In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 18-300V

Filed: October 3, 2025

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DIANA SONGERO,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

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Ronald Craig Homer, Esq. Conway, Homer, P.C., Boston, MA, for petitioner.
Madylan Louise Yarc, Esq., U.S. Department of Justice, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

Roth, Special Master:

On February 28, 2018, Diana Songero ("Ms. Songero" or "petitioner") filed a petition under the National Vaccine Injury Compensation Program, 42 U.S.C. § 300aa-10 *et seq.*[2] ("Vaccine Act" or "the Program"). Petitioner alleged that the influenza ("flu") vaccine she received on September 24, 2016, caused her to suffer from transverse myelitis ("TM"). *See* Petition, ECF No. 1 at 1.

After carefully analyzing and weighing the evidence presented in this case in accordance with the applicable legal standards, I find that petitioner has provided preponderant evidence that her flu vaccine caused her TM, satisfying petitioner's burden of proof under *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274, 1280 (Fed. Cir. 2005). Accordingly, Petitioner is entitled to compensation.

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[1] Because this Ruling 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 Ruling 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 (1986). Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2018).

I. Procedural History

The petition was filed on February 28, 2018, and assigned to me on the same date. ECF Nos. 1, 4. Medical records and affidavits from petitioner were filed in support of the petition on March 5, 2018. Petitioner's Exhibits ("Pet. Ex.") 1-10, ECF Nos. 6-7. Petitioner filed a statement of completion on March 7, 2018. ECF No. 11.

Following his review of the medical records, respondent filed his Rule 4(c) Report on March 14, 2019. ECF No. 19.[3]

Petitioner filed an expert report from Carlo Tornatore, M.D.[4] along with his CV and supporting literature on July 30, 2019. Pet. Ex. 11-26, ECF Nos. 24-25. Respondent filed an expert report of Peter Donofrio, M.D.[5] along with his CV and medical literature on February 26, 2020. Respondent's Exhibits ("Resp. Ex.") A-D, ECF No. 29. A supplemental report from Dr. Tornatore with additional literature was filed on September 24, 2020. Pet. Ex. 27-29, ECF No. 33. On November 4, 2020, respondent filed a status report advising that he did not intend to respond to Dr. Tornatore's supplemental report at that time and requested that the Court schedule an entitlement hearing in the matter. ECF No. 35.

At a status conference held on January 7, 2021, the expert reports were discussed. Also discussed was respondent's decision to defend the case on the 63-day onset and on the ground that an undiagnosed urinary tract infection ("UTI") was responsible for her TM rather than her flu vaccination. ECF No. 36 at 2. The Court also alerted respondent to a prior case in which his expert, Dr. Donofrio, was referenced agreeing with Dr. Tornatore's TM onset period of 63 days. *See Hitt v. Sec'y of Health & Hum. Servs.*, No. 15-1283V, 2020 WL 831822, at *11 (Fed. Cl. Spec. Mstr. January 24, 2020) ("Dr. Donofrio seemed to generally accept Dr. Tornatore's timeframe" of "1 to 63 days" in a case where the flu vaccine caused petitioner's TM.). This case, and Dr. Donofrio's response to it, will be discussed further below. The parties were encouraged to discuss informal resolution. ECF No. 36 at 2.

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[3] Each party requested and was granted several extensions of time in this matter. ECF Nos. 14-15, 18, 20, 22-23, 27-28, 30-32, 39-40, 43, 45, 51.

[4] Dr. Tornatore has an undergraduate degree in neurobiology from Cornell University, an M.S. from Georgetown University, Department of Physiology, and an M.D. from Georgetown University School of Medicine. Pet. Ex. 12. Dr. Tornatore is the Chairman and Neurologist-in-Chief, Department of Neurology, for Medstar Georgetown University Hospital; Chairman, Department of Neurology for Georgetown University Medical Center; and Professor of Neurology at Georgetown University Medical Center. Pet Ex. 11 at 1; Pet. Ex. 12 at 4. He is also the Director of the Multiple Sclerosis Clinic at Georgetown University Hospital. Pet Ex. 12 at 4. He is board certified in neurology. *Id*. at 2.

[5] Dr. Donofrio received his medical degree from Ohio State University School of Medicine in 1975. Resp. Ex. B at 1. He completed an internal medicine residency at Good Samaritan Hospital in Cincinnati, Ohio, in 1978; a neurology residency at the University of Michigan Medical Center in Ann Arbor, Michigan, in 1981; and a neuromuscular fellowship at the University of Michigan in Ann Arbor, Michigan, in 1982. *Id*. at 2. He then worked as a professor of neurology. *Id.* at 2-3. His positions have included Professor of Neurology and Chief of the Neuromuscular Section and Director of the MDA and ALS Clinics at Vanderbilt University Medical Center. Resp. Ex. A at 1. He is board certified in neurology, internal medicine, electrodiagnostic medicine, and neuromuscular disorders. Resp. Ex. A at 1; Resp. Ex. B at 2. He has authored over 100 journal articles, a textbook, and several book chapters and abstracts, among other publications, that touch on GBS, CIDP, and other neuropathies. Resp. Ex. A at 1; Resp. Ex. B at 12-62.

Pursuant to discussions at the January 7, 2021, status conference, respondent filed a supplemental report from Dr. Donofrio along with medical literature on April 7, 2021. Resp. Ex. E-F, ECF No. 44. Petitioner filed a status report on May 19, 2021, confirming that a demand had been submitted to respondent. ECF No. 46. In a June 18, 2021, status report, petitioner advised that respondent was maintaining his position to defend this case and would proceed with litigation. ECF No. 47. A conference was held on July 14, 2021, after which the parties were ordered to advise within 30 days of mutually agreeable dates in January or February 2023 for a hearing. ECF No. 48. A two-day entitlement hearing was scheduled for January 26-27, 2023. ECF Nos. 49-50.

A supplemental expert report of Dr. Tornatore and medical literature were filed on October 29, 2021. Pet. Ex. 32-33, ECF No. 52. Updated medical records were filed on October 13, 2022; November 18, 2022; and November 29, 2022. ECF Nos. 54, 56, 58.

Just prior to hearing and due to Dr. Tornatore being ill, the parties agreed to proceed by Ruling on the Record. ECF No. 66. A briefing schedule was ordered. Petitioner filed her Motion for Ruling on the Record on March 30, 2023. ECF No. 68. Respondent filed his Response on April 14, 2023. ECF No. 69. Petitioner filed a Reply on April 21, 2023. ECF No. 70.

I have determined that the parties have had a full and fair opportunity to present their cases and that it is appropriate to resolve entitlement on the existing record. *See* Vaccine Rule 8(d); Vaccine Rule 3(b)(2); *see also Kreizenbeck ex rel. C.J.K. v. Sec'y of Health & Hum. Servs*., 945 F.3d 1362, 1366 (Fed. Cir. 2020) (noting that "special masters must determine that the record is comprehensive and fully developed before ruling on the record"). Accordingly, this matter is now ripe for resolution.

II. Relevant Medical Terminology

Transverse myelitis ("TM") is an immune-mediated inflammatory process causing damage to the spinal cord, and is often associated with infection, collogen vascular disease, multiple sclerosis, and radiation. Vaccinations, including hepatitis B, rabies, smallpox, influenza, and rubella, have been linked to TM. Pet. Ex. 13 at 1;[6] Pet. Ex. 14 at 1.[7] Up to 40% of TM cases are preceded by infections, including but not limited to influenza, measles, mumps, rubella, cytomegalovirus, and the Epstein-Barr virus. Pet. Ex. 14 at 2.[8] Most cases begin after the patient has recovered from the infection. Thus, TM appears not to be the result of a direct infectious process, but an autoimmune response triggered by the infectious process. *Id*.

The etiology of autoimmune responses is multifactorial, involving genetics, immunology, and hormonal and environmental factors. Pet. Ex. 14 at 2.[9] MRI findings for various forms of TM include spinal cord enlargement, intramedullary increased T2 signal lesions, and variable enhancement. Pet. Ex. 13 at 1.[10] Findings after the flu vaccine have shown extensive, longitudinal

[6] Rohit Bakshi & John C. Mazziotta, *Acute Transverse Myelitis After Influenza Vaccination: Magnetic Resonance Imaging Findings*, 6 J. of Neuroimaging 248 (1996) filed as "Pet. Ex. 13."
[7] N. Agmon-Levin et al., *Transverse Myelitis and Vaccines: A Multi-Analysis*, 18 Lupus 1198 (2009), filed as "Pet. Ex. 14."
[8] *Id*.
[9] *Id*.
[10] Bakshi & Mazziotta, *supra* note 6.

myelitis and diffuse cord enlargement extending over several spinal levels. *Id*. The development of neurological complications ranges from 1 to 63 days after influenza vaccination and occurs, on average, 16.5 days post-vaccination. *Id*. However, *Agmon-Levin, et al.* studied 37 cases of GBS associated with different vaccines given to infants, children, and adults and found the temporal association to be between several days to three months. Pet. Ex. 14 at 5.[11] *Schonberger, et al.* showed an increased risk of vaccine-related GBS to be concentrated within a five-week period after vaccination, but lasting for approximately 9-10 weeks. Pet. Ex. 28 at 1.[12] The *Langmuir, et al.* study, resulting from a court order, computerized summaries of 1,300 cases of GBS reported to the CDC during the swine flu vaccination program of 1976-1977 and found that the effects attributed to the vaccine lasted for at least six weeks and possibly eight weeks but not longer. Resp. Ex. D at 1.[13] The rarity of TM makes it difficult to study. *Id*.; Pet. Ex. 16 at 2.[14]

The pathogenesis of TM is believed to be autoimmune and involves a breakdown of the blood-brain barrier ("BBB") resulting in an inflamed spinal cord in a focal area, pleocytosis,[15] or both. Pet. Ex. 14 at 1.[16] Several mechanisms by which infectious agents may induce autoimmunity include molecular mimicry, epitope spreading, and/or polyclonal activation or bystander activation. *Id*. at 4. The diagnostic criteria include bilateral sensory, motor, or autonomic dysfunction attributable to the spinal cord and a clearly defined sensory level with symptoms peaking within 4 hours to 21 days. *Id*. at 1.

