In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: December 4, 2025

MARCIE UNRUE,	*	
	*	
Petitioner,	*	No. 18-323V
	*	
v.	*	Special Master Young
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
	*	
Respondent.	*	

Lawrence R. Cohan, Saltz Mongeluzzi & Bendesky, Philadelphia, PA, for Petitioner.
Sarah C. Duncan, U.S. Department of Justice, Washington, DC, for Respondent.

DECISION ON ENTITLEMENT[1]

On March 1, 2018, Marcie Unrue ("Petitioner") filed a petition in the National Vaccine Injury Compensation Program ("the Program").[2] The petition alleged that Petitioner received a tetanus, diphtheria, acellular pertussis ("Tdap") vaccine on May 6, 2017, and as a result suffered from transverse myelitis ("TM") and neuromyelitis optica ("NMO"). Pet. at Preamble, ECF No. 1; Am. Pet. at Preamble, ECF No. 15.

A careful analysis and weighing of all the evidence and testimony presented in this case in accordance with the applicable legal standards,[3] reveals that Petitioner has failed to provide

[1] Because this Decision 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 Decision will be available to anyone with access to the internet.** In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, I agree that the identified material fits within this definition, I will redact such material from public access.

[2] National Childhood Vaccine Injury Act of 1986, Pub L. No. 99-660, 100 Stat. 3755 ("the Vaccine Act" or "Act"). Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2018).

[3] While I have reviewed all of the information filed in this case, only those filings and records that are most relevant to the Decision will be discussed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision.") (citation omitted);

preponderant evidence that the Tdap vaccine she received on May 6, 2017, was the cause-in-fact of her TM and NMO. Accordingly, Petitioner is not entitled to an award of compensation.

I. Procedural History

Petitioner filed her petition on March 1, 2018. Pet. Petitioner filed medical records on March 26, 2018. Pet'r's Exs. 1–6, ECF No. 8. Petitioner filed an amended petition and medical records on November 9, 2018. Am. Pet.; Pet'r's Ex. 7, ECF No. 16. Petitioner filed additional medical records on January 4, 2019, February 19, 2019, and April 5, 2019. Pet'r's Exs. 8–9, ECF No. 19; Pet'r's Exs. 10–14, ECF No. 21; Pet'r's Exs. 15–17, ECF No. 24. Respondent filed his Rule 4(c) report, recommending that compensation be denied, on May 7, 2019. Resp't's Rept., ECF No. 26. On September 24, 2019, this case was selected for a pilot ADR program with a third-party neutral mediator. ECF No. 35. That program concluded while this case was still pending, and litigation resumed. ECF No. 39.

On January 29, 2021, Petitioner filed an expert report from Fredreick Nahm, M.D., Ph.D. Pet'r's Ex. 24, ECF No. 47. On June 1, 2021, Respondent filed an expert report from Marc Bouffard, M.D. Resp't's Ex. A, ECF No. 50. Petitioner filed a first supplemental report from Dr. Nahm on August 30, 2021. Pet'r's Ex. 27, ECF No. 53. Respondent filed an expert report from William Hawse, Ph.D., and a supplemental report from Dr. Bouffard on November 22, 2021. Resp't's Exs. C–D, ECF No. 54. Petitioner filed a second supplemental report from Dr. Nahm on June 2, 2022. Pet'r's Ex. 28, ECF No. 59. On August 29, 2022, Respondent filed a supplemental report from Dr. Hawse and a second supplemental report from Dr. Bouffard. Resp't's Exs. F–G, ECF No. 61. On January 19, 2023, Petitioner filed a third supplemental report from Dr. Nahm. Pet'r's E. 29, ECF No. 65. On March 28, 2023, Respondent filed a second supplemental report from Dr. Hawse and a third supplemental report from Dr. Bouffard. Resp't's Exs. H–I, ECF No. 67. Petitioner filed a fourth supplemental report from Dr. Nahm on May 15, 2023. Pet'r's Ex. 30, ECF No. 68.

On March 18, 2024, I scheduled a hearing set to begin on May 20, 2025. ECF No. 69. Petitioner filed her pre-hearing brief on February 18, 2025. Pet'r's Br., ECF No. 73. Respondent field his pre-hearing brief on April 10, 2025. Resp't's Br., ECF No. 74. And on May 12, 2025, Petitioner filed a pre-hearing reply brief. Pet'r's Reply, ECF No. 84. An entitlement hearing was held from May 20 to May 21, 2025. Min. Entry, dated May 21, 2025. There were no post-hearing briefs. This matter is now ripe for consideration.

II. Factual History

A. Relevant Medical Records

Petitioner's pre-vaccination medical history was notable for non-Hodgkin's lymphoma (in remission), hypertension, carpal tunnel surgery, and smoking. *See* Pet'r's Ex. 1 at 12, 83–84, 105; Pet'r's Ex. 3 at 68.

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see also Paterek v. Sec'y of Health & Hum. Servs., 527 F. App'x 875, 884 (Fed. Cir. 2013) ("Finding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered.").

On May 6, 2017, Petitioner presented to the emergency department ("ED") complaining of arm numbness, shoulder pain, and wrist pain after falling two weeks earlier. Pet'r's Ex. 1 at 10. She denied dizziness, seizures, loss of consciousness, pain in other areas of the body, changes to vision, nausea, vomiting or diarrhea, fever or chills, trouble breathing, and trouble with urination or bowel movements. *Id.* at 12. Neurologic examination was normal. *Id.* at 13, 26. Petitioner received an X-ray of her right wrist which showed soft tissue swelling but no fracture. *Id.* at 14. Petitioner was given a splint for her wrist and ordered to follow up with an orthopedist. *Id.* at 15. The diagnoses were wrist pain and neck muscle spasm. *Id.* at 16. At this visit, it was noted that Petitioner was not up to date on tetanus immunization. *Id.* at 12, 16. Accordingly, Petitioner received the Tdap (Adacel) vaccination in her left arm. *Id.* at 26.

Two weeks later, on May 20, 2017, Petitioner presented to the ED where she reported that she woke up "with tingling from her lower ribs all the way down both legs to her feet." Pet'r's Ex. 1 at 82. She also had tingling in her left hand and "altered sensation in her groin," with an episode of urinary incontinence that morning. *Id.* at 82, 93. She reported she also had tingling in her right hand after an injury two weeks prior but that those symptoms had improved. *Id.* at 82. Petitioner reported hiking within the past two days and denied any recent upper respiratory infection ("URI"). *Id.* at 94. Although neurologic examination was essentially normal and a head computed tomography ("CT") scan was negative, she was admitted to the hospital for further evaluation. *See id.* at 84, 87, 90. Upon admission, Petitioner described the "sudden onset of numbness from just below trunk and bilateral lower extremities associated with urinary incontinence." *Id.* at 93. She differentiated numbness in her hands as related to carpal tunnel syndrome. *Id.* Petitioner denied any weakness. *Id.*

After admission, magnetic resonance imaging ("MRI") was obtained. *See* Pet'r's Ex. 1 at 96. Petitioner's thoracic spine MRI showed "mild to moderate degree of degenerative disc disease throughout the thoracic spine with no focal disc herniation or significant spinal canal stenosis or significant neural foraminal encroachment of the thoracic region." *Id.* at 96, 100. Her cervical MRI showed an "elongated elliptical shaped area of high T2 signal intensity expanding the cervical cord from C2-3 level through lower C6 level showing some mild blotchy contrast enhancement with gadolinium infusion imaging most consistent with [TM]." *Id.* at 100, 125–26. Her brain MRI showed "a couple nonspecific high T2 FLAIR signal intensity areas measuring a few millimeters in size in the bilateral frontal white matter." *Id.* at 127. There was "[n]o evidence of acute infarct or abnormal contrast enhancing lesion with gadolinium infusion imaging." *Id.*

That same day, on May 20, 2017, Petitioner saw attending neurologist Sanjay Raikar, M.D., for a neurology consultation. Pet'r's Ex. 1 at 114. Petitioner told Dr. Raiker that three days prior, she was hiking. *Id.* The following day, her feet started to cramp; "[s]he thought it was because she over exerted herself with the hike." *Id.* But then the next day "she noticed that her hands both felt tingling and on the day of admission she felt as though she had tingling that included her hand as well as from her rib cage down" as well as loss of bladder control. *Id.* There was no associated weakness. *Id.* Petitioner denied any tick bites, trauma, out-of-country travel, and recent vaccinations. *Id.* Neurological examination revealed subjective decreased sensation around T6. *Id.* at 115. Dr. Raikar's impression was that Petitioner was having "progression of sensory deficits, the etiology of which [was] unclear." *Id.* Dr. Raikar noted the "abnormal MRI scan of the

cervical cord which raise[d] the possibility of [TM].” *Id.* Dr. Raikar raised the need of an infectious disease consult “to rule out any infective causes which could give a presentation consistent with [TM].” *Id.* at 115–16.

Also on May 20, 2017, Petitioner had an infectious disease consult with Suk Chul Kim, M.D. Pet’r’s Ex. 1 at 99. Dr. Kim wrote that Petitioner “developed sudden onset of sensory loss below chest. MRI of cervical spine showed possible [TM]. She did not have signs of infection before sensory loss occurred. CSF analysis showed no evidence of infection.” *Id.* Due to the possibility of TM, steroids were started. *Id.* An ANA reflex panel was performed and was negative with all antibody levels below cutoffs for systemic autoimmune diseases. *Id.* at 419. A lumbar puncture and rheumatological labs were normal. *Id.* at 422–26.

A neurology progress note on May 26, 2017, indicated that Petitioner was “still having numbness from the chest down,” and that she only had a partial response to steroids. Pet’r’s Ex. 169, 171. That day, Petitioner started plasmapheresis, receiving five total treatments, as well as physical therapy (“PT”) and occupational therapy (“OT”). *Id.* at 169, 176, 249.

On June 2, 2017, Petitioner was discharged from the hospital with a final impression of TM. Pet’r’s Ex. 1 at 274–75, 90–91. She had regained bladder control, but her numbness, though improved, had not fully resolved. *Id.* at 90. At discharge, she could walk the halls slowly. *Id.* at 90–91. She was instructed to follow up with neurology. *Id.* at 275.

