In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 17-1846V
Filed: August 20, 2024

DEBORAH SUE HARDIMAN,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

Special Master Horner

Howard Scott Gold, Gold Law Firm, Wellesley, MA, for petitioner.
Camille Michelle Collett, U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

On November 28, 2017, petitioner, Deborah Sue Hardiman, filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10, *et seq.* (2012),[2] alleging that she suffered significant aggravation of her transverse myelitis as a result of an influenza ("flu") vaccine administered on October 27, 2014. (ECF No. 1.) On January 30, 2023, petitioner filed an amended petition alleging that she suffered a significant aggravation of her neuromyelitis optica spectrum disorder ("NMOSD") as a result of her October 27, 2014 flu vaccination. (ECF No. 80.) For the reasons set forth below, I conclude that petitioner is *not* entitled to an award of compensation.

[1] Because this document contains a reasoned explanation for the action taken in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the document 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, upon review, I agree that the identified material fits within this definition, I will redact such material from public access.

[2] All references to "§ 300aa" below refer to the relevant section of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

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 a number of 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 unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B). 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)(B); § 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).

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 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 but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition, and was a "but for" cause. *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[,]" with the logical sequence being 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 v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). Ultimately, petitioner must satisfy what has come to be known as the *Althen* test, which requires: (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. *Id*.

Where a petitioner in an off-Table case is seeking to prove that a vaccination aggravated a pre-existing injury, the petitioner must establish three additional factors. *See Loving v. Sec'y of Health & Human Servs.*, 86 Fed. Cl. 135, 144 (Fed. Cl. 2009) (combining the first three *Whitecotton* 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 a petitioner 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.

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). Medical records are generally viewed as particularly trustworthy evidence, because they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. § 300aa-13(b)(1). A petitioner may also rely upon circumstantial evidence. *Althen*, 418 F.3d at 1280. The *Althen* court noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279-80. While scientific certainty is not required, that expert's opinion must be based on "sound and reliable" medical or scientific explanation. *Boatmon v. Sec'y of Health & Human Servs*., 941 F.3d 1351, 1359 (Fed. Cir. 2019).

Cases in the Vaccine Program are assigned to special masters who are responsible for "conducting all proceedings, including taking such evidence as may be appropriate, making the requisite findings of fact and conclusions of law, preparing a decision, and determining the amount of compensation, if any, to be awarded." Vaccine Rule 3. Special masters must ensure each party has had a "full and fair opportunity" to develop the record but are empowered to determine the format for taking evidence based on the circumstances of each case, including having the discretion to decide cases without an evidentiary hearing. Vaccine Rules 3(b)(2) and 8(a) and (d). Special masters are not bound by common law or statutory rules of evidence but must consider all relevant and reliable evidence in keeping with fundamental fairness to both parties. Vaccine Rule 8(b)(1). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions."

§ 300aa-13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Human Servs.*, 3 F.3d 413, 417 (Fed. Cir. 1993).

In this case, petitioner has alleged that the flu vaccine significantly aggravated her NMOSD. NMOSD is not listed on the Vaccine Injury Table relative to the flu vaccine. Therefore, petitioner must satisfy the above-described *Althen/Loving* test for establishing causation-in-fact.

II. Procedural History

This case was originally assigned to another special master. (ECF No. 4.) Petitioner filed an affidavit, medical records, and finally a Statement of Completion between January of 2018 and June of 2019. (ECF Nos. 10, 12, 24, 27, 32-33; Exs. 2-12.)[3] The case was then reassigned to the undersigned on August 27, 2019. (ECF No. 38.) Respondent filed his Rule 4(c) Report about a month later, contesting petitioner's entitlement to compensation. (ECF No. 40.)

Petitioner filed additional medical records in March of 2020 (Exhibit 13) and an expert report by neurologist Marcel Kinsbourne, M.D. (Exhibit 14) in June of 2020. (ECF Nos. 45, 50; *see also* ECF No. 51 (medical literature).) Respondent filed a responsive expert report prepared by Michael Wilson, M.D., along with supporting medical literature, the following October. (ECF No. 55; Exs. A-B.) Petitioner filed a supplemental expert report by Dr. Kinsbourne in February of 2021. (ECF No. 58; Ex. 15.) Respondent filed a responsive supplemental report by Dr. Wilson in April of 2021. (ECF No. 60; Ex. C.)

I held a Rule 5 status conference on June 2, 2021. (ECF No. 61.) I explained that "there appear[ed] to be little to litigate within the first three *Loving* prongs; that is, the experts largely appear to agree that a comparison of petitioner's pre- and post-vaccination conditions indicates worsening of likely NMOSD." (*Id.* at 2.) Therefore, this case will likely turn on *Loving* prongs 4 and 5 – "the medical theory (general causation) and the logical sequence of cause and effect (specific causation)." (*Id.* at 2-3.) Petitioner was directed to complete additional filings. (*Id.* at 3.)

Between September of 2021 and January of 2022, petitioner filed additional medical records (Exhibits 16-17), a further report by Dr. Kinsbourne (Exhibit 18), and an affidavit (Exhibit 19). (ECF Nos. 64, 66-67.) Respondent then filed a further report by Dr. Wilson in March of 2022. (ECF No. 70; Ex. D.) Petitioner filed her final expert report by Dr. Kinsbourne the following July. (ECF No. 73; Ex. 20.) Thereafter, the parties agreed that the case was ripe for resolution on the written record. (ECF No. 75.)

Petitioner filed her Motion for a Ruling on the Record on November 21, 2022, and an amended petition on January 30, 2023. (ECF Nos. 77, 80.) Respondent filed a

[3] The petition indicates that Exhibit 1 was intended to be a copy of the petitioner's birth certificate (ECF No. 1, p. 1); however, that document does not appear to have been filed.

response to petitioner's motion on February 21, 2023. (ECF No. 81.) Petitioner filed a reply to respondent's response on March 7, 2023. (ECF No. 82.)

This matter is now ripe for a ruling as to entitlement. I have concluded that the parties have had a full and fair opportunity to develop the record and that it is appropriate to resolve this case without an entitlement hearing. S*ee Kreizenbeck ex rel. C.J.K. v. Sec'y of Health & Human Servs.*, 945 F.3d 1362, 1366 (Fed. Cir. 2020) (citing *Simanski v. Sec'y of Health & Human Servs.*, 671 F.3d 1368, 1385 (Fed. Cir. 2012)); *see also* Vaccine Rule 8(d); Vaccine Rule 3(b)(2).

III. Factual History

a. As reflected in the medical records

Before receiving the vaccine at issue in this case, petitioner had a history of several flares of transverse myelitis. As of October of 2007, petitioner was recovering from a relapse and experiencing "burning paresthesias at the front of her neck and thoracic area," along with incontinence. (Ex. 4, p. 36.) In October of 2008, petitioner experienced another flare, which included numbness and tingling in her legs. (*Id.* at 12.) Petitioner was admitted to the hospital and given steroids. (*Id.* at 13.) At the beginning of 2011, petitioner saw neurologist Sophia Ahmed, M.D., for a follow up regarding her transverse myelitis and ear pain. (Ex. 6, p. 6.) In August of 2012, petitioner returned to Dr. Ahmed, reporting a relapse of her transverse myelitis following a dental procedure. (*Id.* at 3.) Petitioner underwent Solu-Medrol[4] therapy and regained most of her strength; however, at the time of this appointment, she was still experiencing dysesthesias in the lower extremities and frequent micturition. (*Id.*) Petitioner was advised to continue taking Percocet, Neurontin,[5] and follow up with urology. (*Id.* at 4-5.) This flare continued through October of 2012, when petitioner again saw Dr. Ahmed and reported that she continued "to have excruciating, burning pain and dysesthesias from her mid-thoracic region downwards." (*Id.* at 1.) Petitioner was prescribed Percocet, MSIR, Amitriptyline, and Lidocaine gel. (*Id.* at 2.) In January of 2014, petitioner began seeing neurologist Kenten D. Woolhiser, M.D., for weakness that "has been sudden and has been occurring in an intermittent pattern for 20 years." (Ex. 5, p. 19.) It was noted that petitioner had been diagnosed with transverse myelitis based on a lesion in the cervical spine. (*Id.*) He further noted that petitioner was placed

[4] Solu-Medrol is an intramuscularly or intravenously administered glucocorticoid that is used as an anti-inflammatory and immunosuppressant treatment for a variety of disorders. *Methylprednisolone sodium succinate*, DORLAND'S MEDICAL DICTIONARY, https://www.dorlandsonline.com/dorland/definition?id=89219 (last visited Aug. 6, 2024); *Methylprednisolone*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=31014 (last visited Aug. 6, 2024).

[5] Neurontin is the brand name for gabapentin, an orally administered anticonvulsant treatment for partial seizures and postherpetic neuralgia. *Neurontin*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=33803 (last visited Aug. 12, 2024); *Gabapentin*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=19523 (last visited Aug. 12, 2024).

on Imuran[6] following her last flare, which occurred after having her wisdom teeth pulled. (*Id.*)

Petitioner received the flu vaccination at issue in this case on October 27, 2014. (Ex. 3.) Two months later, on December 3, 2014, petitioner received an IV infusion for her transverse myelitis. (Ex. 5, p. 18.) There is no additional information in the record pertaining to this encounter. Petitioner's next encounter was on December 19, 2014. (*Id.* at 15.) She presented to Dr. Woolhiser for a follow up on her weakness. (*Id.*) Dr. Woolhiser noted that petitioner was treated with IV Solu-Medrol during her prior episodes; however, since her last episode, petitioner reported increased pain in her extremities that was not responsive to Solu-Medrol. (*Id.*) A review of petitioner's symptoms was positive for fatigue, neck pain, decreased range of motion, muscle weakness, trouble walking, and headaches. (*Id.* at 15-16.) Her physical examination revealed decreased light touch sensation from the left T7 and right T12. (*Id.* at 16.) Petitioner was continued on Imuran for her transverse myelitis and Neurontin for her intractable cervical neuropathic pain. (*Id.*) On December 23, 2014, petitioner was treated with IVIG by drip method. (*Id.* at 14.) She was subsequently prescribed hydrocodone-acetaminophen for her transverse myelitis on December 24, 2014. (*Id.* at 12.)

On December 30, 2014, petitioner established care with a new primary care physician, Esther F. Adade, M.D. (Ex. 7, p. 6.) Petitioner reported that she was first diagnosed with transverse myelitis in 1994. (*Id.*) At this appointment, petitioner was wheelchair bound due to a transverse myelitis flare that started three weeks prior, which was being treated with IVIG and steroids. (*Id.*) Petitioner also complained of incontinence, constipation, and hypothyroidism. (*Id.*)

Petitioner had a follow up appointment with Dr. Woolhiser on January 2, 2015. (Ex. 5, p. 8.) She again reported no improvement with either Solu-Medrol or IVIG. (*Id.*) Dr. Woolhiser continued petitioner on hydrocodone-acetaminophen, Imuran, Neurontin, Fetzima, and Metanx. (*Id.* at 10.) He also recommended physical therapy. (*Id.*) During this encounter, petitioner underwent a CT scan of the abdomen and pelvis. (Ex. 9, p. 230.) An 11-day history of constipation and a history of transverse myelitis are listed as the reasons for the exam. (*Id.*) The results confirmed constipation and distended bladder. (*Id.*) Two days later, petitioner underwent an MRI of the spine. (*Id.* at 231.) The impression is recorded as follows:

> There is a focal dextro scoliosis in the upper thoracic spine. This along with motion artifact makes evaluation of the segment of the thoracic cord more challenging. There is an abnormal patchy T2 signal in the upper cervical cord. Pronounced T2 signal abnormality is seen in the lower cervical cord

[6] Imuran is the brand name for azathioprine, an orally administered immunosuppressant that is used in the treatment of a number of autoimmune disorders. *Imuran*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=24994 (last visited Aug. 6, 20240; *Azathioprine*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=5231 (last visited Aug. 6, 2024).

