

As detailed in my analysis with respect to *Loving* prong one, I agree with petitioner that his TM pre-dated his flu vaccination. And, as detailed in my analysis under *Loving* prong two, petitioner's symptoms worsened the day after his vaccination and progressed to a nadir over the course of about one week. Thus, comparison of petitioner's pre- and post-vaccination condition indicates that petitioner suffered a significant aggravation under *Loving* prong three insofar as his condition worsened, resulting in greater disability and pain. However, it is also important to stress that my comparison of petitioner's pre- and post-vaccination condition leads to the finding that what petitioner suffered was an acute monophasic TM over the course of approximately three weeks that began prior to vaccination and reached a nadir after vaccination. See *Sword v. United States*, 44 Fed. Cl. 183, 187-89 (1999) (explaining of special masters that "as fact-finders, they may find that truth lies somewhere in between the opposing, uncompromising views of the partisan experts."). Ultimately, this view is consistent with Dr. Gelfand's alternative view that, if one assumes an initial onset of TM occurring 1-2 weeks prior to vaccination, then petitioner suffered a single episode of acute TM. (Ex. E, p. 8; Tr. 279-80.) This finding indicates that, while petitioner may have technically suffered a significant aggravation within the language of the Vaccine Act, there is little reason based on his clinical history to conclude that his condition was actually affected by his vaccination. *Accord Locane*, 685 F.3d at 1381-82 (finding no error in the special master's conclusion that "the preponderance of evidence showed that the course of Ms. Locane's condition was not inconsistent with the disease generally and not affected by the vaccinations"). Several factors contribute to this conclusion.

First, given my findings under *Loving* prong one, petitioner's experts are not persuasive in characterizing petitioner's preexisting TM as merely "smoldering" or "indolent." (Tr. 34, 183.) (For example, Dr. Steinman was relying on "smoldering" TM as something more than subclinical, but less than "the full-blown events that happened" later. (Tr. 215-16.)) Both experts have asserted – and I have accepted – that prior to vaccination petitioner suffered an acute onset of TM symptoms matching his post-vaccination presenting symptoms. Even if the initial symptoms was not as devastating as the later presentation ultimately proved to be, I cannot agree that it constituted

something “less than full-blown” TM. The initial symptom onset was overt, involved the same constellation of symptoms, and was severe enough to leave petitioner temporarily bedridden. And, even though these symptoms improved, the TM did not completely resolve, as petitioner had ongoing symptoms of neck and shoulder pain attributable to his TM at the time of his vaccination. Moreover, Dr. Tornatore was persuasive in opining that petitioner’s spinal lesions likely developed prior to his vaccination.

Second, the time course from petitioner’s initial onset of TM to the nadir of his condition is consistent with a monophasic TM. In resolving the conflicting notations in the medical records, I found under *Loving* prong one that petitioner’s initial episode of symptoms occurred in mid-November. This is much later than what was discussed in much of the expert testimony. Although that acute episode initially occurring in mid-November improved, it never resolved and was ongoing at the time of vaccination. I then found under *Loving* prong two that petitioner’s condition reached its nadir around December 2, 2011. In that regard, both Drs. Tornatore and Gelfand agree that acute TM symptoms generally peak within 4 hours to 21 days after onset of symptoms. (Ex. 81, p. 20; Ex. E, pp. 7-8; Tr. 277-78.) Although it was not his preferred interpretation of the clinical history, Dr. Gelfand agreed that under these assumptions this would reflect a monophasic course of acute TM. (Ex. E, pp. 8-9; Tr. 277-80.) Dr. Tornatore likewise stressed in his testimony that petitioner’s pre- and post-vaccination symptoms represented a continuum arguably consistent with the “ebb and flow” of TM. (Tr. 34, 92-93.) Only Dr. Tornatore’s assessment of the change in the “tempo” of symptoms post-vaccination permitted him to opine that a significant aggravation had occurred. (*Id.* at 68.) However, my findings under *Loving* prong one do not support Dr. Tornatore’s underlying assumption regarding the overall time course of his pre-vaccination symptoms.

Third, both parties’ experts agreed that for monophasic TM, the clinical course from onset to nadir can be variable. (Ex. E, p. 7; Ex. 98, p. 3.) Dr. Gelfand explained that “[t]he most common clinical presentation of acute transverse myelitis is an acute neurological syndrome with continued progression to nadir followed either by gradual recovery or stasis persistence of neurological deficits.” (Ex. E, p. 7; Ex. I, p. 2; Tr. 277-78.) However, he also explained that “[s]ymptoms of myelitis can sometimes appear to stutter or manifest subtly.” (Ex. E, p. 7.) Dr. Gelfand cautions that he would not expect someone who was initially experiencing profound symptoms to recover in just a few days and without medical intervention. (Tr. 281.) However, for the reasons discussed under *Loving* prong one, I have concluded that petitioner’s initial episode was not as profound as Dr. Gelfand assumed and he did not experience a complete recovery. Moreover, consistent with this understanding, I explained relative to *Loving* prong two that petitioner’s subsequent history further confirms that his presentation continued to fluctuate even after vaccination. (*E.g.*, Ex. 1, p. 316 (neurology consultation of December 22, 2011 describing “recent 16 day admission for fluctuating upper and lower extremity weakness, which is now resolving”).)

Fourth, the fact that petitioner had two spinal lesions on MRI does not imply that his condition was not acute and monophasic. Dr. Gelfand stressed that a monophasic

acute TM “can often see several spots in the spinal cord, and the general interpretation, based on the clinical syndrome in those patients is that those spots are all part of the same acute process.” (Tr. 274.) For his part, petitioner’s expert, Dr. Tornatore, at times suggested that petitioner’s TM was non-acute. (See, e.g., *id.* at 59, 129.) This is also the position that petitioner takes. (ECF No. 144, p. 19; Tr. 21.) He further indicates that the location of the two lesions is suggestive of two distinct episodes. (Tr. 107.) Dr. Tornatore suggested that, in his clinical experience, it is “very common” for patients to experience a couple days of feeling worse, recovering, and thereafter seeing a new lesion on MRI. (*Id.* at 163.) Dr. Tornatore suggests that the pathogenesis is such that the immune system “may” have still been activated as a result of a breach in one area of the blood-brain barrier, which subsequently led to a breach in a different area of the blood-brain barrier. (*Id.* at 107-08.) However, he also admits that the variable dates of petitioner’s reported “identical episode” make it difficult to rule out the possibility that his post-vaccination symptoms were a continuation of the prior episode. (*Id.* at 46-48, 75, 122.) Moreover, he separately opined that *both* spinal lesions likely predated the vaccination. (*Id.* at 66-67.)

Thus, based on the record as a whole, I find that petitioner likely experienced a single episode of monophasic TM that began prior to his vaccination. Dr. Gelfand explains that the general understanding that inflammatory and autoimmune processes that typically cause myelitis “take[] time to build,” such that petitioner’s condition may have been “evolving immunologically for some time.” (Tr. 317-18.) As noted above, he also explains that “[s]ymptoms of myelitis can sometimes appear to stutter or manifest subtly at first, but typically this occurs within the context of persistent (even if relatively gradual) progression of such symptoms as the syndrome evolves.” (Ex. E, p. 7.) Dr. Tornatore opines that the medical records include evidence of “transient as well as ongoing symptoms” consistent with TM (Ex. 98, p. 3), and Dr. Gelfand explains that, assuming petitioner’s pre-vaccination symptoms are consistent with TM, petitioner’s pre-vaccination and post-vaccination symptoms would all be part of his evolving myelitis syndrome (Ex. E, p. 8; Tr. 279-80). He also explains that other chronic conditions, such as recurrent TM, were ruled out, and there is no evidence of relapse since this episode. (Ex. E, p. 7.) Though he seemed to sometimes question whether petitioner’s condition was truly acute, Dr. Tornatore likewise agrees that petitioner did not suffer recurrent TM. (Tr. 172.)