On June 13, 2017, Petitioner established care with a primary care physician (“PCP”) office, seeing Jean Swenton, N.P., and James Calson, D.O., at Cedar Lake Health Center. Pet’r’s Ex. 2 at 5. She reported that she was recently in the hospital for TM and had received “a tetanus shot just prior to her symptoms.” *Id.* She reported having back, neck, hip, and wrist pain since the diagnosis of TM “as the numbness [was] wearing off.” *Id.* She also reported having anxiety. *Id.*

On June 14, 2017, Petitioner saw neurologist Subhasree Misra, M.D., for a hospital follow up. Pet’r’s Ex. 3 at 68. Since her discharge from the hospital, Petitioner experienced improvement of numbness and tingling and re-gained bladder control; but she still had some numbness in her bilateral lower extremities up to her mid-thigh. *Id.* Also since discharge, Petitioner developed severe pain in her low back, hip, and neck, and “both her hands and fingers [were] bending inward.” *Id.* Dr. Misra’s history recorded that Petitioner received a tetanus shot 14 days prior to the onset of her TM. *Id.* He also noted that her bloodwork was normal. *Id.* On examination, Petitioner had normal visual fields and vision; intact sensation to light touch in all extremities; a cautious, but normal, gait; and left-hand spasms without spasticity. *Id.* at 70. The assessment was TM and paresthesia.[4] *Id.* Dr. Misra prescribed gabapentin for the paresthesia and repeat MRIs for the TM. *Id.* at 70–71.

Repeat MRIs on June 26, 2017, revealed a “[l]ong segment area of signal abnormality” in the cervical spinal cord with superimposed enhancement.” Pet’r’s Ex. 3 at 74. Petitioner’s thoracic MRI showed no definite evidence of cord signal change or abnormal enhancement. *Id.* at 77. Her

[4] Paresthesia is “an abnormal touch sensation, such as burning, prickling, or formication, often in the absence of an external stimulus.” *Paresthesia*, DORLAND’S ONLINE MED. DICTIONARY, https://www.dorlandsonline.com/dorland/definition?id=37052 (hereinafter, “*Dorland’s*”).

brain MRI showed mild nonspecific white matter changes without any associated abnormal enhancement. *Id.* at 81. Signal abnormality was noted throughout the pons. *Id.*

On July 7, 2017, Petitioner presented to the ED with complaints of face pain that felt as if "an ice pick [was] going through her left eye and report[ed] that it radiates down the face, into the jaw, and towards the clavicle." Pet'r's Ex. 6 at 42. She also reported "an area of 'flashing' in her vision," left hand tingling, and some new right upper extremity weakness. *Id.* A head CT was normal. *Id.* at 48. Nonetheless, Petitioner was admitted to the hospital. *Id.* at 53–54. A brain MRI with contrast revealed a "[d]iscrete high T2 signal lesion involving the left optic nerve as it exits the globe exhibiting postinfusion enhancement present in association with the high cervical cord lesion at the T2 level also exhibiting high signal and postinfusion enhancement concerning for Devic's disease [neuromyelitis optica spectrum disorder ("NMOSD")]." *Id.* at 51. A cervical spine MRI revealed "redemonstration of the abnormal T2 hyperintensity of the cervical cord" with involvement of the central cord that had "mildly progressed [and was] now extending from the level of C1-C7 where it [was] previously seen at the level of C2-3 to C6-7," and "redemonstration of the patchy enhancement . . . [that was] consistent with [NMO]." *Id.* at 89. Petitioner received five days of IV methylprednisolone and was discharged with a steroid taper. *Id.* at 56, 119, 126.

On July 31, 2017, Petitioner had a neuroimmunology evaluation with Adil Javed, M.D., at the University of Chicago for possible NMO. Pet'r's Ex. 4 at 6. She had completed a steroid taper two days earlier and now complained of worsening left eye vision and blurriness in her right eye, right hand tremors, numbness and stiffness in her legs, a tight band around her rib cage, and urinary retention. *Id.* Dr. Javed's impression was NMOSD, and he noted that Petitioner had the tetanus vaccine prior to her symptoms. *Id.* at 9. She was readmitted to the hospital. *Id.* During the admission, aquaporin 4 ("AQP4") antibody testing result was "See NMO TS Reflex."[5] Pet'r's Ex. 12 at 61. A repeat brain MRI was consistent with NMO. Pet'r's Ex. 4 at 29. Petitioner was discharged on August 3, 2017, after improving with three days of IV steroids. *Id.* at 24, 48. She was discharged on CellCept and a steroid taper. *Id.* at 48.

Petitioner presented to the ED on November 13, 2017, with worsening spasticity and stiffness in her right arm, left eye pain (9/10), and vision loss. Pet'r's Ex. 5 at 22. Repeat MRIs revealed lesions were still present. *Id.* at 82; *see also id.* at 113 (cervical MRI showing "subtle focus of vague enhancement and T2 hyperintensity involving the right hemi-medulla"); *id.* at 114 (orbital MRI showing "slightly increased T2 signal within the distal portion of the intraorbital left optic nerve with slight prominence of the CSF space at this level"). The diagnosis throughout her hospitalization was NMO. *See id.* at 83, 91, 105. Petitioner received plasmapheresis and was discharged on November 22, 2017. *Id.* at 123–30.

In December 2017, repeat testing of the presence of anti-AQP4 antibodies yielded positive results with a high titer of >1:100,000. Pet'r's Ex. 9 at 1.

Petitioner experienced another NMOSD flare in April 2018, received plasmapheresis, and was switched from CellCept to rituximab infusions. Pet'r's Ex. 13 at 184–85. In August 2018, she had another flare and received three days of IV steroids. *Id.* at 205. In February 2019, she had a possible flare, but brain and spine MRIs did not show abnormal enhancement and her white matter

[5] Reflex results were not provided.

lesions were stable. Pet'r's Ex. 16 at 24–27, 30–38. She continued receiving rituximab through December 2019. *See* Pet'r's Ex. 21.

B. Petitioner's Affidavit and Testimony

Petitioner submitted one affidavit and testified at the hearing. Pet'r's Ex. 7; Tr. 3, 243. In her affidavit, dated June 27, 2018, Petitioner asserted she received the subject Tdap vaccine on May 6, 2017. Pet'r's Ex. 7 at ¶¶ 2, 4. Prior to that date, she was healthy, active, and had no history of neurological problems. *Id.* at ¶ 3. She recalled that on May 20, 2017, she developed "tingling and numbness from the waist down and urinary incontinence." *Id.* at ¶ 10. She went to the ED where she received an MRI, which showed a cervical spine lesion consistent with TM. *Id.* She was treated with steroids and although she experienced some improvement with that therapy, her symptoms persisted. *Id.* at ¶ 11. On May 26, 2017, Petitioner received the first of five plasmapheresis treatments. *Id.* On July 6, 2017, "the weakness in [her] right arm worsened significantly and [she] lost vision in [her] left eye." *Id.* at ¶ 12. She returned to the ED, and another MRI showed her cervical spine lesion worsened and a new lesion had developed on her left optic nerve. *Id.* She was diagnosed with NMO and again treated with steroids. *Id.* Petitioner maintained in her affidavit that she continued to suffer from "numbness from the waist down, tingling, pins and needles in [her] upper extremities, and substantial pain in [her] right arm." *Id.* at ¶ 13. She was also undergoing rituximab infusions for her symptoms. *Id.*

Petitioner testified why she received the Tdap vaccine in 2017. Tr. 13. She explained that she fell, hurt her wrist, and went to the ED to have it checked out. *Id.* She had an open wound on her hand, and medical personnel recommended that she get the Tdap vaccine, because she had not had one for a long time. *Id.* Two weeks later, she began to experience symptoms of what was ultimately diagnosed as NMOSD. *Id.* She went hiking in new boots and her feet were tingling when she got home and removed the boots. Tr. 13–14. She did not think anything of it and went to bed; when she woke up in the morning, "the bed was wet, and [she] couldn't feel anything from the waist down." Tr. 14. Petitioner testified that she went to the ED and was in the hospital for 10 or 11 days. *Id.* During that time, she received plasmapheresis treatment and received a preliminary diagnosis of TM. *Id.*

Shortly after her initial hospitalization, Petitioner testified she had "really bad" pain in her eye. Tr. 16. She recalled "[i]t felt like a spike was being driven down through [her] head and through [her] eye." *Id.* "They thought it was related to why [she] had been there before." *Id.*

During a visit with neurologist Dr. Misra on June 14, 2017, Petitioner recalled that Dr. Misra told her that "there was a possibility that the tetanus shot could have been part of the cause of the [TM]," but that "it wasn't definitive." Tr. 18. Petitioner testified that treaters at the University of Chicago "did the AQP-4 test and determined that [her] condition [] progressed to include [NMOSD]."[6] Tr. 19. On cross-examination, Petitioner was asked about the fact that none of the medical records said the Tdap vaccine caused her NMO. Tr. 28. Petitioner asserted that her providers "always made reference to it but they couldn't give a definitive answer." Tr. 28. She

[6] Petitioner testified that she refers to her condition as either NMO or NMOSD. Tr. 20. Accordingly, I will use NMO and NMOSD interchangeably throughout this Decision.

testified that her vaccination two weeks prior to her onset of symptoms was always brought up during medical history intake at her appointments. Tr. 30–31.[7]

At the hearing, Petitioner testified she still experiences incontinence related to her condition, calling it neurogenic bladder. Tr. 15. Additionally, she still experiences vision loss—she has no peripheral vision and colors are desaturated in her left eye. Tr. 16–17. Petitioner testified to the current medications she was taking, other treatment she has since tried, and how her condition now affects her day-to-day life. Tr. 21–22, 25–27.

Petitioner was re-called on the second day of the hearing to confirm that she never told her doctors that she had an allergy to the Tdap or tetanus vaccination. Tr. 330–31.

III. Experts

A. Expert Qualifications

1. Petitioner's Expert, Dr. Fredrick Nahm, M.D., Ph.D.

Dr. Nahm submitted five expert reports and testified at the hearing. Pet'r's Exs. 24, 27–30; Tr. 3. Dr. Nahm is board certified in psychiatry and neurology as well as in electrodiagnostic medicine. Pet'r's Ex. 24 at 1; Pet'r's Ex. 25 at 1. He received his Ph.D. in neuroscience from the University of California San Diego, and his M.D. from the University of Michigan Medical School. Pet'r's Ex. 25 at 1; Tr. 34–35. He completed a fellowship in neurophysiology and a residency in neurology. Pet'r's Ex. 25 at 1–2; Tr. 36. Dr. Nahm currently practices medicine "in both acute neurological emergencies as well as outpatient and rehabilitation settings." Pet'r's Ex. 24 at 1; *see also* Pet'r's Ex. 25 at 1. He testified he has seen "well over 100" patients with NMOSD. Tr. 38. At the hearing Dr. Nahm was proffered as an expert in neurology, neurologic sciences, and a "clinical expert in the diagnosis, evaluation, and treatment of TM, NMO, [acute disseminated encephalomyelitis ("ADEM")]-related conditions." Tr. 47.

