

In the United States Court of Federal Claims
OFFICE OF SPECIAL MASTERS
No. 18-1371V
Filed: March 5, 2026

JENNIFER WILLIFORD *and* CHARLES
EDWARD WILLIFORD, III, *parents of*
R.W., a minor,

Petitioners,

v.

SECRETARY OF HEALTH AND
HUMAN SERVICES,

Respondent.

Nichole Glance Booker, Mast Law Firm, Smithfield, NC, for Petitioner.
James Vincent Lopez, U.S. Department of Justice, Washington, DC, for Respondent.

DECISION DENYING ENTITLEMENT¹

Shah, Special Master:

On September 7, 2018, Jennifer and Charles “Eddie” Williford (“Petitioners” or “Mr. and Mrs. Williford”), parents of R.W., filed a petition for compensation under the National Vaccine Injury Compensation Program, 42 U.S.C. §§ 300aa-10, *et seq.*² (the “Vaccine Act” or “Program”). ECF No. 1 (“Pet.”). Petitioners allege that R.W. developed transverse myelitis (“TM”), neurogenic

¹ This Decision will be posted on the United States Court of Federal Claims’ website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means the Decision will be available to anyone with access to the internet.** As provided in 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the Decision’s inclusion of certain kinds of confidential information. To do so, each party may, within 14 days, request redaction “of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy.” Vaccine Rule 18(b). Otherwise, this Decision will be available to the public in its present form. *Id.*

² National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755. For ease of citation, all “§” references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

bladder, neurogenic bowel, scoliosis, and paraplegia caused by the tetanus-diphtheria-acellular pertussis (“Tdap”) and meningococcal vaccines she received on September 11, 2015. *Id.* at 1.

I am very sympathetic to R.W. and the ordeal she and her family have endured. However, for the reasons discussed in this decision, I deny entitlement. The preponderant evidence did not establish that R.W. suffered the condition alleged, TM. The evidence also did not substantiate that either of the subject vaccinations caused R.W.’s injury.

I. PROCEDURAL BACKGROUND

Petitioners filed medical records and medical literature with their petition. Exs. 1-12, 15-18. They also filed affidavits from Mr. and Mrs. Williford. Exs. 13-14. Respondent filed his Rule 4(c) Report on March 13, 2019, indicating that the case was not appropriate for compensation under the Vaccine Act. ECF No. 15 (“Report”) at 1.

Petitioners and Respondent then filed a series of expert reports. Petitioners filed two reports from Lawrence Steinman, M.D. Ex. 23, 49. Respondent filed one report each from Neil Romberg, M.D., and Michael Sweeney, M.D.³ Exs. A, C.

Former Special Master Katherine E. Oler held an entitlement hearing from July 26-28, 2022, at which Mr. and Mrs. Williford, R.W., and Drs. Steinman, Sweeney, and Romberg testified. Minute Entry dated 7/28/2022; Tr. at 3, 191, 343. After the hearing, Special Master Oler directed the parties to state whether they wished to file further expert reports from neuroradiology experts and/or additional reports from their neurology experts. ECF No. 60.

On January 9, 2023, Petitioners filed an expert report, curriculum vitae, and literature from David Wilson, M.D., a neuroradiologist. Exs. 88-96. On April 17, 2023, Respondent filed a responsive report and curriculum vitae from neuroradiologist William Zucconi, D.O. Exs. D-E.

Special Master Oler held a status conference on May 2, 2023, at Respondent’s request. Minute Entry dated 5/2/2023; ECF No. 71. Petitioners’ counsel advised that she wished to file affidavits from R.W.’s physicians at Duke University “to clarify terminology used in the medical record.” ECF No. 71 at 1. Respondent’s counsel stated his potential intent to object to this request as untimely and prejudicial. *Id.* Several weeks later, Special Master Oler held another conference at which the parties revealed that, before Respondent could formally state his position, Petitioners’ counsel had requested the clarifying information from Duke but had received no response. Minute Entry dated 5/22/2023; ECF No. 73. Petitioners’ counsel agreed to withdraw the request to seek further affidavits from Duke. ECF No. 73 at 2.

³ Petitioners filed Dr. Steinman’s curriculum vitae and the medical literature referenced in his first report on August 24, 2020. Exs. 24-48. Shortly before the entitlement hearing, Respondent filed the medical literature referenced in his experts’ reports, along with updated curricula vitae for his experts, and Petitioners filed the literature referenced in Dr. Steinman’s second report. Exs. A, Tabs 1-20; Ex. B, Tab 1; Exs. C, Tabs 1-10; Ex. D, Tab 1.

On August 21, 2023, Petitioners filed a post-hearing brief. ECF No. 75 (“Pets.’ Post-Hearing Brief”). On December 11, 2023, Respondent filed a responsive post-hearing brief. ECF No. 77 (“Resp.’s Post-Hearing Brief”). On February 16, 2024, Respondent filed several pieces of medical literature. Exs. G-M. On February 21, 2024, the parties jointly agreed the record was complete for a decision. ECF No. 80.

On August 13, 2024, this case was reassigned to my docket. ECF No. 81. The case is now ripe for adjudication.

II. FACT EVIDENCE

A. Medical Records

R.W. was born on September 8, 2004, and was 11 years old when she received Tdap and meningococcal vaccines on September 11, 2015, during her well-child checkup. Ex. 2 at 166. She did not have a significant pre-vaccination medical history.

On September 27, 2015, 16 days after receiving her vaccines, R.W. presented to Geeta Subramaniam, M.D., an emergency medicine specialist at the Johnston Medical Center in Clayton, North Carolina, stating “she cannot move her right leg[,] it feels like it is going to sleep.” Ex. 2 at 154, 157. R.W.’s mother reported that R.W. was “sluggish and tired” earlier that day. *Id.* at 154. Dr. Subramaniam noted that R.W. had right posterior thigh pain that began at 12:00 pm that day, which had “progressed to decreased ability to use the right leg and now inability to feel the left.” *Id.* at 156. She had “a low-grade fever” that first began that day but had experienced no other symptoms of infection. *Id.* at 156-57. Dr. Subramaniam noted that R.W. had received two vaccinations “two weeks” prior. *Id.*

Dr. Subramaniam remarked that R.W. was “[g]enerally healthy with no significant past medical history” and that she “[d]enied any respiratory problems or difficulty breathing presently.” Ex. 2 at 157. She suspected Guillain-Barré syndrome (“GBS”) but noted that ascending tick paralysis was another possibility, commenting that R.W. had been at the Benson Mule Day festival the previous day. *Id.* at 158. R.W. was provisionally diagnosed with bilateral leg weakness and transferred to the pediatric intensive care unit (“PICU”) at the WakeMed Hospital in Raleigh, North Carolina (“WakeMed”). *Id.* at 161-63.

1. WakeMed Hospitalization: September 27-October 6, 2015

On arrival to the WakeMed PICU the night of September 27, R.W. was seen by pediatric critical care physicians Bridget Donell, M.D. (attending), and Linh Tran, M.D. (resident). Ex. 4A at 1. Dr. Tran’s exam found 1/5 strength bilaterally in the quadriceps and 0/5 strength bilaterally in the lower legs. *Id.* at 3. R.W. had absent reflexes and “decreased sensation to light touch on the distal right thigh, possibly along the L3-L4 dermatomal distribution [with] decreased 2-point discrimination.” *Id.* The physicians were concerned about possible GBS or an acute spinal cord process such as TM. *Id.* at 4. They noted: “Although her distribution is along the L3-L4 dermatome in the [right] thigh, there is no clearly defined sensory level, making transverse myelitis

a possible etiology.” *Id.* They ordered MRIs of the entire spine, a lumbar puncture (“LP”), and IVIG treatment. *Id.*

On September 28, 2015, R.W.’s thoracic MRI revealed a “very subtle” T2 signal abnormality of the spinal cord at the T11-12 level, with a possible second signal abnormality of the spinal cord at the T7-8 level. Ex. 4A at 107. Her cervical spinal MRI was normal. *Id.* Her lumbosacral spinal MRI showed “[s]ubtle elevation of T2 signal intensity in the conus nodularis.” *Id.* Her brain MRI was normal. *Id.*

R.W. was seen by pediatric critical care specialists Travis Honeycutt, M.D. (attending), and Sara Duffus, M.D. (resident), the morning of September 28, 2015. Ex. 4A at 105. They noted R.W. had been admitted overnight and had undergone an MRI and lumbar puncture. *Id.* at 105, 155-58. She had been given one high-dose steroid treatment. *Id.* at 105. At the time, she reported being able to feel more in her legs and was able to slightly move her toes. *Id.* at 106. She continued to run low fevers intermittently overnight. *Id.*

On exam, R.W. had 1/5 strength in hip flexion and 0/5 strength in her knees and ankles bilaterally. Ex. 4A at 106. She could not move her toes. *Id.* She did have intact sensation to soft touch from the right knee proximally and from the left dorsum of the foot proximally, but she had no sensation from the right knee distally or on the plantar surface of the left foot. *Id.* TM, multiple sclerosis (“MS”), and less likely neoplasm or tick paralysis were included on the differential diagnosis. *Id.* at 108. Dr. Honeycutt believed TM was the most likely diagnosis. *Id.* at 109. The plan was to repeat the thoracic MRI with and without contrast and continue IVIG and steroid treatments. *Id.* at 108. They also planned to run a respiratory viral PCR assay and an arbovirus panel, as well as further testing of the cerebrospinal fluid (“CSF”), as recommended by infectious disease specialists at Duke, with whom the WakeMed team had consulted. *Id.*

The same morning, R.W. was seen by pediatric neurologist John Wooten, M.D. Ex. 4A at 116. The history stated:

[R.W.] noticed that she started to have some pain in her [right] thigh, located around her posterior thigh, at about 3 pm today. Shortly thereafter, she had progressive weakness and numbness of her [right] thigh, and she started to have some weakness spread to her [left] thigh. She then fell over when she tried to get up from a chair to walk. Since that time, she has had progressive numbness and weakness in bilateral lower extremities. Mom checked temperature . . . 100.5 (forehead). No new rashes (has had bumps behind right knee), insect/tick bites. She did get 2 vaccines, possibly her Tdap and HPV, approximately 2 weeks ago. She did not get her flu vaccine[.] She did travel to some areas with pine trees a couple of weeks ago and also attended the Benson Mule Day Festival where she was exposed to horses and dogs.

Id. R.W. also reported experiencing urinary incontinence she could not feel and had significant urinary retention upon arrival to the PICU. *Id.* On exam, she had absent reflexes in the lower

extremities and abdomen and flaccid lower extremities bilaterally. *Id.* at 118. She also had a “gradual transition of sensation from knee to inguinal area with normal sensation of lower abdomen (as best I can tell with sedated patient).” *Id.* Her upper extremities had normal strength and reflexes. *Id.*

Dr. Wooten’s assessment was TM, based on her clinical presentation and MRI showing a “demyelinating lesion of lower thoracic spine[.]” Ex. 4A at 118. He prescribed IVIG and continued high-dose steroids. *Id.* He noted that R.W. had reportedly received the DTaP and meningococcal vaccinations several weeks earlier and commented: “I find no other potential etiology [aside from the vaccinations] in my history and exam.” *Id.* at 116. He recommended that R.W.’s team clarify with her pediatrician which vaccines she received, noting her condition might need to be reported. *Id.*

Later on September 28, R.W. had a repeat thoracic spinal MRI with and without contrast. Ex. 4A at 126-27. This MRI found progression of the T2 hyperintensity between T6 and the distal conus at T12-L1, with mild expansion and questionable patchy enhancement of the ventral cord at T11 and T12. *Id.* This was interpreted to be consistent with inflammatory TM, neuromyelitis optica (“NMO”), MS, vascular disease, or neoplasm less likely. *Id.*

On the morning of September 29, 2015, Drs. Honeycutt and Duffus saw R.W. again. Ex. 4A at 100. They noted that after a second dose of IVIG, R.W. reported some improvement in sensation in the lower extremities but no improvement in motor function. *Id.* at 101. Her repeat MRI with contrast was consistent with TM or acute disseminated encephalomyelitis (“ADEM”), showing a “T2 hyperintensity between T6 and distal conus at T12-L1.” *Id.*

On exam, R.W. exhibited intact sensation to soft touch from the right knee proximally and from the left mid-shin proximally. Ex. 4A at 101. She had 0/5 strength in both legs. *Id.* The MRI findings were thought to be “consistent with inflammatory transverse myelitis.” *Id.* at 103. Her “[h]istory of recent vaccination and a possibility of ADEM should be considered.” *Id.* The team had verified R.W.’s receipt of “TDaP and meningococcal vaccinations on 09/11, possibly the inciting event.” *Id.* They “w[ould] plan to report adverse vaccine event.” *Id.* at 104. Also, R.W.’s Biofore rapid test for rhinovirus/enterovirus was positive, and “[t]here are reports of enterovirus causing similar presentation.” *Id.* Drs. Honeycutt and Duffus believed the issue could be clarified through measures like “[n]asal washing for viral culture” as well as “[s]erum arbovirus and RPR” and a follow-up blood culture. *Id.* The plan was to continue IVIG and high-dose steroids. *Id.*

On October 1, 2015, R.W. was seen by neurologist Traci Sheaffer, M.D. Ex. 4A at 60. R.W. reported that she had “tingling today all the way down to her toes.” *Id.* She reported increased sensation below the knees and was able to urinate. *Id.* She had no improvement in strength. *Id.* Dr. Sheaffer commented that R.W. reported feeling sensation when she was not being touched, making the exam unreliable. *Id.* at 62.