> and upper thoracic cord spanning for approximately C5 to approximately T6. This is very fluidlike in the very upper cervical cord. No gross abnormal enhancement is noted. Findings are consistent with a nonspecific myelitis which could be due to an inflammatory or infectious process or nonspecific etiology/demyelination. In the very upper margin of this signal abnormality, in the lower cervical cord, there . . . appears to be some component of the syrinx. In the remaining portions of the cord signal abnormality is more patchy and diffusely abnormal. No circumferential cord impingement is noted.

(*Id.* at 231-32.)

Petitioner was admitted to a rehabilitation hospital on January 8, 2015. (Ex. 9, p. 301.) In her pre-admission assessment, petitioner reported a chronic history of transverse myelitis, which had been diagnosed over 20 years prior. (*Id.* at 210.) Petitioner reported that "she was doing well, ambulating as usual until about two weeks ago when she lost her ability to ambulate." (*Id.*) She complained of numbness and tingling, as well as intermittent sharp pain in her bilateral feet and legs, which radiated up above her T12 dermatome. (*Id.*) At this time, petitioner could walk with assistance, was able to feed herself, and had good function of her upper extremities. (*Id.* at 211-13.) It was noted that petitioner had been treated with steroids and IVIG by Dr. Woolhiser without improvement and that her "symptoms are usually less pronounced and do not last as long." (*Id.* at 210.) Petitioner underwent an ultrasound of her abdomen, which found no abnormalities. (*Id.* at 233-34.) During her hospital stay, petitioner attended physical and occupational therapy. (*Id.* at 344-65, 371-82.) In addition to her lower extremality weakness, she was also treated for neurogenic bladder and severe constipation. (*Id.* at 235-40.) Petitioner was discharged from physical and occupational therapy on January 30, 2015, and February 4, 2015, respectively. (*Id.* at 366-70, 383-84.) She was directed to continue with outpatient physical and occupational therapy upon discharge. (*Id.* at 367, 383.)

On February 16, 2015, petitioner was prescribed Baclofen for muscle weakness. (Ex. 5, p. 7.) Petitioner presented to Dr. Woolhiser for a follow up on February 19, 2014. (*Id.* at 4.) Petitioner reported that her pain had increased and was radiating down her legs and arms. (*Id.*) Dr. Woolhiser recorded that petitioner "had improvement until recently." (*Id.*) Petitioner was continued on Imuran, Neurontin, and Metanx, and restarted on hydrocodone-acetaminophen. (*Id.* at 6.)

Petitioner had an appointment with Dr. Adade on March 19, 2015. (Ex. 7, p. 24.) Petitioner requested a neurology referral, given that her condition had worsened. (*Id.* at 24-25.) The Review of Systems indicated the presence of fatigue, myalgias, arthralgias, and weakness, but was negative for difficulty urinating. (*Id.* at 25.) She remained wheelchair bound. (*Id.*) The following day, on March 20, 2015, petitioner was admitted to the hospital with "progressive loss of lower extremity strength and left upper extremity strength," as well as shortness of breath. (Ex. 10, p. 35.) She was placed on IV

steroids and underwent 7 treatments of plasmapheresis[7] as recommended by the attending neurologist. (*Id.*) With this treatment, petitioner experienced minimal improvement in her left upper extremity and her shortness of breath was unchanged. (*Id.*) She was discharged to a rehabilitation facility on April 8, 2015. (Ex. 10, pp. 35; Ex. 13, pp. 273-83.) Her diagnoses included myelitis, quadriplegia, quadriparesis, hypothyroidism, neurogenic bladder and bowel, dysphagia, muscle weakness, insomnia, muscle spasm, thrombocytopenia, chronic pain, urinary tract infection, anxiety, and depression. (Ex. 13, p. 46.) On April 9, 2015, petitioner complained of dizziness and shortness of breath, stating that she "just doesn't feel right" and that "something else is wrong." (*Id.* at 383.) Upon physical examination, petitioner appeared sweaty and clammy. (*Id.*) By April 11, 2015, petitioner developed a rash on the right side of her chest that was associated with blistering and pain. (*Id.* at 37.) Petitioner was subsequently diagnosed with shingles. (*Id.* at 380.)

On April 17, 2015, petitioner was transferred back to the hospital due to concerns of low blood pressure, elevated heart rate, and shortness of breath. (Ex. 10, pp. 30-31.) Her primary diagnoses on admission were acute anemia and worsening shingles. (*Id.* at 30.) During her hospital stay, she underwent blood transfusion and was continued on azathioprine for her transverse myelitis. (*Id.* at 33.) She was diagnosed with T4 dermatomal shingles and was placed on famciclovir. (*Id.*) Petitioner underwent a chest x-ray as a part of her hospital stay, and the impression noted "asymmetric left basilar airspace/pleural disease obscuring the left hemidiaphragm." (*Id.* at 137.) Petitioner was also evaluated by physical, speech, and occupational therapists. (*Id.* at 151-58, 160-65, 167-70.) On May 7, 2015, petitioner was discharged to a nursing home for further treatment. (*Id.* at 33-34.) At the time she was discharged, petitioner was still experiencing "generalized weakness on upper and lower extremities with quadriparesis and quadriplegia secondary to transverse myelitis." (*Id.* at 33.) Her primary diagnoses on discharge included transverse myelitis, anemia of chronic disease, neurogenic bladder and bowel, dysphagia, quadriplegia and quadriparesis, and chronic pain. (*Id.*) She was instructed to continue taking azathioprine and to follow up with neurology. (*Id.* at 34.)

Upon admission to a nursing home for inpatient rehabilitation on May 8, 2015, petitioner was examined by Eric D. Aitken, M.D. (Ex. 9, pp. 284, 288-89.) Dr. Aitken summarized petitioner's medical course and noted that, given petitioner's functional limitations, "it was felt she would benefit from acute inpatient rehab." (*Id.* at 284.) A physical examination showed flaccid lower extremities, hands in claw position, and flat affect. (*Id.* at 287.) She remained wheelchair bound and reported banding pain and focal weakness in her bilateral upper extremities, which was worse in the left side. (*Id.*) Petitioner underwent an MRI on May 23, 2015, which again revealed persistent areas of T2 hyperintense signal. (*Id.* at 109.) Specifically, the study showed mild progression of

[7] Plasmapheresis is a therapeutic procedure in which plasma is removed from withdrawn blood before reinfusion with albumin or some other plasma substitute, thus depleting the body's own plasma without depleting its cells. *Plasmapheresis*, STEDMAN'S MEDICAL DICTIONARY (28th ed. 2006); *Plasmapheresis*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=39455 (last visited August 6, 2024).

the T2 hyperintense signal within the lower cervical spinal cord from the C5-T3 levels with possible mild enhancement, although the evaluation was limited by motion artifact. (*Id.*) It was suggested that "[t]his finding may relate to acute flareup of the patient's transverse myelitis." (*Id.*) However, the abnormal signal within the upper cervical spinal cord appeared improved, and the overall degree of degenerative changes appeared stable. (*Id.*)

Petitioner was admitted to a rehabilitation center on June 12, 2015. (Ex. 9, p. 82.) That same day, she underwent an MRI of the brain and cervical spine. (*Id.* at 108-09.) The brain MRI revealed stable areas of hyperintense T2 signal involving both cerebral hemispheres, which were nonspecific findings that could be related to a demyelinating disorder. (*Id.* at 108.) Overall, "[n]o significant change involving the appearance of the brain [was] identified." (*Id.*) The MRI of the cervical spine revealed "persistent, ill-defined, hyperintense T2 signal change involving portions of the spinal cord including involvement of the upper cervical cord extending to the level of the cervical medullary junction." (*Id.* at 109.) However, these findings appeared to be stable, and there was "no abnormal enhancement involving the visualized portion of the spinal cord." (*Id.*) During her stay, petitioner's medication was switched from intravenously administered Solu-Medrol to orally administered prednisone. On the morning of June18, 2015, she developed increasing muscle spasms and pain. (*Id.* at 108.) Petitioner was subsequently discharged and transferred to the hospital "for emergent evaluation of her neurologic changes related to possible transverse myelitis flare." (*Id.*)

On July 30, 2015, petitioner presented to Lael A. Stone, M.D., for a second opinion regarding multiple sclerosis. (Ex. 12, p. 3.) Dr. Stone documented petitioner's history but noted that petitioner could only provide limited information regarding her treatment and course history. (*Id.*) Petitioner reported that had been experiencing sensory problems since 1993, which included tingling, burning in her back, and a "needles" sensation. (*Id.*) She was told that "she had something which was swollen in the spinal cord," and she was diagnosed with transverse myelitis. (*Id.*) She had difficulty walking but noticed improvement after steroid treatment. (*Id.*) Petitioner reported that she had been taking Imuran for 13 years, and although she experienced reasonable recovery "after most of these flares," she still continued to experience flares despite treatment with medication. (*Id.*) She described some of these flares, including the flare she experienced following the subject vaccination. (*Id.* at 3-4.) At the time of this encounter, petitioner reported that she continued to experience spasms in her left hand that were not responsive to botox treatment. (*Id.* at 4.) She further noted a worsening of the "banding sensation" that she had been experiencing for the past 15 years. (*Id.*) Petitioner also reported pain, though the type, location, and frequency were unclear. (*Id.* at 5.) Dr. Stone noted that petitioner's brain MRI showed mild changes, and her cervical spine MRI appeared to show multiple lesions; however, the images were degraded due to movement and/or poor scanning. (*Id.*) Dr. Stone assessed

petitioner with "a [D]evic's[8] like picture although she is said to be [neuromyelitis optica ("NMO")] negative" and confirmed that petitioner has spinal cord demyelination, regardless of whether her proper diagnosis is NMO. (*Id.* at 6.) Her official diagnosis was unspecified demyelinating disease of the central nervous system. (*Id.* at 7.) Dr. Stone described petitioner's medical course as including "a lot of narcotics" and "fragmented care" that made treatment difficult as it was unclear who would be managing her care. (*Id.* at 6.) Dr. Stone further noted petitioner had a "history of exacerbations after infections" and suggested that some of her medications could be contributing to her fatigue and constipation. (*Id.*) He started her on Rituxan and ordered bloodwork to test for pancytopenia. (*Id.*) He also observed that petitioner's left hand was "very distorted" and suggested both that she follow up with a physiatrist and/or surgeon and that she consider alternative medications to address her pain, stiffness, and spasms. (*Id.*)

Petitioner's blood work was negative for the aquaporin-4 antibodies;[9] however, it was noted that negative results could be due to immunosuppression treatment. (Ex. 12, p. 14.) Petitioner was subsequently prescribed Vitamin D based on her lab results. (*Id.* at 20.)

Petitioner had a follow up appointment with her primary care physician, Dr. Adade, on August 24, 2015. (Ex. 7, p. 34.) Dr. Adade noted petitioner's history of transverse myelitis and recent diagnosis of multiple sclerosis. (*Id.* at 40.) In pertinent part, petitioner's physical examination was normal. (*Id.* at 41.) Dr. Adade reiterated that petitioner had been hospitalized in several different hospitals and treated by various neurologists, resulting in fragmented care. (*Id.* at 40.) She noted that she planned to begin weaning petitioner off some of her prescriptions based on Dr. Stone's recommendation, but she refused to begin treating petitioner's multiple sclerosis, explaining that "this is not my area of expertise and that would be inappropriate." (*Id.* at 40, 42.) Dr. Adade's assessment included transverse myelitis and multiple sclerosis, and she noted her plan to begin weaning petitioner off narcotics. (*Id.* at 42.) Petitioner's next primary care appointment was on September 4, 2015. (*Id.* at 49.) Petitioner complained of neurologic pain, and Dr. Adade reported that her neurology referral was "still in process." (*Id.* at 54.) A review of petitioner's symptoms was positive for fatigue, myalgias, arthralgias, and weakness. (*Id.*) Dr. Adade's assessment included multiple sclerosis, and she noted that petitioner opted to forego hand surgery at this time. (*Id.* at 55.) Petitioner had another appointment with Dr. Adade on October 28, 2015. (*Id.* at 66.) She complained of chronic pain and reported that she had not yet been able to see a neurologist or begin treatment of her multiple sclerosis. (*Id.*) A review of petitioner's symptoms was again positive for myalgias, arthralgias, and weakness, as well as gait problems and numbness. (*Id.* at 66-67.) Dr. Adade's

[8] Neuromyelitis optica ("NMO") is also known as Devic's disease. *Devic disease*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=70259 (last visited Aug. 7, 2024).