2. Respondent's Expert, Dr. Marc Bouffard, M.D.

Dr. Bouffard submitted four expert reports and testified at the hearing. Resp't's Exs. A, C, F, H; Tr. 3. Dr. Bouffard is a board-certified neurologist. Tr. 153. He received his M.D. from Tufts University School of Medicine. Resp't's Ex. J at 1. He subsequently completed fellowships in neuro-ophthalmology and autoimmune neurology and a residency in neurology. *Id.* He is currently practicing as neuro-ophthalmologist in which he "routinely evaluate[s] and manage[s] patients with NMOSD." Resp't's Ex. A at 1. Dr. Bouffard is also an Assistant Professor of Neurology at Harvard Medical School. Tr. 152.

[7] On re-direct examination, Petitioner's counsel cited to the record where her vaccination was referenced preceding her symptoms onset. Tr. 32 (citing Pet'r's Ex. 2 at 5; Pet'r's Ex. 3 at 68; Pet'r's Ex. 4 at 9; Pet'r's Ex. 16 at 4, 24, 40, 45; Pet'r's Ex. 17 at 14).

3. Respondent's Expert Dr. William Hawse, Ph.D.

Dr. Hawse submitted three expert reports and testified at the hearing. Resp't's Exs. D, G, I; Tr. 243. Dr. Hawse received his Ph.D. in biophysical chemistry from the Johns Hopkins School of Medicine. Resp't's Ex. D at 1; Resp't's Ex. K at 1. He completed a postdoctoral fellowship in structural immunology. Resp't's Ex. D at 1; Tr. 247–48. He is currently an assistant professor in the Department of Immunology at the University of Pittsburgh School of Medicine. Tr. 248; Resp't's Ex. K at 1. His research laboratory "studies CD4+ T cell differentiation and immune tolerance." Resp't's Ex. D at 1; *see also* Tr. 249–50. Dr. Hawse has published on topics such as cross-reactivity and T cell differentiation. Tr. 251; Resp't's Ex. D at 1.

B. Expert Opinions

1. Petitioner's Expert, Dr. Nahm

Dr. Nahm opined that the Tdap vaccination, "through various mechanisms of molecular mimicry," triggered an inflammatory/autoimmune process leading to Petitioner's TM and optic neuritis ("ON"), otherwise known as NMOSD. Pet'r's Ex. 27 at 5; *see also* Pet'r's Ex. 24 at 16.

Dr. Nahm first explained that TM is "an autoimmune/autoinflammatory demyelination of the spinal cord pathways," and ON is "an inflammatory process leading to demyelination of the optic nerve." Pet'r's Ex. 24 at 11. The combination of TM and ON is referred to as NMO, or an even broader term, NMOSD. *Id.* at 11–12; *see also* Tr. 49–50. Karussis & Petrou[8] defined NMOSD as "an idiopathic, severe, demyelinating disease of the central nervous system that preferentially affects the optic nerve and spinal cord." Pet'r's Ex. 30a at 6. NMOSD can further be divided into antibody positive or negative. Pet'r's Ex. 24 at 12 (citing Pet'r's Ex. 26c);[9] *see also* Tr. 67–68 (discussing the Fujihara article and the relevance of it to this case).

AQP4 is the target NMO antibody. Pet'r's Ex. 24 at 12. "Expression of the AQP4 is notable in brain, spinal cord and optic nerves where astrocytes are closely apposed to endothelial cell basal membranes." *Id.* (citing Pet'r's Ex. 26d).[10] In addition to AQP4, Dr. Nahm asserted that antibodies to myelin oligodendrocyte glycolipid ("MOG") are also present in individuals with NMOSD. *Id.* at 12–13 (citing Pet'r's Ex. 26e);[11] *see also* Tr. 104. However, Jarius et al. wrote that the coexistence of both the anti-MOG antibody and the AQP4 antibody is "highly uncommon." Pet'r's Ex. 26e at 2; *see also* Tr. 106–07. Dr. Nahm explained that anti-MOG antibodies, like anti-AQP4 antibodies are an example of "the immunological basis of NMOSD type conditions." Pet'r's Ex. 28 at 4. On cross-examination, Dr. Nahm acknowledged that literature has discussed whether a

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[8] Dimitrios Karussis & Panayiota Petrou, *The Spectrum of Post-Vaccination Inflammatory CNS Demyelinating Syndromes*, 13 AUTOIMMUNITY REVS. 215 (2014).
[9] Kazuo Fujihara, *Neuromyelitis Optica Spectrum Disorders: Still Evolving and Broadening*, 32 CURRENT OP. NEUROLOGY 385 (2019).
[10] David J. Graber et al., *Neuromyelitis Optica Pathogenesis and Aquaporin 4*, 5 J. NEUROINFLAMMATION 22 (2008).
[11] Sven Jarius et al., *MOG-IgG in NMO and Related Disorders: A Multicenter Study of 50 Patients. Part 1: Frequency, Syndrome Specificity, Influence of Disease Activity, Long-Term Course, Association with AQP4-IgG, and Origin*, 13 J. NEUROINFLAMMATION 279 (2016).

MOG positive is considered separated disease, referred to as MOG-antibody disorder ("MOGAD"). Tr. 105; *see also* Tr. 107 (acknowledging Jarius et al. concluded MOG IgG is a separate entity from AQP4 IgG-positive NMOSD (citing Pet'r's Ex. 26e)). But he considered MOG positive to be in the spectrum of NMOSD. *Id.*

While the precise cause of NMO remains unknown, according to Dr. Nahm, there is overlap between NMO and other autoimmune conditions. Pet'r's Ex. 24 at 12 (citing Pet'r's Ex. 26b);[12] *see also* Pet'r's Ex. 27 at 4 (comparing other CNS demyelinating conditions such as ADEM); Tr. 70–71 (comparing TM and NMO to ADEM); Tr. 144 (acknowledging overlap between ADEM and NMOSD). *But see* Tr. 117–18 (acknowledging on cross-examination the differences between ADEM and NMOSD including the lack of AQP4 antibody in ADEM (citing Pet'r's Ex. 26i at 3)).[13] Dr. Nahm opined that NMO antibodies have been associated with other autoimmune conditions. Pet'r's Ex. 24 at 12–13; *see also* Pet'r's Ex. 27 at 4. For example, he wrote that antibodies to glycolipids play an important role in Guillain-Barré syndrome ("GBS") and chronic inflammatory demyelinating polyneuropathy ("CIDP").[14] Pet'r's Ex. 23 at 13. Therefore, he believed "that NMO may in theory share some pathogenic susceptibility to vaccines as is the case with other demyelination neuropathies." *Id.* He admitted in his testimony that NMO is not analogous to GBS and CIDP. Tr. 104. Dr. Nahm added that although "the precise mechanism by which these antibodies develop and what pathogenetic role they play is uncertain, these data do strongly suggest that this condition, like isolated TM or ON, results from autoimmunological mechanism." Pet'r's Ex. 23 at 12; *see also* Pet'r's Ex. 30a at 6 ("[T]he exact role of antibodies against AQP4 in the pathogenesis of [NMO] is not clear.").

Dr. Nahm proposed molecular mimicry as the medical theory for how the Tdap vaccine can cause NMO.[15] Pet'r's Ex. 24 at 11; Tr. 60. He explained that molecular mimicry "refers to similarities between certain pathogenic elements which are contained in the vaccine, and certain proteins that are found in various tissues of the human body and nervous system." Pet'r's Ex. 24 at 11 (citing Pet'r's Ex. 26j).[16] He added it is "the most widely cited explanation as to how vaccines cause autoimmune neurological injuries," and here, "it is an appropriate and meaningful way to understand how the Tdap vaccine caused the spinal cord and optic nerve injury leading to motor and sensory neurological impairments as well as visual loss." *Id.*; *see also* Pet'r's Ex. 30a at 7 ("Molecular mimicry . . . represents one of the main immunopathogenic mechanism in post-vaccination [central nervous system ("CNS")] demyelination."). Dr. Nahm opined, "[t]he molecular mimic under this theory triggers a lymphocytic proliferation and/or the generation of antibodies and immune complex that attack neural elements leading to neurological dysfunction."

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[12] Amer Awad & Olaf Stuve, *Idiopathic Transverse Myelitis and Neuromyelitis Optica: Clinical Profiles, Pathophysiology and Therapeutic Choices*, 9 CURRENT NEUROPHARMACOLOGY 417 (2011).

[13] Sung-Min Kim et al., *Differential Diagnosis of Neuromyelitis Optica Spectrum Disorder*, 10 THERAPEUTIC ADVANCES NEUROLOGICAL DISORDERS 265 (2017).

[14] Dr. Nahm acknowledged on cross-examination that NMO is not analogues to GBS and CIDP. Tr. 104, 135.

[15] In his first expert report, Dr. Nahm also referenced an aluminum adjuvant theory for how a Tdap vaccine could cause NMO but clarified at the hearing that he withdrew that theory from his opinion. Tr. 124.

[16] Yahel Segal & Yehuda Shoenfeld, *Vaccine-Induced Autoimmunity: The Role of Molecular Mimicry and Immune Crossreaction*, 15 CELLULAR & MOLECULAR IMMUNOLOGY 586 (2018).

Pet'r's Ex. 24 at 11 (citing Pet'r's Ex. 26f);[17] *see also* Tr. 72–74 (explaining the Kerr & Ayetey article).[18] When asked, he believed antibodies are indicative of molecular mimicry. Tr. 142–43.

Dr. Nahm opined that "[w]hile there is no proven homology between the AQP4 protein and the Tdap vaccine, many NMO patients have reported infections prior to the onset of symptoms, suggesting an autoimmunological process which may in theory result from molecular mimicry." Pet'r's Ex. 24 at 12. He did not expand on this. During his testimony, Dr. Nahm reaffirmed that "[t]here is no described homology between . . . any epitope within the Tdap vaccine and a component of NMO." Tr. 61; *see also* Tr. 75 (testifying there is no homology between the Tdap vaccine and AQP4); Tr. 130 (admitting the self-antigen component is unidentified). But he asserted that homology "is not the only way by which molecular mimicry occurs, as the Tdap vaccine also contains certain plant-based carrier proteins that can in theory serve as antigenic triggers." Pet'r's Ex. 24 at 12.

In his second expert report, Dr. Nahm clarified his theory, adding that "in addition to showing structural homology, another way that molecular mimicry has been implicated is to demonstrate cross-reactivity." Pet'r's Ex. 27 at 2.

> Molecular mimicry has been considered a cross-reactive mechanism. It originally defined a situation in which a pathogen expresses an epitope that shares antigenic structures with host tissue-derived protein or peptide, and was originally used for both B- and T-cell responses. In the context of a T-cell response, pathogen-derived peptides when presented by MHC may activate potentially self-reactive T cells. As a consequence, tolerance/ignorance is broken, and the pathogen-specific immune response cross-reacts with host-derived epitopes, which can cause tissue damage and disease.