III. Factual Background

A. Medical History

1. Petitioner's Health Before Receiving the Flu Vaccine

Petitioner was born on August 30, 1948. Pet. Ex. 2 at 1. Her past medical history was not contributory but included, in part, deep vein thrombosis, asthma, melanoma with skin resection, eczema, dry skin, cystocele in need of surgical repair, vitamin D deficiency, and left kidney removal. *See generally*, Pet. Ex. 2; Pet. Ex. 3; Pet. Ex. 4 at 34-35; Pet. Ex. 5 at 2, 11, 133, 144, 222; Pet. Ex. 8 at 122.

Petitioner received a flu vaccine on September 24, 2016, at Sam's Club. Pet. Ex. 1 at 1. She was 68 years old.

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[11] Agmon-Levin et al., *supra* note 7.

[12] Lawrence B. Schonberger et al., *Guillain-Barre Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976-77*, 110 Am. J. of Epidemiology 105 (1979), filed as "Pet. Ex. 28."

[13] Alexander D. Langmuir et al., *An Epidemiologic and Clinical Evaluation of Guillain-Barré Syndrome Reporting in Association with the Administration of Swine Influenza Vaccines*, 119 Am. J. of Epidemiology 841 (1984), filed as "Resp. Ex. D."

[14] Isabelle Korn-Lubetzki et al., *H1N1 Vaccine-Related Acute Transverse Myelitis*, 13 IMAJ 249 (2011), filed as "Pet. Ex. 16."

[15] Pleocytosis is the "presence of a greater than normal number of cells in the cerebrospinal fluid." *Pleocytosis*, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=39556 (last visited August 28, 2025).

[16] Agmon-Levin et al., *supra* note 7.

2. Petitioner's Health After Receiving the Flu Vaccine

Petitioner presented to her dermatologist on November 23, 2016, for a skin check, dry skin, and eczema. She had no other complaints. Pet. Ex. 3 at 8.

On November 26, 2016, sixty-three days following receipt of the flu vaccine, petitioner presented to the emergency room at Community Hospital for numbness in both arms which started that morning around 8:45 while she was folding towels. Pet. Ex. 5 at 2. Her shoulders felt as though "'she had just worked out.'" *Id*. She then experienced weakness and numbness in both hands. She reported being fine when she woke up in the morning and denied injury or other cause. *Id*. Neurological examination was positive for bilateral hand weakness and upper body numbness. *Id*. at 4. She had weak dorsiflexion in both wrists and an inability to maintain any degree of dorsiflexion versus resistance. *Id*. at 5. She had weak to absent hand grasp, right worse than left, and was unable to hold her arms in front of her versus resistance. *Id*. The remainder of the examination was normal or negative. *Id*.

CT scan of the head and MRI of the brain were unremarkable. Pet. Ex. 5 at 6-7, 213, 216. MRI of the cervical spine revealed an abnormal signal and enhancement within the C6 and C7 vertebral bodies suspicious for metastatic disease; degenerative changes at C5 and C6; bulging discs at C4-T1 which narrowed the subarachnoid space ventrally but did not affect the cord; and the neural foramina was patent. Pet. Ex. 5 at 38. The impression was possible metastatic lesions at C6 -7 and T10 [sic] in the setting of prior melanoma. *Id*. at 39. A workup with a bone scan, tissue biopsy, and PET scan were ordered. *Id*. Lumbar puncture was to be considered along with neurology checks and evaluations for physical and occupational therapy. *Id*. at 39-40. MRI of the thoracic spine revealed a 6mm enhancement seen within T10 which could represent metastatic disease. *Id*. at 38.

Petitioner was examined by Dr. Gong of neurology; Dr. Shenoy for asthma; Dr. Shukairy of neurosurgery; Dr. Atassi of hematology; and Dr. Slotar of infectious disease. Pet. Ex. 5 at 22. Following discussions with the multiple specialists, petitioner was admitted. *Id*. at 9.

More specifically, Dr. Gong noted a past medical history of melanoma in remission, a sudden onset of shoulder and arm paresthesia, and bilateral hand weakness. Pet. Ex. 5 at 52. Dr. Gong wrote that, given the sudden onset of bilateral upper arm and hand paresthesia and weakness, there was a need to rule out spinal cord stroke and inflammation. *Id*. A bone scan and consult with Dr. Mbaoma was ordered. *Id*. at 52. Dr. Gong ordered a lumbar puncture, rheumatology and ID workup, acyclovir, and IV solumedrol for five days with calcium and GI prophylaxis. MRI with diffusion weighted imaging and apparent diffusion coefficient showed no ischemic lesion of the cervical spinal cord. *Id*. at 53. Dr. Gong noted mild weakness and positive reflexes on neurological examination. *Id*. at 58. He noted no potential causes in petitioner's medical history, except that petitioner had her flu shot about a month prior.[17]

Petitioner was examined by Dr. Shenoy of neurosurgery. She was noted to be in her usual state of health until that morning when she noticed shoulder soreness, then numbness in her

[17] Petitioner's vaccination records show that she received the flu shot 63 days before she presented to Community Hospital. Pet. Ex. 1.

extremities. Pet. Ex. 5 at 40. She had gotten worse since presenting to the emergency room. Her neurological examination was intact, upper extremity strength was 2/5 bilaterally, with a 3/5 grip strength and normal sensation. *Id*. at 43. Lower extremities were normal. *Id*.

Dr. Shukairy of neurosurgery also noted that her weakness was particularly bad in her wrists. Pet. Ex. 5 at 79. His impression was sudden onset of weakness in the upper extremities, and he was concerned about some type of autoimmune onset versus paraneoplastic syndrome. *Id*. at 80. He noted no cord compression on objective testing and no need for surgical intervention. *Id*.

Dr. Atassi of hematology could not rule out malignancy and ordered a bone scan, D dimer, ESR, serum protein electrophoresis, and serum line chain. Pet. Ex. 5 at 44.

Another MRI of the cervical spine was performed on November 27, 2016, and revealed an abnormal signal from C4 through C7 determined to be transverse myelitis with demyelinating and spondylotic changes of the cervical spine. Pet. Ex. 5 at 219.

Dr. Slotar of infectious disease examined petitioner after the finding of TM or other demyelinating disease on repeat MRI. Pet. Ex. 5 at 81. He ordered a lumbar puncture with full serologic workup. *Id*. IV acyclovir was to continue until test results were in. *Id*. The lumbar puncture was scheduled for that day. *Id*. at 95.

Bone scan revealed mild degenerative or traumatic joint changes with no definite evidence of metastatic bone lesions. Pet. Ex. 5 at 222.

A follow up with Dr. Shukairy on November 28, 2016, confirmed that no surgical intervention was needed. Pet. Ex. 5 at 101. Test results included TM with no expansion of the cord. *Id*. At that time, petitioner reported being able to move her hands better but still had numbness. *Id*.

On November 29, 2016, petitioner was examined by Dr. Zabiega of neurology. Pet. Ex. 5 at 121. The lumbar puncture was negative for white blood cells but was sent for further testing. *Id*. IV solumedrol was continued. *Id*. Petitioner still had significant numbness in her upper extremities but there was some improvement. *Id*.

Dr. Slotar's concern remained TM even though the lumbar puncture showed no pleocytosis. Pet. Ex. 5 at 134. Infectious etiologies were unlikely. *Id*. Acyclovir was to continue until PCR results were received and IV solumedrol continued. *Id*. Petitioner was afebrile with paresthesia and distal weakness that was nominally improved. *Id*.

Dr. Mbaoma of oncology and hematology examined petitioner on November 30, 2016, and noted the C6-7 lesion on MRI but a negative bone scan. Pet. Ex. 5 at 178. There was concern for multiple myeloma due to a high association with TM, though Dr. Mbaoma added he did not see any evidence to suggest it. *Id*. Petitioner had improved with steroids and was referred back to neurology. *Id*. at 179.

Dr. Zabiega examined petitioner on December 1, 2016, for TM and noted that she was doing better and could be discharged on a tapering dose of prednisone with neurological follow up

in a month. Pet. Ex. 5 at 164. She had a zinc deficiency but not enough to cause myelopathy. A supplement was needed. *Id*. Physical therapy evaluation was done that day. *Id*. at 188-92.

Petitioner was discharged to her home on December 1, 2016, with improving symptoms. Pet. Ex. 5 at 21-22. The final diagnosis included acute TM, a demyelinating disease of the central nervous system; other cervical disc degeneration, unspecified; mild intermittent asthma; zinc deficiency; and allergy to penicillin. *Id*. at 21.

At a follow up with Dr. Gong on January 30, 2017, her history included a flu shot about one month prior to onset of symptoms, and no injuries, illness, fever, or tick bites. Pet. Ex. 2 at 114. Her labs largely came back within normal limits, and she tested negative for Lyme. *Id*. at 115. Sensation was intact and reflexes were positive, but she still had mild weakness. *Id*. at 117.

Repeat MRI of the cervical spine performed on February 25, 2017, when compared to her prior films, revealed persistent but improved signal abnormality in the cervical spinal cord compatible with history of myelitis. Pet. Ex. 5 at 578. There was also multi-level spondylosis. *Id*.

Petitioner returned to Dr. Gong on March 20, 2017, with improved weakness. Pet. Ex. 2 at 106-111.

At her visit with pulmonologist Dr. Layous for asthma on May 4, 2017, petitioner was told that the flu vaccine exacerbated her TM and she was not to receive further flu shots. Pet. Ex. 6 at 9-10. He was also considering what type of pneumonia vaccine she was to receive for her second shot. *Id*. at 10.

Dr. Gong documented her TM at her September 18, 2017 visit, noting that her weakness had improved, but she had continued fingertip weakness. Pet. Ex. 7 at 1. She had cervical spondylosis with a questionable vertebral bone lesion of unknown etiology. *Id*. She needed zinc, B12, and Vitamin D supplements. *Id*.

Cervical MRI from March 17, 2018, when compared to one from February 25, 2017, revealed a residual T2 hyperintense signal from C4-C7 with no cord enhancement and no new signal abnormality. Pet. Ex. 35 at 171. There was multilevel cervical spondylosis. *Id*. at 171.

Dr. Gong's impression at petitioner's March 26, 2018 visit remained TM with cervical spondylosis. Pet. Ex. 24 at 36. She needed supplements for vitamin D, zinc, and B12. *Id*. Dr. Gong documented the onset of TM, including petitioner's flu vaccine one month before. *Id*. at 36-37. He detailed petitioner's treatment, continued numbness in both hands, arm weakness, and difficulty with fine motor skills. *Id*. Petitioner also reported neck stiffness with difficulty turning her head to the side. *Id*. at 36.