[9] Aquaporin-4 antibodies are sometimes referred to as "AQP4" and "AQP-4" throughout this decision.

assessment included transverse myelitis, multiple sclerosis, neuropathic pain, neuralgia, and severe pain. (*Id.* at 67.)

There was a significant gap in treatment until June 19, 2018, when petitioner presented to Dr. Adade for a Medicare annual wellness visit. (Ex. 11, pp. 8-9.) Dr. Adade noted that petitioner was taking Rituxan for a "neuromuscular disorder/[multiple sclerosis]," as well as tramadol and Neurontin for chronic pain. (*Id.* at 8.) She reported that she had "been doing well." (*Id.*) A review of her symptoms was positive for arthralgias. (*Id.*) Dr. Adade's assessment included neurogenic bladder, quadriplegia and quadriparesis, multiple sclerosis, and severe pain. (*Id.* at 10, 12.) Petitioner returned to Dr. Adade on July 7, 2018, for a well woman and gynecological exam. (*Id.* at 66, 69.) She complained of cough and chronic constipation. (*Id.* at 66.) A Review of Systems was also positive for rhinorrhea. (*Id.* at 68.) Petitioner was diagnosed with acute bronchitis. (*Id.* at 69.)

b. As reflected in affidavits

Petitioner submitted three affidavits in this case. (Exs. 2, 8, 19.) She explains that she received the subject flu vaccine on October 27, 2014. (Ex. 2, ¶ 3.) Before receiving the vaccine, petitioner worked as a history teacher and enjoyed jogging recreationally. (*Id.* ¶ 4; Ex. 8, ¶ 3.) Petitioner explains that she suffered from transverse myelitis before her vaccination, but it was under control. (Ex. 8, ¶ 4.) She reports that she was taking Imuran for her symptoms; however, she ran out of her prescription "towards the middle to end of November 2014," and "had not been taking Imuran for many days," when she experienced the flare at issue in this case. (Ex. 19.) As a result of the subject vaccination, petitioner believes that her transverse myelitis was significantly aggravated. (Ex. 8, ¶ 8.) She describes paralysis in her bilateral legs, no functionality of her left arm and hand (claw hand), shortness of breath, spinal inflammation, total body pain, and fatigue. (Ex. 2, ¶¶ 5-8.) Additionally, she has limited diaphragm function, bladder and bowel issues, vocal and speech weakness, and hypotension. (*Id.* ¶¶ 9-12.) She states that her injury has impeded her ability to work and severely diminished her quality of life. (*Id.* ¶ 13; Ex. 8, ¶ 9.)

IV. Summary of Expert Opinions and Qualifications

a. Petitioner's Expert, Marcel Kinsbourne, M.D.[10]

Petitioner's expert, Dr. Marcel Kinsbourne, submitted four expert reports in this case. (Ex. 14, Tab A; Ex. 15; Ex. 18; Ex. 20.) Dr. Kinsbourne explained that petitioner's

[10] Dr. Marcel Kinsbourne received his bachelor's and medical degree from Oxford University. (Ex. 14, Tab P, p. 1.) He was conferred a medical degree from North Carolina in 1967. (*Id.*) He is licensed in the United Kingdom, Canada, North Carolina, Massachusetts, and Virginia, and board certified by London's Royal College of Physicians, the Educational Council for Foreign Medical Graduates, and the American Board of Pediatrics. (*Id.*) He has held several academic and hospital positions at various institutions and hospitals since beginning his career in 1964. (*Id.* at 1-2.) He has authored over 400 peer reviewed articles and nine books on pediatrics, neurology, and psychology. (*Id.* at 5-34.)

transverse myelitis was "multiphasic," and the "most common multiphasic inflammatory demyelinating condition that can feature myelitis is multiple sclerosis." (Ex. 14, Tab A, p. 5.) However, the diagnosis of multiple sclerosis is not supported in this case as there was no evidence of dispersion of lesions in space of her recurrences. (*Id.*) Dr. Kinsbourne also noted that petitioner's treating physicians did not prescribe drugs that are normally used to treat multiple sclerosis, "which are known to be detrimental to patients with NMO." Dr. Kinsbourne suggested that petitioner instead had NMOSD. (*Id.* at 5-6.) Dr. Kinsbourne explained that NMO "is a relapsing and remitting inflammatory demyelinating central nervous system disorder that causes longitudinally extensive transverse myelitis (exceeding two spinal segments) as well as optic neuritis." (*Id.* at 5.) He explained that, because petitioner lacked the optic component of neuromyelitis, her condition is more accurately characterized as neuromyelitis optic spectrum disorder ("NMOSD"). (*Id.* (citing Corinna Trebst et al., *Update on the Diagnosis and Treatment of Neuromyelitis Optica: Recommendations of the Neuromyelitis Optica Study Group (NEMOS)*, 261 J. NEUROLOGY 1 (2014) (Ex. 14, Tab K)).)

This diagnosis would usually require a positive aquaporin-4 antibody test, however, Dr. Kinsbourne explains that the test is negative "in a subset of NMOSD that is clinically indistinguishable." (Ex. 14, Tab A, pp. 5-6 (quoting N. Collongues et al., *Neuromyelitis Optica in France: A Multicenter Study in 125 Patients*, 74 NEUROLOGY 736, 741 (2010) (Ex. 14, Tab C, p. 7)).) Specifically, he explained that diagnostic criteria, including identification of certain symptoms and test results, are used in clinical practice to guide care for individual patients, while research diagnostic criteria, or classification criteria, such as aquaporin-4 positivity, are intended to identify relatively uniform groups of patients for clinical research. (*Id.* at 6 (citing Dean M. Wingerchuk & Brian G. Weinshenker, *Neuromyelitis Optica Spectrum Disorder Diagnostic Criteria: Sensitivity and Specificity are Both Important*, 23 MULTIPLE SCLEROSIS J. 182 (2017) (Ex. 14, Tab N)).) The presence of aquaporin-4 antibodies is not necessary to diagnose NMOSD so long as the clinical presentation is consistent with such diagnosis. (*Id.*) In fact, aquaporin-4 antibody positive, myelin oligodendrocyte glycoprotein ("MOG") autoantibody positive, and seronegative cases of NMOSD "have similar clinical characteristics and similar courses of disease." (*Id.*) Therefore, he opined that, even though petitioner's aquaporin-4 antibody test was negative and she was never tested for myelin oligodendrocyte glycoprotein antibodies, she still likely has NMOSD. (*Id.*)

Dr. Kinsbourne also explained that "[p]rimary Sjögren's syndrome . . . is an autoimmune disorder characterized by lymphocytic infiltration of exocrine glands, mainly the lacrimal and salivary glands." (Ex. 14, Tab A, pp. 9-10.) Sjögren's syndrome is characterized by a "chronic sicca syndrome with dry eyes and dry mouth," and may involve the central and peripheral nervous system. (*Id.*) Dr. Kinsbourne noted that multiple case reports have documented the concurrence of Sjögren's syndrome and NMOSD. (*Id.* (citing Timothy W. West et al., *Acute Transverse Myelitis: Demyelinating, Inflammatory, and Infectious Myelopathies*, 32 SEMINARS NEUROLOGY 97 (2012) (Ex. 14, Tab M; *see also* Ex. A, Tab 1)).) Dr. Kinsbourne cited a case report in which a patient presented "with a clinical picture of NMO who had both [Sjögren's syndrome] and NMOSD." (*Id.* (citing Apoorva Jayarangaiah et al., *Sjögren's Syndrome and*

Neuromyelitis Optica Spectrum Disorders (NMOSD) – A Case Report and Review of Literature, 14 BIOMED CENT. NEUROLOGY 1 (2014) (Ex. 14, Tab D)).) Dr. Kinsbourne cited another case report describing "a case of Sjogren's syndrome that initially presented as acute longitudinal myelitis." (T. Yamamoto et al., *Neurological Picture: Acute Longitudinal Myelitis as the Initial Manifestation of Sjogren's Syndrome,* 77 J. NEUROLOGY, NEUROSURGERY & PSYCHIATRY 780, 780 (2006) (Ex. 14, Tab O, p. 1).) However, Dr. Kinsbourne ultimately concluded that "there is no need to speculate whether the NMOSD was related to Sjogren's syndrome or not," because "the applicable medical literature makes no distinction as to the clinical characteristics of NMOSD, whether associated with Sjogren's syndrome or not, or whether [aquaporin-4] antibodies, [myelin oligodendrocyte glycoprotein] antibodies . . . are present or not." (*Id.* at 10.)

Dr. Kinsbourne described NMO/NMOSD as both a parainfectious and a post-infectious disorder, resulting in an autoimmune attack against protein, such as aquaporin-4 or myelin oligodendrocyte glycoprotein. (Ex. 14, Tab A, pp. 6-7 (citing Yoshikazu Nakamura et al., *Influenza-Associated Monophasic Neuromyelitis Optica*, 50 INTERNAL MED. 1605 (2011) (Ex. 14, Tab I)).) Dr. Kinsbourne cites a case report where a patient with aquaporin-4 antibodies was diagnosed with a parainfectious NMOSD that was associated with a concurrent herpes zoster infection. (Ex. 14, Tab A, p. 7 (citing Jin-Sung Park et al., *A Recurrent Longitudinally Extensive Transverse Myelitis with Aquaporin-4 (AQP4) Antibody After Herpes Zoster*, 334 J. NEUROLOGICAL SCIS. 69 (2013) (Ex. 14, Tab J)).) Dr. Kinbourne further notes this case report discusses other prior case reports of NMO following varicella, mumps, and cytomegalovirus infections. (*Id.*) He asserted that vaccinations have also been shown to elicit an autoimmune response that could result in onset or a flare of NMO. (Ex. 14, Tab A, p. 6.)

Dr. Kinsbourne suggested that because vaccines "are constructed to elicit immune response to the same surface epitopes" as the viruses they target, vaccination can also "stimulate NMO onset and/or relapse." (Ex. 14, Tab A, p. 7.) He cites a study in which the authors suggested "that vaccines might trigger onset or relapse of demyelinating [central nervous system] syndromes" and, specifically, that demyelination often occurs in the optic nerves and the myelin (presenting as optic neuritis and myelitis) following the flu and HPV vaccinations. (*Id.* (citing Dimitrios Karussis & Panayiota Petrou, *The Spectrum of Post-Vaccination Inflammatory CNS Demyelinating Syndromes*, 13 AUTOIMMUNITY REVS. 215 (2014) (Ex. 14, Tab E)).) Dr. Kinsbourne also cited "a multi-center retrospective analysis of patients with neuromyelitis optica spectrum disorder for whom immunization history and clinical records from disease onset were available." (*Id.* at 8 (citing Maureen A. Mealy et al., *Vaccines and the Association with Relapses in Patients with Neuromyelitis Optica Spectrum Disorder*, 23 MULTIPLE SCLEROSIS & RELATED DISORDERS 78 (2018) (Ex. 14, Tab G; *see also* Ex. A, Tab 3)).) He explained that Mealy et al. found evidence of increased incidence of NMO flares over a period of 90 days following vaccination. (Ex. 14, Tab A, p. 8 (citing Mealy et al., *supra*, at Ex. 14, Tab G).) The study also found that fewer flares occurred in immunosuppressed patients, noting that only 3 immunosuppressed patients experienced flares as opposed to 7 untreated patients who experienced flares. (*Id.*