Id. at 2–3 (quoting Pet'r's Ex. 28b at 5).[19] Under this scenario, Dr. Nahm opined "molecular mimicry is interpretated as a functional description and not a structural definition." Pet'r's Ex. 30 at 2. Dr. Nham disagreed with Respondent's expert Dr. Hawse that "to invoke the term molecular mimicry, there must be a component of the vaccine that mimics a component of the CNS." *Id.* (quoting Resp't's Ex. G at 2). Dr. Nahm also raised bystander activation and stated that both bystander activation[20] and cross-reactivity are at play; but when asked what the difference is between the two, he said, "it's a little muddy."[21] Tr. 126.

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[17] Douglas A. Kerr & Harold Ayetey, *Immunopathogenesis of Acute Transverse Myelitis*, 15 CURRENT OP. NEUROLOGY 339 (2002).

[18] While Kerr & Ayetey suggested that "vaccination may induce an autoimmune process resulting in [acute] TM," they also noted "extensive data continue to show overwhelmingly that vaccinations are safe and are not associated with an increased incidence of neurological complications." Pet'r's Ex. 26f at 3.

[19] Galina Petrova et al., *Cross-Reactivity of T Cells and Its Role in the Immune System*, 32 CRITICAL REVS. IMMUNOLOGY 349 (2012).

[20] This was the first time Dr. Nahm suggested bystander activation might be at play.

[21] When I questioned Dr. Nahm at the hearing, he was unable to effectively differentiate molecular mimicry, cross-reactivity, and bystander activation. Tr. 128–31. He also stated he would be unable to determine whether NMO is vaccine-induced via molecular mimicry or if it is an idiopathic pathogenesis. Tr. 131–32.

According to Dr. Nahm, "[i]mmunization with tetanus toxoid and diphtheria toxoids can induce antibodies capable of cross-reacting to self-antigen epitopes." Pet'r's Ex. 27 at 3 (citing Pet'r's Ex. 28d).[22] Dr. Nahm explained that in Sutjita et al., patients were immunized with diphtheria and tetanus vaccines and one week later, the patients' serum samples showed antibodies reacted with both toxoids as well as self-antigens, including phospholipids. *Id.* He opined that "[t]hese studies prove cross-reactivity between epitopes on tetanus and diphtheria toxoids and human phospholipids – key components of myelin and known antigenic targets in immune related neurological disorders." *Id.* (opining these data "support the molecular mimicry theory by showing cross-reactive processes which can occur following Tdap vaccination"). Dr. Nahm reiterated in a supplemental report that Sutjita et al. "provides evidence as to how these vaccines in theory can invoke cross-reactive antibodies to neuronal elements known to be injured in autoimmune related polyneuropathies. Pet'r's Ex. 29 at 4 (citing Pet'r's Ex. 28d). He added that these "data show that a disorder like NMOSD can occur through a variety of immunological processes involving the AQP4 antibody, as well as the MOG antibody." *Id.* On cross-examination, Dr. Nahm admitted that Sutjita et al. discussed patients with lupus, not NMO, and that the authors noted that monoclonal antibodies from patients with autoimmune disease may not necessarily be related to the pathogenic autoantibodies found in their serum. Tr. 101 (citing Pet'r's Ex. 28d at 5). He questioned this conclusion regarding the relevance of antibodies. Tr. 103–04.

Dr. Nahm then appeared to present theories of clonal expansion and T cell differentiation. He cited Lindner et al.[23] for the proposition that "[i]ncreased clonality in both CD4+ and CD8+ T cells has been documented in NMO patients." Pet'r's Ex. 27 at 3 (citing Pet'r's Ex. 28g at 2). He added, "[v]accination with tetanus toxoid booster induces a broad T-helper cell response including Th1, Th2, Th17, with the highest concentration being Th1 CD4+ T cells." *Id.* (citing Pet'r's Ex. 28a at 7–11).[24] Dr. Nahm wrote that Livingston et al. shows that the tetanus toxoid booster vaccination "can result in an increase in cell populations which may be involved in the pathogenesis of NMOSD." Pet'r's Ex. 29 at 5 (citing Pet'rs Ex. 28a); *see also* Pet'r's Ex. 30 at 4 (Dr. Nahm opining that Livingston et al. shows "that tetanus containing booster can elicit populations of T cells which are thought to play a pathogenic role in NMO"). Accordingly, Dr. Nahm opined, "[i]f a vaccine can induce a population of T cells which are known to be present and/or play a role in a neurological condition, then a selective increase in those T cells after vaccin[ation] would argue for some degree of molecular mimicry." Pet'r's Ex. 29 at 5.

Dr. Nahm acknowledged that while there is "literature that shows that the AQP4 antibodies, can, in theory, result from exposure to vaccines such as Tdap," he did not believe there was any literature concluding that Tdap vaccination causes production of AQP4 antibodies. Tr. 127.

During the hearing, Dr. Nahm opined his theory holds the same for a variety of neurological conditions. Tr. 135–36. Given that, I asked him what the effect is, if any, on his theory given that some diseases, such as ADEM, are monophasic, and others, like NMO, are not. Tr. 136–37. He

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[22] M. Sutjita et al., *Polyspecific Human and Murine Antibodies to Diphtheria and Tetanus Toxoids and Phospholipids*, 73 CLINICAL EXPERIMENTAL IMMUNOLOGY 191(1988).

[23] Maren Lindner et al., *Characterization of T Cells in NMOSD Patients – An Emerging Role for T Cells in Disease Pathogenesis*, 94 NEUROLOGY 4017 (2020).

[24] Kimberly A. Livingston et al., *CD4 T-Helper Cell Cytokine Phenotypes and Antibody Response Following Tetanus Toxoid Booster Immunization*, 390 J. IMMUNOLOGICAL METHODS 18 (2013).

answered, "[w]e don't know that." Tr. 137. I further questioned how his theory of molecular mimicry contemplates a disease with a relapse; he could not articulate an answer. Tr. 137–38.

To support his position, he cited several case reports of TM, ON, and NMO following tetanus-containing vaccinations. Pet'r's Ex. 24 at 13; Pet'r's Ex. 27 at 4. For example, Jarius et al. reported two cases of anti-MOG NMOSD after Tdap vaccination. Pet'r's Ex. 26e; *see also* Pet'r's Exs. 26h (case report of a 27-year-old who developed ON one day after receiving a diphtheria, tetanus, pertussis, and inactivated poliovirus combined vaccine (DTaP-IPV));[25] Pet'r's Ex. 26m (case report of a 15-month-old who developed acute TM 21 days after receiving the first dose of the measles, mumps, and rubella ("MMR") vaccine and the fourth dose of the DTaP vaccine).[26]

Kumar et al.[27] reported a case of MOG antibody-related NMOSD after the receipt of the tetanus, MMR, and varicella vaccines in a pregnant woman. Pet'r's Ex. 26g at 1–2. Dr. Nahm noted the patient had normal AQP4 levels (AQP4 negative) but was MOG positive. Pet'r's Ex. 29 at 3. While Kumar et al. acknowledged the patient's pregnancy might have contributed to disease onset since "pregnancy is known to trigger NMOSD relapses, especially in anti-MOG-positive patients," the authors also reviewed "the reported cases of postvaccination demyelination in the past decade, with a focus on the relationship between NMOSD and vaccination in patients with [AQP4] or [MOG] antibodies." Pet'r's Ex. 26g at 1, 5. They noted "an increasing number of postvaccination [NMOSD] cases . . . especially patients with [AQP4] antibodies." *Id.* at 1. The authors reviewed all 72 reported cases of postvaccination demyelination from 2008 to 2018. *Id.* at 4. This included 10 with TM, 19 with ON, and nine with NMOSD. *Id.* at 4 tbl. 1. And both AQP4-positive and MOG-positive cases were reported after vaccination. *Id.* at 5. The authors commented that vaccinations can trigger peripheral demyelination and other autoimmune neurologic conditions and suggested that "molecular mimicry (cross-reaction between vaccine antigens and myelin proteins) could trigger autoimmune demyelination." *Id.* at 4.

Agmon-Levin et al.[28] reviewed 37 reported cases of TM associated with different vaccines. Pet'r's Ex. 26a. Four of those were after a diphtheria-tetanus-pertussis ("DTP") or diphtheria-tetanus ("DT") vaccines. *Id.* at 2. The temporal association was between several days and three months. *Id.* at 1, 5. The authors discussed the autoimmune nature of TM and the role of humoral autoimmunity. *Id.* at 2. The authors then identified the mechanisms by which vaccines may induce TM including molecular mimicry, epitope spreading, and polyclonal or bystander activation. *Id.* at 4.

Dr. Nahm also pointed out that "despite the lack of epidemiological or mechanistic evidence, the [Institute of Medicine ("IOM")[29]] did not conclude there was no association between Tdap and a condition such as [TM], but rather that the evidence [was] insufficient, or inadequate to accept or reject an association or causal relationship." Pet'r's Ex. 30 at 2 (citing Pet'r's Ex.

[25] Preston O'Brien & Robert W. Wong, *Optic Neuritis Following Diphtheria, Tetanus, Pertussis, and Inactivated Poliovirus Combined Vaccination: A Case Report*, 12 J. MED. CASE REPS. 356 (2018).
[26] G. Zanoni et al., *Transverse Myelitis After Vaccination*, 9 EUR. J. NEUROLOGY 696 (2002).
[27] Neha Kumar et al., *Postvaccination Anti-Myelin Oligodendrocyte Glycoprotein Neuromyelitis Optica Spectrum Disorder*, 22 INT'L J. MS CARE 85 (2020).
[28] N. Agmon-Levin et al., *Transverse Myelitis and Vaccines: A Multi-Analysis*, 18 LUPUS 1198 (2009).
[29] The IOM is now the National Academy of Medicine ("NAM").

29a).[30] Likewise, Dr. Nahm testified that Baxter et al.[31] found there was not enough evidence to make a general conclusion as to an association between TM and prior immunization. Tr. 68–69, 113–14, 120–21 (citing Pet'r's Ex. 26k).

In sum, Dr. Nahm opined the Tdap vaccine can "trigger[] an immune cross-reaction through molecular mimicry leading to an immune/inflammatory response to antigens affecting the spinal cord and optic nerves as in the condition of NMO." Pet'r's Ex. 24 at 16. Even though Dr. Nahm admitted on cross-examination that "none of the scientific literature says that Tdap causes NMO." Tr. 127. He also did not think there was a discernible difference between vaccine-induced NMO and idiopathic NMO. Tr. 132. When I asked him how he would know what any specific presentation is, he said it is based on a contemporaneous association and if there are no other alternative causes, it is idiopathic unless there is a recent vaccination. Tr. 132–33.