Although petitioner’s symptoms did worsen post-vaccination, what petitioner experienced was a progressive, albeit clinically variable, course of monophasic TM that straddled the date of his vaccination. That is, comparison of petitioner’s pre- and post-vaccination condition indicates that during both periods he was in the midst of an acute course of TM that had not yet reached its nadir, meaning that the ongoing deterioration of his condition was not itself indicative of any aggravating event. Thus, while petitioner may have technically demonstrated the presence of a significant aggravation, this factual finding regarding petitioner’s clinical course is an important predicate that helps inform the analysis under *Loving* prong five that further explains why there is no logical sequence of cause and effect implicating petitioner’s vaccination as a cause of the significant worsening of his condition.

#### d. *Loving* Prong Five / *Althen* Prong Two

The fifth *Loving* prong / second *Althen* prong requires proof of a “logical sequence of cause and effect” linking petitioner’s significantly aggravated post-vaccination condition to his flu vaccination. *Loving*, 86 Fed. Cl. at 144; *Athen*, 418 F.3d at 1278. Petitioners’ showing under this prong is usually supported by facts derived from medical records. *Althen*, 418 F.3d at 1279; *Andreu ex rel. Andreu v. Sec’y of Health & Human Servs.*, 569 F.3d 1367, 1383 (Fed. Cir. 2009); *Capizzano v. Sec’y of Health & Human Servs.*, 440 F.3d 1317, 1326 (Fed. Cir. 2006); *Grant*, 956 F.2d at 1148. However, although they must be considered, medical record and/or statements of a treating physicians do not *per se* bind the special master to adopt such conclusions. § 300aa-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”). Ultimately, a petitioner may support a logical sequence of cause and effect through either medical records or expert medical opinion. § 300aa-13(a). The special master is required to consider all the relevant evidence of record, draw plausible inferences, and articulate a rational basis for the decision. *Winkler v. Sec’y of Health & Human Servs.*, 88 F.4th 958, 963 (Fed. Cir. 2023) (citing *Hines*, 940 F.2d at 1528).

Although there was some suspicion in the medical records that petitioner’s flu vaccination could have caused his TM, this opinion was neither universal nor unequivocal. It was repeatedly noted that the etiology of petitioner’s symptoms was “unclear,” despite extensive work-up. (Ex.1, pp. 422, 429, 446, 465, 477, 480, 496, 498, 514, 731.) Although petitioner’s neurologists noted that TM has been reported after many vaccinations, they did not initially consider whether petitioner’s vaccination and TM may have been related because his presentation did not appear consistent with TM. (*Id.* at 476.) Even after TM became the working diagnosis, the relationship between petitioner’s vaccination and his condition was never explored. Petitioner’s discharge diagnosis was presumed autoimmune myelitis, and it was noted that, despite the “very extensive work up,” the cause of his condition remained unknown. (*Id.* at 3, 7.) It thus appears that petitioner’s discharge diagnosis of autoimmune TM was the result of other etiologies being definitively ruled out. (Ex. 4, pp. 1-7, 456-57; Ex. 55, p. 2; Tr. 262-64.)

During his out-patient neurology appointments, petitioner’s flu vaccine was suggested as a “[p]ossible cause,” although it was also erroneously stated that this vaccine was received “several weeks before initial symptoms.” (Ex. 1, p. 320.) Petitioner’s neurologist explained that “[t]he relationship between the myelopathy and his recent influenza vaccination is uncertain.” (*Id.* at 321.) His neurologist later opined that the association between the flu vaccination and his symptom onset was “unclear.” (*Id.* at 144-45, 199-200.) In his other encounters following his hospitalization, it was noted that petitioner’s “working diagnosis is autoimmune TM following receiving flu and shingles vaccines;” however, “no etiology of the TM was ever confirmed.” (Ex. 4, pp. 72, 125.) In subsequent home health care review, petitioner’s condition was

consistently referred to as idiopathic TM. (*Id.* at 41-42, 62, 84, 112, 166.) Thus, no treater ever confirmed any association between petitioner's vaccination and TM.<sup>27</sup>

Furthermore, my factual findings under *Loving* prongs one through three further suggest that there is little reason based on petitioner's overall clinical history to conclude that he suffered anything other than an acute monophasic TM unaffected by his vaccination. In that regard, Dr. Gelfand further explains that the Transverse Myelitis Consortium Working Group set out a generally accepted approach to clinical diagnosis of acute TM that includes, in pertinent part, some evidence of inflammation in the spinal cord as demonstrated by gadolinium enhancement, CSF pleocytosis, or elevated IgG index. (Tr. 259 (citing Transverse Myelitis Consortium Working Group, *supra*, at Ex. A, Tab 2).) In this case, while there was sufficient evidence to diagnose TM, nothing in the medical testing suggests that the underlying disease progression or pathophysiology changed following petitioner's flu vaccination.

First, petitioner's repeat MRIs revealed stable, non-enhancing T2 lesions. (Ex. 1, pp. 798-806.) Dr. Tornatore explained that active inflammatory lesions enhance, whereas non-enhancing lesions demonstrate the resulting damage. (Tr. 56-57.) Specifically, gadolinium enhancement on MRI evidences a "breakdown of the blood-brain barrier." (*Id.* at 51, 56-58.) Dr. Gelfand agrees. (*Id.* at 275-76.) When enhancement stops, this indicates the blood brain barrier has been reestablished, but not that the inflammation itself has subsided. (*Id.* at 153.) Thus, Dr. Tornatore opines that whether a lesion is enhancing simply informs the age of the lesion, "but it doesn't really tell us anything about the symptoms themselves." (*Id.* at 65.) Non-enhancing lesions do still cause symptoms.<sup>28</sup> (*Id.* at 65-66.) Therefore, Dr. Tornatore does not

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<sup>27</sup> See *Caves v. Sec'y of Health & Human Servs.*, No. 07-443V, 2010 WL 5557542, at \*20 (Fed. Cl. Spec. Mstr. Nov. 29, 2010) ("[T]here is a difference between a statement 'associating' a vaccine with a disease and a statement that a vaccine caused a disease."), *mot. for rev. den'd*, 100 Fed. Cl. 119 (2011), *aff'd*, 463 Fed. App'x 932 (Fed. Cir. 2012); *Cedillo ex rel. Cedillo v. Sec'y of Health & Human Servs.*, 617 F.3d 1328, 1348 (Fed. Cir. 2010) (holding that the special master did not err in refusing to afford significant weight to the opinions of treating physicians that "simply indicat[ed] awareness of a temporal, not causal, relationship" between the vaccination and the condition (emphasis omitted)); see also *Veryzer v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 344, 355 (2011) (finding that the special master properly determined that the statements provided by petitioner's treaters fail to establish causation as "petitioner's physicians doubted that his condition was vaccine-related," and "[w]hen physicians entertained the idea of vaccine-relatedness, the 'driving factor' was the fact that petitioner's condition developed post-vaccination"); *Ruiz v. Sec'y of Health & Human Servs.*, No. 02-156V, 2007 WL 5161754, at \*13-14 (Fed. Cl. Oct. 15, 2007) (reasoning that medical records confirming the temporal proximity between the vaccination and onset without concluding that the vaccine caused onset were insufficient to support vaccine-causation); *Tosches ex rel. Tosches v. Sec'y of Health & Human Servs.*, No. 06-192V, 2008 WL 440285, at \*13-15 (Fed. Cl. Spec. Mstr. Jan 31, 2008) (finding that petitioner's reliance on statements of treating physicians who recognized that the vaccination preceded onset but did not conclude that there was a causal relationship could not support petitioner's burden under the second *Althen* prong); *Egan ex rel. Gum v. Sec'y of Health & Human Servs.*, No. 05-1032V, 2009 WL 1440240, at \*15 (Fed. Cl. Spec. Mstr. May 1, 2009) ("The essence of the undersigned's ruling against a logical sequence of cause and effect and thus finding against petitioner is [in part] that the treating doctors did not consider the vaccine causative of [petitioner's] TM.")