(citing Mealy et al., *supra*, at Ex. 14, Tab G).) However, he explained that, with regard to the 3 immunosuppressed patients, the results did not reach statistical significance, likely due to the small sample size. (*Id.* at 8-9 (citing Mealy et al., *supra*, at Ex. 14, Tab G). Dr. Kinsbourne asserts that vaccines were associated with flares in both untreated and immunosuppressed patients (citing Mealy et al., *supra,* at Ex. 14, Tab G, p. 3 tbl.2) and further that the flu vaccine was the most frequently implicated in triggering NMO (citing Mealy et al., *supra,* at Ex. 14, Tab G, p. 3 tbl.1). Dr. Kinsbourne also included a case report of a patient who developed transverse myelitis with Brown-Séquard syndrome after receiving a flu vaccination. (Ex. 14, Tab A, p. 8 (citing A.J. Larner & S.F. Farmer, *Myelopathy Following Influenza Vaccination in Inflammatory CNS Disorder Treated with Chronic Immunosuppression*, 7 EUR. J. NEUROLOGY 731 (2000) (Ex. 14, Tab F)).) The patient was on immunosuppressants, suggesting that "immunosuppression does not preclude the development of neurological complications following the influenza vaccination." (Larner & Farmer, *supra*, at Ex. 14, Tab F, p. 3.) Dr. Kinsbourne explained that these studies "indicate that the influenza vaccination can cause flares in the course of NMO/NMOSD." (Ex. 14, Tab A, p. 9.) However, he acknowledged that there is a "non-significant result of treatment" with immunosuppressant drugs. (*Id.*) He attributed this to the smaller sample size and explained that "[f]ailure to disconfirm the null hypothesis can never be construed as evidence for the nonexistence of the postulated effect." (*Id.*) As such, he opined that "a retrospective analysis of a small patient sample is of limited use for the detection of rare events." (*Id.*)

In petitioner's case, her NMOSD began in 1994 and resulted in multiple transverse myelitis flares, which she was able to control with medication. (*Id.* at 6-7.) However, Dr. Kinsbourne opined that petitioner had a major relapse in 2014 after her flu vaccination and her condition became "expanded, unremitting, intractable and permanently disabling." (*Id.* at 7.) Dr. Kinsbourne explained that petitioner's symptoms began 35 days after she received her vaccination. (Ex. 14, Tab A, p. 9.) He opined that "[t]his is well within the risk interval for [flu] vaccination of 42 days." (*Id.*)

In his first supplemental report, Dr. Kinsbourne acknowledged that petitioner's medical records are incomplete and, therefore, it is "difficult definitively to diagnose her as having NMOSD." (Ex. 15, p. 1.) Specifically, petitioner's negative aquaporin-4 antibody test complicates this case. (*Id.*) However, Dr. Kinsbourne noted that repeat testing was recommended because petitioner's immunosuppressants could cause a negative result. (*Id.* (citing Ex. 12, p. 14).) Additionally, Dr. Kinsbourne cited a study by Wingerchuck and Weinshenker, which found that "the frequent use of immunosuppressive therapy for a previously diagnosed rheumatologic disease may suppress aquaporin-4 antibodies, increasing the chances of negative serological test for aquaporin-4 autoantibodies in a patient who develops concomitant NMO or NMOSD." (*Id.* (quoting Dean M. Wingerchuk & Brian G. Weinshenker, *The Emerging Relationship Between Neuromyelitis Optica and Systemic Rheumatologic Autoimmune Disease*, 18 MULTIPLE SCLEROSIS J. 5 (2012) (Ex. 15, Tab K)).) Dr. Kinsbourne opined that because no further study was done, nor was there any test for myelin oligodendrocyte glycoprotein autoantibodies, whether petitioner was positive or negative for the

aquaporin-4 antibody "remains indeterminate." (*Id.* at 1-2.) Therefore, in his opinion, the diagnosis has to be verified on clinical and imaging grounds. (*Id.* at 2.)

Dr. Kinsbourne differentiated between multiple sclerosis and NMO/NMOSD. (Ex. 15, pp. 2-3.) He explained that "[t]ransverse myelitis in [multiple sclerosis] is typically 'short segment' (extending over less than two spinal segments), whereas the myelitis in NMO/NMOSD is longitudinally extensive, as it is in [petitioner's] case." (*Id.* at 2.) Dr. Kinsbourne noted that Dr. Wilson suggested that petitioner could still have multiple sclerosis "if multiple flares of [transverse myelitis] had summed up to contribute to its greater length in her case." (*Id.*) However, Dr. Kinsbourne dismissed this suggestion because the radiologists interpreting petitioner's MRIs did not suspect multiple sclerosis as a possibility and because some patients with NMO/NMOSD also have short segment MRI lesions, suggesting that even the summation of short segments would not necessarily support a diagnosis of multiple sclerosis. (*Id.* (citing Eoin P. Flanagan et al., *Short Myelitis Lesions in Aquaporin-4-4-IgG-Positive–Neuromyelitis Optica Spectrum Disorders*, 72 J. AM. MED. ASS'N 81 (2015) (Ex. 15, Tab A)).) Additionally, Dr. Kinsbourne opined that "even multiple flares of [transverse myelitis] in [multiple sclerosis] would be unlikely to implicate the whole length of the cervical cord, reaching down to T3, as well as extending upward to reach the junction of the spinal cord with the brainstem." (*Id.* (citing Ruth Geraldes et al., *The Current Role of MRI in Differentiating Multiple Sclerosis From Its Imaging Mimics*, NATURE REVS. NEUROLOGY 1 (2018) (Ex. 15, Tab B)).)

Dr. Kinsbourne explained that petitioner "had multiple relapses of her transverse myelitis over 20 years." (Ex. 15, p. 2.) He further explained that "[i]t would be highly improbable that a patient with [multiple sclerosis] would have relapses that remained confined to just one region of the [central nervous system] over a period of more than 20 years, without any clinical signs implicating any other region of the nervous system during all those years." (*Id.* (quoting Aksel Siva, *Common Clinical and Imaging Conditions Misdiagnosed as Multiple Sclerosis: A Current Approach to the Differential Diagnosis of Multiple Sclerosis*, 36 NEUROLOGIC CLINICS 69 (2018) (Ex. 15, Tab J)).) Additionally, Dr. Kinsbourne explained that petitioner suffered "extreme neuropathic pain," which is a characteristic of NMO/NMOSD. (*Id.*) While patients with multiple sclerosis and NMO/NMOSD both suffer fatigue, patients with NMO/NMOSD specifically experience more severe pain than patients with multiple sclerosis. (*Id.* (citing Hiroki Masuda et al., *Difference in Fatigue and Pain Between Neuromyelitis Optica Spectrum Disorder and Multiple Sclerosis*, 15 PLOS ONE 1 (2020) (Ex. 15, Tab E); Douglas Kazutoshi Sato et al., *Seronegative Neuromyelitis Optica Spectrum – The Challenges on Disease Definition and Pathogenesis*, 72 ARQUIVOS DE NEURO-PSIQUIATRIA 1 (2014) (Ex. 15, Tab I)).) Finally, Dr. Kinsbourne explained that petitioner was treated with Imuran (azathioprine) and Rituximab, which are normally used to treat NMOSD, not multiple sclerosis. (*Id.* at 3.) In fact, he noted that medication used to treat multiple sclerosis "might dramatically exacerbate NMOSD." (*Id.* (citing Jacqueline Palace et al., *Interferon Beta Treatment in Neuromyelitis Optica: Increase in Relapses and Aquaporin 4 Antibody Titers*, 76 ARCHIVES NEUROLOGY 1016 (2010) (Ex. 15, Tab H)).) Therefore, Dr. Kinsbourne opined that NMOSD was petitioner's proper diagnosis. (*Id.*)

Dr. Kinsbourne described Dr. Wilson's suggestion that petitioner's flare "could have occurred absent any vaccination, given her tendency to recurring and remitting flares of myelitis," as merely speculative. (Ex. 15, p. 3.) He explained that it is unreasonable to argue that petitioner's latest flare, which "totally changed the trajectory of her disease from relapsing-remitting to aggravated, persistent and still relapsing," occurred by coincidence when this "unusually damaging event" occurred "within the risk interval of a vaccination that is known to be able to trigger and to aggravate NMO/NMOSD." (*Id.*) Dr. Kinsbourne further explained that, although petitioner "does have a history of exacerbations after infections" (*Id.* at 4 (citing Ex. 12, p. 6)), infections both trigger and aggravate NMO/NMOSD (*Id.* (quoting Xiaonan Zhong et al., *Infections in Neuromyelitis Optica Spectrum Disorder*, 47 J. CLINICAL NEUROSCI. 14 (2018) (Ex. 15, Tab L))). He argued that "[v]accinations perturb the immune system in ways designed to simulate the impacts of the corresponding infections on immune activation and therefore could similarly trigger NMO/NMOSD onsets or flares." (*Id.*)

Dr. Kinsbourne also addressed the impact of petitioner's immunosuppressant on her flare. (Ex. 15, pp. 4-5.) He clarified that the study by Mealy et al. "documented the triggering effect of flares by vaccinations in untreated patients with NMO/NMOSD." (*Id.* at 4 (citing Mealy et al., *supra*, at Ex. 14, Tab G).) He explained that, while the study found that vaccinations were less likely to trigger flares in patients who were being treated with azathioprine (Imuran), patients on immunosuppressants did still experience flares. (*Id.* (citing Mealy et al., *supra*, at Ex. 14, Tab G).) He continued, "[w]hile it is reasonable to accept that immunosuppressive treatment reduces the probability of provoked flares in NMO/NMOSD, the authors do not conclude that patients on immunosuppressant treatment are immune to flares." (*Id.*) Therefore, petitioner's immunosuppressant treatment could have been overridden by the vaccination, triggering her flare in this case. (*Id.*) Although Dr. Kinsbourne acknowledged that they are "[n]o randomized controlled studies of the effect of vaccinations on NMO/NMOSD are available," he asserted that the findings of Mealy et al. and the case reports previously cited are "persuasive circumstantial evidence that influenza vaccination can trigger NMOSD." (*Id.* at 5.) Dr. Kinsbourne concluded that, in his opinion, "[t]he evidence indicates that, more likely than not, it was the influenza vaccination that cause her disease to become so very significantly worse." (*Id.*)

In Dr. Kinsbourne's second supplemental expert report, he responded directly to three questions posed by the undersigned. (Ex. 18.) I first asked if petitioner relied on aquaporin-4 antibody positivity for the theory of causation. (*Id.*) Dr. Kinsbourne indicated that his theory is not dependent on a positive aquaporin-4 antibody test and that "[t]he identity of the underlying antibodies was not clarified in the medical records of this case." (*Id.*) Second, I asked for clarification on whether petitioner was on immunosuppressants at the time of her vaccination. (*Id.*) Dr. Kinsbourne explained that petitioner was on immunosuppressants during her vaccination, but not during her relapse. (*Id.*) He based his opinion on petitioner's prescription records. (*Id.* (citing Ex. 17, p. 6).) Finally, Dr. Kinsbourne addressed whether the cumulative effect of prior relapses could explain the catastrophic post-vaccination relapse. (*Id.*) He opined that

"[t]here is no evidence in the record that her relapses were cumulative," and that her flares have always "varied in nature or severity." (*Id.*) He further opined that "without evidence that the prior relapses were cumulative, implying that the vaccination was merely coincidental, is speculative." (*Id.*)

Dr. Kinsbourne submitted his final report on July 1, 2022. (Ex. 20.) He explained that petitioner's condition continued for twenty years leading up to her vaccination in December 2014. (*Id.* at 1.) He noted that over those twenty years petitioner "did not succumb to a serious aggravation of her condition." (*Id.*) Additionally, Dr. Kinsbourne explained that petitioner's immunosuppressive therapy did not protect her from flares. (*Id.*) Specifically, petitioner had a flare following a dental procedure in 2012, while she was taking immunosuppressants (Imuran). (*Id.* (citing Ex, 6, pp. 3-4).) Dr. Kinsbourne claimed that this "acute stress" was sufficient to provoke a relapse and suggested that the episode was short-lived because petitioner was taking Imuran. (*Id.*) Dr. Kinsbourne also described a relapse that occurred in 2008 following a bronchitis diagnosis. (*Id.* (citing Ex. 4, pp. 13-14).) In Dr. Kinsbourne's opinion, this relapse was triggered by an infection and was also likely short-lived due to Imuran. (*Id.*) Finally, petitioner had a relapse following a flu vaccination in December 2014. (*Id.* at 1-2.) Dr. Kinsbourne opined that this relapse was more serious because "the reaction to the trigger . . . was not contained by Imuran." (*Id.*) Dr. Kinsbourne explained that "[s]usceptibility as such on account of discontinuation of immunosuppression is not sufficient to explain causation. There also was a trigger." (*Id.*) In petitioner's case, the trigger was her flu vaccination as it was the "only novel factor" that could account for the relapse. (*Id.*) Dr. Kinsbourne asserted that "[t]he resulting immune challenge during a lapse in immunosuppression finally overcame her defenses." (*Id.* at 2.)