Dr. Nahm believed there was a logical sequence of cause and effect showing Petitioner's Tdap vaccine caused her NMO and was within an appropriate temporal timeframe. Pet'r's Ex. 24 at 14–16. He stated that Petitioner received the Tdap vaccine on May 6, 2017, and 14 days later, on May 20, 2017, Petitioner woke up "with sensory symptoms from the level of her lower ribs, down both legs and into the feet. Tingling in the left hand, altered sensation in her groin, and urinary incontinence were also reported." *Id.* at 14 (citing Pet'r's Ex. 1 at 76); *see also* Tr. 53 (testifying onset was 14 days). Dr. Nahm opined that the time between vaccine administration and the development of Petitioner's TM symptoms "is in keeping with a normal tempo for the development of an autoinflammatory/autoimmune response (days to [four] weeks), as is known for other autoimmune neurological vaccine related injuries such as GBS and ADEM." Pet'r's Ex. 24 at 14; *see also* Tr. 54, 94, 115–16, 144–45 (testifying that Baxter et al. reported a time frame of five to 28 days for post-vaccination ADEM). Petitioner later went on to develop ON, "and in the setting of radiographically proven and clinically recurring symptoms of [TM, Petitioner] was diagnosed with NMO." Pet'r's Ex. 24 at 14. Dr. Nham noted that Petitioner initially had a negative AQP4 titer in August 2017, but that it was later shown to be positive in December 2017. *Id.* (citing Pet'r's Ex. 12 at 61; Pet'r's Ex. 9 at 1); Tr. 57–58, 75 (explaining that Petitioner initially being seronegative NMO and later seropositive "speaks to the complex and changing nature of the underlying kind of autoantibody").

It was Dr. Nahm's opinion that Petitioner had no neurological symptoms prior to vaccination. Pet'r's Ex. 24 at 14; Tr. 48. He distinguished Petitioner's musculoskeletal wrist injury (due to fall) that was present on the day of vaccination, with Petitioner's "entirely different array" of post-vaccination neurological symptoms. Pet'r's Ex. 24 at 14. He stated her pre-vaccination symptoms were "post-traumatic, isolated only to the right upper extremity, and musculoskeletal in nature." *Id.* Post vaccination, Petitioner developed symptoms starting "with a thoracic sensory level and neurogenic bladder, progressing to muscle spasticity, and the later development of [ON]." *Id.* at 15. He opined that symptoms of spinal cord injury and visual loss due to TM and ON are "consistent with a neurological injury at the cellular level." *Id.* Therefore, Dr. Nahm concluded, "[t]wo weeks after the Tdap vaccine, [Petitioner] developed acute neurological symptoms

[30] Inst. of Med., *Adverse Events Associated with Childhood Vaccines: Evidence Causality* (Kathleen Stratton et al. eds., 2012).

[31] Roger Baxter et al., *Acute Demyelinating Events Following Vaccines: A Case-Centered Analysis*, 63 CLINICAL INFECTIOUS DISEASES 1456 (2016).

progressing over the ensuing months, that was likely the result of an inflammatory immunological process causing demyelinating injury to the spinal cord and optic nerves." *Id.*

Dr. Nahm asserted that there was no evidence of prior or concurrent infection, trauma, or other conditions, including rheumatological, that would explain Petitioner's TM and/or ON. Pet'r's Ex. 24 at 14–15; Tr. 94. Other infectious causes including cryptococcus, HSV, CMV, Lyme, syphilis, HIV, and EBV were ruled out. Pet'r's Ex. 24 at 15.

2. Respondent's Expert Dr. Bouffard

Dr. Bouffard agreed with Dr. Nahm and Petitioner's treating physicians that NMO or NMOSD is the proper diagnosis. Resp't's Ex. A at 4; Tr. 158, 207–08. He disagreed with Dr. Nahm's proposed theory of molecular mimicry due to the lack of homology between the Tdap vaccination and the AQP4 protein. Resp't's Ex. A at 4; Tr. 175–76. He testified that he does not believe molecular mimicry can lead to any CNS autoimmune disease. Tr. 217.

He began by discussing NMOSD generally. He opined the "central facet of NMOSD pathology" is the pathologic anti-AQP4 antibody, "which defines the disease itself."[32] Resp't's Ex. A at 5 (emphasis omitted); *see also* Resp't's Ex. C at 1 (agreeing with Dr. Nahm that "the presence of absence of the AQP4 antibody may be relevant in the mechanism of NMOSD"); Tr. 161. But the underlying cause of NMOSD is unknown. Resp't's Ex. C at 2; Tr. 166–67. He testified it is also unknown what causes people to develop AQP4 antibodies. Tr. 168–69

However, Dr. Bouffard asserted that "suggesting that there are a 'variety of different immunological processes' which cause NMOSD is simply speculation" and "[c]onflating NMOSD with other [CNS] inflammatory disorders is problematic." Resp't's Ex. C at 1. First, Dr. Bouffard found it problematic to draw a "meaningful comparison between NMOSD and ADEM." Resp't's Ex. C at 2; *see also* Tr. 185–86 (testifying that literature on Tdap vaccination causing ADEM does not support the position that Tdap vaccination can cause NMOSD); Tr. 218–19. The main distinguishing feature is that NMOSD is typically "a chronic demyelinating disorder with intermittent flares" whereas ADEM is typically a monophasic disorder. Resp't's Ex. C at 2; *see also* Tr. 184–85, 188–89 (testifying about the difference between NMOSD and ADEM, including the relapsing remitting versus monophasic characteristics).

Second, Dr. Bouffard asserted MOGAD is not a subtype of NMOSD;[33] they are distinct disorders. Resp't's Ex. C at 1; Tr. 163. He testified that if a patient presents with MOG antibodies and is negative for AQP4 antibodies, the patient will have MOGAD, not NMOSD. Tr. 163. He added that "very rarely" there are patients who have both antibodies, MOG and AQP4. Tr. 163. However, "almost invariably when they do, they have a very, very, very low titer of one of them and a high titer of the other one." *Id.* Dr. Bouffard therefore disagreed with Dr. Nahm's application of Jarius et al. because the article discussed MOGAD, not NMOSD. *See* Resp't's Ex. A at 6 (citing Pet'r's Ex. 26e); Tr. 177–78. Dr. Bouffard testified that at the time Jarius et al. was published,

[32] Although Dr. Bouffard agreed with Dr. Nahm that the AQP4 antibody is not universally found in patients with clinically defined NMOSD. Resp't's Ex. C at 1.

[33] Dr. Bouffard claimed there are only two agreed-upon "types" of NMOSD: AQP4 seropositive and seronegative. Resp't's Ex. C at 2; *see also* Tr. 160–61.

"[p]eople were trying to understand whether MOG antibody positivity represented simply a subset of NMO[SD] or whether it was actually distinctly different." Tr. 177. Since the publication of Jarius et al., Dr. Bouffard stated that MOGAD has become recognized as a separate diagnosis from NMOSD.[34] Tr. 178.[35] Thus, Dr. Bouffard's issue with Dr. Nahm citing Jarius et al. was that MOGAD and NMOSD are not interchangeable and data from one cannot be extrapolated from the other. Resp't's Ex. A at 6; *see also* Tr. 186. Nonetheless, he did not think vaccination is likely to be causal for either NMOSD or MOGAD. Tr. 183.

He continued, "even if it is accepted that data relating vaccine exposure to other CNS autoimmune diseases can be extrapolated to NMOSD, it must be recognized that there is no evidence that vaccines actually cause chronic central nervous system autoimmune diseases." Resp't's Ex. A at 6 (emphasis omitted); *see also* Tr. 197. Dr. Bouffard cited literature that "did not demonstrate any causal association between Tdap vaccination and chronic, relapsing, [CNS] demyelinating disorders." Resp't's Ex. C at 2; *see also* Tr. 187.

First, he cited Langer-Gould et al.,[36] which found vaccination was associated with an increased risk of CNS demyelinating syndromes within the first 30 days after vaccination only in younger (<50 years) individuals. Resp't's Ex. A, Tab 18 at 1. However, they found this increased risk was not statistically significant. *Id.* at 4; *see also* Resp't's Ex. A at 7; Tr. 188 (testifying Langer-Gould et al. "concluded that antecedent vaccination did not cause chronic demyelinating disease"); Tr. 219. Second, he discussed Baxter et al.,[37] which is a case-centered analysis that he opined "directly contradicts Dr. Nahm's suggestion . . . that there is any casual association between vaccines and first-time [ON]." Resp't's Ex. A at 7 (citing Resp't's Ex. A, Tab 16). Baxter et al. did not find any association between ON and any type of vaccine within four to six weeks after vaccination. Resp't's Ex. A, Tab 16 at 1–2; *see also* Tr. 190 (explaining Baxter et al. found the odds of developing ON after vaccination were not increased in 91 patients studied). And third, Dr. Bouffard cited DeStefano et al.[38] which found hepatitis B, influenza, tetanus, measles, and rubella vaccines did not confer a higher risk of developing ON (or multiple sclerosis ("MS")). Resp't's Ex. A at 7 (citing Resp't's Ex. A, Tab 17); Tr. 192–94.

Dr. Bouffard also took issue with the type of evidence Dr. Nham used to "attempt to support a link between Tdap vaccination and the development of chronic demyelinating diseases." Resp't's Ex. F at 1; *see also* Resp't's Ex. H at 1; Tr. 223 (discussing the value of larger population-based studies). He spent his last two supplemental reports discussing the "hierarchy of scientific evidence." Resp't's Ex. H at 1; *see also* Resp't's Ex. F.

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[34] Dr. Bouffard testified MOGAD has only recently, since 2023, been considered a separate disorder with its own diagnostic criteria. Tr. 162; *see also* Tr. 164 (explaining the new clinical entity).

[35] Dr. Bouffard referenced a 2023 Lancet Neuro article when testifying about this, but this article was not filed as an exhibit. *See* Tr. 178.

[36] Annette Langer-Gould et al., *Vaccines and the Risk of Multiple Sclerosis and Other Central Nervous System Demyelinating Diseases*, 71 JAMA NEUROLOGY 1506 (2014).

[37] Roger Baxter et al., *Case-Centered Analysis of Optic Neuritis After Vaccines*, 63 CLINICAL INFECTIOUS DISEASES 79 (2016).

[38] Frank DeStefano et al., *Vaccinations and Risk of Central Nervous System Demyelinating Diseases in Adults*, 60 ARCHIVES NEUROLOGY 504 (2003).