<sup>28</sup> Thus, relatedly, Dr. Gelfand explains that enhancing lesions are diagnostically helpful, but not absolutely required under the diagnostic criteria for acute TM. (Tr. 260.)

suggest that the flu vaccine caused inflammation sufficient to injure the blood-brain barrier, and he could not so suggest as there was never any evidence of post-vaccination enhancement on MRI. Even accounting for Dr. Tornatore's opinion that the two lesions likely occurred separately (*Id.* at 107-08), he nonetheless opines "that you have two unenhanced lesions really strengthens the argument that both of them antedated the vaccination." (*Id.* at 66-68.)

Second, there was no evidence of inflammation in the CSF. (Ex. 1, p. 763; Tr. 50-51.) Petitioner admits that the lack of pleocytosis on CSF shows that "there was not a systemic inflammatory process at work." (ECF No. 144, p. 19, n.16; Tr. 23.) At the hearing, Dr. Tornatore candidly explained that "you would see inflammatory cells in the spinal fluid" when observing an acute TM. (Tr. 51.) Dr. Gelfand interprets the elevated myelin basic protein as "a nonspecific marker of active and ongoing spinal cord injury process." (*Id.* at 268.) Dr. Tornatore agrees, interpreting the elevated myelin basic protein in conjunction with the lack of pleocytosis as evidence of an older injury. (*Id.* at 50-52, 156-57, 454-55.) Although the experts discussed some circumstances that could allow for a false negative CSF result (*Id.* at 158-59, 206-07, 267), this still leaves a lack of supporting evidence of any acute inflammatory process occurring post-vaccination. Dr. Steinman further asserts that petitioner's five-day course of Solu-Medrol treatment during his hospitalization may have concealed the signs of more pronounced inflammation; however, this treatment was initiated on December 1, 2011, and would not have affected the earlier spinal tap results. (Ex. 12, p. 9; Tr. 206-07.) Petitioner did have a positive ANA (Ex. 1, p. 778), which Dr. Tornatore opined this is some evidence of autoimmunity and systemic inflammation (Tr. 454-55); however, it is not a finding of spinal inflammation specifically. As Dr. Gelfand explained, ANA results contribute to the differential diagnosis for TM by speaking to other multi-organ inflammatory syndromes like lupus or connective tissue diseases; it does not speak to the cause of a myelitis. (Tr. 271.) Dr. Gelfand testified that positive ANA "is not a marker of acute inflammation or clinically interpreted as a marker of acute or new inflammation." (Tr. 270-71.)

Dr. Tornatore otherwise discussed petitioner's symptoms as existing on a "continuum" and explained that petitioner's inability to recover from the second episode may arguably be explained as part of the "ebb and flow" of TM. (Tr. 34, 92-93.) He explained that "it's very hard to correlate a patient's symptoms and then the extent of the myelitis." (*Id.* at 162.) And, as discussed above, he testified that older, non-enhancing lesions can still have persisting inflammation even after the blood brain barrier has reestablished. (*Id.* at 153-54.) In this regard, my findings under *Loving* prongs one through three explain that petitioner's overall course of symptom progression remains consistent with a monophasic course of TM.

To be clear, Dr. Tornatore does opine that post-vaccination inflammation can cross the blood brain barrier even after it has been reestablished (Tr. 155); however, he has neither substantiated that such a phenomenon is actually necessary to explain petitioner's presentation nor pointed to any concrete evidence that it actually does explain petitioner's presentation. Rather, his testimony indicates that it would be the nature of the preexisting lesions to cause petitioner's symptoms regardless of the fact

that the blood brain barrier had reestablished prior to the worsening of symptoms. (*Id.* at 71, 93.) Dr. Gelfand likewise testified that it is common for the symptoms of evolving spinal cord syndromes to change over time. (*Id.* at 258.) Specifically, Dr. Tornatore explained that the cervical spine is very narrow – about the circumference of a little finger – and it is compartmented with respect to nerve function. (*Id.* at 71.) A locational difference of as little as five or so grains of salt “just by the nature of them moving just a little bit will cause pretty profound symptoms. And so this is not like an explosion of inflammation.” (*Id.*) “It doesn’t take a lot of inflammation to cause a lot of symptoms. That’s just the nature of the spinal cord.” (*Id.*) Thus, he acknowledged with respect to petitioner’s worsened post-vaccination condition that “it may be that it’s just a location issue. It may be that had it been in a different location, maybe he would have recovered . . . And so in this particular case, I think it was the nature of where the inflammation took place, less so than the actual amount of inflammation.” (*Id.* at 93.)

Nonetheless, Dr. Tornatore presents the Talaat study for the proposition that symptom presentation does not necessarily correlate to absolute levels of inflammatory factors (cytokines and chemokines). (Ex. 130, p. 2 (citing Talaat et al., *supra*, at Ex. 127).) (The Talaat study is also discussed separately under *Loving* prong six with respect to timing of onset.) The Talaat study observed two groups of 10 individuals who received the 2011-2012 trivalent inactivated flu vaccine, drawing blood at baseline, 3 hours, 7 hours, 24 hours, 48 hours, and 14 days to detect, in pertinent part, changes in serum cytokine and chemokine levels post-vaccination.<sup>29</sup> (Talaat et al., *supra*, at Ex. 127, pp. 2-3.) Dr. Tornatore relies on this study for the idea that some patients are immune hyper-responders. The study observed one vaccinee (Subject 8) who experienced markedly higher levels of serum cytokines. (Ex. 130, p. 2.) By comparison, other subjects – immune hyper-responders – reported similar symptoms, despite less robust levels of cytokines or chemokines, suggesting that “[i]n a given cohort of individuals, one may find immune hyper-responders to the influenza vaccination,” and that, in those individuals, “[t]he absolute level of the cytokines and chemokines do not necessarily correlate with the degree of constitutional symptoms.” (*Id.*)

Dr. Tornatore’s reliance on Talaat et al. for this proposition represents an unsupported assumption that petitioner had individual susceptibility.<sup>30</sup> *Flores v. Sec’y of Health & Human Servs.*, No. 10-489V, 2013 WL 5587390, at \*8 (Fed. Cl. Spec. Mstr. Sept. 12, 2013) (finding that the expert’s assumption that petitioner had a “genetic

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<sup>29</sup> Subjects with immunocompromising conditions, such as chronic inflammatory disease and autoimmune diseases, were excluded from the study. (Talaat et al., *supra*, at Ex. 127, p. 2.)