b. Respondent's Expert, Michael Wilson, M.D., M.A.S., F.A.A.N.[11]

Respondent's expert, Dr. Michael Wilson, submitted three expert reports in this case. (Exs. A, C, D.) In his first report, after briefly summarizing petitioner's medical course, Dr. Wilson addressed what he believes are the "relevant diseases" in this case. (Ex. A, pp. 2-5.) He reported that since 1994, petitioner had "neuroimaging showing extensive damage to her spinal cord," and recurrent episodes of transverse myelitis. (*Id.* at 2.) He explained that petitioner's treating physicians noted an incomplete medical history that made it hard to diagnosis her condition. (*Id.* at 2-3.) He explained

[11] Dr. Michael Wilson received his bachelor's degree from the University of Chicago and his medical degree from the University of California, San Francisco School of Medicine. (Ex. B, p. 1.) He completed an internship in Internal Medicine at Massachusetts General Hospital and a residency at Harvard's Neurology Residency Program. (*Id.*) Dr. Wilson also completed a clinical fellowship in neuro-infectious diseases and postdoctoral fellowships in neurovirology and metagenomics. (*Id.*) He is licensed in neurology by the American Board of Psychiatry and Neurology. (*Id.*) He has specialty training in neuroinfectious diseases and neuroimmunology. (Ex. A, p. 1.) He currently works as a neurology professor at the University of California, San Francisco School of Medicine, and as a principal investigator of a lab that has, among other things, pioneered the development of metagenomic next-generation sequencing to diagnose neurologic infections in patients with certain neuroinflammatory conditions and developed comprehensive autoantibody and viral antibody discovery assays to search for antigenic targets and triggers of neuroinflammatory diseases. (Ex. B, p. 2; Ex. A, p. 1.) He has authored 57 peer reviewed articles, 8 review articles, and 11 books and chapters. (Ex. B, pp. 25-31.)

that it is "possible" that Dr. Kinsbourne is correct and petitioner does suffer from aquaporin-4 antibody negative NMOSD, "given her recurrent episodes of transverse myelitis." (*Id.* at 3 (citing Ex. 14).) In fact, he explained that petitioner's positive Sjögren's syndrome antibody test "is consistent with the diagnosis of NMOSD;" however, he indicated that these antibodies are not in themselves diagnostic for NMOSD as they can be coincidentally found in patients with other neuroinflammatory diseases. (*Id.* (citing West et al., *supra*, at Ex. 14, Tab M).)

Additionally, Dr. Wilson explained that petitioner's MRI showed "chronic and diffuse signal abnormality in the spinal cord," which "is consistent either with [one] or more prior episodes of longitudinally extensive transverse myelitis (which would be consistent with NMOSD or other disorders including neurosarcoidosis or primary central nervous system vasculitis), or with recurrent short segment transverse myelitis from relapsing remitting multiple sclerosis." (Ex. A, p. 3.) In relapsing remitting multiple sclerosis, many short segment lesions in the spinal cord "can become confluent over years," culminating in a diffuse spinal cord signal abnormality like what was observed in petitioner's 2015 MRI. (*Id.*) Additionally, Dr. Wilson described how petitioner's "early attacks of transverse myelitis caused short lived motoric disability" with some recovery, and it was only after the 2014 flare that she developed more permanent paraparesis. (*Id.*) He opined that this course is more consistent with transverse myelitis from multiple sclerosis, rather than NMOSD. (*Id.* (citing West et al., *supra*, at Ex. 14, Tab M).) Dr. Wilson explained that, based on the limited records presented in this case, there is not enough information about the "acute appearance of the inflammatory lesions early in [petitioner's] clinical course to differentiate between these different neuroinflammatory diseases, all of which can result in progressive paraparesis as a result of recurrent episodes of transverse myelitis." (*Id.* (citing West et al., *supra,* at Ex. 14, Tab M).) Dr. Wilson noted that petitioner has not met the diagnostic criteria for aquaporin-4 antibody negative NMOSD due to the lack of cerebrospinal fluid examination, systemic imaging to look for evidence of granulomas that could be consistent with neurosarcoidosis, or more detailed serologic testing, including myelin oligodendrocyte glycoprotein antibody testing. (*Id.* (citing Wingerchuk & Weinshenker, *supra*, at Ex. 14, Tab N).)

While Dr. Wilson does not offer a specific diagnosis, he does agree that petitioner "has a neuroinflammatory disease that causes recurrent transverse myelitis which is variably responsive to a variety of immunomodulatory and immunosuppressive therapies which had been present for 20 years before her severe exacerbation [five] weeks after an influenza vaccination at the end of 2014." (Ex. A, pp. 3-4.) He opined that "[b]ecause of her significant pre-existing injuries from prior episodes of transverse myelitis, she was more vulnerable to longer lasting disability from any subsequent relapses." (*Id.* at 4.) He explained that, because petitioner's prior episodes included similar symptoms, her pre-existing injury likely affected the same nerve pathways as were implicated by her late 2014 episode. (*Id.*)

Dr. Wilson also acknowledged that "a [five] week immune response to a flu vaccination is not impossible." (Ex. A, pp. 4-5.) However, Dr. Wilson explained that petitioner's past "flares could independently (in the absence of vaccination) cause the

same constellation of symptoms that [petitioner] experienced in December 2014." (*Id.* at 4.) Dr. Wilson noted that none of petitioner's doctors attributed the flare at issue in this case to her flu vaccination. (*Id.*) Dr. Wilson explained that petitioner was on an immunosuppressant at the time of her 2014 flare. (*Id.* (citing Ex. 5, p. 20).) Dr. Wilson acknowledged "there is some correlational (not causal) evidence of increased risk of relapse in patients with NMOSD" following the flu vaccination; however, he noted that "this increased risk was not seen in patients on preventive immunotherapy." (*Id.* (citing Mealy et al., *supra*, at Ex. 14, Tab G).) Although Dr. Wilson agreed with Dr. Kinsbourne's opinion that the lack of statistically significant results could be "due to an under powered study as a result of a small sample size," he countered that "associations can also fail to reach statistical significance because there is simply no statistically significant association." (*Id.*) Additionally, he explained that retrospective observational studies "cannot affirm or contradict causation" and "[o]nly randomized controlled studies can imply causation." (*Id.*)

Dr. Wilson submitted a supplemental expert report on April 12, 2021. (Ex. C.) In this report, he continued to agree with Dr. Kinsbourne that petitioner "may very well have NMOSD," but reiterated that, because of petitioner's incomplete diagnostic work up, he was not confident in the diagnosis. (*Id.* at 1 (citing Ex. 12).) Although Dr. Wilson agreed that petitioner's negative aquaporin-4 antibody test could have been a false negative due to her immunosuppression treatment, he suggested that petitioner could have been seronegative for aquaporin-4 antibodies, which would make a diagnosis of NMOSD even less secure. (*Id.*) He acknowledged Dr. Kinsbourne's assertion that petitioner's MRIs make it more likely that she has NMOSD and not multiple sclerosis, but explained that "the dearth of MRIs during her acute attacks (especially early on in the disease) leaves us making these probabilistic arguments because we do not have the definitive imaging studies to confidently make one diagnosis or another." (*Id.*) He also opined briefly that another possible diagnosis for petitioner could be neurosarcoidosis. (*Id.*)

Dr. Wilson opined that, regardless of petitioner's underlying disease, two points are relevant to determining whether her vaccination caused her 2014 flare: "1) before any vaccine was given, the petitioner had a longstanding inflammatory disease that caused many bouts of spinal cord inflammation, many of which occurred without any apparent exogenous trigger," and "2) repeated injury to the spinal cord (for any reason) – especially injuries that resulted in a similar constellation of symptoms . . . increases the risk for any subsequent injury to be more permanently disabling." (Ex. C, p. 1 (citing Ex. 4, p. 9; Ex. 6, p. 1).) Dr. Wilson clarified that, in his first report, he was not opining that petitioner's most recent flare was a coincidence but instead that petitioner's repeated injuries as exhibited by her multiple flares could have led to worse symptoms during her most recent flare. (*Id.* at 2.) He explained that there is "no evidence that the petitioner was having a continuous relapse after November/December 2014," and any suggestion that petitioner was experiencing a persistent relapse is "directly contradicted by the lack of enhancement on her December 2014 spinal cord MRI." (*Id.* (citing Ex. 9, p. 231).) In fact, "we only have evidence that the petitioner was more disabled after her 2014 flare." (*Id.*)

Dr. Wilson then addressed Dr. Kinsbourne's reliance on Mealy et al. (Ex. C, p. 2.) He explained that the study "doesn't even find correlational evidence for an increased risk of relapse in the days and weeks after vaccination for patients with NMOSD . . . who are on an immunosuppressant medication like azathioprine." (*Id.* (citing Mealy et al., *supra*, at Ex. 14, Tab G).) He explained that "while we may wish for better, larger, more rigorous studies that will support our arguments, we nevertheless have to rely on the scientific evidence that we actually have," and the existing evidence does not support Dr. Kinsbourne's claims. (*Id.*)

Dr. Wilson's second supplemental report addressed both Dr. Kinsbourne's second supplemental report and the undersigned's Rule 5 Order. (Ex. D.) Dr. Wilson explained that, although Dr. Kinsbourne conceded that petitioner was taking azathioprine at the time of her vaccination and for at least 25 days thereafter, Dr. Kinsbourne asserted that she may have been off the prescription for the next 10 or 11 days while waiting for a refill and that the 2014 relapse occurred during the period she was off her medication. (Ex. D, p. 1.) He explained his understanding of petitioner's "new theory of the case" as including that petitioner was not at risk of a relapse at the time of vaccination due to immunosuppression treatment, but upon discontinuing immunosuppressants, her immune system "rapidly reconstituted and somehow 'remembered' the immune stimulus it had received a month prior," resulting in the 2014 flare. (*Id.* (citing Mealy et al., *supra*, at Ex. 14, Tab G).) Dr. Wilson countered that "the status of the immune system on the day of the vaccination is most critical for determining the immune response to it, not the status of the immune system 30-35 days after the fact." (*Id.*) Dr. Wilson explained that if Dr. Kinsbourne is correct and petitioner suffers from NMOSD, was taking azathioprine until 10 days before her flare, and "her immune system rapidly reconstituted after stopping azathioprine, then it is much more reasonable to conclude that her NMOSD flared simply because she abruptly stopped taking the only medication that was keeping it in check." (*Id.*)

Dr. Wilson explained that "NMOSD is attack/flare/relapse related, and any individual attack (even the first) can be catastrophic." (Ex. D, p. 2 (citing Sean J. Pittock & Claudia F. Lucchinetti, *Neuromyelitis Optica and the Evolving Spectrum of Autoimmune Aquaporin-4 Channelopathies: A Decade Later*, 1366 ANNALS N.Y. ACAD. SCIS. 20 (2015) (Ex. D, Tab 2)).) Therefore, Dr. Wilson opined that petitioner was always at risk of a catastrophic attack and "no special trigger or exacerbating factor needs to be invoked to explain the fact that she had a severe attack other than" her NMOSD diagnosis and her pause in immunosuppressive medication. (*Id.*) Dr. Wilson stressed that there is "no doubt that repeated injuries to the spinal cord, whether it be repeated trauma, repeated ischemia, or in this case, repeated bouts of inflammation . . . makes the likelihood of a substantial recovery after every subsequent injury less likely." (*Id.*) He explained that, in this case, petitioner has suffered repeated attacks, causing significant neuropathic pain, problems with urinary retention, and lower extremity weakness. (*Id.* (citing Ex. 6, p. 1).) Petitioner's December 2014 MRI showed "no areas of contrast enhancement, but it did show old scaring," demonstrating "extensive evidence of prior damage throughout the spinal cord that would put anyone at risk for

significant decline with any new injury," but "there was no big, new (i.e., enhancing) MRI lesion to explain why this attack alone would be so consequential." (*Id.* (citing Ex. 9, p. 231).) Therefore, Dr. Wilson explained that a cumulative theory in this case is not speculative, but rather "driven by [petitioner's] pre-existing disability, many prior attacks and the clinicoradiologic dissociation of this catastrophic flare." (*Id.*)