As to prong two, Dr. Bouffard testified Petitioner's clinical course was typical for seropositive NMOSD. Tr. 170. He also opined that Petitioner was never AQP4 negative and that the initial test result impression from July 2017 was "just a little misunderstanding in how the test report was interpretated."[39] Tr. 171. In fact, Dr. Bouffard asserted that Petitioner was actually positive for AQP4 antibodies in July 2017. Tr. 172–73. Explaining the process of antibody testing for his reasoning, he testified that when a specimen is first tested it is only minimally diluted. Tr. 172. "[I]f it comes back positive at that low titer, what you see is NMO TS reflex." *Id.* And if it is positive, it undergoes serial dilution in which the specimen is diluted then run again and again until it is so diluted it tests negative. *Id.* "[T]he principle there is that if you have a lot of antibody, you can dilute it a bunch of times before there becomes so little that it tests negative." *Id.* Ultimately, he said testing does not move on to this serial dilution unless the initial test is positive. Tr. 173. Thus, he interpreted Petitioner's July 2017 testing result of "see NMO TS Reflex" as positive. *Id.*

Dr. Bouffard did not dispute that 14 days was an appropriate timeframe assuming the vaccination was the triggering event. Tr. 215 (testifying he would expect to see "B cell and T cell activity with the beginning of a generation of antibodies" around that time).

He also asserted "it is not necessary to invoke another, non-vaccinal cause in this case" because "NMOSD, like the cause of most autoimmune disease in general and demyelinating disease in particular, is unclear." Resp't's Ex. A at 7; *see also* Tr. 215.

3. Respondent's Expert Dr. Hawse

Dr. Hawse agreed with Dr. Nahm that Petitioner received the Tdap vaccine on May 6, 2017, and subsequently developed TM, ON, and NMOSD. Resp't's Ex. D at 11. He also agreed with Dr. Nahm that the cause of TM is idiopathic. *Id.* at 12. However, he disagreed that the Tdap vaccine "contributed in any way" to Petitioner's condition. *Id.* at 11.

Dr. Hawse believed Dr. Nahm "equate[d] the concept of cross reactivity with molecular mimicry, but [that] these two concepts are not always the same."[40] Resp't's Ex. G at 2. Dr. Nahm stated that "[i]n addition to showing structural homology, another way that molecular mimicry has been implicated is to demonstrate crossreactivity." *Id.* (quoting Pet'r's Ex. 27 at 2). Dr. Hawse opined this definition "confounds two immunological concepts." *Id.* He explained, "[t]o invoke the term molecular mimicry, there must be a component of the vaccine that mimics a component of the CNS to elicit an immune response to cause damage to the CNS." *Id.* Whereas in a cross-reactive mechanism, "a component of a vaccine or pathogen would activate T cells or B cells that have multiple specificities." *Id.*

He agreed with Dr. Nahm that "NMO patients have CD4+ and CD8+ T cells that clonally expand," and he acknowledged that "CD4 T cells react to a component of a vaccine and undergo

[39] The test result did not say positive or negative. It said, "See NMO TS Reflex." Pet'r's Ex. 12 at 61.

[40] Dr. Hawse also believed Dr. Nahm "intertwine[d] the concepts of clonal expansion, cross-reactivity and T cell differentiation in a way that leads to an incorrect conclusion." Resp't's Ex. I at 1–3. However, because Dr. Nahm only continued to pursue a molecular mimicry theory, I will not address this response in depth here. *See* Tr. 266.

differentiation and clonal expansion. Resp't's Ex. I at 2 (citing Pet'r's Ex. 28a; Pet'r's Ex. 28g). He did not question the position that an immune process contributes to NMO. However, Dr. Hawse opined that Dr. Nahm combining these two "unrelated findings" to conclude that "Th1 T cells . . . that develop because of vaccination must cause NMO" is incorrect. *Id.* Dr. Hawse averred that neither clonal expansion nor generating different CD4 populations is evidence of cross-reactivity. *Id.* He stated it is simply expected that Th1, Th2, and Th17 cells result from vaccination as it is a characteristic response to vaccination. *Id.* Moreover, he added that Lindner et al. did not propose that T cells in NMO patients cross-react with a component of a vaccine; they simply showed that NMO patients have clonally expanded T cells. *Id.* (citing Pet'r's Ex. 28g).

Dr. Hawse responded to Dr. Nahm's primary theory of causation, molecular mimicry. Resp't's Ex. D at 2–3. He began by stating that there are three types of molecular mimicry:

> 1) Complete identity at the protein level between a vaccine component and a human protein, 2) Homology between a vaccine component and a human protein[,] and 3) structural similarities between a vaccine component and a human protein in the CNS. There are two major types of immune cells typically implicated in molecular mimicry, which are B cells and T cells.

Id. at 3; *see also* Tr. 267–69. Dr. Hawse opined that for Dr. Nahm's theory to hypothetically work, whether B cells or T cells are implicated, "a specific epitope in a component of the Tdap vaccine must have shared structural or chemical similarity to a protein in the CNS." Resp't's Ex. D at 3, 5. In other words, "[f]or molecular mimicry to be operative, there must be a specific component in the Tdap vaccine that triggers an autoreactive response," and Dr. Hawse asserted such "is not identified by Dr. Nahm nor the current body of scientific literature." *Id.* at 6. He added that the unknown causative agents for TM also complicates a molecular mimicry theory. *Id.*

Dr. Hawse cited Benoist & Mathis[41] and Ang et al.[42] to show there are five criteria that must be established to invoke molecular mimicry. Resp't's Ex. D at 9 (citing Resp't's Ex. D, Tab 11; Resp't's Ex. D, Tab 12). He opined neither Dr. Nahm nor the literature he cited satisfied the criteria. Resp't's Ex. D at 9; Resp't's Ex. G at 3–6. However, on cross-examination, Dr. Hawse admitted that the five criteria are not required for Dr. Nahm to establish his molecular mimicry theory and that he did not know of any vaccines that have demonstrated these criteria in connection with causing a CNS injury. Tr. 293–94. While conceding that it is not required, he specifically identified how Petitioner fails to meet the criteria.

> 1) The association between the Tdap vaccine and [TM], [ON,] and NMO is not established; 2) The component of the Tdap vaccine that mimics a human self-antigen is not identified; 3) That the Tdap vaccine causes a cross-reactive response to self-epitopes to cause [TM], [ON,] and NMO is not established; 4) A requirement that both the Tdap and self-epitopes cause [TM], [ON,] and NMO was not demonstrated; and 5) It was not established that T cells and B cells elicited by the

[41] Christophe Benoist & Diane Mathis, *Autoimmunity Provoked by Infection: How Good is the Case For T Cell Epitope Mimicry?*, 2 NATURE IMMUNOLOGY 797 (2001).
[42] C. Wim Ang et al., *The Guillain-Barré Syndrome: A True Case of Molecular Mimicry*, 25 TRENDS IMMUNOLOGY 61 (2004).

> Tdap vaccine that are cross-reactive to the Tdap vaccine and self-epitopes are necessary to provoke [TM], [ON,] and NMO.

Resp't's Ex. D at 11; *see also* Resp't's Ex. G at 3–6; Tr. 275, 280, 282, 284, 287–88. Notwithstanding these critiques, Dr. Hawse acknowledged on cross-examination that it is unknown in the current state of scientific and medical knowledge what, if any, antigen or component of the Tdap vaccine is capable of producing that response in a recipient that would support molecular mimicry. Tr. 310–11.

Dr. Hawse disagreed with Dr. Nahm that any vaccine could cause NMO via molecular mimicry due to antigen specificity. Tr. 271–72, 274–275, 318. Additionally, Dr. Hawse explained that with molecular mimicry, hypothetically, "you are exposed to a vaccine component[, e]ventually that vaccine component gets used up." Tr. 279. "It's taken up by cells, it's processed, it's degraded and goes away." *Id.* And so, he opined the theory of pure molecular mimicry "does not explain the relapsing remitting course of a chronic condition" such as NMO. Tr. 279–80; *see also* Tr. 317 ("[M]olecular mimicry in itself doesn't explain how you keep this chronic condition churning."); Tr. 322–24.

Nonetheless, Dr. Hawse addressed each of the components Dr. Nahm listed that could be possible antigenic triggers, as well as the proposed self-antigens for molecular mimicry. Resp't's Ex. D at 6; Tr. 277. First, as to AQP4, Dr. Hawse agreed with Dr. Nahm that the mechanism by which AQP4 develops in patients with TM is unknown. Resp't's Ex. D at 6. He added it is unknown whether these antibodies cause, are the result of, or have no role in disease progression. *Id.* He also agreed with Dr. Nahm that there is no homology between the Tdap vaccine and AQP4. *Id.* Dr. Hawse wrote, "Dr. Nahm can use the term homology, shared epitopes or cross reactivity interchangeably, but the conclusion is the same." *Id.* Thus, based on the current literature, Dr. Hawse opined Dr. Nahm's argument on AQP4 being causative in TM or ON "is not defined." *Id.*

Second, as to MOG, Dr. Hawse noted that there is no evidence that Petitioner has MOG antibodies, it is unknown whether anti-MOG antibodies cause TM or ON, and Dr. Nahm did not provide evidence that a component of the Tdap vaccine results in anti-MOG antibodies. Resp't's Ex. D at 7; *see also* Tr. 278. Dr. Hawse quoted Jarius et al. which found "(i) that MOG-IgG are associated with ON and myelitis in a substantial proportion of cases; (ii) that MOG-IgG and AQP4-iGG do not usually co-exist in patients with ON and/or myelitis, which is in support of the notion of MOG-IgG denoting an entity distinct from AQP4-IgG-positive NMO spectrum disorder." Resp't's Ex. D at 7 (quoting Pet'r's Ex. 26e at 10). Because Petitioner has AQP4-IgG antibodies, Dr. Hawse surmised that "[b]ased on this study cited by Dr. Nahm, MOG antibodies are unlikely. Therefore, . . . Dr. Nahm's theory regarding MOG antibodies is not supported by current scientific knowledge." *Id.*; *see also* Resp't's Ex G at 4–5 ("Petitioner does not have anti-MOG antibodies, so there are no anti-MOG antibodies to cause disease. Therefore, discussion of MOG antibodies is not relevant to [P]etitioner's case."); Tr. 278.