<sup>30</sup> Dr. Forsthuber also challenges the idea that the Talaat study demonstrates that the flu vaccine produces a causally meaningful cytokine response. (Tr. 420-22.) In particular, he stresses that the fact that a flu vaccine can produce circulating cytokines and constitutional symptoms does not suggest that it produces a cytokine response sufficient to affect the permeability of the blood brain barrier, as can be seen in more serious conditions like septic shock. (*Id.* at 422; *accord Kaltenmark ex rel. A.J.K. v. Sec’y of Health & Human Servs.*, No. 17-1362V, 2023 WL 8870299, at \*31-35 (Fed. Cl. Spec. Mstr. Nov. 27, 2023).)

predisposition” in support his causal theory was “mere speculation or guesswork” not shown to be probable), *mot. for rev. den’d*, 115 Fed. Cl. 157 (2014), *aff’d per curiam*, 586 F. App’x 588 (Fed. Cir. 2014); *Boatmon ex rel. J.B. v. Sec’y of Health & Human Servs.*, 941 F.3d 1351, 136263 (Fed. Cir. 2019) (explaining that a brain stem abnormality could not be inferred from statistics “[i]n the absence of actual evidence.”). Moreover, Dr. Tornatore also raised the issue of petitioner’s age-related immunosenescence, or the gradual deterioration of the immune system with age. (Tr. 171-73.) While this point was initially noted in support of the notion that petitioner’s flare would have been unlikely absent an additional trigger, Dr. Tornatore ultimately testified that the significance of immunosenescence “could be argued both ways” – the immune system in older individuals may be slower to heal and it may also be less susceptible to augmented inflammation. (*Id.* at 84-85.) This underscores the speculative nature of attempting to characterize petitioner’s expected immune response to vaccination in the complete absence of any evidence of that immune response. Even if I accepted Dr. Tornatore’s premise that some people are immune hyper-responders, the only evidence that Dr. Tornatore can point to in support of his suggestion that petitioner is one of these susceptible individuals is petitioner’s progressing symptoms themselves. However, this is circular logic – with the clinical presentation constituting the only evidence of the underlying susceptibility that is itself intended to prove the cause of the clinical presentation. See, e.g., *Holmes v. Sec’y of Health & Human Servs.*, No. 08-185V, 2011 WL 2600612, at \*14 (Fed. Cl. Spec. Mstr. Apr. 26, 2011) (observing that “[t]o rely on the initial seizures themselves as evidence of a lowered seizure threshold would be circular reasoning” and rejecting Dr. Kinsbourne’s opinion for seeking to rely on facts not supported by the medical records); *Dodd ex rel. S.S. v. Sec’y of Health & Human Servs.*, No. 09-0585V, 2013 WL 3233210, at \*14 (Fed. Cl. Spec. Mstr. June 5, 2013) (explaining that “Dr. Kinsbourne’s circular logic, that one event was caused by another simply because the second event occurred, is also unavailing”), *rev. den’d*, 114 Fed. Cl. 43 (2013); *Gram ex rel. A.L.M. v. Sec’y of Health & Human Servs.*, No. 15-515V, 2022 WL 17687972, at \*46 (Fed. Cl. Spec. Mstr. Nov. 16, 2022) (same).

Ultimately, Dr. Tornatore opines that “it’s the tempo of [petitioner’s symptoms] that really to me is the significant aggravation.” (Tr. 68.) This *post hoc ergo propter hoc* reasoning cannot support petitioner’s burden of proof. See *Wu ex rel. Qian v. Sec’y of Health & Human Servs.*, No. 21-1811V, 2023 WL 7304919, at \*10 (Fed. Cl. Spec. Mstr. Oct. 11, 2023); *Bulman v. Sec’y of Health & Human Servs.*, No. 19-1217V, 2023 WL 5844348, at \*14 (Fed. Cl. Spec. Mstr. Aug. 16, 2023); *Galindo v. Sec’y of Health & Human Servs.*, No. 16-203V, 2019 WL 2419552, at \*20 (Fed. Cl. Spec. Mstr. May 14, 2019). Moreover, Dr. Tornatore’s opinion regarding the “tempo” of petitioner’s symptoms is based in part on his assumption that the initial onset of petitioner’s first episode occurred a month prior to vaccination whereas I have concluded that onset of the TM occurred in mid-November, only about ten days prior to the onset of the second episode. As discussed under *Loving* prongs one through three, even if petitioner’s clinical presentation did fluctuate, his overall clinical course from onset to nadir is consistent with acute monophasic TM.

Given all of these factors, Dr. Tornatore is not persuasive in relying on the “tempo” of petitioner’s symptom presentation, without more, as a basis for opining that there is a logical sequence of cause and effect that explains how petitioner’s vaccination actually did affect, or significantly aggravate, his preexisting TM. Even as Dr. Tornatore does seek to explain the absence of any markers of post-vaccination inflammation, the absence of such markers on both MRI and CSF results leaves his opinion speculative, especially, but not only, because the overall clinical history is consistent with acute monophasic TM.

**e. *Loving* Prongs Four and Six / *Althen* Prongs One and Three**

Petitioner’s burden under the fourth *Loving* prong / first *Althen* prong is to preponderantly show “a medical theory causally connecting such a significantly worsened condition to the vaccination.” *Loving*, 86 Fed. Cl. at 144; *Althen*, 418 F.3d at 1278. While petitioner’s theory needs not be “medically or scientifically certain,” it must be “legally probably” and based on a “sound and reliable medical or scientific explanation.” *Knudsen ex rel. Knudsen v. Sec’y of Health & Human Servs.*, 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioner’s burden under *Loving* prong four varies from his burden under *Althen* prong one in that a significant aggravation claim requires a showing that the subject vaccine can worsen the condition at issue, rather than be its cause. *Sharpe*, 964 F.3d at 1083 (explaining that “[u]nder *Loving* prong 4, a petitioner need only provide ‘a medical theory causally connecting [petitioner]’s significantly worsened condition to the vaccination.’ In other words, Petitioner was required to present a medically plausible theory demonstrating that a vaccine ‘can’ cause a significant worsening of [petitioner’s injury]”).

Petitioner presents two overarching theories for how the flu vaccine can significantly aggravate TM: the fertile field model and molecular mimicry. These two theories are challenged by respondent’s experts; however, there is not any dispute that TM is a condition that theoretically could be aggravated. Dr. Gelfand agrees that it is a theoretically possibility. (Tr. 324.) Therefore, for the purpose of brevity, I will assume, without deciding, that there are certain circumstances in which the flu vaccine can cause or aggravate acute CNS demyelinating syndromes. Even assuming *arguendo* that petitioner’s proffered theories are sound and reliable as a general matter, respondent’s experts are persuasive for all the reasons discussed relative to *Loving* prong six in explaining why these theories cannot reasonably be applied to explain the actual onset of TM at issue in this case.