V. Analysis

a. Diagnosis

The Vaccine Act requires a petitioner to present a claim for compensation for a "vaccine-related injury or death," as well as preponderant evidence supporting her claim. § 300aa-11(c); § 300aa-13(a)(1)(A); *Stillwell v. Sec'y of Health & Human Servs.*, 118 Fed. Cl. 47, 56 (2014), *aff'd*, 607 F. App'x 997 (Fed. Cir. 2015). Accordingly, a petitioner must specify her "vaccine-related injury and shoulder the burden of proof on causation." *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339, 1346 (Fed. Cir. 2010). Where the identity and nature of the vaccine-related injury is in dispute, the Federal Circuit has concluded that it is "appropriate for the special master to first determine what injury, if any, [is] supported by the evidence presented in the record before applying the *Althen* test to determine causation." *Lombardi v. Sec'y of Health & Human Servs.*, 656 F.3d 1343, 1352-53 (Fed. Cir. 2011). However, "the function of a special master is not to 'diagnose' vaccine-related injuries." *Andreu ex rel. Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1382 (Fed. Cir. 2009). Instead, the special master must determine, "based on the record evidence as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the [petitioner's] injury." *Id.* (citing *Knudsen ex rel. Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 549 (Fed. Cir. 1994)).

In this case, petitioner initially pleaded that the flu vaccine significantly aggravated her pre-existing transverse myelitis. (ECF No. 1, pp. 1-2.) Following her expert's assessment, petitioner subsequently filed an amended petition alleging significant aggravation of NMOSD. (ECF Nos. 78, 80.) The parties dispute the applicability of this latter injury. (ECF No. 77, pp. 9-13; ECF No. 81, pp. 15-17.)

There is a wide variety of central nervous system ("CNS") demyelinating conditions, including multiple sclerosis, transverse myelitis, optic neuritis, and NMO/NMOSD. (Karussis & Petrou, *supra*, at Ex. 14, Tab E.) These conditions are distinguished by their clinical presentations and by which CNS areas they affect. (*Id.* at 2.) Multiple sclerosis is a chronic, immune-mediated inflammatory and demyelinating disease that is generally characterized by recurrent episodes of neurological impairment, including loss of motor and sensory functions, that eventually lead to more permanent axonal damage. (*Id.* at 3.) Optic neuritis is an inflammatory demyelinating condition of the optic nerve that is often associated with multiple sclerosis. (*Id.*) While optic neuritis is an acute disease, patients often experience residual visual dysfunction. (*Id.*) Transverse myelitis is also usually monophasic and is generally characterized by inflammation and demyelination across the spinal cord, resulting in symptoms of

neurological disconnection and dysfunction below the level of the demyelinating area. (*Id.* at 6.) Finally, NMO is "an idiopathic, severe, demyelinating disease of the central nervous system that preferentially affects the optic nerve and spinal cord." (*Id.*) Although NMO was once believed to be a variant of multiple sclerosis, the condition is distinguishable by clinical, neuroradiological, and pathological criteria. (*Id.*; Trebst et al., *supra*, at Ex. 14, Tab K, p. 2.) Most patients with NMO have detectable serum antibodies against aquaporin-4, and the typical presentation includes both transverse myelitis and bilateral optic neuritis. (Dean M. Wingerchuk et al., *International Consensus Diagnostic Criteria for Neuromyelitis Optica Spectrum Disorders*, 85 NEUROLOGY 177 (2015) (Ex. A, Tab 2, p. 1).) The term NMOSD was initially introduced to include aquaporin-4 seropositive patients with atypical presentations. (*Id.* at 2; Zhong et al., *supra*, at Ex. 15, Tab L, p. 1.) However, "[t]he consensus definition of NMOSD unifies NMO and modern NMOSD definitions," and there now exists distinct diagnostic criteria for NMOSD with and without aquaporin-4 antibodies. (Wingerchuk et al., *supra*, at Ex. A, Tab 2, pp. 3 tbl.1, 10.)

Petitioner's expert, Dr. Kinsbourne, has singled out NMOSD as petitioner's most likely diagnosis based on her clinical course and work up. (Ex. 14, Tab A, pp. 5-6.) However, petitioner's treaters described her clinical course as including "fragmented care" that hindered their ability to confidently diagnose her condition. (Ex. 12, p. 6; Ex. 7, p. 40.) Although she spent a substantial amount of time in hospitals and rehabilitation centers as a result of the post-vaccination flare, no physician was able to narrow her diagnosis. (Ex. 9, pp. 108, 280-81; Ex. 10, p. 33, 35.) Given her persistent and progressing symptoms following the subject flare, petitioner presented to Dr. Stone for a second opinion, and although Dr. Stone suspected NMOSD, she could only confidently diagnose petitioner with an unspecified CNS demyelinating disease. (Ex. 12, pp. 1-2, 6-7.) Thus, while the medical records reflect that petitioner's treating physicians appear to agree that petitioner suffers from a CNS demyelinating condition, there is no consensus regarding which diagnosis best fits her presentation. (*Compare* Ex. 5, pp. 15-16, *with* Ex. 12, pp. 6-7.)

On behalf of respondent, Dr. Wilson agrees with the more limited assessment of unspecified CNS demyelinating disease. (Ex. A, pp. 2-4.) He concedes that petitioner's recurrent flares and the presence of Sjögren's antibodies is consistent with NMOSD, though Sjögren's antibodies can also be coincidentally present in patients with other neuroinflammatory disease, such as multiple sclerosis. (*Id.* at 3.) He further acknowledges that petitioner's MRI could be consistent with either NMOSD or recurrent short segment transverse myelitis in multiple sclerosis. (*Id.*) Ultimately, although Dr. Wilson does not agree that a diagnosis of NMOSD has been definitively established, he did concede that petitioner "may very well" have NMOSD and respondent does not offer any compelling alternative diagnosis.[12] (Ex. C, p. 1; *see also* ECF No. 81, p. 16 (asserting that "petitioner's actual diagnosis remains in question").)

[12] Discussing my prior Rule 5 Order, which indicated that Dr. Wilson does not dispute the NMOSD diagnosis, respondent argues against this interpretation of Dr. Wilson's opinion. (ECF No. 81, p. 16 n.9.) In the interest of completeness, it is worth quoting Dr. Wilson's statement in full. He states:

Although not definitive, given petitioner's history and presentation, I find Dr. Kinsbourne's proposed diagnosis of NMOSD to be reasonable. This diagnosis was also among the diagnoses considered by the treating physicians. (Ex. 12, p. 6.) However, even granting petitioner Dr. Kinsbourne's assumption regarding diagnosis, my conclusion is that petitioner has not established that her condition was aggravated or caused-in-fact by the flu vaccine. Thus, for the purposes of the analysis below, I will merely assume, without deciding, that petitioner suffered from NMOSD. Moreover, this would necessarily be aquaporin-4 seronegative NMOSD.[13] (Ex. 15, pp. 1-2.)

b. Petitioner's condition prior to vaccination (*Loving* prong one)

The first *Loving* prong requires an examination of petitioner's pre-vaccination condition. *Loving*, 86 Fed. Cl. at 144. There is no dispute that, prior to the subject vaccination, petitioner had a chronic inflammatory condition that resulted in periodic flares throughout the more than twenty-year course of her illness. (ECF No. 77, p. 14; ECF No. 81, pp. 22-23.) Two points regarding petitioner's pre-vaccination history are important to the analysis that follows. First, the evidence preponderantly suggests that petitioner's condition was well controlled on Imuran at the time of vaccination. Second, Dr. Wilson is persuasive in opining that petitioner's prior flares had a cumulative effect that left her more susceptible to a catastrophic attack.

There is record evidence of at least three distinct flares that occurred in 2007, 2008, and 2012. (Ex. 4, pp. 12, 36; Ex. 6, p. 3.) These flares were characterized by burning paresthesias, dysesthesias, tingling, numbness, pain, weakness, and incontinence. (Ex. 4, pp. 12-13, 36; Ex. 5, p. 19; Ex. 6, p. 1-6.) Her condition was noted as being responsive to steroids and IVIg treatment. (Ex. 6, pp. 1, 3; Ex. 4, p. 13; Ex. 5,

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> The petitioner's expert points out again that [petitioner] likely has neuromyelitis optica spectrum disorder (NMOSD) (Ex. 15, pp. 1-2). I continue to agree with him that she may very well have NMOSD, but because of the incompleteness of her diagnostic work up, I agree with Dr. Stone (Ex. 12) that we cannot be confident in the diagnosis for reasons I outlined in my original report.

(Ex. C, p. 1.) It must be noted that Dr. Wilson explicitly expresses that he "agree[s]" with Dr. Kinsbourne. (*Id.*) Moreover, that agreement is in specific regard to the fact that petitioner "likely" or "may very well" have NMOSD. (*Id.*) Respondent stresses the latter part of the statement – that "we cannot be confident" in the diagnosis. (ECF No. 81, p. 16 n.9.) However, while this is clearly a caveat to Dr. Wilson's opinion, it does not actually contradict the first part of his statement. Taken as a whole, I understand Dr. Wilson to be expressing that he agrees NMOSD is a reasonably likely diagnosis, but there is not sufficient clinical data to actually confirm it. In that regard, respondent himself does not affirmatively argue that petitioner does not have NMOSD, he argues only that her "actual diagnosis remains in question." (*Id.* at 16.)

[13] In fact, although petitioner did have a negative test result for aquaporin-4, Dr. Kinsbourne asserts that petitioner's status with regard to aquaporin-4 is "indeterminate." (Ex. 15, pp. 1-2.) Dr. Kinsbourne explains that it is possible petitioner's negative aquaporin-4 result was due to immunosuppression; however, he also acknowledges that the record lacks any follow up test that could have confirmed that suspicion. (*Id.*) Accordingly, even if an undetected seropositive NMOSD cannot be definitively excluded, it remains the case that petitioner has not preponderantly established that her NMOSD could be considered seropositive.

p. 19.) Petitioner was first prescribed Imuran in 2007 and was noted to be taking Imuran when she presented to Dr. Woolhiser on January 31, 2014, with complaints of a sudden onset of weakness that was consistent with prior flares. (Ex. 4, p. 36; Ex. 5, pp. 19-20.) There was then a gap in treatment between January 31, 2014, and December 19, 2014. (Ex. 5, pp. 15-20.) During that gap in treatment, petitioner received the subject flu vaccination at Med Check on October 27, 2014. (Ex. 3; Ex. 2, ¶ 3.) Other than the record of vaccination, there are no records for any other encounters during this period. Given the lack of contemporaneous treatment records, the description of a subsequent onset of symptoms in November of 2014 (as discussed under *Loving* prong two, below), and the experts' opinions that petitioner was at least variably responsive to immunosuppressive treatment throughout her course (Ex. A, pp. 3-4; Ex. 15, pp. 3-4; Ex. 20, p. 1), it is reasonable to conclude that petitioner's symptoms were well controlled with Imuran during the period leading up to November of 2014 and that she was not in the midst of a flare at the time of vaccination.