Third, Dr. Hawse wrote that "Dr. Nahm's proposal regarding antibodies against glycolipids is wildly speculative." Resp't's Ex. D at 7. He opined there is no evidence that antibodies against glycolipids are involved in TM or ON and no evidence that a component of the Tdap vaccine results in antibodies towards glycolipids. *Id.* at 8. While Dr. Nahm referenced the role of antibodies

against glycolipids in GBS and CIDP, Dr. Hawse opined GBS and CIDP are very different diseases from TM, ON, and NMO and there is no basis to extrapolate between them. *Id.* at 7–8. Dr. Hawse also responded to Dr. Nahm's propositions on plant-based carrier proteins and adjuvants; however, because Dr. Nahm did not continue to pursue those components in his theory, I will not discuss Dr. Hawse's responses here. *Id.*

Further, Dr. Hawse believed the case reports cited by Dr. Nahm were inapplicable here. Resp't's Ex. D at 10–11; *see also* Resp't's Ex. G at 4 (opining Sutjita et al. is not relevant here because there is no evidence Petitioner has antibodies to cardiolipin or phospholipids); Resp't's Ex. G at 5–6 (writing that Livingston et al. did "not demonstrate that [tetanus-toxoid] vaccination generates T cell populations capable of recognizing and cross-reacting with CNS antigens and does not support Dr. Nahm's theory of cross-reactivity or molecular mimicry causing [P]etitioner's disease"); Tr. 281–82.

IV. Applicable Legal Standards

To receive compensation under the Vaccine Act, a petitioner must demonstrate either that: (1) the petitioner suffered a "Table injury" by receiving a covered vaccine and subsequently developing a listed injury within the time frame prescribed by the Vaccine Injury Table set forth at § 14, as modified by 42 C.F.R. § 100.3; or (2) that petitioner suffered an "off-Table injury," one not listed on the Table, as a result of his receiving a covered vaccine. *See* § 11(c)(1)(C); *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1319–20 (Fed. Cir. 2006). Petitioner does not allege a Table injury in this case; thus, she must prove that her injury was caused-in-fact by a Table vaccine.

To establish causation-in-fact, a petitioner must demonstrate by a preponderance of the evidence that the vaccine was the cause of the injury. § 13(a)(1)(A). A petitioner is required to prove that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321–22 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)).

In the seminal case of *Althen v. Sec'y of the Dept. of Health & Hum. Servs*, the Federal Circuit set forth a three-pronged test used to determine whether a petitioner has established a causal link between a vaccine and the claimed injury. *See* 418 F.3d 1274, 1278–79 (Fed. Cir. 2005). The *Althen* test requires petitioners to set forth: "(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 a proximate temporal relationship between vaccination and injury." *Id.* at 1278. To establish entitlement to compensation under the Program, a petitioner is required to establish each of the three prongs of *Althen* by a preponderance of the evidence. *Id.* "[C]lose calls regarding causation are resolved in favor of injured claimants." *Id.* at 1280. Further, evidence used to satisfy one prong of the test may overlap to satisfy another prong. *Capizzano*, 440 F.3d at 1326.

Under the first prong of *Althen*, a petitioner must offer a scientific or medical theory that answers in the affirmative the question: "can the vaccine[] at issue cause the type of injury alleged?" *Pafford v. Sec'y of Health & Hum. Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed.

Cl. Spec. Mstr. July 16, 2004), *mot. for rev. den'd*, 64 Fed. Cl. 19 (2005), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2006). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such theory must only be "legally probable, not medically or scientifically certain." *Id.* at 548–49. Petitioners are not required to identify "specific biological mechanisms" to establish causation, nor are they required to present "epidemiologic studies, rechallenge[] the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities." *Capizzano*, 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280). Scientific and "objective confirmation" of the medical theory with additional medical documentation is unnecessary. *Althen*, 418 F.3d at 1278–81; *see also Moberly*, 592 F.3d at 1322. However, as the Federal Circuit has made clear, "simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof." *LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) (citing *Moberly*, 592 F.3d at 1322). Indeed, the Federal Circuit has "consistently rejected theories that the vaccine only 'likely caused' the injury and reiterated that a 'plausible' or 'possible' causal theory does not satisfy the standard." *Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1360 (Fed. Cir. 2019) (citing *Moberly*, 592 F.3d at 1322 and *LaLonde*, 746 F.3d at 1339). Rather, "[a] petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case." *Moberly*, 592 F.3d at 1322. In general, "the statutory standard of preponderance of the evidence requires a petitioner to demonstrate that the vaccine more likely than not caused the condition alleged." *LaLonde*, 746 F.3d at 1339.

Furthermore, establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). The Supreme Court's opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.* requires that courts determine the reliability of an expert opinion before it may be considered as evidence. 509 U.S. 579 (1993). However, in the Vaccine Program, the *Daubert* factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66–67 (2010) ("[U]niquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted."); *see also Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999)). Under *Daubert*, the

> factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community.

Terran, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

The *Daubert* factors are "meant to be helpful, not definitive." *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 151 (1999). The factors do not "constitute 'a definitive checklist or

test'" and may be applied differently depending on the facts of a particular case. *Id.* at 150 (quoting *Daubert*, 509 U.S. at 593).

"In short, the requirement that an expert's testimony pertain to 'scientific knowledge' establishes a standard of evidentiary reliability." *Daubert*, 509 U.S. at 590 (citation omitted). Thus, for Vaccine Act claims, a "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly*, 592 F.3d at 1324. Nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder v. Sec'y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 743 (2009) (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)); *see also D'Tiole v. Sec'y of Health & Hum. Servs.*, No. 15-085V, 2016 WL 7664475, at *24 (Fed. Cl. Spec. Mstr. Nov. 28, 2016) (stating that the Vaccine Act "require[s] a chain of reliable propositions supporting [a] petitioner's theory").

Under the second prong of *Althen*, a petitioner must prove that the vaccine actually did cause the alleged injury in a particular case. *See Pafford*, 2004 WL 1717359, at *4; *Althen*, 418 F.3d at 1279. 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; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner does not meet this obligation by showing only a temporal association between the vaccination and the injury; instead, the petitioner "must explain *how* and *why* the injury occurred." *Pafford*, 2004 WL 1717359, at *4 (emphasis in original). The special master in *Pafford* noted petitioners "must prove [] both that her vaccinations were a substantial factor in causing the illness . . . and that the harm would not have occurred in the absence of the vaccination." *Id.* (citing *Shyface*, 165 F.3d at 1352). A reputable medical or scientific explanation must support this logical sequence of cause and effect. *Hodges v. Sec'y of Health & Hum. Servs.*, 9 F.3d 958, 961 (Fed Cir. 1993) (citation omitted). Nevertheless, "[r]equiring epidemiologic studies . . . or general acceptance in the scientific or medical communities . . . impermissibly raises a claimant's burden under the Vaccine Act and hinders the system created by Congress." *Capizzano*, 440 F.3d at 1325–26. "[C]lose calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F.3d at 1280.

In Program cases, contemporaneous medical records and the opinions of treating physicians are favored. *Capizzano*, 440 F.3d at 1326 (citing *Althen*, 418 F.3d at 1280). Indeed, when reviewing the record, a special master must consider the opinions of treating physicians. *Capizzano*, 440 F.3d at 1326. This is because "treating physicians are likely to be in the best position to determine whether 'a logical sequence of cause-and-effect show[s] that the vaccination was the reason for the injury.'" *Id.* In addition, "[m]edical records, in general, warrant consideration as trustworthy evidence. The records contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium. These records are also generally contemporaneous to the medical events." *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). However, there is no "presumption that medical records are accurate and complete as to all of the patient's physical conditions." *Kirby v. Sec'y of Health & Hum. Servs.*, 997 F.3d 1378, 1383 (Fed. Cir. 2021) (finding that a special master must consider the context of a medical encounter before concluding that it constitutes evidence regarding the absence of a

condition). While a special master must consider these opinions and records, they are not "binding on the special master or court." § 13(b)(1). Rather, when "evaluating the weight to be afforded to any such . . . [evidence], the special master . . . shall consider the entire record." *Id.*

In determining the accuracy and completeness of medical records, special masters will consider various explanations for inconsistencies between contemporaneously created medical records and later given testimony. The Court of Federal Claims has identified four such explanations for explaining inconsistencies: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *LaLonde v. Sec'y of Health & Hum. Servs.*, 110 Fed. Cl. 184, 203 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014).

To satisfy the third *Althen* prong, a petitioner must establish a "proximate temporal relationship" between the vaccination and the alleged injury. *Althen*, 418 F.3d at 1281. This "requires preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). Typically, "a petitioner's failure to satisfy the proximate temporal relationship prong is due to the fact that onset was too late after the administration of a vaccine for the vaccine to be the cause." *Id.* However, "cases in which onset is too soon" also fail this prong; "in either case, the temporal relationship is not such that it is medically acceptable to conclude that the vaccination and the injury are causally linked." *Id.*; *see also Locane v. Sec'y of Health & Hum. Servs.*, 685 F.3d 1375, 1381 (Fed. Cir. 2012) ("[If] the illness was present before the vaccine was administered, logically, the vaccine could not have caused the illness.").

Although a temporal association alone is insufficient to establish causation, under the third prong of *Althen*, a petitioner must also show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d at 1278. The special master cannot infer causation from temporal proximity alone. *See Thibaudeau v. Sec'y of Health & Hum. Servs.*, 24 Cl. Ct. 400, 403–04 (1991); *see also Grant*, 956 F.2d at 1148 ("[T]he inoculation is not the cause of every event that occurs within the ten[-]day period . . . [w]ithout more, this proximate temporal relationship will not support a finding of causation." (quoting *Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1983))).

A petitioner who satisfies all three prongs of the *Althen* test has established a prima facie showing of causation. *Hammitt v. Sec'y of Health & Hum. Servs*., 98 Fed. Cl. 719, 726 (2011). A petitioner who demonstrates by a preponderance of the evidence that he suffered an injury caused by vaccination is entitled to compensation unless the respondent can demonstrate by a preponderance of the evidence that the injury was caused by factors unrelated to the vaccination. *See Althen*, 418 F.3d at 1278; *Knudsen*, 35 F.3d at 547. In such a case, the government must not merely prove the existence of an alternative cause, but that such an alternative actually caused the injury. *Knudsen*, 35 F.3d at 549. Consequently, when and if the petitioner establishes a prima facie case, the burden then shifts to the government to prove that an alternative cause, unrelated to the administration of the vaccine, was the "sole substantial factor" in causing the alleged injury. *See de Bazan*, 539 F.3d at1354; *see also Hammitt*, 98 Fed. Cl. at 726 (explaining that the Respondent's

burden is to show that the "factor unrelated" was the "sole substantial factor" in causing the injury). Additionally, a factor unrelated "may not include 'any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness or condition.'" § 13(a)(2); *see also Doe v. Sec'y of Health & Hum. Servs.*, 601 F.3d 1349 (Fed. Cir. 2010) (stating that an idiopathic diagnosis cannot be a "factor unrelated," as it is idiopathic).