Petitioner visited neurologist Dr. Joseph on January 28, 2021, with continued complaints of difficulty with hand coordination, making it difficult to type and do fine motor tasks, following post-flu vaccine TM. Pet. Ex. 34 at 102-03. Repeat cervical MRIs were noted as stable. *Id*. at 105.

Petitioner's relevant medical records end here.

B. Petitioner's Affidavit

Petitioner affirmed that prior to the flu vaccine she was in good health. Pet. Ex. 9 at 1. She saw a doctor occasionally for a bad cold, skin checks for moles, and asthma for which she used an inhaler. *Id*. She was diligent in receiving her flu and other vaccinations. *Id*.

Petitioner affirmed receipt of a flu vaccine on September 24, 2016, at Sam's Club. Pet. Ex. 9 at 1. On the morning of November 26, 2016, while folding laundry at about 9:30 am, she suddenly felt a prickly feeling in her shoulders that spread to her arms and hands. *Id*. at 1-2. She became anxious and walked to keep moving. *Id*. Thinking she was having a stroke or heart attack, she tried to get ready to go to the hospital, but lost feeling in her hands and arms. *Id*. By the time she got to the emergency room at Community Hospital she could not use her hands. *Id*.

Petitioner affirmed that she saw many doctors, had many tests, and was ultimately diagnosed with TM. Pet. Ex. 9 at 2. Doing routine tasks was difficult and she was concerned about losing her job. *Id*. She was discharged from the hospital on December 1, 2016, and was prescribed prednisone, which allowed her to better control her arms and hands. *Id*. She returned to work the next day. *Id*. Initially she was driven to work as she was still unable to use her hands to turn the key or use the gear shift. *Id*.

Petitioner affirmed that her hands and arms are still weak. Pet. Ex. 9 at 3. Although she can now perform some tasks, petitioner is aware of every movement and still has a lack of coordination. *Id*. at 3-4. At work she performs a variety of clerical tasks, including switchboard, typing, taking minutes, and stapling hundreds of labels to single sheets of paper. *Id*. Her typing is slower with more mistakes. *Id*. She drops papers because she does not feel them in her hands. *Id*. When she became a grandmother, she could not carry the baby while walking due to fear of dropping the baby. *Id*. at 4. She has difficulty changing a diaper and her arms are sore and weak from holding the baby. *Id* at 4-5. She cannot be relied upon to babysit. *Id*.

Petitioner affirmed that her doctors have advised against receiving further flu vaccines. Pet. Ex. 9 at 5.

IV. The Experts

Dr. Tornatore authored three reports in this matter: Pet. Ex. 11; Pet. Ex. 27; and Pet. Ex. 32. Dr. Donofrio issued two reports: Resp. Ex. A and Resp. Ex. E.

A. Dr. Tornatore's First Report – Pet. Ex. 11

Following an in-depth recital of petitioner's medical history, Dr. Tornatore summarized that petitioner received a flu vaccine on September 24, 2016, at the age of 68, had an onset of neurologic symptoms in the upper extremities on November 26, 2016, an MRI on November 27, 2016, consistent with transverse myelitis, and other than the vaccination, no other etiology for transverse myelitis was found. Pet. Ex. 11 at 2-9.

Dr. Tornatore described transverse (meaning inflammation across the width of the spinal cord) myelitis (meaning inflammation of the spinal cord) as a rare clinical syndrome in which an immune-mediated process causes neural injury to the spine, resulting in varying degrees of weakness, sensory alterations, and autonomic dysfunction. Pet. Ex. 11 at 9. The inflammation in TM destroys or damages the myelin, the fatty substance that insulates and covers the nerve fibers, causing scars that interrupt communications between the nerves and the rest of the body. *Id*. TM is part of a continuum of neuroimmunologic disorders which include Guillain-Barré syndrome (GBS), multiple sclerosis (MS), and acute disseminated encephalomyelitis ("ADEM"). *Id*. However, TM and MS are central nervous system ("CNS") disorders, while GBS and CIDP (chronic inflammatory demyelinating polyneuropathy) are peripheral nervous system ("PNS") disorders. *Id*.

Dr. Tornatore explained that with TM there is a breakdown of the blood-brain barrier with cerebral spinal fluid (CSF) pleocytosis within a focal area of the spinal cord. Pet. Ex. 11 at 11; Pet. Ex. 14 at 2.[18] Vaccines, including the flu vaccine, and various infectious agents have been implicated in the pathogenesis of TM, which appears to be an autoimmune response triggered by foreign antigens rather than a direct infectious process. Pet. Ex 11 at 11. In ADEM, a related condition, "the presumptive mechanism is immune-mediated demyelination although immune-complex mediated vasculopathy has also been postulated." *Id*.; Pet. Ex. 19 at 1-2.[19]

Dr. Tornatore explained that the body's immune system has the ability to distinguish self from non-self, which is essential for self-defense and protection from autoimmune destruction. Pet. Ex. 11 at 11. However, a breakdown of self-tolerance to autoantigens is necessary to the development of autoimmunity. *Id*. Therefore, it is reasonable that if an infectious antigen can cause autoimmunity so can recombinant or live attenuated antigens in a vaccine. *Id*.

Dr. Tornatore then proposed several mechanisms by which autoimmunity can occur. Pet. Ex. 11 at 11-12. Molecular mimicry between infectious antigens and self-antigens is the most common. *Id*. at 11. Epitope spreading involves invading antigens that accelerate an ongoing autoimmune process by local activation of antigen presenting cells and over-processing of antigens. *Id*. at 12. Polyclonal activation of B lymphocytes or bystander activation, which enhances cytokine production, may further induce the expansion of auto-reactive cells in response to infectious agents. *Id*. Bystander activation has been associated with TM due to elevated IL-6 levels found in the CSF of TM patients. *Id*. at 12; Pet. Ex. 14 at 4.[20]

Dr. Tornatore added that molecular mimicry has more than one biologic process. Pet. Ex. 11 at 12. Classically, antibodies cross-react directly with viral and cellular proteins. *Id*. However, another well-established model shows T-cell activation cross-reacting against myelin basic protein. *Id*. The process of T-cell activation against an antigen can damage nearby cells, leading to collaterally damaging effects to cell structures from the release of cytokines and macrophage activation. *Id*. "[I]nteractions of the immune cells and the potential for a negative cascade of auto-immunity have led to postulation of what is termed the 'fertile field' model." *Id*. This model

[18] Agmon-Levin et al., *supra* note 7.
[19] William Huynh et al., *Post-Vaccination Encephalomyelitis: Literature Review and Illustrative Case*, 15 J. of Clinical Neuroscience 1315 (2008), filed as "Pet. Ex. 19."
[20] Agmon-Levin et al., *supra* note 7.

features the activation of an immune response by an immunogen with sequence homology to self-proteins which may prime autoreactive T-cells in the host, but which lack the momentum to initiate an adverse autoimmune reaction by themselves. *Id*. A later or coincidental immune stimulation from a vaccine or other immunogen, even one without cross-reactive antigens or sequence similarity, could initiate an autoimmune reaction in a susceptible host that could lead to inflammatory demyelination. *Id*. at 12; *see generally* Pet. Ex. 19.[21] Receptors on B and T cells once thought to have a high level of specificity for individual foreign antigens are now known to recognize peptide sequences with no shared homology. Pet. Ex. 11 at 13. A single T-cell receptor may recognize thousands of different peptide sequences. *Id*.; *see generally* Pet. Ex. 26.[22] Therefore, microbiologic antigens from bacteria or viruses that bear no similarity to nervous system antigens could activate a B- or T-cell receptor causing the B or T cell to mount an autoimmune response in the nervous system. Pet. Ex. 11 at 13. The general principle of antigenic stimulation or vaccination as a trigger for autoimmune nervous system disease is well accepted. An example is allergic encephalitis. *Id*. at 13.

Dr. Tornatore submitted that the clinical presentation of TM includes bilateral sensory, motor or autonomic dysfunction attributable to the spinal cord, a clearly defined sensory level, and peaking symptoms within four hours and 21 days. Pet. Ex. 11 at 10; Pet. Ex. 14 at 1.[23] Evidence of TM includes inflamed spinal cord manifesting as cerebrospinal fluid pleocytosis, elevated IgG index, or gadolinium enhancement by MRI. Pet. Ex. 11 at 10. The exclusion of "extra-axial compressive etiology by neuroimaging should be observed." *Id*. MRI findings for TM are nonspecific, and may include spinal cord enlargement, intramedullary increased T2 signal lesions, and variable enhancement. *Id*.; Pet. Ex. 13 at 1;[24] *see* Pet. Ex. 15 at 2.[25] Petitioner presented with the typical presentation and progression for TM. *Id*. An inflammatory lesion was seen on MRI extending across more than three vertebral segments longitudinally (C4/5 to C7). *Id*.

Dr. Tornatore referenced case studies associating TM with vaccination. *Bakshi, et al*. reported on cases involving TM following vaccines, including the flu vaccine. Pet. Ex. 11 at 9; Pet. Ex. 13 at 1.[26] *Korn-Lubetzki, et al.* was a case study involving the H1N1 influenza vaccine, where cervical MRI revealed a hyperintense lesion at C6 and C7 with mild expansion of the cord and enhancement with gadolinium. Pet. Ex. 11 at 10; Pet. Ex. 16 at 1.[27] The data supported the diagnosis of post-vaccinal TM "due to an immunological reaction to the vaccine" and negative results for alternative causes. Pet. Ex. 11 at 10; Pet. Ex. 16 at 1-2.[28] *Akkad* was a case study of a patient with longitudinally extensive TM following the H1N1 flu vaccine, who presented with a two-week history of back and lower extremity pain, gradual weakness, paresthesia of the legs, and urinary retention which progressed to all extremities, leaving the patient unable to stand. Pet. Ex.

[21] Huynh et al., *supra* note 19.
[22] Don Mason, *A Very High Level of Crossreactivity is an Essential Feature of the T-Cell Receptor*, 19 Immunology Today 395 (1998), filed as "Pet. Ex. 26."
[23] Agmon-Levin et al., *supra* note 7.
[24] Bakshi & Mazziotta, *supra* note 6.
[25] Wafa Akkad et al., *Longitudinally Extensive Transverse Myelitis Following Vaccination with Nasal Attenuated Novel Influenza A(H1N1) Vaccine*, 67 Archives of Neurology 1018 (2010), filed as "Pet. Ex. 15."
[26] Bakshi & Mazziotta, *supra* note 6.
[27] Korn-Lubetzki et al., *supra* note 14.
[28] *Id*.