Under *Loving* prong six / *Althen* prong three, petitioner must establish a “proximate temporal relationship” between the flu vaccine and his significantly aggravated TM. *Loving*, 86 Fed. Cl. at 144; *Althen*, 418 F.3d at 1278. To make this showing, a petitioner must present “preponderant proof that the onset of symptoms occurred within a time frame for which, given the medical understanding of the disorder’s etiology, it is medically acceptable to infer causation-in-fact.” *de Bazan*, 539 F.3d at 1352. There are two components at issue: (1) the timing of onset or significant aggravation of the condition for which petitioner seeks compensation, and (2) the time

frame for which it is “medically acceptable to infer causation.” *Shapiro v. Sec’y of Health & Human Servs.*, No. 99-552V, 2011 WL 1897650, at \*13 (Fed. Cl. Spec. Mstr. Apr. 27, 2011), *vacated in part on other grounds*, 101 Fed. Cl. 532 (2011). Regarding the first point, petitioner argues that the significant aggravation of his TM occurred on or about November 24, 2011. (ECF No. 159, pp. 6-7.) This is consistent with my findings under *Loving* prong two and places onset of petitioner’s alleged significant aggravation approximately 24 hours post-vaccination. Whether a proposed time frame is “medically acceptable” depends on the specific circumstances of the case, *Knudsen*, 35 F.3d at 548-49; *Capizzano*, 440 F.3d at 1327; *Moberly ex rel. Moberly v. Sec’y of Health & Human Servs.*, 592 F.3d 1315, 1322 (Fed. Cir. 2010), and “will vary according to the particular medical theory advanced,” *Day ex rel. B.K.D. v. Sec’y of Health & Human Servs.*, No. 12-630V, 2015 WL 8028393, at \*18 (Fed. Cl. Spec. Mstr. Nov. 13, 2015). As explained above, petitioner’s two experts proposed differing theories of causation. Accordingly, they present distinct rationales with respect to timing of onset.

i. Dr. Tornatore

Dr. Tornatore opines that “the kinetics and anatomy of draining lymph nodes and their proximity to the spinal cord” supports a rapid onset of clinical symptoms of TM within one day following vaccination. (Ex. 98, pp. 8-11; ECF No. 144, pp. 35-36.) He relies on two studies by Liang & Lore and Jacob et al., respectively, to “support the scientific basis for a rapid vaccine-mediated inflammatory cascade in the proximal musculature with rapid drainage of antigen bearing cells to draining lymphatics” that are in close proximity to the spinal cord. (Ex. 98, pp. 8-11 (citing Liang & Loré, *supra*, at Ex. 101; Jacob et al., *supra*, at Ex. 99).)

Dr. Forsthuber rebuts Dr. Tornatore’s reliance on Jacob et al., explaining that the article is not helpful as it deals with lymphatic drainage of the epidural space and dura matter around the spinal cord, which he explains is “the other way around” from the lymphatics drainage from muscle cells to axillary lymph nodes as a result of vaccination. (Ex. H, p. 24.) The study by Liang & Loré looked at the effect of vaccine adjuvants on the innate immune response to vaccination. (Liang & Loré, *supra*, at Ex. 101, p. 1.) However, Dr. Forsthuber is persuasive in explaining that none of the adjuvants studied were contained in the subject flu vaccination. (Ex. H, p. 22, n.28.) Even if such adjuvants were contained in the subject vaccines, Dr. Forsthuber disputes that the study supports a 24-hour onset. (*Id.* at 22-23.) Dr. Forsthuber explains that the article by Laing & Loré provides a time frame of 3 hours (but more typically 6-24 hours) for local activation of inflammatory cells, followed by an approximately 24-hour time frame for migration of inflammatory cells to lymph nodes. (*Id.*) Additional time is needed for T cells in the lymph nodes to become activated, expand, and acquire their effector functions once encountered by the inflammatory cells. (*Id.* at 23; Ex. G, pp. 6-7.) The authors conclude, “The kinetics of mobilization of specific cell subset to the injected muscle and subsequent homing to [draining lymph nodes] induced by adjuvants is therefore multifaceted, and the profile and degree of innate immune response vary with time and adjuvant formulation.” (Liang & Loré, *supra*, at Ex. 101, p. 6.) Dr. Tornatore has not suggested that any specific adjuvant in the flu vaccine at issue can and did

induce a more rapid antigen uptake and migration to the lymph nodes. Indeed, Dr. Tornatore acknowledges that the flu vaccine received by petitioner did not contain any adjuvants at all. (Tr. 102.) Even viewing the time frames proposed by Laing & Loré in the light most favorable to petitioner, the immune response following vaccination would still take more than 24 hours.

Dr. Tornatore also asserts that the fertile field theory demonstrates how vaccination can induce a “very, very rapid increase in chemokine and cytokine levels” in “hyper-responders,” citing the above-discussed article by Talaat et al., in particular. (Tr. 442-43 (citing Talaat et al., *supra*, at Ex. 127).) Importantly, however, Dr. Tornatore does not suggest that cytokines or chemokines can cause a CNS injury, but instead opines that an increase of cytokines and chemokines may be the initial immune response and “the subsequent triggering of the cellular and other portions of the humoral arm of the immune system can result in downstream CNS inflammatory effects.” (Ex. 130, p. 4.) Even setting aside Dr. Forsthuber’s criticisms of the Talaat study (Ex. J), that study measured only peripheral cytokine activity from blood draws and tracked reports of post-vaccination body aches. (Talaat et al., *supra*, at Ex. 127, p. 2.) Although the study detected circulating cytokines within 24 hours of vaccination, it does not speak to whether or how quickly this cytokine response would affect the CNS. The fact that vaccines can produce a cytokine response within 24 hours simply does not meet petitioner’s burden of proof under *Loving* prong six/*Althen* prong three. Nothing in the Talaat study is inconsistent with above-discussed understanding of the Laing & Loré study, which strongly suggests that greater than 24-hours is required for the complete innate immune response to unfold.<sup>31</sup>

None of the other articles cited to support of Dr. Tornatore’s reliance on the fertile field theory provide any details on an expected symptom onset under this process. Dr. Tornatore cites an epidemiologic study by Langer-Gould et al. that looked at the incidence of CNS acquired demyelinating syndromes following vaccination. (Ex. 98, p. 5 (citing Langer-Gould et al., *supra*, at Ex. 102); Tr. 88-92.) The authors concluded that “this mechanism would be expected to hasten symptom onset” without providing any further detail. (Langer-Gould et al., *supra*, at Ex. 102, p. 7.) Instead, Figure 2 indicates that researchers did not look for symptoms of disease until 14 days post-vaccination. (*Id.* at p. 6, fig. 2.) In contrast, Dr. Forsthuber cites an animal model study by Theil et al. that examined the fertile field model and found that, when primed with a viral infection

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<sup>31</sup> I note that Dr. Steinman additionally cited a mouse model of EAE for the proposition that T cells can cross the blood brain barrier within 24 hours. (Tr. 201-02 (discussing Bartholomäus et al., *supra*, at Ex. 17).) Dr. Steinman’s reliance on this study has been questioned by respondent’s expert, Dr. Forsthuber, as discussed below. However, it is also worth noting vis-à-vis Dr. Tornatore’s opinion that he does not agree that the EAE model is necessarily helpful with respect to TM. (*Id.* at 149.) He explained, in a different context, that

EAE is not a great model for multiple sclerosis because of, you know, the nature of what you have to do to induce the inflammation. So, yes. You’re going to get gadolinium enhancement, but is that a reflection of what’s really happening in somebody with a disease like MS or TM that, you know, we don’t – we don’t really know what the trigger is?