V. Discussion

The parties do not dispute diagnosis. Tr. 6. They agree the proper diagnosis is NMO or NMOSD. *Id.*; Resp't's Br. at 10. The parties also agree that Petitioner's onset of symptoms was after vaccination. Tr. 6; Resp't's Br. at 21. The issue in dispute revolves around *Althen* prong one, and subsequently *Althen* prongs two and three to the extent they rely on *Althen* prong one. Tr. 7.

A. *Althen* Prong One – Medical Theory

Petitioner's expert, Dr. Nahm, opined the Tdap vaccine can cause NMO. He based his opinion on (1) "the reports in the literature of cases, not just NMO, but other cases that are central inflammatory autoimmune disorders in response to vaccines like Tdap and other vaccines;" and (2) "invocation of the molecular mimicry theory that has, you know, been used in other cases in the literature as well as in the Court." Tr. 147. I find Petitioner has failed to provide preponderant evidence of a sound and reliable medical theory explaining how the Tdap vaccine can cause NMO.

At different times throughout his reports and testimony, Dr. Nahm raised molecular mimicry, cross-reactivity, bystander activation, and aluminum adjuvants as causal theories. He clarified at the hearing that he was no longer pursuing an aluminum adjuvant theory. At times he intertwined the concepts of molecular mimicry, cross-reactivity, and bystander activation, and when asked, was unable to distinguish them and/or explain how each concept works in conjunction with the other(s). *See, e.g.*, Pet'r's Ex. 24 at 16 (opining the Tdap vaccine can "trigger[] an immune cross-reaction through molecular mimicry leading to an immune/inflammatory response to antigens affecting the spinal cord and optic nerves"); Tr. 128–31. Notwithstanding, his opinion focused on molecular mimicry.[43]

Dr. Nahm conceded that the precise cause of NMO remains unknown. But, he argued NMO is similar enough to other CNS demyelinating diseases such that "NMO may in theory share some pathogenic susceptibility to vaccines as is the case with other demyelination neuropathies." Pet'r's Ex. 23 at 13. An expert may "extrapolate from existing data" where the reasons for extrapolation are transparent and persuasive. *K.O. v. Sec'y of Health & Hum. Servs.*, No. 13-472V, 2016 WL 7634491 (Fed. Cl. July 7, 2016) (quoting *Snyder v. Sec'y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 743 (2009)). Dr. Nahm, however, did not provide any meaningful similarities between NMO and other CNS conditions. In fact, the only difference he identified was the lack of AQP4 antibody in ADEM, compared to NMO. Dr. Hawse pointed out that ADEM is monophasic and NMO is not, and opined molecular mimicry by itself does not explain a relapsing remitting chronic condition such as TM or NMO. Dr. Nahm was unable to answer how molecular mimicry contemplates a

[43] I find Petitioner would also fail to satisfy prong one with any of the other theories suggested (combined or standalone) for lack of sufficient evidence as Dr. Nahm did not adequately describe them or their application to Tdap and NMO.

chronic condition. When I asked Dr. Nahm to address how his theory would hold true for both monophasic and relapsing conditions, he replied "[w]e don't know." Tr. 137. He also was unable to explain how literature on ADEM or other CNS demyelinating diseases could be extrapolated to NMO.[44] Dr. Nahm further acknowledged that NMO is not analogous to GBS and CIDP. Therefore, I do not find the evidence provided here on other vaccine-caused demyelinating conditions to constitute preponderant evidence of vaccine-caused NMO without comparative analysis and/or supportive medical literature that acknowledges pathogenic similarity.

All the experts agreed that AQP4 is the target antibody in NMO.[45] Dr. Nahm conceded that "there is no proven homology between the AQP4 protein and the Tdap vaccine." Pet'r's Ex. 24 at 12; *see also* Tr. 61 (testifying that "[t]here is no described homology between . . . any epitope within the Tdap vaccine and a component of NMO"); Tr. 75 (testifying there is no homology between the Tdap vaccine and AQP4); Tr. 130 (admitting the self-antigen component is unidentified). Further, he admitted that there is no literature concluding the Tdap vaccination causes production of AQP4 antibodies or causes NMO.

To the extent that molecular mimicry is offered as a theory, it must be supported by a sound and reliable medical or scientific explanation." *Knudsen*, 35 F.3d at 548. There must also be some degree of selectivity. *See W.C. v. Sec'y of Health & Hum. Servs.,* 704 F.3d 1352, 1360 (2013) (finding that a petitioner cannot prevail by simply invoking a biological term, or by showing that the mechanism is a valid theory to explain how *other* triggers may have induced *other* diseases and determining that a petitioner must produce additional evidence that the mechanism can cause that vaccine to cause a specific disease); *Caves v. Sec'y of Health & Hum. Servs.,* 100 Fed. Cl. 119, 135 (2011), *aff'd*, 463 F. App'x. 932 (2012); *McKown v. Sec'y of Health & Hum. Servs.,* No. 15-1451, 2019 WL 4072113, at *50 (Fed. Cl. Spec. Mstr. July 15, 2019). Petitioner does not have to provide a specific mechanism, but it must be detailed enough to apply to the administered vaccine and alleged injury in this case. Otherwise, any vaccination, by nature of its purpose to illicit an immune response, could be asserted as the cause of any autoimmune disease that later developed in an individual, and *Althen* prong one "would be rendered meaningless." *See Caves*, 100 Fed. Cl. at 135; *see also McKown*, 2019 WL 4072113, at *50 ("[M]erely chanting the words 'molecular mimicry' in a Vaccine Act case does not render a causation theory scientifically reliable, absent additional evidence specifically tying the mechanism to the injury and/or the vaccine in question."). Petitioner is not limited to any one type of evidence in support of a molecular mimicry mechanism. A non-exhaustive list of potential evidence includes homology evidence, epidemiology studies, pathogenic antibodies, relevant animal models, or disease etiology specific to the vaccine's live virus counterpart. *See Broekelschen*, 618 F.3d 1339; *Dougherty v. Sec'y of Health & Hum. Servs.*, 141 Fed. Cl. 223 (2018); *Brayboy v. Sec'y of Health & Hum. Servs.*, No. 15-183, 2021 WL 4453146, (Fed. Cl. Spec. Mstr. August 30, 2021). I reiterate, Petitioner is under no obligation to provide any one or more of those types of evidence. This list serves only to illustrate that even in cases of rare and understudied phenomena, petitioners must

[44] As in this case, NMO is often initially diagnosed as TM. However, Petitioner also did not explain how the literature could be extrapolated to TM.

[45] While there was ample discussion on the anti-MOG antibody and MOGAD, it is undisputed that Petitioner did not have the MOG antibody and that the diagnosis was NMO, not MOGAD. Therefore, I will not analyze the relevance, if any, of the MOG antibody.

provide preponderant evidence of causation in support of any identified mechanism. Here, however, Petitioner did not provide such evidence.

Dr. Hawse referenced five criteria that must be established for molecular mimicry and that Petitioner did not satisfy the criteria. However, this not the standard used in establishing preponderant evidence of a sound and reliable medical theory in the Vaccine Program. One of the criterion was the establishment of an epidemiolocal association. Petitioner acknowledged the lack of epidemiological evidence supportive of her position. While epidemiological studies are not necessary for petitioner to prevail, Dr. Nahm did cite Baxter et al., a large-scale epidemiological study that found no association between vaccination and subsequent development of TM. Pet'r's Ex. 26k. Epidemiological studies are unnecessary, and in fact, are rarely invoked in the Program, due to the uncommon nature of many of the alleged conditions. However, in instances where such studies have been undertaken, the results can provide persuasive evidence in support of, or rebuttal to, a petitioner's petition. And, even if relevant studies are available, they would not be the sole piece of evidence upon which a special master would determine if causation has been established. Here, Petitioner also cited case reports of various tetanus-containing vaccinations with subsequent developments of TM, ON, and NMO. These case reports alone, however, provide limited value in the absence of a cogent theory deduced from the facts and circumstances of the reported patients, that can then be applied to Petitioner's medical history.

After consideration of the evidence, I find that Petitioner has not presented preponderant evidence of a sound and reliable explanation that the Tdap vaccine can cause NMO. Therefore, Petitioner does not meet her burden pursuant to *Althen* prong one.

B. *Althen* Prong Two – Actual Causation

All of the experts agreed that Petitioner's symptoms first presented as TM that evolved into NMO. *See* Tr. 140, 149. While Petitioner's medical records note that she received a vaccine prior to the onset of her symptoms, none of her treating providers opined on the cause of her TM or NMO.

Petitioner presented an association between her vaccine and her condition, specifically that the former preceded the latter. However, a chronological relationship and lack of alternative cause, without more, are insufficient to meet the preponderant standard. Dr. Nahm did not analyze Petitioner's clinical presentation in the context of his theory to distinguish an idiopathic NMO from a vaccine-induced NMO, or from what happened in Petitioner's case. *See* Tr. 131–32 (testifying that he would be unable to determine in a clinical setting whether NMO is vaccine-induced via molecular mimicry of if it is an idiopathic pathogenesis). When I asked Dr. Nahm how he would recognize the cause of any specific patient's NMO, he said it is based on a contemporaneous association and if there are no other alternative causes,[46] it is idiopathic unless there is a recent vaccination. Tr. 132–33. He asserted that the specifics of the immune pathogenesis of NMO are unknown. Petitioner's burden to establish actual causation cannot be met by simply declaring that if a vaccine preceded illness, then the illness is vaccine caused. This

[46] None of the experts proposed alternative causes for Petitioner's condition nor do I find preponderant evidence of alternative causes in the medical records.

acknowledgment that there is no mechanism or subsequent application to Petitioner's presentation best illustrates the lack of preponderant evidence here to satisfy *Althen* prong two.

C. *Althen* Prong Three – Temporal Association

Althen prong three is also somewhat dependent on a reliable causation theory. Petitioner's inability to meet her burden demonstrating how the Tdap vaccine can cause NMO effectively precludes her from being able to show that her symptoms were temporally appropriate according to said theory. While I find preponderant evidence Petitioner suffered from NMO, she did not offer a sound and reliable theory of vaccine causation. Therefore, she cannot demonstrate that her NMO arose in a medically acceptable timeframe consistent with vaccine causation. I do note, however, that Respondent's experts did not dispute a 14-day onset as proposed by Petitioner. Nonetheless, I find Petitioner has not met her burden with respect to *Althen* prong three.

VI. Conclusion

After a careful review of the record, Petitioner has failed to provide preponderant evidence that that her May 6, 2017 Tdap vaccine caused her TM and NMO. Accordingly, Petitioner's claim is **DENIED**. Absent a timely motion for review, the Clerk is directed to enter judgment dismissing this case for insufficient proof in accordance with Vaccine Rule 11(a).[47]

IT IS SO ORDERED.

s/Herbrina D. S. Young
Herbrina D. S. Young
Special Master

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