11 at 10; Pet. Ex. 15 at 1.[29] Examination revealed proximal muscle weakness with sensory loss in the lower extremities and diminished sensation in the trunk with a T4 sensory level. There was diffuse hyperreflexia, silent plantar response, and no clonus. MRI revealed extensive non-enhancing T2 hypersensitivity from the cervical medullary junction throughout the length of the thoracic cord. A brain MRI was negative for demyelinating lesions. Nerve conduction studies were normal. Pet. Ex. 11 at 10-11; Pet. Ex. 15 at 1-2.[30] The diagnosis was arrived at by CSF and blood testing for infectious causes and by ruling out MS, ADEM, vascular lesions, and neuromyelitis optica. Pet. Ex. 11 at 11. *Akkad* linked the patient's TM to the recent H1N1 vaccination fewer than 30 days before neurologic onset. *Id*. at 11; *see* Pet. Ex. 15.[31] *Nakamura, et al.* showed TM following vaccination as just as plausible as GBS. *Id*.; *see* Pet. Ex. 18.[32]

In Dr. Tornatore's opinion, the foregoing supports a biologically plausible hypothesis, as well as a reasonable sequence of cause and effect. Petitioner received the flu vaccine which has been causally associated with TM. Her medical records show that extensive testing ruled out any other potential alternative cause. Pet. Ex. 11 at 13.

Relying on *Agmon-Levin,* Dr. Tornatore argued that most cases of TM have an onset between several days and 3 months. Pet. Ex. 11 at 13; Pet. Ex. 14 at 5.[33] Neurological onset of symptoms can develop with a latency ranging from 1 to 63 days with a mean of 16.5 days. Pet. Ex. 11 at 13. Petitioner's onset was 63 days. *Id*. at 14. Therefore, petitioner's flu vaccine played a significant causal role in initiating or triggering her TM and onset was within an appropriate timeframe. *Id*.

B. Dr. Donofrio's First Report – Resp. Ex. A

Following a recital of petitioner's medical history, Dr. Donofrio focused on the 63-day onset being too long for an immune response following vaccination and that petitioner had an undiagnosed and untreated UTI that was the cause of her TM. Resp. Ex. A at 5-6.

Dr. Donofrio submitted that no epidemiological studies exist that show that the flu vaccine can cause TM. The best evidence that can be offered is data about GBS from the swine flu epidemic of 1976-1977. Resp. Ex. A at 5; Resp. Ex. D.[34] Dr. Donofrio noted that when considering that the first licensed flu vaccine in the US was in 1943 with billions of vaccines administered over the past 80 years, the absence of an epidemiologic relationship between the flu vaccine and the development of TM was notable: "[A]ny reports of TM following flu vaccination are best explained by chance occurrence rather than causality." Resp. Ex. A at 6. Further, the 2012 Institute of Medicine report, Adverse Effects of Vaccines, concluded that the epidemiological evidence was insufficient or absent to assess an association between the influenza vaccine and TM and that the mechanistic evidence was weak based on the knowledge of natural infection. Resp. Ex. A at 6;

[29] Akkad et al., *supra* note 25.
[30] *Id*.
[31] *Id*.
[32] Naoko Nakamura et al., *Neurologic Complications Associated with Influenza Vaccination: Two Adult Cases*, 42 Internal Medicine 191 (2003), filed as "Pet. Ex. 18."
[33] Agmon-Levin et al., *supra* note 7.
[34] Langmuir et al., *supra* note 13.

Resp. Ex. C.[35] Therefore, the evidence was inadequate to accept or reject a causal relationship between the flu vaccine and TM. Resp. Ex. A at 6.

Dr. Donofrio argued that a 63-day onset was not medically appropriate. The latency or lag phase between primary exposure and the development of the primary antibody response is seven to ten days or shorter for subsequent exposure to the same antigen. Resp. Ex. A at 5; Resp. Ex. C.[36] *Langmuir, et al.* showed an increase of GBS within six weeks of swine flu vaccination which led to the Vaccine Injury Table timeline of 3-42 days for GBS associated with flu vaccination. Resp. Ex. A at 5; Resp. Ex. D at 1.[37] Therefore, a cause-and-effect determination should be much shorter than the 63 days in this case.

Additionally, Dr. Donofrio argued that petitioner had an undiagnosed UTI. Pet. Ex. A at 6. He referenced *Agmon-Levin* as showing that 40% of the 37 cases of TM studied between 1970 and 2009 were associated with preceding infectious illness: "[Petitioner's] urinalysis from [November 26, 2016] showed 11 white blood cells, 2 red blood cells, and an elevated white blood cell esterase 25 (reference negative)." *Id*. at 5.; *see* Pet. Ex. 5 at 37. The "lab results were highlighted as abnormal (A)." *Id*. According to Dr. Donofrio, petitioner's UTI was a sufficient inciting event for TM and much more likely the precipitating event than the flu vaccine. Resp. Ex. A at 5.

Dr. Donofrio added that TM is a monophasic illness and, because petitioner "denied weakness, tremor, paresthesia or numbness" at her January 5, 2017, visit, her complaints of ongoing numbness in her fingertips and difficulty with activities of daily living worsening after January 2017 must be indicative of another cause. Resp. Ex. A at 6; Pet. Ex. 6 at 4. He did not however indicate what that other cause was.

In Dr. Donofrio's opinion, petitioner's onset of injury 63 days after receipt of the subject flu vaccine was "well beyond any interval considered reasonable for an immune reaction to the flu vaccine." Additionally, petitioner had an undiagnosed urinary tract infection which was more likely the cause of her TM because infection precedes TM in 40% of patients. Resp. Ex. A at 6.

C. Dr. Tornatore's Second Report – Pet. Ex. 27

In his second report, Dr. Tornatore maintained that a 63-day onset was medically appropriate for TM and supported by the literature. The latency period for the development of neurologic symptoms typically ranges from 1 to 63 days with a mean of 16.5 days, though there are cases stretching to three months as well. Pet. Ex. 27 at 2; Pet. Ex. 13 at 1.[38] Further, *Schonberger, et al.* reported an increased risk period of autoimmune disorders concentrated within the five-week period after vaccination but lasting for approximately nine to ten weeks. *Schonberger, et al.* found that post vaccinal autoimmune disorders of the nervous system can occur up to 70 days post-vaccination. Pet. Ex. 27 at 2; Pet. Ex. 28.[39] Dr. Tornatore added that in

[35] Institute of Medicine of the National Academies, *Adverse Effects of Vaccines: Evidence and Causality* (Kathleen Stratton et al. eds., 2012), filed as "Resp. Ex. C."
[36] Institute of Medicine of the National Academies, *supra* note 34.
[37] Langmuir et al., *supra* note 13.
[38] Bakshi & Mazziotta, *supra* note 6.
[39] Schonberger et al., *supra* note 12.

discussing GBS, Dr. Donofrio conceded that vaccinations can result in an autoimmune disorder of the nervous system. Pet. Ex. 27 at 2.

Dr. Tornatore disagreed that petitioner had a UTI that was more likely the cause of her TM. Pet. Ex. 27 at 2. Dr. Tornatore pointed out that the urinalysis performed on November 26, 2016, showed no bacteria or cause for repeat testing and petitioner had no complaints of any symptoms related to a UTI. *Id*.; Pet. Ex. 5 at 218. He discussed a phenomenon called sterile pyuria, where patients with systemic autoimmune processes have white blood cells found in the urine even in the absence of infection. In this case, the presence of white blood cells in the absence of infection could have been caused by post-vaccinal immune activation that spilled into the bladder. Pet. Ex. 27 at 2. In his over 40 years of practice, Dr. Tornatore has encountered this phenomenon many times in the TM patients he has treated. *Id*.

Dr. Tornatore maintained that petitioner's September 24, 2016, flu vaccine triggered her TM with lingering neurologic symptoms and deficits. He relied on his first report as detailing the biologically plausible theory and logical sequence of cause and effect between the flu vaccine and petitioner's TM with no evidence of alternative cause seen in the medical records. The onset of symptoms was within an appropriate time. Pet. Ex. 27 at 2.

D. Dr. Donofrio's Second Report – Resp. Ex. E

In his second report, Dr. Donofrio again discussed the 63-day onset of petitioner's TM following her flu vaccine. He referenced *Langmuir, et al.* as the best data available showing that "[t]he effect attributed to the vaccine lasted for at least six weeks and possibly for eight weeks but not longer. . . . 00The authors did not consider any patients who developed GBS after 8 weeks (56 days) to have developed GBS from the flu vaccine." Resp. Ex. E at 1. He noted that the *Langmuir* study was ordered by the court five years after the *Schonberger* study and was a more rigid study than *Schonberger. Langmuir* looked at cases of extensive motor involvement or weakness due to concerns that patients with milder disease may not have GBS. *Id*.

Dr. Donofrio repeated that there is no epidemiologic data relating TM and flu vaccination. The best data regarding immunologic response to the vaccine relates specifically to GBS from 1976-77. Pet. Ex. E at 1.

Dr. Donofrio maintained that petitioner's undiagnosed UTI was the cause of her TM. He disagreed that she had sterile pyuria resulting from a systemic autoimmune process that spilled into the bladder. Pet. Ex. E at 2. He added that Dr. Tornatore did not mention what systemic autoimmune disease to which he referred, and that petitioner did not have a systemic disease. *Id*. at 2. Dr. Donofrio relied on *Stamm,* a 1984 study which measured pyuria, or white blood cells in urine, in female patients with acute simple cystitis, concluding that white blood cells in urine are the best indicator of infection. *Id*. at 1; Resp. Ex. F.[40] "Ten or more WBCs per mm3 occur in less than 1 percent of asymptomatic, non-bacteriuric patients but in greater than 96 percent of the symptomatic men and women with significant bacteriuria." Resp. Ex. E at 1. Petitioner's urinalysis

[40] Walter E. Stamm, *Measurement of Pyuria and Its Relation to Bacteriuria*, 75 Am. J. of Medicine 53 (1983), filed as "Resp. Ex. F."

revealed 11 white blood cells, 2 red blood cells, and white blood cell esterase elevated at 25 (reference negative). *Id*. at 2. Therefore, petitioner had an undiagnosed and untreated UTI. *Id*.