(*Id.*)

and injected with a strong adjuvant that is known to be highly inflammatory and result in severe adverse events, mice did not exhibit clinical symptoms until 10 days following adjuvant administration. (Ex. J, pp. 14-15 (citing Theil et al., *supra*, at Ex. J, Tab 11, p. 3).) Dr. Tornatore has not called into question this study's findings with respect to timing. (Ex. 130, pp. 8-10.) Accordingly, Dr. Tornatore has not substantiated that the proposed "proinflammatory cofactor" or "redundant enhancer[]" effect of vaccination could support a 24-hour onset within the fertile field model of disease.

ii. Dr. Steinman

At the heart of Dr. Steinman's opinion as to why a one-day onset is "medically acceptable" is his theory regarding a recall response based on molecular mimicry between myelin basic protein and the zoster and flu vaccines. He contends that

a recall response to myelin mimics in the zoster vaccine on Sept. 21, 2011 and the influenza vaccine on November 23, 2011 could trigger neuroinflammation in a time interval of less than even one day, with full blown symptoms in 72 hours from the immunization on Nov. 23, 2011. Within this time frame of onset aggravation of a smoldering myelitis from the Sept. 21, 2011 zoster vaccine became clinically apparent. The influenza vaccine on Nov. 23, 2011 aggravated the smoldering symptoms initially triggered by the Zoster immunization on Sept. 21, 2011.

(Ex. 12, p. 27 (emphasis omitted).)

As a threshold matter, there is no basis on this record for finding that the flu vaccine can trigger a recall response to an unrelated vaccine. Reaching this conclusion would require several steps, all of which Dr. Forsthuber challenges. Fundamentally, Dr. Steinman has not articulated any reason to conclude that there would be epitope spreading relative to these vaccines and this condition. (Ex. 12, pp. 2, 10, 24-25; Tr. 184-95.) The "mere invocation of [a] scientific term," without proof "that the mechanism likely does link the vaccine in question to the relevant injury," does not carry petitioner's burden. *Deshler v. Sec'y of Health & Human Servs.*, No. 16-1070V, 2020 WL 4593162, at \*20 (Fed. Cl. Spec. Mstr. July 1, 2020) (rejecting "mere invocation" of molecular mimicry). Dr. Forsthuber has indicated that, in his opinion, it is unlikely that this process would have happened. (Ex. B, pp. 17-20; Tr. 400-11.) Furthermore, Dr. Steinman explained that it takes "a few weeks" for epitope spreading to occur. (Tr. 195.) Thus, Dr. Steinman opined that, with two and a half months between vaccinations, there was "more than enough time" for epitope spreading to occur in this case. (*Id.*) Dr. Forsthuber explained, however, that the process of epitope spreading does not occur until an autoimmune process has already resulted in significant tissue damage. (*Id.* at 405, 07.) Accordingly, in order for epitope spreading to in turn explain the presence of a recall response to the flu vaccine, the time period at issue is not the time between the two vaccinations, but the time from the initial onset of petitioner's TM to the time of his flu vaccine. Thus, given my findings with respect to *Loving* prong one, it is unlikely that there was enough time for epitope spreading to occur, even by Dr. Steinman's measure

of the appropriate timeframe. (*Id.* at 411.) But in any event, even assuming that a recall response is even possible in this context, petitioner has not preponderantly shown that a 24-hour onset of TM is “medically acceptable” even following a recall response.

A recall response involves a secondary or “memory” immune response to a previously-encountered viral infection or vaccination. (Tr. 186-87.) Dr. Steinman explains that the idea is “that once you’re immunized, you can call in the troops, meaning your immune system, and fight back real hard, real fast.” (*Id.* at 187.) Because memory B and T cells are developed during the primary immune response, *i.e.*, the prior viral infection or vaccination, the latency phase between a subsequent exposure to the same antigen and development of the immune response will generally be between 1-3 days. (Ex. 98, p. 8.) The logarithmic (“log”) phase takes a further 3-5 days. (*Id.*) Although Dr. Steinman indicates that it takes “a few days” to “hit” the log phase, he suggests “whether a few days could be one day” is “certainly within the realm that it can happen that fast.” (Tr. 220.) Dr. Forsthuber disagrees. (Ex. H, pp. 2-5; Ex. G, pp. 4-8.) Despite acknowledging that a “memory” response “accelerates initiation of immune responses after re-infection,” Dr. Forsthuber persuasively opines that such response cannot result in onset of clinical symptoms within 24 hours. (Ex. G, p. 7.) Instead, he explains that it “will still take a few days” for clinical symptoms to manifest because the memory T and B cells must proliferate, migrate to the spinal cord, and cause damage to the CNS before neurologic symptoms will be apparent. (*Id.* at 7-8; Ex. H, pp. 2-5.) He contends that, even in a secondary immune response, it still takes at least 5 days for an antibody response to form. (Ex. H, p. 5 (citing Scharer et al., *supra*, at Ex. H, Tab 5); Ex. G, p. 7; Tr. 416-18.) That time frame is well outside the 24 hours proposed by petitioner, and petitioner’s experts have not adequately rebutted Dr. Forsthuber’s detailed explanation of the timing of the secondary immune response.

Dr. Steinman references several studies concerning tuberculin tests to support his contention that “recall responses to specific antigens can be read within 24 hours.” (Ex. 12, pp. 24-25 (citing Serane & Kothendaraman, *supra*, at Ex. 47; Fan et al., *supra*, at Ex. 48; Kardjito & Grange, *supra*, at Ex. 49).) He notes one study found that “an initial reaction occurred within 30 minutes.” (*Id.* at 25 (citing Kardjito & Grange, *supra*, at Ex. 49); Tr. 203-04.) However, Dr. Forsthuber explains that the phenomenon of cell-mediated skin reaction following tuberculin injection is a different form of immune reaction known as “delayed-type hypersensitivity response” and usually take 1-2 days. (Ex. B, p. 19; *see also* Serane & Kothendaraman, *supra*, at Ex. 47, pp. 3-4 (explaining that “tuberculin reaction is a type of delayed hypersensitivity reaction, which has been noted to peak at 48-72 [hours],” and thus, “it is logical that this test is read at that time”).) Dr. Steinman does not attempt to refute Dr. Forsthuber’s explanation. (Ex. 64, p. 8; Ex. 75, p. 16.) Moreover, I have reviewed these sources, and I am not persuaded that they are applicable here. Both the studies by Serane & Kothendaraman and by Fan et al. looked at patients who did not have tuberculosis prior to undergoing a tuberculin test. (Serane & Kothendaraman, *supra*, at Ex. 47, p. 1; Fan et al., *supra*, at Ex. 48, p. 5.) Thus, nothing about the timing of a recall response can be extrapolated from these two studies. The study by Kardjito & Grange found that there were five distinct peaks of reactivity following tuberculin injection. (Kardjito & Grange, *supra*, at

Ex. 49, p. 6.) However, this study does not attempt to uncover what causes tuberculin hypersensitivity, and Dr. Steinman does adequately explain why it is relevant here.<sup>32</sup>