On October 4, 2015, Dr. Honeycutt noted that R.W. was making “very slow but some notable improvement.” Ex. 4A at 43. Her family was not ready to consider plasmapheresis (“PLEX”) treatment. *Id.* By October 6, however, R.W. still had experienced “only very mild

improvement of sensory and motor [symptoms].” *Id.* at 17. After further discussions with Dr. Honeycutt, the family opted for PLEX treatment at Duke Children’s Hospital (“Duke”). *Id.* at 18.

2. Duke Hospitalization: October 6-30, 2015

In an admission exam on October 6, 2015, medical resident William Fox, M.D., noted that “[o]ther than the fever at presentation,” R.W. had not been experiencing “preceding fevers, cough, rhinorrhea, sore throat, rash, or diarrhea” before the onset of her symptoms. Ex. 5 at 12. She did have “mild lumbar back pain” in the two weeks prior to onset “that she attributed to her heavy backpack.” *Id.*

On October 7, 2015, pediatric neurologists William Gallentine, D.O. (attending), and Sarah Neuhaus, M.D. (fellow), had an initial consult with R.W. Ex. 5 at 15. On exam, R.W. had flaccid lower extremities, no spontaneous movement in those limbs, and mild response to pain stimulation. *Id.* at 19. She could feel cool touch but was not able to clearly distinguish vibration. *Id.* She had no strength in her lower extremities and absent reflexes bilaterally in those limbs. *Id.* Drs. Gallentine and Neuhaus ordered lab work and planned to review R.W.’s spinal MRI from WakeMed with Neuroradiology. *Id.* at 19-20. That day, ophthalmologist Andrew Lee, M.D., opined that R.W. had “a normal ophthalmic exam with no evidence of current optic neuropathy,” which ruled out NMO. *Id.* at 25.

R.W. saw Dr. Gallentine again on October 8, 2015. Ex. 5 at 34. Dr. Gallentine noted Neuroradiology had reviewed the spinal MRI and it was “thought to be consistent with TM.” *Id.* They did not believe R.W. had a vascular lesion or had suffered a spinal cord stroke. *Id.* R.W. began the first of five PLEX treatments on October 8, 2015. *Id.* at 35.

On October 9, 2015, Dr. Neuhaus observed a sensory level at the T6-7 level, below which there was decreased sensation. Ex. 5 at 39. Drs. Gallentine and Neuhaus characterized R.W.’s condition as “Acute Flaccid Paralysis due to likely Transverse Myelitis,” which was being further evaluated. *Id.*

On October 16, 2015, the results of R.W.’s nasopharynx studies were negative for Enterovirus D68 (“D68”) and Human Parechovirus but “[p]ositive for Human Rhinovirus A-29” (“A29”). Ex. 4A at 185. R.W.’s arboviral panel from the state lab revealed she was negative for West Nile Virus IgM, Eastern Equine Encephalitis IgM, and La Crosse Encephalitis IgM, but positive for West Nile Virus IgG. *Id.* at 185-87. The Duke physicians did not feel the positive West Nile Virus result was clinically relevant because the labs were drawn after IVIG was given. Ex. 5 at 40.

Also on October 16, 2015, R.W. underwent a repeat spinal MRI that revealed a “[d]iffuse enhancement of the [ventral] cauda equina nerve roots and the ventral and dorsal aspects of the conus medullaris.” Ex. 5 at 1725. The MRI further revealed “significant interval increase of extent and degree of expansion of the abnormal intramedullary cord signal abnormality extending from T3 to the conus,” suggesting “[w]orsening ascending inflammatory myelitis[.]” *Id.*

On October 17, 2015, Dr. Neuhaus and attending neurologist Edward Smith, M.D., noted that R.W. “ha[d] not changed much other than subjective sensory finding and [was] still not able to discriminate right from left reliably,” but she had “increased hip strength” since October 15. Ex. 5 at 183. R.W. had undergone five sessions of PLEX “without improvement,” and her repeat MRI revealed “evidence that long segment TM ha[d] extended further to T3; marked enhancement of ventrally predominant nerve roots [was] also appreciated on repeat imaging, significant for possible virally mediated process.” *Id.*

On October 18, 2015, R.W. was seen by pediatric infectious disease specialists Robert Drucker, M.D. (attending), and Nazario Chaparro, M.D. (fellow). Ex. 5 at 51. R.W. and her family “[denied] recalling any illnesses (cough, headache, diarrheas, dysuria, emesis, bloody stools)” or “prior episode, travel, sick contacts or abdominal pain.” *Id.* at 52. Her parents recalled she had rhinitis two weeks before her initial presentation. *Id.* They also went to a carnival where there were horses and other animals, but R.W. denied having contact with the animals. *Id.* She received her Tdap and meningococcal vaccines two weeks before her symptoms began. *Id.* Drs. Drucker and Chaparro noted that R.W. did not have “significant exposure or risk factors” except rhinitis, but “[i]nfectious causes of transverse myelitis are multiple and most of them are viral etiology causing in most cases a post-infectious transverse myelitis.” *Id.* at 55-56. They recommended a repeat LP to test the CSF for enteroviruses, herpesviruses, HIV, and other viral and bacterial antigens. *Id.* at 56.

The same day, R.W. saw pediatric rheumatologist Heather Vanmater, M.D. Ex. 5 at 57. Dr. Vanmater assessed “acute onset [long] segment transverse myelitis of unclear etiology” and noted that R.W. received her immunizations two weeks before the onset of neurological symptoms and had experienced some back pain in the preceding two weeks, which was not associated with any numbness or weakness. *Id.* at 68-69. R.W. “ha[d] not improved and ha[d] in fact had progression of her disease despite IV and oral steroids, IVIG and pheresis.” *Id.* at 69. She had no signs or symptoms of a connective tissue disease. *Id.* “Her PCR was positive for rhinovirus, [and] numerous infectious studies are pending.” *Id.* Dr. Vanmater ordered a complete autoimmunity workup and stated that “[i]t [was] unclear if her progression in the size of the lesion [was] from an infectious process not yet resolved [versus] ongoing inflammatory/autoimmune process.” *Id.* She recommended a repeat brain MRI with “thin cuts of orbits for any evidence of more extensive disease that would indicate seronegative NMO which may benefit from rituximab⁴.” *Id.*

On October 20, 2015, pediatric neurologists Carolyn Pizoli, M.D. (attending), and Suma Das, M.D. (resident), noted R.W. had “paraplegia secondary to spinal cord findings of unknown etiology” and stated “[a]t this point, unclear etiology, though high suspicion for virally mediated myeloradiculopathy.” Ex. 5 at 71. They also noted that R.W. had a “low serum copper level

⁴ Rituximab: a chimeric murine/human monoclonal antibody that binds the CD 20 antigen; used as an antineoplastic in the treatment of CD20-positive, B-cell non-Hodgkin lymphoma; administered intravenously. DORLAND’S MEDICAL DICTIONARY ONLINE, <https://www.dorlandsonline.com/dorland/definition?id=43977&searchterm=rituximab> (last visited Mar. 4, 2026) (“DORLAND’S”).

raising suspicion for copper myelopathy.” *Id.* They cited literature discussing copper deficiency-mediated myelopathy. *Id.* at 71-72.

On October 22, 2015, Dr. Pizoli noted that R.W. would receive a five-day copper infusion because her “repeat copper level also returned low,” and the reason for her low copper levels was unclear. Ex. 5 at 78. The cause of R.W.’s paraplegia secondary to spinal cord findings was unknown, but there remained a “high suspicion for virally mediated myeloradiculopathy.” *Id.* Dr. Pizoli explained that a neuroradiology review from that morning revealed “concern about viral infection” and that “[p]ropensity for ventral cauda equina enhancement was noted, raising suspicion for viral tropism.” *Id.* She stated: “Given the peripheral nerve as well as spinal cord involvement in this process, will consult neurosurgery for consideration of sural nerve biopsy. Also recommend [electron microscopy (“EM”)] on CSF for viral particles.” *Id.* The EM on R.W.’s CSF was negative. *Id.* at 81.

That same day, R.W. was seen by pediatric rheumatologists Jeffrey Dvergsten, M.D. (attending), and Stephen Balevic, M.D. (fellow). Ex. 5 at 203. They noted that R.W. did not have any clinical features of an underlying rheumatologic disorder and had negative serologies for rheumatologic/connective tissue diseases. *Id.* at 205. She did not have “a significant clinical response to immunosuppression with IVIG, corticosteroids, and plasmapheresis,” and they “would expect plasmapheresis to rapidly improve any antibody mediated inflammatory process.” *Id.* As such, “it may be reasonable to consider repeat MRI now that she has finished a second course of pulse corticosteroids,” because “there may be some thought that immunosuppression can potentially worsen post-infectious processes.” *Id.* They also felt that it might be helpful for WakeMed to run Antinuclear Antibody (“ANA”) and Extractable Nuclear Antigen (“ENA”) panels on blood drawn before the initiation of IVIG treatment. *Id.*

On October 23, 2015, Drs. Drucker and Chaparro documented that R.W.’s state lab tests were negative for enterovirus and positive for Rhinovirus A29. Ex. 5 at 207. She had been screened for “many of the treatable causes from a viral standpoint that include most of the DNA viruses ([Epstein-Barr virus, cytomegalovirus, herpes simplex virus]) and the bacterial causes such as bartonella and mycoplasma pneumonia all of which are negative.” *Id.* at 208. They further commented:

From the RNA viruses the most common causes [are] Enteroviruses but she has a positive rhinovirus. Rhinovirus is of the same family as the enterovirus (picornaviridae) and for many years Rhinovirus wasn't diagnosed . . . thus the literature and data that have been published state enterovirus and it isn't clear how many of these were actually rhinovirus since rhinovirus has been mistaken for enterovirus. Post infectious myelitis thus can still be a possible and the duration and recovery from this is very variable to week, months and even years. And treatment is aimed at the inflammatory component of the syndrome.

Id. The plan was to continue with current therapies. *Id.*

On October 24, 2015, R.W. saw Dr. Gallentine for a follow-up consult. Ex. 5 at 79. Dr. Gallentine commented that “[a]t this point, unclear etiology, though high suspicion for virally mediated myeloradiculopathy.” *Id.* at 79, 81. A repeat MRI was scheduled for October 26, 2015, to “evaluate for questionable changes in spinal cord as well as re-evaluation of nerve root enhancement.” *Id.* at 81. The repeat MRI showed no changes. *Id.* at 88-89.

On October 27, 2015, pediatric neurologists Edward Smith, M.D. (attending), and Dr. Das assessed “ongoing flaccid paralysis.” Ex. 5 at 88. They said R.W.’s condition had an “unclear etiology, though high suspicion for virally mediated myeloradiculopathy.” *Id.* Dr. Smith advised Mr. Williford that Duke planned to report the case to the CDC as a case of acute flaccid myelitis (“AFM”). *Id.* On October 28, 2015, Drs. Smith and Das documented that the CDC report had been completed that day. *Id.* at 91. However, Petitioners produced a letter from Duke’s senior manager of health information management stating that “all efforts to locate written communication between the CDC and [Duke] for the above captioned patient has [sic] been unsuccessful.” Ex. 53 at 1.

At the time of R.W.’s discharge from Duke on October 30, 2015, she continued to have “flaccid paralysis of lower extremities” but could use her “abdominal/side muscles to roll and perform lateral transfers [with] moderate assistance.” Ex. 5 at 4. She had minimal to no sensation to light touch at L3, L4, L5, and S1. *Id.* She had no patellar reflexes and reduced Achilles reflexes. *Id.* She was experiencing urinary retention and sometimes had urinary or stool incontinence. *Id.* The discharge summary, prepared by Ashley Naughton, M.D. (resident), and David Ming, M.D. (attending), characterized her condition as “Post infectious/Post-inflammatory (likely virally mediated) Myeloradiculopathy.” *Id.* at 5. The summary further explained:

Given [R.W.’s] lack of response to 5 plasmapheresis treatments, T and C spinal cord were reimaged with MRI twist protocol to re-evaluate for spinal infarction. Repeat imaging was significant for inflammatory progression, suggesting inflammatory myelitis, with potential etiologies including lupus, sarcoidosis, or other viral or autoimmune causes. Rheumatology and infectious disease [were] consulted to help further guide work up. The patient underwent extensive lab workup for infectious and primary autoimmune etiologies at the request of the above services, which was only remarkable for antibodies to rhinovirus and a low serum copper of 38 ug/dl. Pertinently, patient underwent workup and imaging to rule out SLE, seronegative NMO, and multiple esoteric infectious etiologies. Patient underwent further therapy with high dose methylprednisone, repeat IVIG, and 5 days of copper chloride therapy. She underwent re-imaging with MRI following this which showed stable T2 hyperintense lesion from T3 through the cauda equina with multiple nerve roots. ***After extensive discussion between neurology, rheumatology, and infectious disease, it was determined that her lesion was most likely virally mediated, though the exact etiology was never determined.*** She began extensive inpatient PT/OT, and was discharged to an inpatient rehab facility

at Levine Children's Rehabilitation hospital in Charlotte, NC with planned follow up with neurology in roughly 6-8 weeks (they will be coordinating with patient). ***Her case was reported to the North Carolina Department of Public Health and CDC as a case of unexplained acute flaccid myelitis.***

Id. at 5-6 (emphases added). Dr. Ming also provided an addendum stating R.W. had a “lengthy hospital course for management of acute flaccid paralysis” and noting that he “favor[ed] post-viral as most likely etiology (of note, state lab testing was positive for rhinovirus A29 and negative for enterovirus D068).” *Id.* at 10.