Dr. Donofrio denied that in *Hitt*, 2020 WL 831822, he agreed to a 63-day onset of TM from flu vaccine. Resp. Ex. E at 1. He disagreed that *Langmuir*'s data showed a bell-shaped curve with an increased relative risk of GBS after eight weeks. Though *Langmuir, et al.* might have noted patients whose GBS onset was more remote than eight weeks, the study did not consider these patients to have developed GBS from the flu vaccine. Resp. Ex. E at 2.

E. Dr. Tornatore's Third Report – Pet. Ex. 32

In his third report Dr. Tornatore addressed Dr. Donofrio's reliance on *Langmuir, et al.* which stated that the risk interval for the development of GBS following flu vaccine was restricted to eight weeks. Pet. Ex. 32 at 1. Dr. Tornatore argued that a 63-day onset was an acceptable timeframe for TM. He provided a paper by *Freedman and Stark* entitled, "The swine flu vaccine and Guillain-Barré syndrome. A case study in relative risk and specific causation." Pet. Ex. 33.[41] This paper detailed the history of the first recorded influenza pandemic in 1918 that killed 20 million people worldwide. This was followed by the 1976-77 influenza pandemic, a virus with a similar antigenic type to the 1918 virus, which led the federal government to organize a massive immunization campaign. 151 million people over the age of 18 were targeted, with 43 million people ultimately vaccinated. *Id*. at 3-6. The CDC set up a nationwide surveillance system to collect data on GBS from state health authorities and hired Langmuir and associates to analyze the data. *Id*. at 4. Unvaccinated GBS rates were used for comparison. *Id*.; Pet. Ex. 32 at 1-2. Notably, *Langmuir* distinguished cases with extensive paralysis from limited paralysis showing strong association for the extensive cases. Pet. Ex. 33 at 7.[42] The federal government took responsibility for the over 4,000 claims filed as a result of the swine flu vaccine when insurance companies refused to cover the injuries and drug companies refused to produce the vaccine without protection. Over four billion dollars was paid in damages. *Id*. at 8.

One of those claims was detailed in the case of *Manko v. United States*, 636 F. Supp. 1419 (W.D. Mo. 1986) *aff'd in part*, 830 F. 2d 831 (8th Cir. 1987). The defendant argued that there was only a small excess risk for developing GBS after the eighth week following vaccination. Pet. Ex. 32 at 2-3; Pet. Ex. 33 at 8.[43] The defendant did not agree with the methods and data results relied on by the plaintiff's experts but conceded that the plaintiff's presentation was very different than the data set used in the *Langmuir* paper. They concluded that the mathematical models showed how individual differences can be represented in a more general but abstract setting with results confirming that epidemiological data cannot determine the probability of causation in a meaningful way because of those differences. Pet. Ex. 32 at 3. Dr. Tornatore concluded this was a compelling argument for a prolonged onset interval for GBS following flu vaccine depending on how complete the data is, how it is analyzed, and individual differences. Pet. Ex. 32 at 3; Pet. Ex. 33 at 15-16.[44] He concluded that, where biological plausibility and logical sequence of cause and effect exist,

[41] David A. Freedman & Philip B. Stark, *The Swine Flu Vaccine and Guillain-Barré Syndrome: A Case Study in Relative Risk and Specific Causation*, 64 Law and Contemporary Problems 49 (1999), filed as "Pet. Ex. 33."
[42] *Id*.
[43] *Id*.
[44] *Id*.

they buttress the argument that the flu vaccine can result in the development of TM with an onset of 63 days. Pet. Ex. 32 at 4.

Dr. Tornatore maintained that petitioner did not have a UTI and UTI was not the cause of her TM; rather, the 11 white blood cells on urinalysis was sterile pyuria. Pet. Ex. 32 at 4. He argued that the table in *Stamm* demonstrated that pyuria can be found in 1.6% of asymptomatic, abacteriuric patients, not the less than 1% as opined by Dr. Donofrio. Dr. Tornatore showed that, like the petitioner, up to 3.1% of asymptomatic abacteriuric patients have sterile pyuria. *Id*. Therefore, *Stamm* supported rather than rebutted the argument that sterile pyuria can exist in a patient with WBC >10wbc/mm. *Id*. at 4; Resp. Ex. F.[45] Further, the presence of "[l]eukocyte esterase is evidence of leukocytes, not infection."[46] Pet. Ex. 32 at 4.

Dr. Tornatore maintained his opinion that the flu vaccine received by petitioner on September 24, 2016, triggered her TM with lingering neurologic symptoms and deficits attributable to the initial inflammatory insult. Pet. Ex. 32 at 4.

V. Legal Framework

A. Legal Standard Regarding Causation

The Vaccine Act provides two avenues for petitioners to receive compensation. First, a petitioner may demonstrate a "Table" injury—i.e., an injury listed on the Vaccine Injury Table that occurred within the provided time period. § 11(c)(1)(C)(i). "In such a case, causation is presumed." *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006); *see* § 13(a)(1)(B). Second, where the alleged injury is not listed on the Vaccine Injury Table, a petitioner may demonstrate an "off-Table" injury, which requires that the petitioner "prove by a preponderance of the evidence that the vaccine at issue caused the injury." *Capizzano*, 440 F.3d at 1320; *see* § 11(c)(1)(C)(ii). Initially, a petitioner must provide evidence that he or she suffered, or continues to suffer, from a definitive injury. *Broekelschen v. Sec'y of Health & Hum. Servs*., 618 F.3d 1339, 1346 (Fed. Cir. 2010). A petitioner need not show that the vaccination was the sole cause, or even the predominant cause, of the alleged injury; showing that the vaccination was a "substantial factor" and a "but for" cause of the injury is sufficient for recovery. *See Pafford v. Sec'y of Health & Hum. Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006); *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999).[47]

To prove causation for an "off-Table" injury, petitioners must satisfy the three-pronged test established in *Althen v. Sec'y of Health & Hum. Servs*., 418 F.3d 1274 (Fed. Cir. 2005). *Althen* requires that petitioners show by preponderant evidence that a vaccination caused petitioner's injury "by providing: (1) a medical theory causally connecting the vaccination and the injury; (2)

[45] Stamm, *supra* note 39.

[46] "Leukocyte [] esterase is a screening test used to detect leukocytes in the urine." Kathleen Deska Pagana & Timothy J. Pagana, Mosby's Manual of Diagnostic and Laboratory Tests 900 (6th ed. 2018). Leukocytes are "white blood cells [] that fight infections." *Id*. at 648.

[47] The Vaccine Act also requires petitioners to show by preponderant evidence the vaccinee suffered from the "residual effects or complications" of the alleged vaccine-related injury for more than six months, died from the alleged vaccine-related injury, or required inpatient hospitalization and surgical intervention as a result of the alleged vaccine-related injury. § 11(c)(1)(D). It is undisputed that this requirement is satisfied in this case.

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. Together, these prongs must show "'that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury.'" *Id*. at 1278 (quoting *Shyface*, 165 F.3d at 1352-53). Causation is determined on a case-by-case basis, with "no hard and fast *per se* scientific or medical rules." *Knudsen v. Sec'y of Health & Hum. Servs*., 35 F.3d 543, 548 (Fed. Cir. 1994). 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). "[C]lose calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F.3d at 1280.

Each of the *Althen* prongs requires a different showing. The first *Althen* prong requires petitioner to provide a "reputable medical theory" demonstrating that the vaccines received *can* cause the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citation omitted). To satisfy this prong, petitioner's "theory of causation must be supported by a 'reputable medical or scientific explanation.'" *Andreu ex rel. Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1379 (Fed. Cir. 2009) (quoting *Althen*, 418 F.3d at 1278). This theory need only be "legally probable, not medically or scientifically certain." *Id.* at 1380 (emphasis omitted) (quoting *Knudsen*, 35 F.3d at 548-49). Nevertheless, "petitioners must proffer trustworthy testimony from experts who can find support for their theories in medical literature." *LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1341 (Fed. Cir. 2014).

The second *Althen* prong requires proof of a "logical sequence of cause and effect." *Capizzano*, 440 F.3d at 1326 (quoting *Althen*, 418 F.3d at 1278). In other words, even if the vaccinations can cause the injury, petitioner must show that it did so in this particular case. *See Hodges v. Sec'y of Health & Hum. Servs.*, 9 F.3d 958, 962 n.4 (Fed. Cir. 1993) (finding that even though petitioner's expert showed that a particular vaccine could cause death, the expert failed to show that it caused the death of petitioner, specifically). "A reputable medical or scientific explanation must support this logical sequence of cause and effect," *id.* at 961 (citation omitted), and "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," *Paluck v. Sec'y of Health & Hum. Servs.*, 786 F.3d 1373, 1385 (Fed. Cir. 2015) (quoting *Andreu*, 569 F.3d at 1375). Petitioner is not, however, required "to eliminate alternative causes as part of establishing [their] prima facie case." *Doe v. Sec'y of Health & Hum. Servs.*, 601 F.3d 1349, 1357-58 (Fed. Cir. 2010); *see Walther v. Sec'y of Health & Hum. Servs.*, 485 F.3d 1146, 1152 (Fed. Cir. 2007) (holding that a "petitioner does not bear the burden of eliminating alternative independent potential causes").

To satisfy the third *Althen* prong, petitioner must establish a "proximate temporal relationship" between the vaccination and the alleged injury. *Althen*, 418 F.3d at 1278. 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.").

B. Legal Standard Regarding Fact Finding

The process for making determinations in Vaccine Program cases regarding factual issues begins with analyzing the medical records, which are required to be filed with the petition. § 11(c)(2). Medical records created contemporaneously with the events they describe are generally considered to be more trustworthy. *Cucuras v. Sec'y of Health & Hum. Servs*., 993 F.2d 1525, 1528 (Fed. Cir. 1993); *but see Kirby v. Sec'y of Health & Hum. Servs*., 993 F.3d 1378, 1382-83 (Fed. Cir. 2021) (clarifying that *Cucuras* does not stand for proposition that medical records are presumptively accurate and complete). While not presumed to be complete and accurate, medical records made while seeking treatment are generally afforded more weight than statements made by petitioners after-the-fact. *See Gerami v. Sec'y of Health & Hum. Servs*., No. 12-442V, 2013 WL 5998109, at *4 (Fed. Cl. Spec. Mstr. Oct. 11, 2013) (finding that contemporaneously documented medical evidence was more persuasive than a letter prepared for litigation purposes), *mot. for rev. denied*, 127 Fed. Cl. 299 (2014). Indeed, "where later testimony conflicts with earlier contemporaneous documents, courts generally give the contemporaneous documentation more weight." *Campbell ex rel. Campbell v. Sec'y of Health & Hum. Servs*., 69 Fed. Cl. 775, 779 (2006); *see United States v. U.S. Gypsum Co*., 333 U.S. 364, 396 (1948).