However, despite petitioner's condition being well controlled around the time of vaccination, Dr. Wilson opines that patients with NMOSD are always at risk of a catastrophic attack. (Ex. D, p. 2.) He explains that long-term disability in NMOSD is attack-related and any individual attack could be catastrophic. (*Id.* (citing Pittock & Lucchinetti, *supra*, at Ex. D, Tab 2).) Specifically, patients with NMOSD experience more severe attacks of myelitis, and recovery is less complete, when compared to multiple sclerosis, where disability generally occurs as part of the progressive phase of the illness. (West et al., *supra*, at Ex. 14, Tab M, p. 9; Pittock & Lucchinetti, supra, at Ex. D, Tab 2, p. 2.) In petitioner's case, Dr. Wison submits that petitioner's "many short signal lesions in the spinal cord" became "confluent over years, culminating in the diffuse spinal cord signal abnormality" seen on MRI. (Ex. A, pp. 2-3.) These short signal lesions were likely related to petitioner's "short lived motoric disability" following flares. (*Id.* at 3.) Dr. Wilson opines that these prior flares, which caused extensive scarring in the spinal cord, made petitioner "more vulnerable to developing permanent neurologic sequelae with every subsequent attack." (*Id.* at 4-5; Ex. C, p. 1; Ex. D, p. 2.) Dr. Wilson contends that petitioner's medical records support his position. Specifically, he argues that petitioner's previous attacks resulted in lasting urinary retention issues and significant neuropathic pain in her legs and trunk. (Ex. D, p. 2 (citing Ex. 6, p. 1).) He also points to the lack of enhancement and significant residual scarring on petitioner's 2014 MRI to support his opinion that petitioner was predisposed to a catastrophic attack, regardless of the trigger, as a result of her pre-existing condition. (*Id.* (citing Ex. 9, p. 231).) He states that the "extensive evidence of prior damages throughout the spinal cord . . . would put anyone at risk for significant decline with any new injury." (*Id.*) Dr. Wilson's assessment is well supported, and Dr. Kinbourne was not effective in seeking to rebut this point, ultimately offering only his own dissatisfaction with the idea that petitioner's disabling flare would have been coincidental to vaccination. (Ex. 15, pp. 4-5; Ex. 20.)

Accordingly, I find that, prior to vaccination, petitioner was suffering from a chronic inflammatory condition that was subject to flaring over time. I further find that petitioner's longstanding history of recurrent flares had a cumulative damaging effect

that predisposed her to catastrophic injury upon subsequent attacks. However, petitioner was not in the midst of a flare at the time of vaccination.

c. Petitioner's condition after vaccination (*Loving* Prong Two)

The second *Loving* prong requires an examination of petitioner's post-vaccination condition. *Loving*, 86 Fed. Cl. at 144. Petitioner received the flu vaccination at issue in this case on October 27, 2014. (Ex. 3.) While there is no record evidence precisely dating onset of petitioner's symptoms, she asserts that a flare began after she discontinued Imuran "towards the middle to end of November of 2014." (Ex. 19, ¶ 2.) Considering the medical records and petitioner's affidavit, I find that there is preponderant evidence supporting an onset of petitioner's post-vaccination flare beginning at some point between late November and early December of 2014, approximately 5 weeks following vaccination.[14] Petitioner's records show that her prescription for Imuran (60 tablets) was filled on October 22, 2014, and she was directed to take one tablet twice daily. (Ex. 17, p. 6; Ex. 5, p. 19.) In that regard, petitioner submits that her prescription had run out, and she had not taken Imuran for "many days," before her relapse. (Ex. 19, ¶ 2; ECF No. 77, p. 20.) Accordingly, the record evidence indicates petitioner was on Imuran at the time of vaccination and for close to a month afterward.

On December 3, 2014, petitioner received an IVIG infusion for transverse myelitis. (Ex. 5, p. 18.) Petitioner presented to Dr. Woolhiser on December 19, 2014, with complaints of increased pain in her extremities. (*Id.* at 15.) She reported that her condition had not responded as it had in the past to treatment with Solu-Medrol. (*Id.*) A review of her symptoms revealed symptoms that were consistent with prior episodes, including fatigue, neck pain, decreased range of motion, muscle weakness, trouble walking, and headaches. (*Compare* Ex. 5, pp. 15-16, *with* Ex. 5, pp. 19-20.) Petitioner was restarted on Imuran and Neurontin. (Ex. 5, p. 16.) However, by December 30, 2014, she was wheelchair bound. (Ex. 7, p. 6.) Petitioner also suffered from severe constipation and incontinence. (*Id.*; Ex. 9, pp. 235-36.) During her initial post-vaccination hospitalization, petitioner underwent 7 treatments of plasmapheresis with only minimal improvement in her left upper extremity weakness. (Ex. 10, p. 35.) Over the course of her flare, petitioner underwent extensive physical, occupational, and speech therapies. (Ex. 9, pp. 344-65, 371-82; Ex. 10, pp. 151-70.) When petitioner was discharged in May of 2015, she was still experiencing "generalized weakness on upper and lower extremities with quadriparesis and quadriplegia secondary to transverse myelitis." (Ex. 10, pp. 33, 35.) Her discharge diagnoses also included neurogenic bladder and bowel, dysphagia, and chronic pain. (*Id.* at 33.) At this point,

[14] Although the medical records include reports by petitioner of various dates of onset post-dating this time frame (See Ex. 7, p. 6; Ex. 9, p. 210), these dates of onset appear to relate to specific symptoms. For instance, on December 30, 2014, petitioner reported that her flare "started 3 weeks ago" (Ex. 7, p. 6); however, I understand this notation to be referring to when petitioner became wheelchair-dependent at some point in late December (Ex. 5, p. 12). Similarly, petitioner's report of a 2-week onset during her pre-admission assessment on January 8, 2015, appears to be related to her complete loss of the ability to ambulate. (Ex. 9, pp. 210, 235.) This squares with the record noting petitioner received IV treatment on December 3, 2014. (Ex. 5, p. 18.)

petitioner was discharged to a nursing home due to her functional limitations. (Ex. 9, p. 284.) She remained wheelchair bound with reports of pain and weakness in her upper extremities. (*Id.* at 287.) In June of 2015, petitioner was again admitted to a rehabilitation center, but she was subsequently transferred back to the hospital for "emergent evaluation of her neurologic changes related to a possible transverse myelitis flare." (*Id.* at 82,108.) Because her symptoms were not abating, petitioner sought a second opinion in July of 2015. (Ex. 12, p. 6.) Dr. Stone assessed petitioner with an unspecified CNS demyelinating disease after reviewing her medical history and treatment. (*Id.* at 6-7.) In September of 2015, petitioner reported continued neurologic pain, fatigue, myalgias, arthralgias, and weakness. (Ex. 7, p. 54.) In October of 2015, petitioner continued to complain of chronic pain, fatigue, myalgias, arthralgias, and weakness, as well as gait problems and numbness. (*Id.* at 66-67.) Petitioner continued to seek care for her CNS demyelinating condition through 2018. (Ex. 11, pp. 8-12.)

As previously discussed, petitioner's treaters did not come to a consensus regarding what specific disease plagued her, but they did agree that she suffered from some form of CNS demyelinating condition and continued to treat her accordingly throughout the course of her illness. In that regard, I find that petitioner experienced a flare of her underlying CNS demyelinating condition in late November of early December of 2014, after discontinuing her immunosuppressive treatment and following vaccination.

d. Whether there was significant aggravation (*Loving Prong* Three)

The third *Loving* prong requires an examination of petitioner's pre- and post-vaccination conditions and a determination of whether petitioner's current condition constitutes a "significant aggravation" of her pre-vaccination condition. *Loving*, 86 Fed. Cl. at 144. Under the Vaccine Act, a "significant aggravation" is "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). As indicated in my analysis for *Loving* prongs one and two, above, petitioner suffered from a preexisting CNS demyelinating condition with recurrent flares, but she was not in the midst of a flare, and her condition was well controlled with immunosuppressive treatment, at the time of vaccination. However, following vaccination, petitioner experienced a flare that resulted in permanent sequalae. Accordingly, there is preponderant evidence that petitioner's post-vaccination condition is a "significant aggravation" of her pre-vaccination condition under *Loving* prong 3.

Respondent argues that the analysis under the third *Loving* prong does not stop at simply showing a markedly worse post-vaccination condition. (ECF No. 81, pp. 22-23.) He asserts that "[n]othing in *Sharpe* prohibits respondent from introducing, or the special master from considering, evidence that petitioner's post-vaccination clinical course is consistent with the expected clinical course of the condition, and that the vaccine was therefore not a 'substantial factor' in aggravating that condition." (*Id.* (citing *Sharpe v. Sec'y of Health & Human Servs.*, 964 F.3d 1072 (Fed. Cir. 2020); *Locane v. Sec'y of Health & Human Servs.*, 685 F.3d 1375 (Fed. Cir. 2012)).) He relies on Dr.

Wilson's opinion concerning the nature of the disease and petitioner's clinical course to support his argument that "there is no persuasive evidence in the record that petitioner's alleged significant aggravation deviated from the expected clinical course of her disease." (*Id.* at 23.) In this case, I find that respondent's argument is better addressed under *Loving* prongs 4-6/*Althen* prongs 1-3.

e. Medical theory of causation (*Loving* prong four/*Althen* prong one)

Under *Althen* prong one, petitioner must provide a "reputable medical theory," demonstrating that the vaccine received can cause the type of injury alleged. *Pafford v. Sec'y of Health & Human Servs.,* 451 F.3d 1352, 1355-56 (Fed. Cir. 2006) (quoting *Pafford v. Sec'y of Health & Human Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004)). Such a theory must only be "legally probable, not medically or scientifically certain." *Knudsen*, 35 F.3d at 548-49. Petitioner may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *See Andreu ex rel. Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1325-26 (Fed. Cir. 2006)). However, "[a] petitioner must provide a 'reputable medical or scientific explanation' for [her] theory. While it does not require medical or scientific certainty, it must still be 'sound and reliable.'" *Boatmon*, 941 F.3d at 1359 (quoting *Knudsen*, 35 F.3d at 548-49).

The literature filed by petitioner explains that "[i]t is widely accepted that NMOSD is a humeral-mediated autoimmune astrocytopathy that begins with the entry of AQP4-IgG into the [central nervous system] via an impaired blood brain barrier." (Zhong et al., *supra*, at Ex. 15, Tab L, p. 2.) Although the mechanism remains unsettled, it is generally accepted that the process involves an antibody dependent cellular cytotoxicity." (*Id*.) Thus, Zhong et al. indicate that it may be possible that any infection can result in NMOSD if it perturbs the immune system in such a way as to result in self-reactive lymphocytes and AQP4-IgG production. (*Id*. at 5.) In that regard, Dr. Kinsbourne opines that "[s]ince infections and vaccines designed to prevent them are constructed to elicit immune responses to the same surface epitopes, it comes as no surprise that vaccination can also stimulate NMO onset and/or relapse." (Ex. 14, Tab A, p. 7.) Speaking of the post-infectious nature of NMO, Dr. Kinsbourne opines more specifically that "NMO is not held to be due to direct invasion by the organism in question, but to an autoimmune attack against a protein such as AQP4 or MOG." (*Id.* at 6.)

In a subsequent report, despite having invoked aquaporin-4 in his causal explanation, Dr. Kinsbourne specifically disclaimed that his theory of causation is predicated on aquaporin-4 antibody involvement. (Ex. 18, p. 1.) However, he did not explain how or why he felt he was able to disclaim reliance on aquaporin-4. Dr. Kinsbourne had previously cited literature explaining that "[i]n experimental studies, purified immunoglobulin G (IgG) from AQP4 antibody seronegative patients did not reproduce NMO-like pathology with astrocytic destruction as seen with the infusion of

the same material from AQP4 antibody seropositive patients. Therefore, it is unclear if AQP4 antibody seronegative NMO patients have the same autoimmune astrocytopathic disease as seropositive patients." (Sato et al., *supra*, at Ex. 15, Tab I, p. 6.) The same paper also suggests there is differing pathophysiology between AQP4-positive and MOG-positive NMO. (*Id*.) To the extent 10-20% of NMOSD patients are seronegative for aquaporin-4, it remains an open question whether those patients are experiencing a separate, as of yet unknown, pathomechanism. (Zhong et al., *supra*, at Ex. 15, Tab L, p. 2.) Because that alternative pathogenesis is hypothesized yet unknown, it does not help petitioner meet her burden of proof in this case. Although Dr. Kinsbourne has substantiated that aquaporin-4 seronegativity is not dispositive as to diagnosis, he has neither asserted nor substantiated any theory of vaccine causation that does not involve the understanding that NMO/NMOSD is a product of the aquaporin-4 autoimmune pathway.