3. Later Treatment

On October 30, 2015, R.W. was discharged to Levine Children’s Rehabilitation Hospital while on antibiotics for a urinary tract infection (“UTI”). Ex. 5 at 5-6, 10. She remained there until November 24, 2015. Ex. 2 at 118. An MRI of the thoracic spine on November 21, 2015, revealed “[m]ultiple T2 hyperintense cord signal abnormalities, compatible with demyelination,” and an MRI of the lumbar spine showed “[a]bnormal T2 hyperintensity and enhancement of the conus, along with enhancement of the cauda equine nerve roots,” which were thought to represent an inflammatory process. *Id.* at 115-16.

On December 23, 2015, R.W. had a follow-up with Dr. Gallentine and Lyndsey Prange, a nurse practitioner. Ex. 5 at 1726. The assessment was “transverse myelitis and demyelinating lower extremity neuropathy,” and while she had “regained some of her truncal strength[,]” there was not any “significant movement” in her lower extremities. *Id.* The records stated that R.W. “had a clinical course and poor response to treatment that is somewhat atypical for acute transverse myelitis” and noted “there is evidence of lumbar nerve root involvement, this can be seen [with] more late imaging findings of enterovirus D68.” *Id.* at 1724. R.W.’s “lack of improvement with [plasmapheresis], IVIG, and steroids, suggests that further immunotherapy is not indicated,” though she “[m]ay continue to show some improvement up to 18 months.” *Id.* at 1726.

On April 12, 2016, R.W. presented to Dr. Smith for “[f]ollow-up [on] acquired paraparesis 10/6/15 due to myeloradiculitis (T3-conus).” Ex. 5 at 1800. She had been doing well but had experienced no real change in lower extremity strength, function, or sensation. *Id.* at 1801. She had been “experiencing what sound like brief episodes of neuropathic pain in the posterior thighs,” and she had been self-catheterizing and using a manual wheelchair. *Id.*

On April 14, 2016, R.W. saw John Wiener, M.D., a pediatric urologist, “for management of neurogenic bladder secondary to transverse myelitis” that had affected her T10 spinal level. Ex. 5 at 1836. On April 18, 2016, she saw Lloyd Hey, M.D., an orthopedic surgeon, for “scoliosis without pain.” Ex. 2 at 71. Her physical therapist had advised she had a curvature in her spine, which had not been observed before onset. *Id.* An x-ray revealed a curvature of 64 degrees. *Id.* at 72. Dr. Hey commented that “[a]nything greater than 10 degrees on x-ray is scoliosis. This is due to your Transverse Myelitis.” *Id.* Surgery was discussed as a treatment option. *Id.*

On April 20, 2016, R.W. saw Tobias Tsai, M.D., a physiatrist, for her “acute onset of paraplegia in 2015, TM vs. acute flaccid paralysis, neurogenic bladder and bowel.” Ex. 2 at 70. Dr. Tsai noted that it was unclear whether R.W.’s paraplegia “was a manifestation of TM or (possibly more likely) acute flaccid paralysis.” *Id.* at 68. R.W. saw Dr. Tsai on October 5, 2016, for a follow-up evaluation of scoliosis. *Id.* at 56.

On May 10, 2017, R.W. received arthrodesis⁵ to treat her scoliosis. Ex. 2 at 46. On November 28, 2017, she saw physiatrist Patrick O’Brien, M.D., at Carolina Rehabilitation. Ex. 12 at 11-12. It was noted that she had tolerated her spinal fusion surgery well. *Id.* at 11. After the surgery, however, she experienced increased bilateral hip contractures, for which Botox injections were recommended. *Id.* at 11-12. She continued to experience neurogenic bladder and bowel. *Id.* at 12. On December 15, 2017, R.W. received her first Botox treatment. *Id.* at 8.

On February 5, 2018, R.W. returned to Dr. Gallentine. Ex. 5 at 3910. Her diagnoses remained acute flaccid paralysis and TM/polyradiculoneuropathy. *Id.* Dr. Gallentine noted that she had regained some of her truncal strength but that there was not any significant movement in her lower extremities. *Id.* at 3913. He did not believe there would be much improvement going forward. *Id.*

On April 24, 2018, R.W. saw Cheryl Bennett, a physical therapist. Ex. 4D at 4692. She was doing well and planned to continue working out with a personal trainer once or twice a week and use a functional electrical stimulation cycle at home. *Id.* It was recommended that R.W. continue to receive Botox every three months to preserve the range of motion in her hips. *Id.*

On August 28, 2018, Boyd Gray Howell of B3 Fitness noted that he was working with R.W. on “stretching her hips, core strength, over all body strength, and exercise” and had seen her 50 times between November 11, 2017, and August 28, 2018. Ex. 16 at 1.

B. Affidavits and Fact Witness Testimony

1. Mrs. Williford

Mrs. Williford is R.W.’s mother and works as a paralegal. Ex. 13 (“Mrs. Williford Aff.”) at 1; Tr. at 8-9. In her affidavit, executed October 4, 2021, she stated that R.W. was healthy prior to the subject vaccinations, was social, excelled in school, was active in her church youth group, and participated in various forms of dance, pageants, gymnastics, and softball. Mrs. Williford Aff. at 1.

R.W. was in fifth grade at the time of her September 11, 2015 vaccinations. Tr. at 13. Mrs. Williford testified that R.W. did not have a cold or rhinitis before the vaccinations, which were

⁵ Arthrodesis: the surgical fixation of a joint by a procedure designed to accomplish fusion of the joint surfaces by promoting the proliferation of bone cells; called also artificial ankylosis. DORLAND’S, <https://www.dorlandsonline.com/dorland/definition?id=4247&searchterm=arthrodesis> (last visited Feb. 26, 2026).

given at a well-child visit; medical records indicating otherwise were in error. *Id.* at 14, 16-17. R.W. did complain of arm pain and fatigue at the time of the vaccinations, as well as low back pain leading up to her September 27, 2015 hospitalization. *Id.* at 15-16; Mrs. Williford Aff. at 1. She had to ask to sit down during her clogging practice about four days before going to the hospital. Tr. at 17-18.

On September 27, 2015, R.W. complained of leg pain. Mrs. Williford Aff. at 1. She asked to take a nap after church, which was unusual. Tr. at 18-19. Shortly thereafter, she complained of right leg pain, and she then fell trying to stand up from the bed. *Id.* at 19. Her parents decided to take her to the hospital; Mr. Williford had to carry her to the car. *Id.* at 20.

At the local hospital, R.W. was asked to provide a urine sample, but when she attempted to sit on the toilet, her body became “stiff,” and she had an episode of urinary incontinence that she could not feel. Tr. at 22. After this, she was taken by private transport to WakeMed. *Id.* at 23-24. At WakeMed, R.W. was diagnosed with TM. *Id.* at 26. Later, her parents were advised to transfer R.W. to Duke for PLEX treatment, “the next step for her care.” *Id.* at 29. The physicians at Duke also characterized R.W.’s diagnosis as “TM.” *Id.* at 30. After a conversation with a friend, Mrs. Williford inquired with the medical team about AFM and requested that they test R.W. for that condition. *Id.* at 30-31. She was told that the test was negative. *Id.* at 33.

R.W. remained hospitalized and in inpatient rehabilitation until November 23, 2015. Mrs. Williford Aff. at 2. Later, she was diagnosed with scoliosis, for which surgery was recommended. Tr. at 42. The physicians treating the scoliosis advised that the condition was secondary to R.W.’s TM. *Id.* at 42-43.

At the time of hearing, R.W. continued to do exercises and personal training at home, as well as outpatient physical therapy. Tr. at 43. She remained paralyzed from the mid-torso down and was wheelchair bound and incontinent. *Id.* at 45.

2. Mr. Williford

Mr. Williford’s affidavit was materially identical to Mrs. Williford’s. *See* Ex. 14 (“Mr. Williford Aff.”). He testified that, while R.W. was hospitalized, a nasal swab was taken to test her for enterovirus and rhinovirus. Tr. at 47-48. The purpose of the test was to determine whether R.W. had AFM or TM. *Id.* at 48. He recalled that the test ultimately ruled out AFM. *Id.* at 50-51.

3. R.W.

R.W. testified that she was in “normal health” prior to her vaccinations. Tr. at 54. She recalled that the day of vaccination, her arm “hurt a lot, but I just figured it was since I had gotten the shot, so I just pushed through.” *Id.* at 55. Over the next few days, she had a “little bit of back pain” but no other problems. *Id.* at 56. A few days before her hospitalization, she felt more tired than usual. *Id.* On September 27, 2015, after church and lunch, her leg was hurting, so she lay down. *Id.* at 56-57. She got up to use the restroom and felt like she was struggling to walk. *Id.* at 57. When she got up again, she fell. *Id.* She was seen by paramedics at a nearby fire station, after

which she was taken to the hospital. *Id.* at 57-58. At the time of hearing, she still could not feel anything from her hips down, she was incontinent, and her skin had difficulty healing and was sensitive to the sun. *Id.* at 61.

III. EXPERT EVIDENCE

A. Pre-Hearing Expert Reports and Affidavits

1. Petitioners' Expert Lawrence Steinman, M.D.: First Expert Report

Dr. Steinman filed two reports in this case. Ex. 22 (“First Steinman Rep”); Ex. 49 (“Second Steinman Rep.”). Dr. Steinman received his medical degree from Harvard University and was a NIH Fellow in Chemical Neurobiology at Harvard Medical School. Ex. 24 (“Steinman CV”) at 1. He completed his residency in pediatrics and pediatric/adult neurology at Stanford University Hospital. *Id.* He is the GA Zimmermann Professor of Neurological Sciences, Neurology, and Pediatrics at Stanford. *Id.* He is board certified in neurology and is involved in the American Academy of Neurology as a fellow, along with the American Neurological Association, the American Association of Immunologists, and the Clinical Immunology Society. *Id.* at 2. He has published nearly 600 articles on many different topics. *Id.* at 5-46. He runs an active research laboratory “investigating neuroimmunology in conditions like [TM] and [NMO].” First Steinman Rep. at 1.

Over the course of his 40-year career, Dr. Steinman has cared for many patients, both adult and pediatric, with neuroinflammatory diseases, including TM, NMO, GBS, optic neuritis, multiple sclerosis, chronic inflammatory demyelinating polyneuropathy (“CIDP”), ADEM, and others. First Steinman Rep. at 1. At the time of hearing, he had six pediatric patients with AFM and 15-20 with TM. Tr. at 180. He has served as an expert for the Institute of Medicine of the National Academy of Sciences (“IOM”) on matters relating to vaccines. *Id.* at 67; Steinman CV at 2. He was elected to the National Academy of Sciences in 2015. Steinman CV at 2.

Dr. Steinman opined that R.W. suffered an “extensive transverse myelitis of undetermined etiology, with competent academic teams . . . having ruled out a wide set of competing diagnoses.” First Steinman Rep. at 6.

Dr. Steinman advanced a molecular mimicry theory to explain how the DTaP and meningococcal vaccines could cause TM. First Steinman Rep. at 7. He described molecular mimicry as “an evolutionary adaptation whereby viruses and bacteria attempt to fool the body into granting them free access. Such mimicry works by showing the immune system stretches of amino acids that look like self.” *Id.*

An autoimmune response can occur even where the mimicry is not exact. First Steinman Rep. at 7. For example, Drs. Fujinami and Oldstone induced experimental autoimmune encephalitis (“EAE”) in rabbits via immunization with proteins from the Hepatitis B virus, which “shared a stretch of just six amino acids with myelin basic protein [‘MBP’].” *Id.* at 8 (quoting Lawrence Steinman, *Autoimmune Disease*, 269 SCI. AM. 107, 109 (1993) (Exs. 30, 62) (“Steinman 1993”)). Other experiments similarly demonstrated that limited, nonconsecutive homologies

could trigger EAE in animal models. *Id.* at 9-11 (citing Anand M. Gautam et al., *A Polyalanine Peptide with only Five Native Myelin Basic Protein Residues Induces Autoimmune Encephalomyelitis*, 176 J. EXP. MED. 605 (1992) (Exs. 35, 67) (“Gautam 1992”); Anand M. Gautam et al., *Minimum structural requirements for peptide presentation by major histocompatibility complex class II molecules: Implications in induction of autoimmunity*, 91 PROC. NATL. ACAD. SCI. 767 (1994) (Ex. 36, 68) (“Gautam 1994”); Anand M. Gautam et al., *A Viral Peptide with Limited Homology to a Self Peptide Can Induce Clinical Signs of Experimental Autoimmune Encephalomyelitis*, 161 J. IMMUNOL 60 (1998) (Exs. 37, 69) (“Gautam 1998”)). As a result, cross-reactivity between viral and self proteins is relatively common: one study showed nearly 4% of antiviral monoclonal antibodies also reacted with self proteins. *Id.* at 7-8 (citing Robert S. Fujinami et al., *Molecular Mimicry, Bystander Activation, or Viral Persistence: Infections and Autoimmune Disease*, 19 CLIN MICROBIOL. REV. 80 (2006) (Exs. 33, 65) (“Fujinami”); Javaraiah Srinivasappa et al., *Molecular Mimicry: Frequency of Reactivity of Monoclonal Antiviral Antibodies with Normal Tissues*, 57 J. OF VIROLOGY 397 (1986) (Exs. 34, 66) (“Srinivasappa”)).