Despite the weight afforded medical records, special masters are not bound rigidly by those records in determining facts such as the onset of a petitioner's symptoms. *Vallenzuela v. Sec'y of Health & Hum. Servs*., No. 90-1002V, 1991 WL 182241, at *3 (Fed. Cl. Spec. Mstr. Aug. 30, 1991); *see also Eng v. Sec'y of Health & Hum. Servs*., No. 90-175V, 1994 WL 67704, at *3 (Fed. Cl. Spec. Mstr. Feb 18, 1994) (explaining that § 13(b)(2) "must be construed so as to give effect to § 13(b)(1) which directs the special master or court to consider the medical record . . . but does not require the special master or court to be bound by them"); *see also Burns v. Sec'y of Health & Hum. Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (holding that it is within the special master's discretion to determine whether to afford greater weight to medical records or to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is rational).

In short, "the record as a whole" must be considered. § 13(a).

C. Evaluating Expert Testimony

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 or her 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 Pharms., Inc.*, 509 U.S. 579 (1993), requires that courts determine the reliability of an expert opinion before it may be considered as evidence. "In short, the requirement that an expert's testimony pertain to 'scientific knowledge' establishes a standard of evidentiary

reliability." *Id*. 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 ex rel. Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1324 (Fed. Cir. 2010). 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 (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."). Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen*, 618 F.3d at 1347 (citing *Lampe*, 219 F.3d at 1362). And 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 ex rel. 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)).

D. Consideration of Medical Literature

Finally, although this decision discusses some but not all of the literature in detail, the undersigned reviewed and considered all of the medical records and literature submitted in this matter. *See Moriarty ex rel. 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 [s]he does not explicitly reference such evidence in h[er] decision."); *Simanski v. Sec'y of Health & Hum. Servs.*, 115 Fed. Cl. 407, 436 (2014) ("[A] Special Master is 'not required to discuss every piece of evidence or testimony in her decision.'") (citation omitted), *aff'd*, 601 F. App'x 982 (Fed. Cir. 2015).

VI. Discussion & Analysis

There is no dispute that petitioner had an onset of TM symptoms 63 days after receipt of the subject flu vaccination. Dr. Donofrio does little to dispute Dr. Tornatore's theory of causation in this case. Rather, his focus is twofold: 1) the 63-day onset is too long for an immune response to flu vaccination, and 2) petitioner had a urinary tract infection which was the cause of her TM. Dr. Donofrio submitted three publications in support of his opinions – the section of the 2012 IOM report for flu vaccination and TM, *Langmuir, et al.* for onset, and *Stamm* discussing urinary tract infection. Resp. Ex. C;[48] Resp. Ex. D;[49] Resp. Ex. F.[50]

A. *Althen* Prong One

For *Althen* prong one, petitioner must establish a "reputable" medical theory that the flu vaccination can cause her injury by a preponderance of the evidence, but she does not need to prove that theory to the level of scientific certainty. *Althen*, 418 F.3d at 1278 ("A persuasive medical theory is . . . supported by reputable medical or scientific explanation.") (internal citations omitted). In a later case, the Federal Circuit required that the theory be "legally probable." *Moberly*

[48] Institute of Medicine of the National Academies, *supra* note 34.
[49] Langmuir et al., *supra* note 13.
[50] Stamm, *supra* note 39.

ex rel. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 (Fed. Cir. 2010) (citation omitted).

Dr. Tornatore opined that the flu vaccine can cause TM via molecular mimicry. Pet. Ex. 11 at 11-12. He relied on *Agmon-Levin, et al.* which noted that "[t]he pathogenesis of [TM] is mostly of an autoimmune nature, triggered by various environmental factors, including vaccination." Pet. Ex. 14 at 1.[51] *Agmon-Levin, et al.* was a systemic review of journals published between 1970 and 2009 analyzing cases of TM following vaccination. *Id*. at 1. Their initial search included 43 cases, but six were excluded due to insufficient data. *Id*. at 2. Of the remaining 37 cases, two were reported after influenza vaccine. *Id*. at 2, 3. "In most of these cases the temporal association was between several days and 3 months." *Id*. at 5. Twenty-seven of the 37 cases (73%) developed symptoms of TM within the first month after vaccination, three developed symptoms between one and two months after vaccination, and seven developed symptoms more than two months after vaccination. *Id*. at 2, 3. Of the two cases of TM following influenza vaccine, onset was seven and nine days. *Id*. at 3. The authors added that a "host's response to a vaccine, originally generated to produce protective immunity, is similar to its response to an infectious invasion." *Id*. at 4. They concluded that "the temporal association between [ ] vaccines and TM, and the possible mechanism associating these phenomena cannot be ignored. The rarity of TM makes it a difficult disease to study." *Id*. at 5.

Dr. Tornatore detailed how structural similarities between an antigen and self-peptides can cause them to cross-react, resulting in the development of autoreactive B and T cells which can cause inflammation and can lead to demyelination. Pet. Ex. 11 at 12-13. He added that homology in amino acid sequences between an antigen and self-peptides is not the only mechanism that can cause an autoimmune response. *Id*. at 13. Receptors on the B and T cells initially thought to have a high level of specificity for individual foreign antigens are now known to recognize peptide sequences that share no homology, with one T cell able to recognize thousands of peptide sequences. This is called "degeneracy." *Id*. at 13; Pet. Ex. 26 at 2-3.[52] Further, the mechanism of bystander activation is the process by which activated T cells react to an antigen damaging cells nearby, both releasing cytokines and by macrophage activation. Pet. Ex. 11 at 12; Pet. Ex. 25 at 2.[53]

Finally, Dr. Tornatore discussed the concept of the fertile field model which includes both aspects of molecular mimicry and bystander activation. Here, an antigen with sequence homology to self-proteins may prime autoreactive T cells but lacks sufficient "momentum" to trigger an autoimmune response by itself. Instead, a later immune stimulation, whether by infection or vaccination, even without cross-reactive antigens or sequence homology, initiates an autoimmune reaction in a susceptible host leading to inflammatory demyelination. Pet. Ex. 11 at 12; Pet Ex. 25 at 4.[54] Dr. Tornatore added that it is accepted that flu vaccination can cause autoimmune demyelinating disease resulting from these various mechanisms which may occur sequentially or

[51] Agmon-Levin et al., *supra* note 7.
[52] Mason, *supra* note 22.
[53] Robert S. Fujinami et al., *Molecular Mimicry, Bystander Activation, or Viral Persistence: Infections and Autoimmune Disease*, 19 Clinical Microbiology Reviews 80 (2006), filed as "Pet. Ex. 25."
[54] *Id*.

concurrently. Pet. Ex. 11 at 13. Dr. Tornatore states that the flu vaccine "has been causally associated with [TM]" in the cited literature. *Id*.

Dr. Tornatore submitted case studies to support the association between the flu and/or H1N1 influenza vaccine(s) and TM and ADEM. Pet. Ex. 13;[55] Pet. Ex. 14;[56] Pet. Ex. 15;[57] Pet. Ex. 16;[58] Pet. Ex. 17;[59] Pet. Ex. 20.[60] Dr. Donofrio argued that case reports carry little weight. Resp. Ex. A at 6. Case reports are generally not sufficient to prove causation; but in the context of rare conditions, such as TM, where epidemiologic studies are unavailable, they provide some evidence of causation. *See, e.g.*, *Irwin v. Sec'y of Health & Hum. Servs.*, No. 16-1454V, 2024 WL 863690, at *18 (Fed. Cl. Spec. Mstr. Jan. 23, 2024) (finding that case reports do not, by themselves, establish causation, but that they do provide evidence in favor of causation). Here, where medical literature has reported TM associated with flu vaccines, the evidence weighs in favor of causation.

Importantly, Dr. Donofrio offered little disagreement with Dr. Tornatore's medical theories. He provided only that the 2012 IOM report concluded that there was insufficient evidence to accept or reject a causal relationship between flu vaccine and TM. Resp. Ex. A at 4; Resp. Ex. C.

In 2009, the IOM committee reviewed *Vellozzi, et al.*, a study in which the committee found data was gathered from a passive surveillance system and lacked an unvaccinated comparison group. Resp. Ex. C at 3.[61] It also identified six other publications, *Bakshi*, *Buchner*, *Larner*, *Nakamura*, *Sugimoto*, and *Wells*, all of which addressed post-flu vaccine TM and concluded that there was no supporting evidence beyond temporality, some being too short a timeframe based on the mechanism involved. *Id*. However, the IOM noted that influenza infection has been, rarely, associated with TM and it considered the effects of natural infection as one type of mechanistic evidence. *Id*. Autoantibodies, T cells, and molecular mimicry may contribute to the symptoms of TM, but the publications did not provide evidence linking the mechanisms to flu vaccine. *Id*. Therefore, the IOM considered the mechanistic evidence weak between the vaccine and TM, but not nonexistent, concluding that the evidence was inadequate to accept or reject a causal relationship between flu vaccine and TM. *Id*. at 3-4.

Further, in a prior case, in which Dr. Tornatore and Dr. Donofrio were the experts, *Hitt v. Sec'y of Health & Hum. Servs.*, No. 15-1283V, 2020 WL 831822, at *10 (Fed. Cl. Jan. 24, 2020), Dr. Donofrio conceded that the medical theories presented by Dr. Tornatore, which mirrored those presented here, describing how a flu vaccine could cause TM, were valid. His position and lack of criticism of Dr. Tornatore's medical theories in this case preponderates in favor of petitioner.

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[55] Bakshi & Mazziotta, *supra* note 6.
[56] Agmon-Levin et al., *supra* note 7.
[57] Akkad et al., *supra* note 25.
[58] Korn-Lubetzki et al., *supra* note 14.
[59] Christopher S. Ambrose et al., *A Case Report of Transverse Myelitis Following Influenza Vaccination*, 68 Archives of Neurology 1085 (2011), filed as "Pet. Ex. 17."
[60] Isabelle Van Ussel et al., *Encephalitis Related to an H_1N_1 Vaccination: Case Report and Review of the Literature*, 124 Clinical Neurology and Neurosurgery 8 (2014), filed as "Pet. Ex. 20."
[61] Institute of Medicine of the National Academies, *supra* note 34.