Nor does the medical literature available on this record otherwise indirectly point to a causal relationship between the flu vaccine and aquaporin-4 seronegative NMO/NMOSD. A 2014 review of CNS demyelinating syndromes by Karussis & Petrou did not identify any reports of NMO following the flu vaccine despite observing that there otherwise were a "high number" of reports of CNS demyelination following release of the H1N1 flu vaccine in 2009. (Karussis & Petrou, *supra*, Ex. 14, Tab E, pp. 4-5, 7.) Instead, Karussis & Petrou noted that most reported cases of NMO followed the HPV vaccine, hypothesizing cross-reactivity between the vaccines' viral antigens and aquaporin-4. (*Id*. at 6.) However, a subsequent retrospective analysis by Mealy et al. was able to detect an increased risk of NMOSD relapse within 90 days of vaccination, including the flu vaccination. (Mealy et al., *supra*, at Ex. 14, Tab G.) However, the study was inadequately sized with respect to aquaporin-4 seronegative subjects and, in fact, none of the relapsing seronegative subjects received the flu vaccine. (*Id*. at 5.) Dr. Kinsbourne has cited literature including several case reports of post-vaccination aquaporin-4 seronegative NMO. (*E.g.*, Nakamura et al., *supra*, at Ex. 14, Tab I; Aimen Vanood & Dean Wingerchuk, *Systematic Review Investigating Relationships Between Neuromyelitis Optica Spectrum Disorder (NMOSD) and Vaccination (P1.2-003)*, 92 (15 Supp.) NEUROLOGY, Apr. 9, 2019 (Ex. 14, Tab L).[15]) However, isolated case reports are not strong evidence even though they are not entirely without evidentiary value. *Paluck ex rel. Paluck v. Sec'y of Health & Human Servs.*, 104 Fed. Cl. 457, 475 (2012) (quoting *Campbell v. Sec'y of Health & Human Servs.*, 97 Fed. Cl. 650, 668 (2011)); *see also Crutchfield v. Sec'y of Health & Human Servs.*, No. 09-0039V, 2014 WL 1665227, at *19 (Fed. Cl. Spec. Mstr. Apr. 7, 2014) ("[S]ingle case reports of Disease X occurring after Factor Y . . . do not offer strong evidence that the *temporal* relationship is a *causal* one—the temporal relationship could be pure random chance."), *aff'd*, 125 Fed. Cl. 251 (2014). Moreover, because aquaporin-4 positivity is not 100% sensitive (Trebst et al.,

[15] Petitioner filed only an abstract for the Vanood and Wingerchuk paper. I directed petitioner to file a complete copy, but petitioner confirmed that the abstract did not result in the publication of a complete article. (ECF No. 68.) Accordingly, this exhibit at best supports the mere identification of the fact of the prior case reports. The paper cites the existence of 15 case reports, ten of which were seropositive. The flu vaccine was among ten different vaccines implicated among the different case reports. It is impossible to discern from the abstract whether the flu vaccine was involved in any of the seronegative cases.

Ex. 14, Tab K, p. 4), even if these subjects did have vaccine-caused NMO it would not necessarily follow that the case reports evidence a vaccine-related pathomechanism unrelated to aquaporin-4. In contrast to these case reports, a further case report cited by Dr. Kinsbourne stressed the patient's positive aquaporin-4 antibody test as strong support of a "parainfectious pathogenesis" of NMOSD. (Park et al., *supra*, at Ex. 14, Tab J, p. 1.)

Petitioner must present a theory that applies to her condition. *Broekelschen,* 618 F.3d at 1346 (explaining that "[b]ecause causation is relative to the injury, a petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case"). Here, petitioner has not met her burden under *Loving* prong 4 because, even assuming *arguendo* that aquaporin-4 seropositive NMO can be triggered by vaccination, there is not preponderant evidence that vaccination can cause seronegative NMO/NMOSD. Although petitioner claims that she does not rely on aquaporin-4 positivity to prove her case, Dr. Kinsbourne's theory, based on the medical literature he provided, does rely on a disease pathology related to aquaporin-4. The fact that patients can be diagnosed with either seronegative of seropositive NMO/NMOSD does not resolve or overcome that issue.[16]

f. Logical sequence of cause and effect connecting the vaccination and significant aggravation (*Loving* prong five/*Althen* prong two)

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326-27; *Grant*, 956 F.2d at 1147-48. Medical records are generally viewed as particularly trustworthy evidence. *Cucuras*, 993 F.2d at 1528. However, medical records and/or

[16] The conclusion reached herein is also consistent with prior cases. A seropositive test combined with homology between the subject vaccine has been a successful theory for vaccine causation of NMO in the program. *Day v. Sec'y of Health & Human Servs.*, No. 12-630V, 2015 WL 8028393, at *14 (Fed. Cl. Spec. Mstr. Nov. 13, 2015) (finding that there is preponderant evidence that petitioner's Gardasil and FluMist vaccinations caused petitioner's NMO through the mechanism of molecular mimicry based on homology between the HPV vaccine and aquaportin-4). However, special masters have denied compensation in cases where either the petitioner was seronegative for the aquaporin-4 antibody or there is no evidence of homology between the aquaporin-4 antibody and the vaccine received. *Broussard v. Sec'y of Health & Human Servs.,* No. 18-302V, 2024 WL 1829210, at *18 (Fed. Cl. Spec. Mstr. Apr. 4, 2024) (petitioner failed to present preponderant evidence under *Althen* prong one by failing to provide any evidence of homology between the aquaporin-4 antibody and hepatitis B vaccine); *Morgan v. Sec'y of Health & Human Servs.*, No. 15-1137V, 2019 WL 7498665, at *19 (Fed. Cl. Spec. Mstr. Dec. 4, 2019) (petitioner with seronegative NMO failed to provide preponderant evidence under *Althen* because, "[f]or molecular mimicry to have utility herein as a reliable mechanism, there should be some evidence that the relevant autoantibodies that are known to drive, or are at least associated with, the resulting demyelinating disease are likely produced as a result of the flu vaccine"), *mot. for rev. den'd*, 148 Fed. Cl. 454 (2020), *aff'd*, 850 F. App'x 775 (Fed. Cir. 2021); *Wei-Ti Chen v. Sec'y of Health & Human Servs.*, No. 16-634V, 2019 WL 2121208, at *21 (Fed. Cl. Spec. Mstr. Apr. 19, 2019) (petitioner with seronegative NMO "offered no evidence tending to suggest that the flu vaccine might produce, directly or indirectly, *any* NMOSD-associated autoantibodies – but at a minimum the MOG antibodies, since that was the sole relevant biomarker for which Petitioner tested positive").

statements of a treating physician's views do not *per se* bind the special master. *See* § 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"); *Snyder ex rel. Snyder v. Sec'y of Health & Human Servs.,* 88 Fed. Cl. 706, 745 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). A petitioner may support a cause-in-fact claim 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).

As respondent explained, "no special trigger or exacerbating factor needs to be involved to explain the fact that petitioner had a severe attack." (ECF No. 81, p. 21.) Instead, respondent argues that petitioner's repeated relapses "made the likelihood of a substantial recovery after every subsequent injury less likely." (*Id.*) As explained above, Dr. Wilson persuasively contends that petitioner's previous attacks had resulted in urinary retention issues, neuropathic pain in her legs and trunk, and prior damage on her MRI, which suggest that petitioner was, in fact, at risk for a cumulative attack. (Ex. D, p. 2 (citing Ex. 6, p. 1; Ex. 9, p. 231).) In that regard, none of petitioner's treating physicians attributed her condition to her vaccination. Most of petitioner's treating physicians did not opine on the cause of her flare and, instead, focused on petitioner's treatment. Petitioner's physicians did attribute past flares to a dental procedure and infections, generally. (Ex. 6, p. 3; Ex. 12, p. 6.) One of petitioner's treating physicians also opined that petitioner's medications could be contributing to petitioner's symptoms. (Ex. 12, p. 6.)

Additionally, petitioner acknowledges that, especially given her reliance on Mealy et al., the fact that petitioner was on immunosuppressants at the time of vaccination does make it less likely that she would have suffered a vaccine-related flare. (ECF No. 77, p. 21.) Mealy et al. found that patients treated with immunosuppressives at the time of vaccination had a lesser risk of relapse. (Mealy et al., *supra*, at Ex. 14, Tab G, p. 3.) In fact, the study determined that "the association of vaccines to relapses is not present among patients who are using preventative immunotherapy." (*Id.* at 3.) Petitioner indicates that she had stopped taking her immunosuppressive medication at the time of onset of her post-vaccination flare; however, as discussed above, the evidence indicates that at the time of her vaccination, she was still taking immunosuppressants. Mealy et al. found that patients are protected when they are taking immunosuppressants *at the time of vaccination*, which petitioner was. (*Id.* at 1.) In fact, onset of petitioner's flare more readily correlates to her discontinuance of her immune suppressive treatment, which, according to Mealy et al., would make petitioner more susceptible to a relapse. (*Id.*) Dr. Wilson also noted this point. (Ex. D, p. 1.) Even accounting for Dr. Kinsbourne's opinion that immunosuppressant therapy would not entirely eliminate the possibility of a flare, petitioner's discontinuance of her medication shortly before her flare remains a more likely cause of the flare as compared to her earlier vaccination.

Finally, the theory of causation petitioner has actually presented applies to aquaporin-4 positive NMO/NMOSD. Even without treating petitioner's negative aquaporin-4 finding as diagnostically dispositive, the lack of a positive aquaporin-4 result still constitutes a lack of evidence supporting a logical sequence of cause and effect, given the nature of petitioner's theory under *Loving* prong four. Petitioner cannot rely on a mere likelihood that the antibodies are present but undetected, especially because, as discussed under *Loving* prong four, aquaporin-4 negative NMOSD is a known clinical syndrome suspected of having a distinct pathomechanism. *Boatmon,* 941 F.3d at 1362-63 (explaining that a brain stem abnormality could not be inferred from statistics "[i]n the absence of actual evidence").

For all the reasons included above, petitioner has failed to prove by preponderant evidence that there was a logical sequence of cause and effect between her vaccination and her NMOSD relapse.

g. Proximate temporal relationship between vaccination and significant aggravation (*Loving* prong six/*Althen* prong three)

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1278. A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorders etiology, it is medically acceptable to infer causation-in-fact." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *mot. for recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd*, 503 Fed. App'x 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877, at *26 (Fed. Cl. Spec. Mstr. May 30, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

Respondent's expert admitted that "onset at approximately [five] weeks after [petitioner's flu] vaccination could be considered to be related to a vaccine-triggered complication." (Ex. A, p. 5.) Additionally, respondent did not contest that petitioner had met her burden and established that there was a temporal relationship between petitioner's vaccination and her injury. (ECF No. 81, p. 17 n.10.) However, a proximate temporal relationship is not enough to carry petitioner's burden for causation. *Chuisano v. United States*, 116 Fed. Cl. 276, 287 (2014); *Veryzer v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 344, 356 (2011). Therefore, because petitioner failed to establish her burden under *Loving* prong four/*Althen* prong one and *Loving* prong five/*Althen* prong two, petitioner has failed to prove that her injury was caused in fact by her flu vaccination.

VI. Conclusion

Petitioner has clearly suffered and for that she has my sympathy. This decision is in no way meant to minimize her condition or the impact it has had on her life. However, for all the reasons discussed above, petitioner has not met her burden of proof with specific respect to demonstrating that her condition (in whole or in part) was vaccine caused. Accordingly, this case is dismissed.[17]

IT IS SO ORDERED.

s/Daniel T. Horner
Daniel T. Horner
Special Master

[17] In the absence of a timely-filed motion for review of this Decision, the Clerk of the Court shall enter judgment accordingly.