Turning to the vaccine and injury involved here, Dr. Steinman used the basic local alignment search tool (“BLAST”) to compare the “DTaP vaccine and two myelin antigens, [myelin oligodendrocyte glycoprotein (‘MOG’)] and MBP[,] known to be targeted in transverse myelitis.” First Steinman Rep. at 12 (citing Oden Abramsky & Dvora Teitelbaum, *The Autoimmune Features of Acute Transverse Myelopathy*, 2 ANN. NEUROL 36 (1977) (Exs. 38, 70) (“Abramsky & Teitelbaum”); Claus G. Haase & Stephan Schmidt, *Detection of brain-specific autoantibodies to myelin oligodendrocyte glycoprotein, S100b and myelin basic protein in patients with Devic’s neuromyelitis optica*, 307 NEUROSCIENCE LETTERS 131 (2001) (Exs. 39, 71) (“Haase & Schmidt”); Scott S. Zamvil & Anthony J. Slavin, *Does MOG Ig-positive AQP4-seronegative opticospinal inflammatory disease justify a diagnosis of NMO spectrum disorder?*, 2 NEUROL. NEUROIMMUNOL. & NEUROINFLAMM. e62 (2015) (Exs. 40, 72) (“Zamvil & Slavin”); Til Menge et al., *Neuromyelitis Optica Following Human Papillomavirus Vaccination*, 79 NEUROLOGY 285 (2012) (Exs. 41, 73) (“Menge”); Steinman et al., *Polypeptide Pertussis Toxin Vaccine*, US PATENT NUMBER 5,000,952 (1991) (Ex. 42) (“Steinman Patent”)). He found the tetanus toxin shared four identical amino acids within an eight-acid sequence (KDSAGEVR) with the MBP segment. *Id.* at 13. This would be “sufficient to trigger an immune response with paralysis.” *Id.* The pertussis toxin contained a sequence (AELRGSGDL) with five of nine identical amino acids to a sequence in MBP. *Id.* at 14.

Dr. Steinman then entered the sequences he identified as homologous into the Immune Epitope Database (“IEDB”), which lists epitopes that have been described as immunologically relevant in the scientific literature. First Steinman Rep. at 15. He reported that the homologous sequence in the pertussis toxin was listed in the IEDB. *Id.* In his opinion, this information provided “a compelling theory that molecular mimics in the DTaP received by petitioner *could* trigger immunity to myelin basic protein culminating in transverse myelitis.” *Id.* at 16 (emphasis in original).

Dr. Steinman also opined there was a molecular mimic between the carbohydrate component of the meningococcal vaccine and glycans involved in neurological disease. First Steinman Rep. at 17-18. In particular, he claimed that mannose-containing glycans, which are in

the vaccine, have been shown to induce EAE in an animal model. *Id.* at 18 (citing Denong Wang et al., *Uncovering Cryptic Glycan Markers in Multiple Sclerosis (MS) and Experimental Autoimmune Encephalomyelitis (EAE)*, 75 DRUG DEV. RES. 172 (2014) (Exs. 45, 79) (“Wang”)).

Regarding onset, Dr. Steinman opined that R.W. developed TM approximately 16 days after vaccination. First Steinman Rep. at 18. He stated: “The best surrogates for this timing are found in epidemiologic studies on other neuroinflammatory diseases including [GBS], ADEM. A sixteen day delay post-immunization is concordant with these studies[.]” *Id.* at 19 (citing Lawrence B. Schonberger et al., *GBS Following Vaccination from the National Immunization Program, U.S., 1976-1977*, 110 AM. J. OF EPIDEMIOLOGY 105 (1979) (Ex. 46, 77) (“Schonberger”); L. Bennetto & N. Scolding, *Inflammatory/Post-Infections Encephalomyelitis*, 75 J. NEUROL NEUROSURG. PSYCHIATRY i22 (2004) (Exs. 47, 78) (“Bennetto & Scolding”), Dimitrios Karussis & Panayiota Petrou, *The spectrum of post-vaccination inflammatory CNS demyelinating syndromes*, AUTOIMMUNITY REV. (2013), <http://dx.doi.org/10.1016/j.autrev.2013.10.003> (Exs. 48, 79) (“Karussis & Petrou”)).

2. Respondent’s Expert Neil Romberg, M.D.: Expert Report

Dr. Romberg submitted one expert report in this case. Ex. A (“Romberg Rep.”). He earned a medical degree from Pennsylvania State College of Medicine. Ex. B (“Romberg CV”) at 1. He completed his residency at New York University and was an immunology fellow at Yale University. *Id.* He has held various teaching positions in immunology and pediatrics for the past 10 years and is an Assistant Professor of Pediatrics at the Children’s Hospital of Philadelphia (“CHOP”), which is affiliated with the University of Pennsylvania School of Medicine. *Id.* He practices as an attending physician in CHOP’s Immunology Department. *Id.* He is board certified in allergy/immunology and is board eligible in pediatrics. *Id.* at 2. He has received several awards and grants for his work and holds membership in several immunology societies. *Id.* He is on the board of three immunology journals and has published approximately 45 peer-reviewed articles. *Id.* at 3-5.

Dr. Romberg opined that R.W.’s condition was consistent with “acute flaccid paralysis,” also known as AFM. Romberg Rep. at 4. AFM is “caused by damage to the anterior cell horns.” *Id.* (citing Yasaman Fatemi & Rana Chakraborty, *Acute Flaccid Myelitis: A Clinical Overview for 2019*, 94 MAYO CLIN. PROC. 875 (2019) (Ex. A, Tab 1) (“Fatemi”)). He explained: “Traditionally, acute flaccid paralysis was synonymous with epidemic poliomyelitis but there are many viruses (enterovirus D68, rhinovirus/non-D68 enteroviruses, adenoviruses and flaviviruses) that exhibit tropism for spinal gray matter.” *Id.* Furthermore, rhinoviruses have genetic similarities to non-D68 enteroviruses; thus, “routine clinical PCR-based screening tests used by hospitals” cannot distinguish between rhinoviruses and non-D68 enteroviruses. *Id.* “For this reason, acute flaccid paralysis patients are typically divided into enterovirus D68 positive cases or rhinovirus/non-D68 enterovirus positive cases.” *Id.* He cited a case series in which 18% of patients diagnosed with AFM “had evidence of rhinovirus or non-D68 enterovirus.” *Id.* (citing Kevin Messacar et al., *Acute Flaccid Myelitis: A Clinical Review of US Cases 2012–2015*, 80 ANN. NEUROL. 326 (2016) (Ex. A, Tab 3) (“Messacar”)). After more sophisticated testing was developed to distinguish these viruses, another case series reported that rhinovirus had been detected in 12 of 305 pediatric AFM patients. *Id.* (citing Tracy Ayers et al., *Acute Flaccid Myelitis in the United States: 2015–2017*,

144 PEDIATRICS 1 (2019) (Ex. A, Tab 4) (“Ayers”)). Dr. Romberg concluded that the fact that R.W. was infected with rhinovirus at the outset of her symptoms suggests her case “appears to share many typical disease features with other pediatric patients affected by this disorder.” *Id.*

On causation, Dr. Romberg contended that, for molecular mimicry to be considered a “potential contributor” to an autoimmune disease, several criteria must be satisfied. Romberg Rep. at 5 (citing Christophe Benoist & Diane Mathis, *Autoimmunity provoked by infection: how good is the case for T cell epitope mimicry?*, 2 NATURE IMMUNOLOGY 797 (2001) (Ex. A, Tab 5) (“Benoist & Mathis”); C. Wim Ang, Bart C. Jacobs & Jon D. Laman, *The Guillain–Barre syndrome: a true case of molecular mimicry*, 25 TRENDS IN IMMUNOLOGY 61 (2004) (Ex. A, Tab 7) (“Ang”)). First, there must be an epidemiologic association between the vaccine antigen and the immune-mediated disease. *Id.* Here, is little epidemiologic data concerning AFM and vaccines aside from the live oral polio vaccine, which is not at issue. *Id.* at 5 (citing David Bearden et al., *Enteroviruses in X-Linked Agammaglobulinemia: Update on Epidemiology and Therapy*, 4 J. ALLERGY CLIN. IMMUNOL. PRACT. 1059 (2016) (Ex. A, Tab 8) (“Bearden”)). A 2016 study in the Morbidity and Mortality Weekly Report (“MMWR”) catalogued 10 AFM cases, none of which were vaccine caused. *Id.* (citing Jesse Bonwitt et al., *Acute Flaccid Myelitis Among Children — Washington, September–November 2016*, 66 MMWR 826 (2017) (Ex. A, Tab 9) (“Bonwitt”)).

Second, there must be “[i]dentification of autoreactive T cells or autoantibodies that recognize a human structure (target antigen) that if perturbed could explain symptomology.” Romberg Rep. at 5. R.W.’s serum did not contain any autoantibodies, nor did she have oligoclonal banding in her CSF, suggesting she was not producing autoantibodies. *Id.*

Third, Dr. Romberg opined that the “vast majority” of homologies identified by BLAST search are not immunologically relevant. Romberg Rep. at 6. He believed Dr. Steinman’s homology metric of five of nine identical, nonsequential amino acids was too broad. *Id.* This is signified by the high “E-values” assigned to the homologies Dr. Steinman identified in this case, which were “consistent with random pairing.” *Id.* at 6-7. Dr. Steinman’s citation of the Gautam articles was inapposite, because those experiments used an epitope that was “definitively known” to cause EAE in mice. *Id.* at 7. Dr. Steinman, by contrast, selected peptide segments that were not known to be immunogenic in either mice or humans. *Id.* Furthermore, in comparison to the tetanus/pertussis toxins tested by Dr. Steinman, MBP has equal or greater homology with numerous proteins that are “ubiquitous in nature.” *Id.* In fact, the rhinovirus A29 protein (for which R.W. tested positive) had greater homology with MBP than the vaccine components. *Id.*

Dr. Romberg pointed out that the IEDB was not designed to be a “tool to prove or disprove molecular mimicry.” Romberg Rep. at 8. The database contains information from a variety of sources and reports findings in a simplified manner. *Id.* Dr. Steinman used very broad parameters to query the IEDB, using the least stringent filter available. *Id.* at 9. Dr. Romberg applied a more stringent filter based on an exact match with the sequence in question, which returned negative results. *Id.* He concluded that Dr. Steinman’s methodology did not attempt to “filter” irrelevant homologies; instead, it “explode[d] the list of possible mimics by layering the loose fit of the Gautam references on top of a permissive 70% IEDB filter.” *Id.*

Dr. Romberg also argued that the nine-peptide sequences identified in Dr. Steinman's IEDB search have not been shown to have the ability to activate B or T cells. Romberg Rep. at 9. He would find it surprising for the second sequence Dr. Steinman identified to have a role in R.W.'s injury, because any pathogenic reaction triggered by that sequence would be expected to primarily affect the adrenal glands. *Id.* R.W.'s presentation was not consistent with this type of damage. *Id.*

With respect to the alleged mimics identified in the meningococcal vaccine, Dr. Romberg noted that mannose-containing carbohydrates in the brain have a different chemical structure than those in the vaccine. Romberg Rep. at 10 (citing Pumtiwitt C. McCarthy, Abeer Sharyan & Laleh Sheikhi Moghaddam, *Meningococcal Vaccines: Current Status and Emerging Strategies*, 6 VACCINES 1 (2018) (Ex. A, Tab 18) ("McCarthy")). Furthermore, later experiments by Dr. Steinman have shown mice exposed to mannose-containing carbohydrates had significantly less severe EAE, suggesting those carbohydrates do not have a role in the pathogenesis of neuroinflammation. *Id.* at 10-11 (referencing Wang). Dr. Romberg concluded that if R.W. did generate anti-mannose antibodies in response to her meningitis vaccination, these experiments would "suggest[] those antibodies would have protected, not damaged her [central nervous system]." *Id.* at 11 (emphasis in original).