Dr. Steinman also relies on an animal study that he claims shows T cells that are already sensitized to myelin basic protein can enter the CNS within 24 hours. (Ex. 12, pp. 25-26 (citing Bartholomäus et al., *supra*, at Ex. 17).) Dr. Steinman quotes the study's finding that the cells appeared in the CNS "on days 1-2.5 after transfer." (*Id.* at 25 (quoting Bartholomäus et al., *supra*, at Ex. 17, p. 1).) Although he acknowledges that onset of clinical symptoms were not observed until day 3, Dr. Steinman suggests that the animal subjects could have been experiencing neurologic symptoms prior to day 3 but were unable to convey their condition to researchers. (*Id.* at 4, 26; Tr. 220-21.) He emphasizes that "humans are more eloquent in communicating symptoms than rodents are" (Tr. 221) and cautions that I "not become overly rigid about the extrapolation of neurology in the rat to neurology in the human" (*Id.* at 222; Ex. 12, p. 4). While Dr. Steinman's point may be logical, it is inherently speculative. The study's finding was that clinical symptoms manifested at 3 days. The fact that mice cannot report subjective complaints is a limitation of the study, not evidence that onset was earlier than actually observed. In any event, Bartholomäus et al. presents a "passive transfer model of EAE," in which T cells are activated in tissue culture for several days before being transferred in large number to naïve recipients. (Tr. 412; Ex. B, p. 18.) Dr. Forsthuber suggests a true understanding of the study's results as to timing should include this incubation period. (Tr. 418.) Thus, Dr. Forsthuber explains that this model does not reflect the immune response to vaccination, which "takes at least several days to develop and fully form." (Ex. B, pp. 18 (citing Sosa et al., *supra*, Ex. B, Tab 13), 20; Tr. 413.) He further explains that, when relying on activation of memory T cells in a separate experiment within the same study, Bartholomäus et al. found that cells did not enter the brain and begin causing disease until day 5. (Tr. 414-16.) Therefore, even in an experimental model that "bypassed many additional steps" that would normally occur in the immune response to vaccination, the Bartholomäus study still did not find that disease onset can occur within 24 hours. (Ex. B, p. 20.)

Taken together, this evidence suggests that, even if the flu vaccine could trigger a recall response following an unrelated vaccine, the immune system still would not respond quickly enough to cause symptoms of CNS injury to appear within 24 hours.

### iii. Case reports and onset of TM more generally

Petitioner further relies on several case reports to support a time frame for onset of TM following flu vaccination. Dr. Tornatore asserts the importance of case reports, "given that the bedside approach to every patient is essentially a case report." (Ex. 98, p. 6.) Although I have previously acknowledged that "case reports are not wholly without evidentiary value," *Skinner-Smith v. Sec'y of Health & Human Servs.*, No. 14-

<sup>32</sup> In a prior case, another special master similarly found that literature concerning tuberculin tests was not helpful in resolving timing of onset for TM. See *Contreras v. Sec'y of Health & Human Servs.*, No. 05-626V, 2013 WL 6698382, at \*48 n.41 (Fed. Cl. Spec. Mstr. Nov. 19, 2023), *vacated on other grounds*, 116 Fed. Cl. 472 (2014).

1212V, 2022 WL 13461862, at \*5 (Fed. Cl. Spec. Mstr. Sept. 9, 2022), the case reports presented do not support the 24-hour onset in this case. The case report by Akkad et al. reported symptom onset 4 days after flu vaccination. (Akkad et al., *supra*, at Ex. 86, p. 1.) The case reports by Bakshi & Mazziotta and Korn-Lubetzki et al. both reported symptom onset 4 weeks after flu vaccination. (Bakshi & Mazziotta, *supra*, at Ex. 88, p. 1; Korn-Lubetzki et al., *supra*, at Ex. 92, p. 1.) Dr. Tornatore also cites a literature review by Agmon-Levin et al., which he contends found onset in most cases to be “between several days and 3 months” post-vaccination. (Ex. 81, p. 23 (quoting Agmon-Levin et al., *supra*, at Ex. 84).) However, of the reported cases of TM following flu vaccination reviewed by Agmon-Levin et al., the earliest onset was 7 days post-vaccination. (Agmon-Levin et al., *supra*, at Ex. 84, p. 3, tbl.1 (citing Nakamura et al., *supra*, at Ex. 93).) The Nakamura case report observed that a 70-year-old man with pre-existing rheumatic arthritis and diabetes mellitus suffered backache followed by dysuria and paraplegia 7 days after receiving the flu vaccine. (Nakamura et al., *supra*, at Ex. 93, pp. 1-3.) Dr. Gelfand did acknowledge one case report of a 77-year old woman who suffered TM one day after a 2009 H1N1 flu vaccination. (Ex. A, p. 17 (citing Nozomu Sato et al., *Acute Transverse Myelitis and Acute Motor Axonal Neuropathy Developed After Vaccinations Against Seasonal and 2009 A/H1N1 Influenza*, 50 INTERNAL MED. 503 (2011) (Ex. A, Tab 6)).) However, a single case report is inherently anecdotal and Dr. Gelfand therefore opines that this case report does not establish the flu vaccine to have been causal. (*Id.*; see also *Paluck ex rel. Paluck v. Sec’y of Health & Human Servs.*, 104 Fed. Cl. 457, 475 (2012) (noting that, despite carrying some evidentiary weight, “case reports ‘do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value’” (quoting *Campbell v. Sec’y of Health & Human Servs.*, 97 Fed. Cl. 650, 668 (2011))), *mot. for rev. den’d*, 111 Fed. Cl. 160 (2013).)

Dr. Steinman further presents an epidemiologic study by Schonberger et al., which he describes as “the best supportive evidence for the rapid onset of neuroinflammation following influenza immunization.” (Ex. 64, p. 8.) Dr. Steinman highlights the Schonberger study’s finding of “an increased incidence of GBS within 0-1 day” (Ex. 12, pp. 2-3) and contends that the study is relevant, despite focusing on a disease of which petitioner did not suffer, because there is a blood-neural barrier (or blood-nerve barrier) in the peripheral nervous system that is “akin” to the blood-brain barrier in the CNS. (Ex. 75, p. 2 (citing Kanda, *supra*, at Ex. 14).) From my review of the paper, however, Dr. Steinman is incorrect to assert that the Schonberger study actually identifies increased incidences of GBS within 0-1 days of vaccination.<sup>33</sup>

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<sup>33</sup> Figure 5 within the paper is a bar graph showing imprecisely that somewhere between 8-12 cases of GBS were reported on days 0-1. (Schonberger et al. *supra*, at Ex. 13, p. 8 fig. 5.) This is higher than the totals for other (less causally controversial days) such as days 29-30 or 35-36. (*Id.*) This is the basis for Dr. Steinman’s assertion. However, nothing in the paper actually indicates that this constitutes increased incidences of GBS nor is there any calculation in the study that details the relative risk of GBS by day. Figure 6 within the same paper compares the incidences of post-vaccination GBS against expected incidences; however, that figure presents the data by one-week increments. (*Id.* at 9 fig. 6.) Figure 6 shows that 0.22 cases of GBS are expected per million persons per week and that 1.03 cases of GBS were reported in the first week post-vaccination per million vaccinated individuals. (*Id.*; see also *id.* at 7.) However, Figures 4 and 5 show that the incidences occurring on days 0-1 represent only about a quarter

Moreover, Dr. Gelfand disagrees that the findings are useful given that GBS and TM “are distinct pathophysiological and disease entities.” (Ex. A, p. 18.) Dr. Forsthuber similarly notes that “GBS differs from TM in many key aspects, including clinical features, pathogenesis, diagnostic features, and efficacy of treatments.” (Ex. B, p. 17 (citing Krishnan et al., *supra*, at Ex. 100, p. 6 tbl. 3); see also Ex. C, p. 1.) He further explains that there are several differences between the blood-brain barrier and the blood-nerve barrier, including the possibility that different mechanisms for T cell migration are involved. (Ex. B, p. 18.)