I am not bound by decisions of other special masters, but I do take guidance from my colleagues and their opinions in similar cases. *See Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1358 (Fed. Cir. 2019). Many petitioners have been found entitled to compensation for vaccine-induced TM and other demyelinating diseases based on molecular mimicry, as provided by Dr. Tornatore and detailed above.[62]

Based on the foregoing, I agree with the reasoning of other special masters who have found molecular mimicry to be a sound and reliable mechanism for explaining how the flu vaccine can cause TM and find that petitioner has satisfied her burden under *Althen* prong one.

B. *Althen* Prong III

Althen prong three requires petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1278. That term has been defined as a "medically-acceptable temporal relationship." *Id*. at 1281. Petitioner must offer "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*, 539 F.3d at 1352. The explanation for what is a medically-acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause the injury alleged under *Althen* prong one. *Id*.; *Koehn v. Sec'y of Health & Hum. Servs.*, 773 F.3d 1239, 1243 (Fed. Cir. 2014); *Shapiro v. Sec'y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011) ("The etiology of the disorder determines the appropriate temporal relationship") (cleaned up). *See also Pafford*, 451 F.3d at 1358.

The parties agree that petitioner's onset of TM was 63 days following her receipt of the flu vaccine. Dr. Tornatore proposed a medically-acceptable range of 1 to 63 days but noted that

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[62] *See, e.g.*, *J.G. v. Sec'y of Health & Hum. Servs.*, No. 20-664V, 2023 WL 2752634, at *30 (Fed. Cl. Spec. Mstr. Feb. 13, 2023) (observing that "[t]he experts do not dispute the theory of molecular mimicry, or that it is a sound and reliable theory generally as it relates to GBS" and that "[m]olecular mimicry has been accepted as a sound and reliable theory in many Vaccine Program cases dealing with demyelinating conditions"); *Osso v. Sec'y of Health & Hum. Servs.*, No. 18-575V, 2023 WL 5016473, at *21 (Fed. Cl. Spec. Mstr. July 13, 2023) (finding that molecular mimicry is accepted as a "sound and reliable theory" in a case in which the hepatitis B vaccine was found to cause GBS); *Introini v. Sec'y of Health & Hum. Servs.,* No. 20-176V, 2022 WL 16915818, at *25 (Fed. Cl. Spec. Mstr. Oct. 19, 2022) (finding that the theory of molecular mimicry is sound and reliable for many demyelinating conditions including TM); *Palattao v. Sec'y of Health & Hum. Servs.*, No. 13-591V, 2019 WL 989380, at *37 (Fed. Cl. Spec. Mstr. Feb. 4, 2019) ("[M]any of the existing Program decisions in which TM has been found to be caused by a vaccine rely on a mechanism" of molecular mimicry.); *Hitt*, 2020 WL 831822 (flu vaccine caused TM/MS); *Mura v. Sec'y of Health & Hum. Servs.*, No. 08–819V, 2012 WL 2402590 (Fed. Cl. Spec. Mstr. May 30, 2012) (flu vaccine caused ADEM); *Jane Doe 93 v. Sec'y of Health & Hum. Servs.*, 2011 WL 2326966 (Fed. Cl. Spec. Mstr. May 9, 2011) (flu vaccine causing TM); *Moore v. Sec'y of Health & Hum. Servs.*, No. 07-0645V, 2010 WL 5113199 (Fed. Cl. Spec. Mstr. Aug. 31, 2010) (flu vaccine causing TM); *Schmidt v. Sec'y of Health & Hum. Servs.*, No. 07-20V, 2009 WL 5196169 (Fed. Cl. Dec. 17, 2009) (flu vaccine causing TM); *Raymo v. Sec'y of Health & Hum. Servs.*, No. 11-0654V, 2014 WL 1092274, at *21 (Fed. Cl. Spec. Mstr. Feb. 24, 2014) (Molecular mimicry is a "biologically probable" explanation of how the tetanus vaccine can cause TM.); *Roberts v. Sec'y of Health & Hum. Servs.*, No. 09-427V, 2013 WL 5314698, at *6-7 (Fed. Cl. Spec. Mstr. Aug. 29, 2013) (entitlement found in a Tdap/TM case with the theory of molecular mimicry). *Compare Palattao*, 2019 WL 989380, at *35-37 (denial of entitlement in a TM case where the facts did not support application of molecular mimicry), *with I.J. v. Sec'y of Health & Hum. Servs.*, No. 16-864V, 2022 WL 277555, at *4-7 (Fed. Cl. Spec. Mstr. Jan. 4, 2022) (entitlement found on remand in a Tdap/TM case that relied upon the theory of molecular mimicry).

Agmon-Levin contained a risk period of several days and up to three months. Pet. Ex. 11 at 13; Pet. Ex. 14.[63] While *Schonberger, et al.* focused on the five weeks following vaccination, the authors noted that the risk period lasted approximately for 9-10 weeks or 70 days post-vaccination for GBS. Pet. Ex. 28 at 1, 9.[64]

Dr. Donofrio argues that 63 days is too long a timeframe for onset. The Vaccine Table provides for a 3- to 42-day onset for GBS, although he agreed that *Langmuir* proposed up to "8 weeks or 56 days." Resp. Ex. A at 5; Resp. Ex. D at 1;[65] Resp. Ex. E at 1-2.

The table in *Langmuir* shows that there were those who developed GBS up to nine and ten weeks after vaccination. Resp. Ex. D at 13.[66] Experts in the Program generally rely on either or both *Schonberger* and *Langmuir* since *Langmuir* analyzed the findings of *Schonberger* but on a smaller group of patients, with both analyzing the onset of weakness following influenza vaccination. Resp. Ex. D at 1-3;[67] Resp. Ex. E at 1.

The Federal Circuit in *Paluck* cautioned against set deadlines for onset of injuries following vaccination. 786 F.3d at 1383-84. In *Paluck*, the court advised that, given the high degree of difference between cases of even the same disorder, "hard and fast deadline[s]" are inapposite for the onset of symptoms post-vaccination. *Id*. at 1384. While the Vaccine Table sets a timeframe of 3 to 42 days for flu/GBS cases to be qualified as Table injuries, the Program does not preclude a case from proceeding as a causation in fact case where the onset is less than three days or more than 42 days. *Id*. (finding that "the fact that [petitioner's] first clinically evident sign" was documented slightly outside the Table timeframe "does not preclude a finding" of causation).

Cases in the Program have found entitlement, albeit rarely, in TM, ADEM, and GBS cases up to 65 days after vaccination.[68] Sixty-three days falls within the timeframe of prior decisions.

Based on the facts of this case, the medical records, extensive testing, opinions of her treating physicians, and medical literature, I find that preponderant evidence exists to support an onset of TM 63 days after receipt of the flu vaccine as medically appropriate. That is not to say that there is no limit for onset of demyelinating disease following vaccination or infection, only that literature supports that on rare occasion, onset TM and/or ADEM which are diseases of the central nervous system may be up to 65 days due to individual differences. *See* Resp. Ex. D.[69]

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[63] Agmon-Levin et al., *supra* note 7.
[64] Schonberger et al., *supra* note 12.
[65] Langmuir et al., *supra* note 13.
[66] *Id*.
[67] *Id*.
[68] *See, e.g.*, *Brown v. Sec'y of Health & Hum. Servs.*, No. 09-426V, 2011 WL 5029865, at *43-44 (Fed. Cl. Spec. Mstr. Sept. 30, 2011) (onset of ADEM 60 days after flu vaccine based on *Schonberger, et al*. and *Langmuir*); *Doe v. Sec'y of Health & Hum. Servs.*, 2010 WL 4205677, at *25 (Fed. Cl. Spec. Mstr. Oct. 20, 2010), *vacated sub nom. on other grounds Doe 93 v. Sec'y of Health & Hum. Servs.*, 98 Fed. Cl. 553 (2011) (onset of TM 65 days after flu vaccine); *Spayde v. Sec'y of Health and Hum. Servs.*, No. 16-1499V, 2021 WL 686682, at *19 (Fed. Cl. Spec. Mstr. Jan. 27, 2021) (60 days is "reasonable and appropriate" in a flu/GBS case); *Cooper v. Sec'y of Health & Hum. Servs.*, No. 18-1885V, 2024 WL 1522331, at *20 (Fed. Cl. Spec. Mstr. Mar. 12, 2024) (60-day onset acceptable period for causation in a Prevnar/GBS case).
[69] Langmuir et al., *supra* note 13.

Petitioner has satisfied *Althen* prong three.

C. *Althen* Prong Two

Under *Althen* prong two, petitioner must prove by a preponderance of the evidence that there is a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." *Capizzano*, 440 F.3d at 1324 (quoting *Althen*, 418 F.3d at 1278). "[P]etitioner must show that the vaccine was the 'but for' cause of the harm . . . or in other words, that the vaccine was the 'reason for the injury.'" *Pafford*, 451 F.3d at 1356 (internal citations omitted).

It is undisputed that petitioner suffers from TM. Having established that the influenza vaccine can cause demyelinating disease, that TM is a demyelinating disease, and that onset of TM, while rare, can take place 63 days post-inciting event, there is little to dispute that a logical sequence of cause and effect exists showing that petitioner's flu vaccine was the cause of her TM.

Dr. Donofrio previously acknowledged that demyelinating diseases, which include TM, can be caused by infection and vaccination. *Hitt*, 2020 WL 831822, at *10 (Fed. Cl. Spec. Mstr. Jan. 24, 2020) ("Dr. Donofrio agreed that the medical theories that flu vaccine could cause either transverse myelitis or multiple sclerosis were 'valid.'"); Resp. Ex. A at 5 (A urinary tract infection "would be sufficient to serve as the inciting event for TM.") In this case, he argued that petitioner's TM was caused by an undiagnosed UTI. Resp. Ex. A at 5. As further discussed below, the contemporaneous medical records and objective testing do not support a finding of a UTI. Further, Dr. Donofrio provided no persuasive support that a UTI, specifically, could cause TM.

By themselves, treating physicians' references in their records to a temporal relationship of a vaccine with the onset of disease or injury do not advance proof of causation or logical sequence of cause and effect. But where they mention the two without any other potential contributing factor or, as here, caution against receipt of additional flu vaccines, their records garner some weight. *See Capizzano*, 440 F.3d at 1326 ("[T]reating 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.'") (internal citations omitted); *Andreu*, 569 F.3d at 1375 (finding that, where petitioner satisfies prongs one and three of *Althen*, the testimony of treating physicians is "quite probative.") (internal citations omitted).