Fourth, to show molecular mimicry, there must be reproduction of the relevant disease in an animal model. Romberg Rep. at 11. Dr. Romberg could find no animal studies relating to AFM and either of the vaccines at issue here, though he did find literature describing animal models of AFM induced by "direct intracranial injections of live enteroviruses." *Id.* (citing Alison M. Hixon et al., *A mouse model of paralytic myelitis caused by enterovirus D68*, 13 PLOS PATHOGENS 1 (2017) (Ex. A, Tab 19) ("Hixon")).

Dr. Romberg agreed that the timing of the onset of R.W.'s condition after vaccination was consistent with the range observed between swine flu vaccination and GBS onset. Romberg Rep. at 12. He pointed out, however, that R.W. had been given five prior doses of the DTaP vaccine with no neurological effects, making it unlikely that her condition was caused by that vaccine. *Id.*

Dr. Romberg concluded that there was "no factual or scientific basis for the claim of injury by vaccine in this case." Romberg Rep. at 12. Furthermore, "there is an alternative, more likely trigger for R.W.'s disease, the rhinovirus A29[.]" *Id.* "As rhinoviruses are detected in nasal swabs from many acute flaccid paralysis patients, I must agree with R.W.'s discharge summary: A post-viral etiology was the most likely cause of R.W.'s neurological disease." *Id.* (citing Ayers; Ex. 5 at 10).

3. Respondent's Expert Michael Sweeney, M.D.: Expert Report

Dr. Sweeney filed one expert report in this case. Ex. C ("Sweeney Rep."). He earned his M.D. from the Medical College of Wisconsin in 2010, and he is an Assistant Professor of Child Neurology and Neuroimmunology at the University of Louisville School of Medicine. Ex. D, Tab 1 ("Sweeney CV") at 1; *Id.* at 5. He completed his residency training at Cincinnati Children's Hospital and the University of Cincinnati, followed by a fellowship in autoimmune neurology at the University of Utah. Sweeney Rep. at 1. He is a pediatric neurologist who is board certified in

neurology, with special qualifications in child neurology. *Id.* His clinical practice specializes in autoimmune and inflammatory conditions affecting the nervous system, including multiple sclerosis, NMO, anti-MOG related demyelinating disease, acute disseminated encephalomyelitis ADEM, post-infectious/autoimmune encephalitis, and paraneoplastic syndromes. *Id.*

Dr. Sweeney opined that the appropriate diagnosis in R.W. was AFM. Sweeney Rep. at 3. He explained: “Though AFM has been described as a subtype of transverse myelitis (TM), it is largely considered a separate entity with a different pathophysiology.” *Id.* (citing Cynthia Wang & Benjamin Greenberg, *Clinical Approach to Pediatric Transverse Myelitis, Neuromyelitis Optica Spectrum Disorder and Acute Flaccid Myelitis*, 6 CHILDREN 1 (2019) (Ex. C, Tab 1) (“Wang & Greenberg”)). AFM usually affects the gray matter of the spinal cord, but it can affect the white matter in more severe cases. *Id.* By contrast, TM is “a demyelinating disease which affects predominantly white matter in the spinal cord.” *Id.* AFM can be distinguished from TM based on its rapid onset of symptoms, flaccid weakness, depressed/diminished deep tendon reflexes, and predominance of gray matter involvement on imaging. *Id.*

Further, AFM presents with asymmetric paralysis of one or more limb “in the setting of recent or current febrile illness.” Sweeney Rep. at 3-4. Weakness can be preceded by pain and may progress over hours to several days. *Id.* at 4. The patient will have low muscle tone and absent reflexes but often will have normal sensation. *Id.* (citing Ayers, Messacar, Sarah E. Hopkins, Jay Desai & Leslie Benson, *Acute Flaccid Myelitis: A Call for Vigilance and an Update on Management*, 114 PEDIATRIC NEUROLOGY 26 (2021) (Ex. C, Tab 2) (“Hopkins”)). Bowel and bladder dysfunction are often present. *Id.*

Dr. Sweeney pointed out that, different from AFM, TM often presents with a specific sensory level, along with weakness and bladder/bowel dysfunction. Sweeney Rep. at 4. Usually reflexes are brisk, and “spasticity develops over time.” *Id.* Generally, TM is responsive to “acute immunotherapies such as steroids, plasmapheresis and IVIG.” *Id.* Finally, about 50% of pediatric TM patients will have a full recovery within two years of onset, though outcomes can be variable. *Id.* (citing Michael Absoud, *Pediatric transverse myelitis*, 87 (Suppl. 2) NEUROLOGY S46 (2016) (Ex. C, Tab 3) (“Absoud”)).

AFM is “thought to be caused by acute viral infection.” Sweeney Rep. at 4. There is “mounting evidence that supports enterovirus D68 as the cause for biennial outbreaks” of AFM. *Id.* Other enteroviruses, such as A71, and coxsackie virus have also been implicated. *Id.* (citing Ryan D, Schubert, et al., Pan-viral serology implicates enteroviruses in acute flaccid myelitis, 25 NATURE MED. 1748 (2019) (Ex. C, Tab 4) (“Schubert”)). As a general matter, it is “well known that many virus species cause AFM,” including poliovirus, West Nile virus, enteroviruses, and Japanese encephalitis virus. *Id.* (citing James J. Sejvar et al., *West Nile Virus–associated Flaccid Paralysis*, 11 EMERGING INFECTIONS DISEASE 1021 (2005) (Ex. C, Tab 5) (“Sejvar”); Chao-Ching Huang et al., *Neurologic Complications in Children with Enterovirus 71 Infection*, 341 NEW ENGLAND J. OF MED. 936 (1999) (Ex. C, Tab 6) (“Huang”); Tom Solomon et al., *Poliomyelitis-like illness due to Japanese encephalitis virus*, 351 LANCET 1094 (1998) (Ex. C, Tab 7) (“Solomon”)).

Dr. Sweeney noted there have been sporadic reports of TM preceded by rhinovirus infection, as well as at least one case report of AFM in a patient positive for rhinovirus. Sweeney Rep. at 4 (citing Gary R. Nelson et al., *Recognition and Management of Acute Flaccid Myelitis in Children*, 55 PEDIATRIC NEUROLOGY 17 (2016) (Ex. C, Tab 8) (“Nelson”). He pointed out that it is very difficult to identify a specific virus from the CSF in patients with AFM, “a fact that has contributed largely to the uncertainty in pathogenesis of AFM.” *Id.* Of the AFM cases reported to the CDC in 2018, 29% were positive for enterovirus A71, 37% were positive for enterovirus D68, and 34% were positive for other viruses, including several that were positive only for rhinoviruses. *Id.* (citing Susannah L. McKay et al., *Increase in Acute Flaccid Myelitis — United States, 2018*, 67 MMWR 1273 (2018) (Ex. C, Tab 9) (“McKay”).

Dr. Sweeney acknowledged that R.W.’s case was unusual because she had sensory loss. Sweeney Rep. at 5. Some research has shown up to 44% of AFM patients have sensory involvement, though the evidence on this aspect of AFM is “inconclusive.” *Id.* (citing Messacar, Riley Bove et al., *Unmet Needs in the Evaluation, Treatment, and Recovery for 167 Children Affected by Acute Flaccid Myelitis Reported by Parents Through Social Media*, 102 PEDIATRIC NEUROLOGY 20 (2020) (Ex. C, Tab 10) (“Bove”).

On MRI, AFM patients can have enhancement of nerve roots, which is not typical for TM. Sweeney Rep. at 5 (citing J.A. Maloney et al., *MRI Findings in Children with Acute Flaccid Paralysis and Cranial Nerve Dysfunction Occurring during the 2014 Enterovirus D68 Outbreak*, 36 AJNR AM. J. NEURORADIOL. 245 (2015) (Ex. 93) (“Maloney”). Such enhancement was seen on R.W.’s imaging. *Id.* While the radiologists who reviewed R.W.’s imaging did not comment on white matter versus gray matter involvement, the fact that her abnormal signal was located in the central cord, combined with her persistent flaccid weakness, suggests “significant gray matter involvement.” *Id.* Furthermore, the inflammation in R.W.’s central nervous system (“CNS”) was limited to the lower spinal cord and did not extend to the brain or optic nerves. *Id.*

Finally, Dr. Sweeney commented that no causal link has been found between any vaccination and AFM. Sweeney Rep. at 5 (citing Bonwitt). He concluded R.W. developed AFM, as her case was consistent with other AFM cases reported in the literature. *Id.*

4. Dr. Steinman: Second Expert Report

Dr. Steinman first addressed Special Master Oler’s directive to address the significance of R.W.’s rhinovirus infection, which was stated in a non-PDF order dated October 19, 2020. Second Steinman Rep. at 1. He contended that AFM falls “under the heading” of TM. *Id.* He opined that R.W.’s case was consistent with AFM except for the presence of sensory loss, but the “diagnosis of transverse myelitis accounts for the clinical picture[.]” *Id.*

Dr. Steinman acknowledged that the Messacar paper identified some cases of AFM in which the patients tested positive for “rhinovirus/enterovirus,” but the low rate of such cases makes it “difficult to consider rhinovirus as a principal factor in the etiology of acute flaccid myelitis in this case.” Second Steinman Rep. at 2. Also, the Ayers paper reported only 4% of AFM patients tested positive for rhinovirus. *Id.* (citing Ayers). Those patients had a variety of subtypes of rhinovirus, making it difficult to implicate any particular subtype in causing AFM. *Id.* It was

more likely that R.W.’s injury was caused by the subject vaccines than a rhinovirus, particularly because rhinoviruses are widespread in children. *Id.*

Dr. Steinman disagreed that his molecular mimicry theory of causation did not meet the criteria identified by Dr. Romberg. Second Steinman Rep. at 3. He opined that the first criterion – “a susceptible host whose genetic background and adaptive immune responses allows emergence of self-reactive immunity” – was likely met because R.W. suffered an injury “where the immune system attacks the motor neuron and the spinal cord.” *Id.* He argued that he met the second criterion through his methodology identifying immunologically relevant homologies between the subject vaccines and host tissues. *Id.* The third criterion – a showing of a cross-reactive response in the host to the exogenous mimic – could not be demonstrated at this point because R.W. has already undergone immunotherapy. *Id.*

Furthermore, Dr. Steinman stressed that he was not attempting to scientifically *prove* that the subject vaccines caused R.W.’s injury, only that they *could*. Second Steinman Rep. at 4-5. He pointed out that to prove his theory, he would need to test R.W.’s blood, which would be infeasible. *Id.* at 5. He asserted that his methodology reliably answered the “could” question in favor of Petitioners. *Id.* at 5-7.

5. Treating Physician Travis Honeycutt, M.D.: Affidavits

R.W.’s critical care physician at WakeMed, Dr. Honeycutt, filed two separate affidavits addressing diagnosis and causation. Exs. 10, 84. He did not file his CV. The first affidavit, executed July 26, 2018, stated that, on September 27, 2015, he and other WakeMed physicians diagnosed R.W. with TM, “thought to be the result of an adverse vaccine event.” Ex. 10 at 1. Although she had a normal white blood count and was asymptomatic for a respiratory viral infection, “viral polymerase chain reaction assay was positive for enterovirus or rhinovirus.” *Id.* Her sample was sent to the state lab for further viral culture. *Id.*

Dr. Honeycutt noted that “[t]ransverse myelitis after vaccination is reported in medical literature.” Ex. 10 at 2 (citing N. Agmon-Levin et al., *Traverse myelitis and vaccines: a multi-analysis*, 18 LUPUS 1198 (2008) (Exs. 7, 58) (“Agmon-Levin”)). Furthermore, the National Institutes of Health “acknowledges that vaccines appear to cause transverse myelitis when the body’s immune system mistakenly attacks the body’s own tissue while responding to a vaccine.” *Id.* (citing *Traverse Myelitis*, U.S. Dept. of Health & Hum. Servs., Nat. Inst. of Health (Ex. 8, 59) (“NIH”); *Traverse Myelitis Fact Sheet*, Nat. Inst. of Neurological Disorders & Stroke (Ex. 9) (“TM Fact Sheet”)). Because R.W.’s symptoms appeared 16 days after her vaccinations and because no other cause of her condition was identified, Dr. Honeycutt concluded that her TM “resulted from the vaccination.” *Id.*

The second affidavit from Dr. Honeycutt, executed July 15, 2022, noted that his first affidavit erroneously stated that the Duke physicians diagnosed R.W. with AFM. Ex. 84 at 1. Her actual discharge diagnosis from Duke was acute flaccid paralysis, not AFM. *Id.* Dr. Honeycutt’s diagnosis of R.W. remained TM. *Id.*

B. Expert Testimony

1. Dr. Steinman's Testimony

Dr. Steinman was recognized as an expert in neurology. Tr. at 78. He concluded R.W. had TM, though there were “some elements” of her presentation in common with AFM. *Id.* at 82. AFM is a “subset” of or overlaps with TM. *Id.* The Tdap and meningococcal vaccines R.W. received were, more likely than not, a substantial factor causing her condition. *Id.*

TM is an inflammatory condition of the spinal cord. Tr. at 84. R.W.'s imaging showed extensive inflammation of her spinal cord, extending to the nerve roots. *Id.* She also had sensory abnormalities, “which can happen in AFM but are more a hallmark of transverse myelitis.” *Id.* She had no sensation from about T10 down, which Dr. Steinman believed represented a sensory level, a hallmark of TM, and not “just a motor neuron disease.” *Id.* at 85.