Although I have previously accepted a one-day onset of GBS following Tdap vaccination, I noted that one-day onset of GBS was “not unprecedented, but neither was it the norm.” *Harris v. Sec’y of Health & Human Servs.*, No. 18-944V, 2023 WL 2583393, at \*35 (Fed. Cl. Spec. Mstr. Feb. 21, 2023). I emphasized that respondent’s experts in *Harris* did not adequately rebut petitioner’s experts’ opinion regarding timing. *Id.* at \*34. Dealing with a different vaccine and a different injury, I clarified in *Harris* that “[o]n a different record it is likely that I would reach a different conclusion.” *Id.* at \*35; see also *McGill v. Sec’y of Health & Human Servs.*, No. 15-1485V, 2023 WL 3813524, at \*33-36 (Fed. Cl. Spec. Mstr. May 11, 2023) (finding that a 7-9 hour onset of small fiber neuropathy was not medically acceptable). Indeed, prior program cases generally do not support the proposition that a vaccine can cause or aggravate CNS demyelination within 24 hours of vaccination. *L.R. v. Sec’y of Health & Human Servs.*, No. 16-922V, 2024 WL 1912575, at \*26-27 (Fed. Cl. Spec. Mstr. Mar. 28, 2024) (finding that a 3- to -4-day onset was medically acceptable time frame for onset of anti-NMDAR encephalitis following a recall response); *Gardner v. Sec’y of Health & Human Servs.*, No. 17-1851V, 2023 WL 9288070, at \*43-46 (Fed. Cl. Spec. Mstr. Dec. 21, 2023) (finding that significant aggravation of MS from a more mild form “beginning several days post vaccination” was medically acceptable based on recall response); *Rowan v. Sec’y of Health & Human Servs.*, No. 17-760V, 2020 WL 2954954, at \*16-18 (Fed. Cl. Spec. Mstr. Apr. 28, 2020) (finding that a 30- to 36-hour onset of GBS based on a post-vaccination recall response to previously-encountered antigens was not medically acceptable); *Forrest v. Sec’y of Health & Human Servs.*, No. 14-1046V, 2019 WL 925495, at \*3-8 (Fed. Cl. Spec. Mstr. Jan. 28, 2019) (finding that 36-hour onset of TM following recall response triggered by flu vaccination was not medically acceptable); *Quackenbush-Baker v. Sec’y of Health & Human Servs.*, No. 14-1000V, 2018 WL 1704523, at \*19-23 (Fed. Cl. Spec. Mstr. Mar. 14, 2018) (finding a 40- to 41-hour onset of TM based on recall response to be medically acceptable). In a recent decision, Special Master Dorsey found a 24-hour onset of TM to be too soon following vaccination to be considered medically acceptable based on recall response. *Brancheau v. Sec’y of Health & Human Servs.*, No. 21-1209, 2024 WL 1619606, at \*23-26 (Fed. Cl. Spec. Mstr. Mar. 21, 2024). I found only one case where a special master

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of the cases that were reported during that first week. (*Id.* at 8 fig. 4, 5.) This strongly suggests to me that the relative risk the authors calculated by week (see Figure 7) cannot be readily applied to days 0-1 in isolation. (A quarter of the 1.03 cases noted for week one on Figure 6 would be about 0.26 cases of GBS per million vaccinated, which appears very close to the .22 expected incidences per million per week.) But in any event, no calculation of any kind was ever performed by the study’s authors to examine whether there was any significance to the 8-12 GBS cases occurring on days 0-1 and the paper includes no specific assertion by the authors of a relative risk of GBS on days 0-1 post-vaccination.

accepted a 24-hour onset based on recall response. *E.M. v. Sec’y of Health & Human Servs.*, No. 14-753V, 2021 WL 3477837, at \*42-44 (Fed. Cl. Spec. Mstr. July 9, 2021). In *E.M.*, Dr. Steinman opined that petitioner experienced the first symptoms of small fiber neuropathy within hours of her flu vaccination and that this time frame was medically acceptable based on a recall response to several prior flu vaccinations. *Id.* at \*43. The special master credited Dr. Steinman’s opinion over respondent’s expert’s opinion in part because Dr. Steinman was better qualified to opine on this issue, stating that “based on Dr. Steinman’s specified knowledge and understanding of immunology, I must afford his account of Petitioner’s autoimmune reaction greater weight,” and because respondent’s expert changed his opinion regarding onset at the hearing, prompting the special master to afford his changed opinion not much, “if any, weight.” *Id.* In the instant case, Drs. Steinman and Forsthuber are both sufficiently qualified to opine on issues of immunology and Dr. Forsthuber’s opinion is not subject to any of the issues affecting respondent’s expert in *E.M.* (Ex. 129; Ex. K.)

Based on the record as a whole, I cannot conclude that a one-day onset of significant aggravation of TM following petitioner’s flu vaccination is medically acceptable.

## VI. Causation-in-Fact

Petitioner argues in the alternative that his acute TM was caused-in-fact by his flu vaccination. (Ex. 144, p. 1.) As a threshold matter, this argument is fatally undercut by my findings with respect to *Loving* prongs one through three. *L.Z. v. Sec’y of Health & Human Servs.*, No. 14-920V, 2018 WL 5784525, at \*18 (Fed Cl. Spec. Mstr. Aug. 24, 2018) (“Petitioner’s direct causation claim cannot succeed, as she cannot demonstrate a vaccine ‘caused’ an illness predating vaccination.”); *W.C. v. Sec’y of Health & Human Servs.*, 100 Fed. Cl. 440, 452-53 (2011) (holding that the special master did not abuse his discretion in denying petitioner’s direct causation claim after determining that petitioner’s condition predated his vaccination), *aff’d*, 704 F.3d 1352 (Fed. Cir. 2013). However, even setting those findings aside and assuming a *de novo* TM occurring post-vaccination as Dr. Gelfand had asserted, the 24-hour period of onset for post-vaccination symptoms in this case is no more plausible with regard to a *de novo* TM than it is with respect to the significant aggravation claim discussed above. Accordingly, any alternative cause-in-fact claim fails for the same reasons discussed above with respect to *Loving* prong six.

Additionally, regardless of whether one assesses this case under *Loving* or *Althen*, Dr. Tornatore agrees that the objective testing on MRI and CSF is not consistent with an acute inflammatory process occurring post-vaccination for all the reasons discussed in greater detail under the *Loving* prong five analysis above. Accordingly, petitioner has little basis for contending that his TM was caused-in-fact by his vaccination. Dr. Tornatore opines that petitioner’s “clinical course is by far the most important” indicator of augmented inflammation implicating vaccine-causation. (Tr. 158.) However, “a proximate temporal association alone does not suffice to show a causal link between the vaccination and the injury.” *Grant*, 956 F.2d at 1148. Dr.

Tornatore opined that the position of petitioner's lesions as much or more so than the degree of inflammation explains his clinical course and further opined that the lack of enhancement on MRI suggests an older injury and that "if all of this was completely de novo new transverse myelitis, we should be seeing enhancement." (Tr. 58.) Thus, for the same reasons petitioner fails to meet his burden under *Loving* prong five, petitioner cannot prove under *Althen* prong two that his TM was caused-in-fact by the flu vaccine he received on November 23, 2011.

Accordingly, petitioner also fails to preponderantly prove that his TM was caused-in-fact by the subject flu vaccination.

## **VII. Conclusion**

Petitioner has clearly suffered a profound, life-altering injury. For that he has my sympathy. However, for all the reasons described above, there is not preponderant evidence that petitioner's TM was significantly aggravated or caused-in-fact by his flu vaccination administered on November 23, 2011. Therefore, this case is dismissed.<sup>34</sup>

**IT IS SO ORDERED.**

**s/Daniel T. Horner**

Daniel T. Horner  
Special Master

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<sup>34</sup> In the absence of a timely-filed motion for review of this Decision, the Clerk of the Court shall enter judgment accordingly.