Here, petitioner's treating physicians noted petitioner's flu vaccine weeks prior to her onset of TM on several occasions. Pet. Ex. 5 at 53; Pet. Ex. 2 at 114; Pet. Ex. 34 at 105. She was also advised not to receive additional flu vaccines. Pet. Ex. 6 at 9-10; Pet. Ex. 31 at 16-17.

Accordingly, I find that petitioner has satisfied her burden under *Althen* prong two.

D. Urinary Tract Infection as an alternative cause for Petitioner's TM.

1. The Expert Opinions

Dr. Donofrio argued that petitioner had a UTI because "[h]er urinalysis from [November 26, 2016] showed 11 white blood cells, 2 red blood cells, and an elevated white blood cell esterase

25 (reference negative)" which is indicative of active infection. Resp. Ex. A at 5; Pet. Ex. 5 at 37. *Agmon-Levin, et al.* shows that 40% of TM is associated with preceding infection. Resp. Ex. A at 5; Pet. Ex. 14.[70] Therefore, petitioner had an undiagnosed UTI, and her UTI was a sufficient and more likely inciting event for TM than the flu vaccine. Resp. Ex. A at 5.

Dr. Tornatore disagreed, pointing out the November 26, 2016, urinalysis was negative for bacteria, showed no need for repeat testing, and petitioner had no complaints or symptoms of a urinary tract infection. Pet. Ex. 27 at 2; Pet. Ex. 5 at 218. Dr. Tornatore explained a phenomenon called sterile pyuria, in which patients with a systemic autoimmune process can have benign white blood cells, called pyuria, in their urine in the absence of infection. Pet. Ex. 27 at 2. Petitioner's post-vaccinal immune activation could have resulted in white blood cells spilling into the bladder. *Id*. Dr. Tornatore submitted that in over 40 years of practice he has seen this phenomenon many times in the TM patients he has treated. This phenomenon is reported in lupus patients as well. *Id*.; Pet. Ex. 29.[71]

Dr. Donofrio disagreed that petitioner had sterile pyuria, arguing that Dr. Tornatore did not mention what systemic autoimmune disease petitioner suffered from; indeed, she did not suffer from any systemic autoimmune disease. Resp. Ex. E at 2. Dr. Donofrio relied on *Stamm* in support of his opinion that petitioner suffered from a UTI which was the cause of her TM. *Id*. at 1.

Dr. Tornatore countered, citing to the table in *Stamm* which he argued demonstrated that pyuria is actually found in 1.6% of asymptomatic, abacteriuric patients, not less than 1% as opined by Dr. Donofrio. Additionally, 3.1% of asymptomatic, abacteriuric patients have sterile pyuria, like petitioner. Therefore, *Stamm* supports rather than rebuts the argument that sterile pyuria can exist in a patient with WBC>10wbc/mm. Pet. Ex. 32 at 4; Resp. Ex. F.[72] Further, "[l]eukocyte esterase is evidence of leukocytes, not infection." Pet. Ex. 32 at 4.

Dr. Tornatore referenced the *Rahman* study to show that sterile pyuria is frequently seen in lupus patients and at a higher rate than seen in the normal population. Pet. Ex. 29 at 1, 4.[73] Isolated sterile pyuria was defined as >5 white blood cells per high powered field in the absence of urinary infection and other renal manifestations. *Id*. at 1. The study found that isolated sterile pyuria are manifestations of active lupus. Dr. Donofrio did not address the *Rahman* study.

2. Analysis

Once petitioner satisfies her burden on each of the three *Althen* prongs, "she is entitled to recover unless the government can show by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine." *Althen*, 418 F.3d at 1278 (cleaned up) (citations omitted). "[T]he standards that apply to a petitioner's proof of actual causation in fact in off-table cases should be the same as those that apply to the government's proof of alternative actual causation in fact." *Knudsen*, 35 F.3d at 549. The petitioner having met her burden on each of the

[70] Agmon-Levin et al., *supra* note 7.
[71] P. Rahman et al., *Significance of Isolated Hematuria and Isolated Pyuria in Systemic Lupus Erythematosus*, 10 Lupus 418 (2001), filed as "Pet. Ex. 29."
[72] Stamm, *supra* note 39.
[73] Rahman et al., *supra* note 70.

three *Althen* prongs, shifts the burden to respondent to demonstrate that the alleged undiagnosed UTI was the "sole substantial factor in bringing about" petitioner's TM. *de Bazan*, 539 F.3d at 1354.

The subject urinalysis results for November 26, 2016, revealed:

Lab Data:
Recent Results (from the past 24 hour(s))
UA WITH MICRO REFLEX TO CULTURE
Collection Time: 11/26/16 10:18 PM

Result	Value	Ref Range
Type	Clean Catch	
Color	YELLOW	YELLOW
Appearance	CLEAR	CLEAR
Specific Gravity	1.015	1.005 - 1.030
pH	5.0	4.5 - 8.5
Protein	NEGATIVE	NEGATIVE mg/dL
Glucose	NEGATIVE	NEGATIVE mg/dL
Ketones	NEGATIVE	NEGATIVE mg/dL
Bililrubin	NEGATIVE	NEGATIVE mg/dL
Blood	NEGATIVE	NEGATIVE /uL
Nitrites	NEGATIVE	NEGATIVE
Urobilinogen	NORMAL	NORMAL mg/dL
WBC Esterase	25 (A)	NEGATIVE /uL
RBC	2	0 - 3 /[HPF]
WBC	11 (A)	0 - 3 /[HPF]
Epithelial Cells	2	0 - 5 /[HPF]
Hyaline Casts	0	0 - 3 /[LPF]
Bacteria	NEGATIVE	NEGATIVE-TRACE

Urine Culture Reflex
Collection Time: 11/26/16 10:18 PM

Pet. Ex. 5 at 37. Notably the urinalysis lists "Bacteria NEGATIVE". Petitioner was also noted to have no fever or viral or bacterial infection on blood work and CSF testing. *Id*. at 36, 53, 121, 176.

The *Stamm* article distinguished bacteriuria and pyuria, defining bacteriuria as indicating "either urinary colonization (replication of bacteria in urine without evidence of tissue invasion) or urinary tract infection (bacteriuria associated with clinical, histologic, or immunologic evidence of host injury)." Resp. Ex. F at 1.[74] The study stated, and Dr. Donofrio quoted, that "10 leukocytes/mm^3 or greater occur in less than 1 percent of asymptomatic, nonbacteriuric patients but in greater than 96 percent of symptomatic men and women with significant bacteriuria." Resp. Ex. F at 1; Resp. Ex. E at 1. However, the study cautioned that bacteriuria arises for many reasons including contamination of the urine specimen, colonization of the urine, or urinary tract infection. Resp. Ex. F at 1. Colonization and infection can be distinguished by, among other things, the presence of symptoms or signs indicating tissue invasion. *Id*. at 2. Of the patients studied, the data suggested that a portion of the patients with asymptomatic bacteriuria "actually ha[d] a transient, self-limited colonization state rather than true infection." *Id*. at 3. Transient bacteriuria can last one or two days with spontaneous resolution; in some cases, it may not be associated with pyuria, suggesting that not all asymptomatic bacteriuria is actually infection. *Id*. Due to the many variables involved, *Stamm* concluded that the measurement of pyuria in routine clinical practice "needs reassessment." *Id*. at 5.

[74] Stamm, *supra* note 39.

Relying on *Stamm,* Dr. Donofrio argued that what Dr. Tornatore called sterile pyuria was in fact evidence of an acute infection, a diagnosis that was not made by her treating physicians. Resp. Ex. E at 1-2. However, *Stamm* did not support the reliability of that testing in asymptomatic patients due to the many variables that could affect the accuracy of the testing and the findings. *Stamm* noted that the most commonly used method for measuring pyuria does not correlate well with the leukocyte excretion rate for this reason. Resp. Ex. F at 3.[75]

There is insufficient evidence in the record and objective testing to show that petitioner suffered from an asymptomatic, undiagnosed UTI on November 26, 2017, when she presented to the hospital with symptoms of TM. She underwent extensive testing which did not reveal any bacterial or viral infection, and her urinalysis was negative for bacteria. Pet. Ex. 5 at 37, 53, 79. Further, Dr. Donofrio failed to provide any persuasive evidence that a UTI can cause TM.

While up to 40% of TM cases are preceded by infections, the infections associated with TM include but are not limited to influenza, measles, mumps, rubella, cytomegalovirus, and Epstein-Barr virus. Pet. Ex. 14 at 2.[76] Further, most cases of TM begin *after* the patient has recovered from the infection. TM is believed to be the result of an autoimmune response triggered by infectious antigens not the result of the infection itself. *Id*. Assuming petitioner did have an active UTI as suggested by Dr. Donofrio, that would not be the cause of her simultaneous TM.

Simply raising an alternative cause without showing that it can cause and did cause that alternative condition within a medically accepted timeframe does not satisfy respondent's burden of an alternative cause. To meet this standard, respondent must "present sufficient evidence to prove that the alternative factor was the sole substantial factor in bringing about the injury." *Deribeaux ex rel. Deribeaux v. Sec'y of Health & Hum. Servs.*, 717 F.3d 1363, 1367 (Fed. Cir. 2013) (citing *de Bazan*, 539 F.3d at 1352). The Vaccine Act limits the scope of unrelated factors by excluding any "idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness, or condition." § 13(a)(2)(A). "In other words, alternative causes that are 'idiopathic, unexplained, unknown, hypothetical or undocumentable' cannot overcome a petitioner's prima facie case." *Doe*, 601 F.3d at 1357 (quoting § 13(a)(2)(A)).

Respondent has not provided preponderant evidence to support a UTI as the sole substantial cause of petitioner's TM.

VII. Conclusion

Upon careful evaluation of all the evidence submitted in this matter, including the medical records, affidavit of the petitioner, expert reports, and medical literature, I find that petitioner has shown that she is entitled to compensation under the Vaccine Act. Accordingly, this matter shall proceed to damages with a separate damages order to issue.

IT IS SO ORDERED.

[75] Stamm, *supra* note 39.
[76] Agmon-Levin et al., *supra* note 7.

s/ Mindy Michaels Roth
Mindy Michaels Roth
Special Master