Dr. Steinman stated that there is a reported association between TM and vaccines, with onset occurring from “days to months” after vaccination. Tr. at 86-88. He referenced various literature items on this. *Id.* R.W.'s presentation fell within the reported timeframe. *Id.* The best estimate of the date of onset was 16 days after vaccination, September 27, 2015. *Id.* at 86-87.

TM can also be caused by infections, metabolic deficiencies, or other factors. Tr. at 89-90. It often involves a longitudinally extensive lesion, as was seen in R.W.'s case. *Id.* at 90. It can present with gray matter involvement. *Id.* There is some overlap with AFM, but R.W.'s case more closely resembled TM. *Id.* at 90-91.

Regarding diagnosis, Dr. Steinman discussed R.W.'s test results. Tr. at 91. Her protein level was consistent with TM but might also be consistent with AFM. *Id.* at 92-94. It was unlikely that R.W.'s condition was virally mediated because no viruses were found in her CSF, which is near her spinal lesion. *Id.* at 94.

Dr. Steinman testified that a disease like AFM that affects the anterior horns of the spinal cord, where the motor neurons are, should not “have any sensory disturbance if it's predominantly involving the motor neurons,” as the motor neurons are in a separate location from the sensory neurons. Tr. at 96-97. R.W. had sensory involvement, as shown by her inability to feel her bladder. *Id.* Exams where she had a T10 sensory level, meaning decreased/absent sensation below that point, also suggested she had TM. *Id.* at 104-05.

The MRI taken at Duke on October 16, 2015, showed an increasing, longitudinally extensive lesion, which would be seen in TM but likely not in AFM. Tr. at 98, 105-06. Her next MRI on October 26, 2015, was also consistent with TM. *Id.* Her MRIs also showed cauda equina nerve root enhancement and enhancement of the dorsal aspects of the conus medullaris. *Id.* at 99. The inflammation of the dorsal aspects responsible for sensory function was, in Dr. Steinman's view, more characteristic of a diffuse myelitis than AFM. *Id.* at 99-100. He also felt the fact that R.W.'s MRIs had enhancing lesions meant AFM was less likely. *Id.* at 101-02.

Dr. Steinman explained that AFM results predominantly in motor impairment and usually affects limited parts of the body, “not usually both legs.” Tr. at 106. It does have overlapping characteristics with other CNS disorders. *Id.* at 107. If he had to make a diagnosis of R.W., he would diagnose TM. *Id.*

Dr. Steinman testified that enterovirus D68 has been causally linked to AFM. Tr. at 109. Rhinoviruses and D68 do “share a lot of sequence homology.” *Id.* Rhinoviruses, however, are quite prevalent and responsible for most “common” colds. *Id.* at 109-10. Thus, it is unsurprising to find a rhinovirus in a person’s nose. *Id.* at 110. He described a study that found no statistical association between AFM and non-D68 enterovirus or rhinovirus infections. *Id.* (discussing Negar Aliabadi et al., Enterovirus D68 Infection in Children With Acute Flaccid Myelitis, Colorado, USA, 2014, 22 EMERGING INFECTIOUS DISEASE 1387 (2016) (Exs. 6, 57) (“Aliabadi”)). Just because rhinovirus A29 was detected in R.W. does not mean the virus caused her condition. *Id.* at 113.

Turning to causation, Dr. Steinman explained that his experiments have shown a homology of five of 12 identical amino acids can trigger an immune response in animals, when the antigen is combined with Complete Freund’s Adjuvant to enhance the response. Tr. at 123-24. Homologies of fewer than five identical amino acids did not cause disease in animals, even with the adjuvant. *Id.*

With respect to the vaccines at issue here, Dr. Steinman used MBP and MOG as comparators. Tr. at 129-30. He did not find any relevant homologies between the subject vaccines and MOG, but he did with MBP, using BLAST. *Id.* The “E value” provided in BLAST searches is inapplicable in this context, as it was designed to identify proteins that are genetically similar, not molecular mimics. *Id.* at 125-26. Dr. Steinman acknowledged that BLAST might not be frequently used to compare short protein sequences, as he did. *Id.* at 135.

Addressing the point that the MBP sequence purportedly homologous with Tdap is primarily expressed in the adrenal glands, Dr. Steinman acknowledged that this was a legitimate critique, but he noted that the aquaporin-4 water channel targeted in NMO is present in organs outside the nervous system, but NMO patients do not develop disease in other organs. Tr. at 130-31. Here, the IEDB revealed the sequence in question had been identified as an immunologically relevant epitope. *Id.* at 136.

Dr. Steinman clarified that “the main weight of the evidence comes from . . . protein similarities,” not the purported homologies between the meningococcal vaccine and mannose clusters within the nervous system. Tr. at 144. He acknowledged that in later experiments by his lab, “we were able to actually use those mannose clusters coupled to another protein to suppress inflammation.” *Id.* at 144-45.

On *Althen* prong two, Dr. Steinman stated:

Well, she got the vaccine. The vaccine has a component which has a sequence similarity to myelin basic protein. The literature tells me that myelin basic protein is one of the targets of the immune system.

So that could explain how [R.W.] developed transverse myelitis after getting the vaccine. Is there a better alternative explanation? So I looked hard, and the reports from my colleagues showed they looked hard too. There's been a lot of discussion and there will be more about D68 and rhinovirus. My argument is the vaccines were given for sure. They are given to give you an immune response. Whether or not a rhinovirus caused transverse myelitis, I think that's never been ruled in. And whether this is just flaccid myelitis and rhinovirus is a trigger for flaccid myelitis is also controversial.

Tr. at 138. He acknowledged that there was a potential molecular mimic between rhinovirus and MBP, suggesting that the "rhinovirus could be a substantial factor" causing R.W.'s disease. *Id.* at 138-39. However, "by the preponderance of evidence the vaccine is a stronger piece of evidence, especially for transverse myelitis, than rhinovirus," given the prevalence of rhinovirus infections. *Id.* at 139.

Concerning timing, Dr. Steinman relied on the Schonberger study relating to GBS following flu vaccination, as well as the Bennetto and Scolding study on encephalomyelitis and the Karussis review of post-vaccination inflammatory CNS demyelinating syndromes. Tr. at 139-40 (citing Schonberger; Bennetto & Scolding; Karussis & Petrou). The timing of the onset of R.W.'s symptoms, 16 days after vaccination, was consistent with the latency ranges reported in these studies. *Id.* at 140. Likewise, the Agmon-Levin study on TM and vaccinations found the appropriate interval for vaccine causation was "several days to three months," consistent with R.W.'s case. *Id.* (citing Agmon-Levin).

On cross, Dr. Steinman explained that he used BLAST and IEDB searches because it would not be feasible to experiment on actual specimens. Tr. at 150. In response to Special Master Oler's questioning, he said that "TM is hundreds of times more common as a diagnosis" than AFM. *Id.* at 160. R.W.'s poor response to IVIG, PLEX, and steroid treatment did not rule out TM in favor of AFM, because up to 25% of TM patients do not have a positive response to these treatments. *Id.* at 161-62. He clarified that his causation theory focused on the Tdap vaccine, not the meningococcal vaccine. *Id.* at 163-64.

2. Dr. Sweeney's Testimony

Dr. Sweeney was recognized as an expert in the field of neurology with a specific focus on clinical pediatric neurology. Tr. at 186.

Dr. Sweeney opined the correct diagnosis for R.W. was AFM. Tr. at 192. AFM is a newer term than "acute flaccid paralysis," which derived from the time when polio was prominent. *Id.* at 193. Acute flaccid paralysis has been found to be caused by various viruses, including enterovirus, West Nile virus, and parvovirus. *Id.* Beginning in 2012, there were flare-ups of cases of acute flaccid paralysis in children, often linked to D68, and the term "AFM" began to be used instead. *Id.* at 193-94. The terms are still sometimes used interchangeably. *Id.* To him, it appeared the treating physicians at Duke used those terms synonymously. *Id.* at 194.

A patient with AFM typically presents with an acute, rapid onset of symptoms, including weakness affecting one or more limbs. Tr. at 196. They will have decreased muscle tone in the affected limb, along with decreased or absent reflexes and pain. *Id.* MRIs will typically show predominantly gray matter involvement. *Id.* Most will have a prodromal or concurrent illness or fever at the time of onset. *Id.* Pain is often the “heralding sign,” indicating the onset of weakness. *Id.*

According to a CDC AFM working group article, AFM cases are classified as either “definite,” “probable,” “possible,” or “uncertain.” Tr. at 197-98. The first symptom is “acute onset of limb weakness where you have a period from onset to nadir, hours to 10 days.” *Id.* at 198. The second sign is a “prodromal fever or illness,” which can include nonspecific respiratory symptoms like rhinorrhea, pharyngitis, or cough, or, less commonly, gastrointestinal symptoms. *Id.* Another feature is weakness “involving one or more limbs, the neck, face or cranial nerves.” *Id.* Cranial nerve involvement has not been consistently reported during spikes of AFM cases. *Id.* The involved limbs have decreased muscle tone and absent reflexes, different from classic demyelinating illnesses in which reflexes and tone increase after the initial presentation. *Id.* at 198-99.

Nerve root enhancement sets AFM apart from other forms of myelitis. Tr. at 199. CSF will show a white blood cell “WBC” count of greater than five cells per liter. *Id.* If the CSF results show this, the case will be classified as “definite” AFM. *Id.*

In R.W.’s case, “she had rapid onset of weakness,” with a nadir of 4-5 hours. Tr. at 200. From the time R.W. complained of pain to when she had flaccid limbs upon first presentation to the hospital was a matter of hours. *Id.* at 200-01. She had a fever at the time of presentation, meeting the criterion of a prodromal or concurrent illness, even though she did not have other symptoms. *Id.* at 201-02. She had weakness in both legs, as well as decreased muscle tone and absent reflexes that persisted throughout her hospitalization.⁶ *Id.* at 201-04.

Dr. Sweeney reviewed R.W.’s MRIs. Tr. at 204. Her MRIs at WakeMed showed “T2 hyperintense signal between T6 and the conus with mild expansion of the cord. And along the ventral surface of the cord, there was patchy enhancement, which corresponds to nerve root enhancement.” *Id.* at 205. Her next MRI, taken at Duke, showed “diffuse enhancement of the cauda equina nerve root in the ventral and dorsal aspects of conus medullaris,” with “significant interval increase in the extent and degree of expansion of the abnormal intramedullary core signal, extending from T3 to the conus.” *Id.* These collectively showed the expansion of the lesion from the T6 to the T3 level, as well as increased swelling within the spinal cord. *Id.* Dr. Sweeney also pointed out that the imaging showed enhancement in the nerve roots and cauda equina, but not the spinal cord itself, as would be expected in “classic demyelinating myelitis.” *Id.* at 206.

Dr. Sweeney testified that R.W.’s CSF results did not meet the criteria for “definite” AFM, because she only had five white blood cells in her fluid. Tr. at 206, 277. Thus, he classified her

⁶ Dr. Sweeney could not explain why Mrs. Williford observed R.W.’s body to be very rigid in the emergency room bathroom, but he said that true spasticity would not be transient. Tr. at 202-03.

case as “probable.” *Id.* He was not surprised a virus was not detected in the spinal fluid itself, as that rarely occurs. *Id.* at 208. Her later course was also consistent with AFM, as she did not have a favorable response to immunotherapy, which is unusual in pediatric TM. *Id.* at 216-17. He would expect at least a modest response to these treatments in TM, but he would not expect a recovery of motor function in AFM, because the causal virus destroys the anterior horn cells in the spinal cord. *Id.* at 217.

Dr. Sweeney walked through the MRI images, pointing out where the gray matter involvement was seen. Tr. at 220-22. He also identified the enhancement of the nerve roots, showing damage to the anterior portion of the spine. *Id.* at 223-25. The predominant inflammation was “more anterior and central, which is where the gray matter lives.” *Id.* at 227. Dr. Sweeney interpreted R.W.’s MRIs as showing predominantly gray matter involvement. *Id.*

In Dr. Sweeney’s view, the general term “myelitis” encompasses a range of different diagnoses, including AFM. Tr. at 230. Idiopathic TM typically presents with bilateral symptoms and a sensory level. *Id.* There will also be evidence of inflammation within the spinal fluid, such as an elevated WBC count, enhancement on imaging, or oligoclonal banding. *Id.* TM is not applicable to R.W. because she mostly had gray matter involvement, not white matter. *Id.* at 232.

Asked about R.W.’s sensory involvement, Dr. Sweeney did not believe it ruled out AFM, because the sensory symptoms were secondary to her weakness, which developed first. Tr. at 232-33. He attributed her sensory deficits to swelling and inflammation of her spinal cord, which led to dysfunction of the nerve cells. *Id.* at 233, 275-76. Nonetheless, the initial assignment of “TM” as a diagnosis at WakeMed was appropriate, given what was known at the time. *Id.* at 234. TM is a broadly used term and refers to sensory loss across the body. *Id.*

Given R.W.’s overall course, Dr. Sweeney disagreed that her sensory level was dispositive against an AFM diagnosis; her flaccid weakness, fever, and absent reflexes instead signified a viral-mediated illness like AFM. Tr. at 234-35. Also, AFM can present with sensory involvement, as documented in the medical literature. *Id.* at 237-38.

On cross, Dr. Sweeney clarified that AFM and “acute flaccid paralysis” can be used interchangeably; AFM refers to acute flaccid paralysis with a specific viral etiology. Tr. at 242-43. TM, by contrast, is a distinct condition that does not tend to present with acute flaccid paralysis. *Id.* at 243. AFM can present with secondary demyelination due to inflammation. *Id.* R.W. did not have evidence of demyelination on imaging, but her sensory loss implies she had some “demyelination or damage to the sensory tract.” *Id.* at 244.

Dr. Sweeney acknowledged that the physicians at Duke referred to R.W.’s condition as “acute flaccid paralysis” due to “likely transverse myelitis” and frequently used the term “transverse myelitis” to describe her condition. Tr. at 245. He also acknowledged that a sensory level is “uncommon” in AFM and “more common in idiopathic or demyelinating transverse myelitis.” *Id.* at 251. Bowel and bladder incontinence is common in TM but can also occur in AFM. *Id.* at 252. He was asked about R.W. having tingling in her leg as an initial symptom; this, he said, was a “positive sensory symptom.” *Id.* at 256. He admitted that R.W. was noted to have “profound” sensory level loss. *Id.* at 257-58.

Dr. Sweeney explained that R.W. developed spasticity in her hips only after “she had instrumentation of her spinal cord, so after she had surgery for her scoliosis.” Tr. at 259. However, because it is “very unusual to develop spasticity in only one muscle group,” he believed she more likely developed contractures, meaning the “shortening of a muscle group because of disuse,” rather than spasticity. *Id.* at 259-60.

Dr. Sweeney opined that the A29 rhinovirus detected in R.W. was the principal cause of her AFM. Tr. at 268. If she had not contracted the A29 virus, he did not believe she would have developed AFM at that time. *Id.* at 271.

In response to questioning by Special Master Oler, Dr. Sweeney noted that, although R.W. did not complain of upper respiratory symptoms before or at the time her weakness began, she had a fever and was positive for A29, which, to him, was “enough for me to include that as a prodromal illness.” Tr. at 280.

3. Dr. Romberg’s Testimony

Dr. Romberg was qualified as an expert in clinical immunology and pediatrics. Tr. at 299. He testified that AFM is caused by a virus. *Id.* at 302. However, “[t]he Tdap or DTaP, both of them, and Menactra are killed or dead vaccines. They are not living. They cannot reproduce, and therefore, I cannot imagine a scenario in which they can cause AFM.” *Id.* Only a living pathogen could damage the anterior horn cells and produce the damage seen in AFM. *Id.* at 307. There is also no epidemiologic evidence linking the subject vaccines and AFM. *Id.*

With respect to the detection of A29 in R.W., Dr. Romberg explained that rhinoviruses are part of the enterovirus family and are genetically similar to enteroviruses. Tr. at 305-06. Before 2015, rhinoviruses and enteroviruses could not be distinguished from one another through testing. *Id.* at 306.

Turning to Dr. Steinman’s molecular mimicry theory, Dr. Romberg criticized Dr. Steinman’s reliance on BLAST searches to identify potential mimics, noting that BLAST was not designed for this purpose. Tr. at 310-11. He explained:

So I think what BLAST does is it looks at an amino acid sequence like you or I would read letters on a page, in a linear fashion. But the immune system can't read amino acid sequences. What it does is it feels the surface of these peptides, both their hydrophobicity, how attracted they are to water, and their charges, are they positively or negatively charged, how bulky the amino acids are. And so it's not really reading these sequences in a linear fashion. It's really feeling them sort of like braille. And I think for this reason, the National Academy of Science warned against using BLAST support[ed] theories of molecular mimicry in their IOM report.

Id. at 311. Also, Dr. Steinman's method was too broad to accurately identify immunologically relevant homologies. *Id.* Instead, it was likely to produce false positive results. *Id.* at 311-12. Furthermore, the E-value associated with Dr. Steinman's findings was very high, suggesting the finding was due to chance alone. *Id.* at 313-14.

Dr. Romberg testified that the Gautam experiments were not relevant here, because those experiments tested an immunologically relevant epitope in mice. Tr. at 315-16. The sequences identified by Dr. Steinman are unrelated to those used in Gautam. *Id.* at 316.

Dr. Romberg further pointed out that Dr. Steinman only required a 70% sequence match when querying the IEDB, which could produce false positive results. Tr. at 316-17. And just because a sequence is contained in the IEDB does not mean it is immunogenic. *Id.* at 317. One of the sequences Dr. Steinman searched for was an "imaginary" protein. *Id.* at 318. The other primarily exists in the adrenal gland, but R.W. did not have any clinical symptoms relating to the adrenal gland. *Id.*

With respect to the purported molecular mimicry between the meningococcal vaccine and mannose 9, Dr. Romberg pointed out that the vaccine has a phosphodiester bond, "which is really molecularly bulky and charged. So I would predict that that difference would significantly change antibody binding and recognition." Tr. at 320-21. Later experiments by Dr. Steinman's group found that the mice with anti-mannose 9 antibodies had less severe EAE, pulling against Dr. Steinman's theory and actually suggesting mimicry with the meningococcal vaccine would have a protective effect. *Id.* at 321-22.

In response to questions from Special Master Oler, Dr. Romberg explained that he did not believe the molecular mimicry theory could apply to AFM, but it could apply to TM because TM is an autoimmune disease. Tr. at 335.

4. Rebuttal Testimony

a. *Dr. Steinman*

Dr. Steinman testified on rebuttal that, in his opinion, the data were not "anywhere near settled for understanding whether D68 or D68 and rhinovirus are the causes of AFM." Tr. at 345. On the question of the expected response to immunotherapy in TM, he cited a website from the TM Society reporting that about one-third of patients have "virtually no recovery and are left severely functionally disabled." *Id.* at 351 (referencing Rare Disease Database, *Transverse Myelitis*, NORD RARE DISEASE ADVOCACY (2018) <https://raredisease.org/rare-disease/transverse-myelitis> (Ex. 86) ("NORD")). A study on treatments of TM and AFM, called the CAPTURE study, found 24% of TM patients and 34% of AFM patients had no improvement with corticosteroids, while 15% of TM and 11% of AFM patients were "mostly recovered" after treatment. *Id.* at 355-56 (citing Benjamin Greenberg et al., *Acute flaccid myelitis: long-term outcomes recorded in the CAPTURE study compared with paediatric transverse myelitis*, 3 BJM NEUROL. OPEN 1 (2021) (Ex. C, Tab 12) ("CAPTURE")). Similar results were reported in response to IVIG therapy. *Id.* Thus, R.W.'s lack of improvement with treatment did not rule out a TM diagnosis. *Id.*

Dr. Steinman testified that R.W.'s WakeMed MRI showed inflammation in both the motor and sensory portions of her spinal cord. Tr. at 357. The differential diagnosis of the radiologist included TM, but not AFM. *Id.* at 361. Dr. Steinman would generally defer to the radiologist to interpret imaging like this. *Id.* The Duke MRI showed a longitudinally extensive lesion, which had increased since the last imaging was done, as well as diffuse enhancement of the cauda equina nerve root and "patchy nodular enhancement along the ventral and dorsal aspects of the thoracic cord." *Id.* at 362-63. Again, this showed involvement of both the sensory and motor neurons. *Id.* at 363. The differential included inflammatory myelitis, which Dr. Steinman agreed was correct. *Id.* at 364-65. However, "this case has elements of acute flaccid myelitis. It also has elements that are transverse myelitis." *Id.* at 366.

Special Master Oler asked for Dr. Steinman's interpretation of the notation in the Duke MRI report that there was "no abnormal enhancement of the spinal cord." Tr. at 368-69. He acknowledged that if he saw an TM case with no abnormal enhancement of the spinal cord, he "would really have to scratch [his] head," as he had never seen a TM patient without such enhancement. *Id.* at 369. He pointed out, though, that another portion of the report stated there was increased spinal cord signal at the T3-T4 level, along with mild cord enlargement "concerning for transverse myelitis." *Id.* He admitted that her imaging showed "elements of AFM with this kind of patchy T2 hyperintensities not only in the motor areas but in the dorsal. So there's elements of both, but I think it's certainly inflammatory myelitis, myelitis being a term that connects AFM to TM anyway." *Id.* at 372.

Responding to Special Master Oler, Dr. Steinman opined that the likely reason R.W. did not develop brisk reflexes was because her disease involved inflammation of both the posterior and anterior aspects of the lower spinal cord. Tr. at 381. He had seen that presentation in about 15-20% of his TM cases. *Id.* While R.W. initially had a fever, she did not have respiratory symptoms, which "certainly goes against AFM." *Id.* at 383. She had asymmetric weakness, which can be seen in TM but weighs a bit more toward AFM. *Id.* at 383-84. The complaints of numbness and paresthesia pulled toward TM. *Id.* at 384. The sensory level and bowel and bladder dysfunction "[u]ndeniably" suggested TM. *Id.* Her WBC count remained low for TM, but the true count might have been masked by the early treatment with steroids. *Id.* at 384-85.

Special Master Oler asked Dr. Steinman to comment on R.W.'s pattern of weakness. Tr. at 386. He said that normally, AFM presents with asymmetric weakness. *Id.* at 387. R.W.'s presenting complaint was right leg weakness, but over time she became weak and flaccid on both sides. *Id.* However, "[c]ertainly classically she presents asymmetrically." *Id.* Thus, this was an ambiguous aspect of her condition. *Id.* at 387-88.

On cross, Dr. Steinman maintained that the physicians at Duke could have used the terms "hyperintensity" and "enhancement" interchangeably in describing R.W.'s MRI. Tr. at 395-96. He believed her pattern of weakness was consistent with TM or AFM. *Id.* at 396. The lack of oligoclonal banding did not rule out TM, as it is seen in TM only in about half of cases. *Id.* at 400.

Dr. Steinman testified that AFM could be an autoimmune disease, as stated in the Ayers paper. Tr. at 400 (citing Ayers). You can see fever and inflammatory cells in the CSF. *Id.* at 401.

b. R.W.

R.W. testified that when she lay down for a nap on September 27, 2015, she “started having a little bit of numbness, but nothing extreme. But once I went to the bathroom and when I was coming out of the bathroom, my [right] leg, it felt numb, and I was struggling to walk because I think my leg was just numb. I really couldn’t feel much of it.” Tr. at 405. She was able to walk back to her bed at that time. *Id.* at 406. When she later tried to stand up, her leg buckled. *Id.* When she was first seen by paramedics, she could still feel “something,” including the touch of metal on her foot, but the sensation was reduced. *Id.* at 406-07.

c. Mrs. Williford

Mrs. Williford’s recollection of events was similar to R.W.’s. Tr. at 408. By the time the family left the house to seek medical attention, R.W. could not walk. *Id.* Her parents attempted to put her on the toilet at the hospital to procure a urine sample, but “we couldn’t bend her,” and then she urinated on herself without being able to feel it happening. *Id.* at 409. A nurse attempted to mark the level where R.W. could and could not still feel. *Id.* at 410. By the time R.W. was admitted to WakeMed, the demarcation was at her belly button. *Id.* at 411.

d. Dr. Sweeney

Dr. Sweeney testified that a T2 MRI image cannot show enhancement indicating inflammation of the lower spinal cord. Tr. at 413. He explained that a “T2 hyperintensity” is not synonymous with “enhancement,” which cannot be seen on a T2 sequence MRI. *Id.* at 414. Enhancement is seen by comparing T1 sequences with and without contrast. *Id.* The “T2 hyperintensity” showed a “hyperintensity within the cord itself.” *Id.* This hyperintensity extended from T6 to the distal conus, with “mild expansion, indicating that there is already significant inflammation or swelling within the spinal cord itself.” *Id.* at 414-15. The enhancement pattern on the second WakeMed MRI scan, which was given with and without contrast, was “described as patchy and only at one to two levels. I don’t feel that the extent of her weakness, her flaccid weakness at that point would be explained by involvement of those nerve roots alone.” *Id.* at 415.

Furthermore, R.W.’s very sudden onset of weakness was not consistent with a “neuropathic process.” Tr. at 415. Instead, in his view, it was “the findings within the cord itself, which is the T2 hyperintense signals . . . driving the weakness, the flaccid weakness at that time.” *Id.* He noted that AFM has a range of “hours to days” from onset to nadir, while TM progresses over days to weeks.” *Id.* at 416.

Dr. Sweeney agreed with Dr. Steinman that both AFM and TM can present with asymmetric weakness. Tr. at 417. The lack of facial and bulbar involvement did not point away from AFM, as those symptoms were seen in early-reported cases with cervical cord involvement. *Id.* Numbness/sensory loss can occur in AFM and almost always does so in TM. *Id.* at 418. Both diseases can involve bowel and bladder dysfunction. *Id.* R.W.’s MRI imaging showed far more gray matter than white matter involvement, suggesting AFM. *Id.* at 418-19.

With respect to R.W.'s sensory symptoms, Dr. Sweeney cited medical records documenting that, after her admission to Duke, she had an exam where "[s]he could feel cold on the lateral and medial aspect of the things as well as in the feet and could feel the reflex hammer on the bottom of her feet." Tr. at 421. At discharge, she was noted to have "minimal to no sensation to light touch at [the] L3, L4, L5 and S1" dermatomal distributions. *Id.* Other exam notes indicated she had some degree of sensation. *Id.* at 421-22. However, Dr. Sweeney acknowledged that "right around her lower abdomen there is what could be referred to as a sensory level." *Id.* at 422. He found it anomalous that she had such a low sensory level when her scans showed signal abnormality all the way up to the T3 level. *Id.* at 422-23.

Concerning the causes of AFM, Dr. Sweeney stated that "we are so much further along in understanding how enterovirus D68 causes acute flaccid myelitis than anyone could be in describing how a potential autoimmune or molecular mimic pattern could cause acute flaccid myelitis." Tr. at 425. Both human epidemiology and animal models support D68 causation. *Id.* at 425-26.

Commenting on the CAPTURE study, Dr. Sweeney testified that the study classified patients as those with predominantly white matter involvement (TM) and those with predominantly gray matter involvement (AFM). Tr. at 429 (citing CAPTURE). The study showed that pediatric AFM was as prevalent, if not more prevalent, than TM for the timeframe reviewed. *Id.* Furthermore, 30% of the AFM patients in the study had sensory symptoms and 38% had bowel or bladder symptoms at onset. *Id.* at 430. Twenty-eight percent of AFM patients had "mixed" involvement of both gray and white matter. *Id.* Thus, although R.W. likely had some white matter involvement, that did not point away from AFM. *Id.* The authors commented that the "epidemiologic and animal model data both support the theory that AFM is the result of a viral infection causing the death of the anterior motor neurons." *Id.* at 431. D68 likely causes the majority of cases. *Id.* In "mixed" AFM patients with both white and gray matter involvement, "the vast majority" had no or minimal improvement with steroid or IVIG treatment. *Id.* at 432.

In response to Special Master Oler, Dr. Sweeney opined that AFM is not currently believed to be an autoimmune condition. Tr. at 438. It has a non-relapsing course, which is atypical for autoimmune conditions. *Id.* It does not respond well to immunotherapy. *Id.* at 438-39. "So all of those point against an autoimmune process." *Id.*

C. Post-Hearing Neuroradiology Expert Reports

1. Petitioners' Expert: David Wilson, M.D., Ph.D.

After the hearing, Petitioners filed an expert report from Dr. David Wilson. Ex. 88 ("Wilson Rep."). Dr. Wilson is a professor of radiology and biomedical imaging at the University of California, San Francisco ("UCSF"). *Id.* at 1. He earned his M.D. and Ph.D. at Columbia University and completed his residency and a fellowship in neuroradiology at UCSF. *Id.*; Ex. 89 ("Wilson CV") at 1. He is board certified by the American Board of Radiology in both general radiology and neuroradiology, and he served as the Chief of Neuroradiology at San Francisco's VA hospital. Wilson Rep. at 1. He is active in several radiology societies and has held committee roles in them. *Id.* He has published more than 60 peer-reviewed articles with an emphasis on

molecular imaging. *Id.* He has interpreted more than 3,000 images of known or suspected demyelinating and/or autoimmune injuries. *Id.* at 1-2.

Dr. Wilson reviewed a series of six of R.W.'s MRIs, from both WakeMed and Duke, with reference to a review article by Helfferich, which set forth the MRI findings typically seen in a case of AFM. Wilson Rep. at 2 (referencing Jelte Helfferich et al., *Acute flaccid myelitis and enterovirus D68: lessons from the past and present*, 178 EUR. J. OF PEDIATRICS 1305 (2019) (Ex. 90) ("Helfferich")). According to that paper,

In AFM, the classical MRI feature is a longitudinally extensive slight T2-hyperintense signal in the central cord, affecting the central gray matter, often most pronounced in the cervical regions. Initially, there is usually more diffuse spinal cord edema, evolving over several days to T2-hyperintensity that is restricted to the anterior horn. Enhancement of the caudal roots and sometimes of the cranial nerves can be seen. MRI of the brain commonly reveals an area of slight hyperintensity typically located in the dorsal pons in the region of the nuclei of the abducens and facial nerve. The corticospinal tracts, located ventrally, are not affected, while the caudate nucleus may be involved. These findings may help in securing the diagnosis, but the correlation between symptoms and radiologic findings is usually poor, making MRI unsuitable as a prognostic tool for AFM.

Id. at 2-3.

Dr. Wilson did not observe any evolution of the signal localization in R.W.'s MRIs to hyperintensities limited to the anterior horn, though the variable quality of the MRIs made comparison challenging. Wilson Rep. at 3. He stated:

Overall, all studies show a process of the distal thoracic cord (including the end or 'terminus' of the cord at T12-L1 also called the 'conus medullaris' or just 'conus') and more distally the cauda equina nerve roots. This process spans at least 5 vertebral body segments and involves the conus, with clear cord expansion (increased volume) and somewhat patchy/diffuse T2 signal abnormality.

Id. He interpreted the studies as showing "equivocal" enhancement of the cord itself, which he did not believe was relevant to the differential diagnosis. *Id.* He did observe clear enhancement of the ventral cauda equina nerve roots. *Id.* Overall, he agreed with the observations made by the Duke radiologists. *Id.*

Below are the images referenced in Dr. Wilson's report, with his comments:⁷

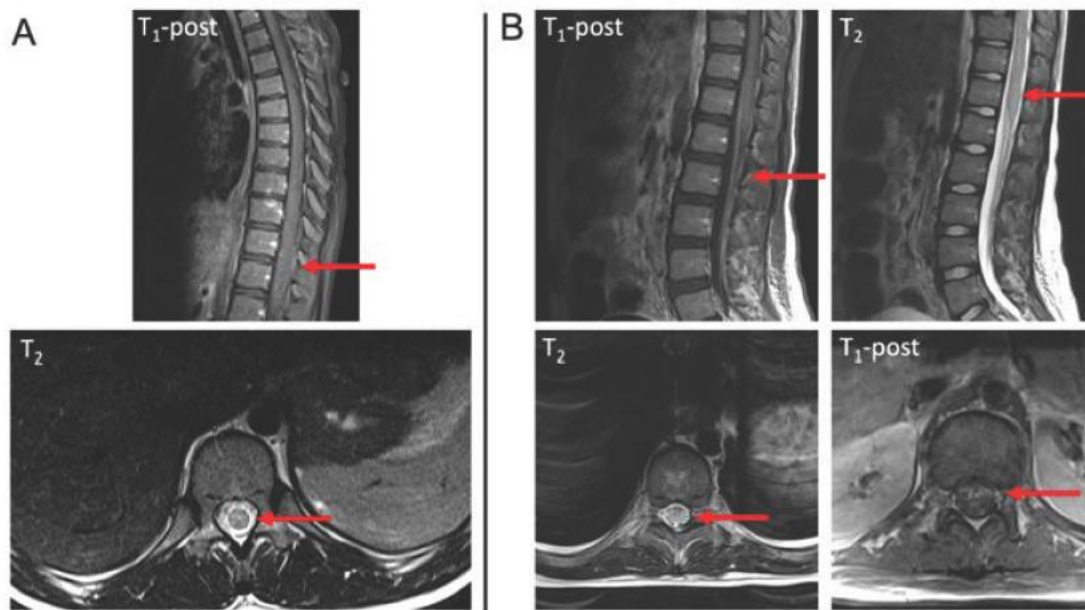


Figure 1. [REDACTED] MRI studies. (A) shows images from WakeMed MRI's and (B) shows images from Duke MRI's. There is some apparent worsening between the two imaging time points, but no change in the differential considerations. T₂-weighted images show "hyperintensity" with cord expansion that is more apparent on the Duke images. T₁-post weighted images show some signal heterogeneity of the distal cord (may reflect subtle enhancement) with images through the cauda equina showing diffuse, smooth ventral nerve root enhancement.

Wilson Rep. at 4.

Dr. Wilson explained the difference between "hyperintensity" and "enhancement." Wilson Rep. at 4. "Hyperintensity" within the spinal cord refers to bright signal on T₂-weighted imaging. *Id.* "Many spinal diseases (demyelinating, infectious/inflammatory, post-traumatic, degenerative, vascular, neoplastic) have associated hyperintensities in the cord[.]" *Id.* Hyperintensity will persist over time. *Id.* "Enhancement" refers to the breakdown of the blood-spine barrier, with "associated bright signal on T₁-weighted sequences." *Id.* Enhancement generally signifies an acute or subacute process, and it will abate over time and with treatment. *Id.* "Enhancement of the cord itself can be variable especially in likely infectious/inflammatory or autoimmune cases like [R.W.'s]." *Id.*

Dr. Wilson observed that

[t]he presence of cauda equina enhancement is useful, to the extent that expert neuroradiologists and published reports can agree on its relevance. When we see the type of cauda equina enhancement in

⁷ The MRI images from Dr. Wilson's and Dr. Zucconi's expert reports have been redacted to remove R.W.'s identifying information.

[R.W.'s] case we almost always invoke [GBS] which like most possible diseases in her case is considered [autoimmune].

Wilson Rep. at 4. With respect to AFM, “[t]he overall central nervous system findings include brainstem and cranial nerve abnormalities, long-segment spinal involvement, non-existent or slight cord enhancement, and in some cases cauda equina enhancement (in many cases, according to the Okumura et al. study).” *Id.* at 5 (citing Akihisa Okumura et al., *Serial MRI findings of acute flaccid myelitis during an outbreak of enterovirus D68 infection in Japan*, 41 *BRAIN & DEV.* 443 (2019) (Exs. 95, G) (“Okumura”)). Cauda equina enhancement is not typical of TM, though it can occur. *Id.*

To investigate the MRI findings in R.W. further, Dr. Wilson searched the mPower database for cases at UCSF using the descriptors “flaccid” with either “acute” or “myelitis,” finding 20 cases of suspected AFM. Wilson Rep. at 5. None of these cases reported cauda equina enhancement. *Id.* He concluded that R.W.’s MRIs were distinct from the AFM cases reported in the literature and UCSF database, because there was no involvement of her brainstem, the abnormalities extended to gray and white matter, the cord abnormalities were “patchy,” and the most distinctive abnormalities were in the distal thoracic cord and conus. *Id.* at 6.

Dr. Wilson felt other diseases should be included on R.W.’s differential, including TM and GBS. Wilson Rep. at 5. The MRIs most likely indicated an autoimmune process, though no diagnosis could definitively be assigned. *Id.* The cord enhancement in her case was “equivocal” and did not suggest a specific diagnosis. *Id.* The cauda equina enhancement observed in R.W. has also been reported with AFM but was more consistent with GBS, in Dr. Wilson’s view. *Id.*

2. Respondent’s Expert: William Zucconi, D.O.

After the hearing, Respondent filed an expert report from Dr. William Zucconi. Ex. D (“Zucconi Rep”). Dr. Zucconi earned his D.O. from the New York College of Osteopathic Medicine in 2001, is a board-certified radiologist with a certificate in neuroradiology, and is a professor at Dartmouth’s Geisel School of Medicine. Zucconi Rep. at 1; Ex. E (“Zucconi CV”) at 1. He previously served as an associate professor of radiology and biomedical imaging at Yale School of Medicine and was the Neuroradiology Section Chief and Fellowship Director at Yale. *Id.* Over the past five years, Dr. Zucconi has cared for numerous patients with myelopathies, including dozens with TM. Zucconi Rep. at 1. He has treated two patients with AFM and has considered that diagnosis in other cases. *Id.*

On R.W.’s MRI imaging, Dr. Zucconi commented:

The [first set of] MRIs performed on 9/28/15 demonstrate abnormal T2 signal hyperintensity within the central gray matter of the spinal cord, with anterior horn predominance. The anterior grey matter involvement is most notable in the mid thoracic segments (along the upper aspect of the abnormality). The cord involvement spans T6 through the inferior aspect of the cord (the conus medullaris). The

signal abnormality in the lower portion of the cord is also confined to the central gray matter.

Zuconci Rep. at 2. The repeat thoracic and lumbar MRIs, taken 13 hours later with and without contrast, showed a similar disease pattern, with equivocal enhancement of the ventral nerve roots of the cauda equina. *Id.* That report concluded the cord abnormality had progressed, involving levels T6-12. *Id.* It also noted possible enhancement of the ventral cord at T11-12, which Dr. Zuconci interpreted to refer to the anterior nerve roots. *Id.*

Below are Dr. Zuconci's annotated copies of images from R.W.'s September 28, 2015 MRIs:



Figure 1, axial and sagittal T2 weighted images from 9/28/15 MRIs. **A:** axial image through an unaffected area of the cord, at T5, corresponding to the level of the green arrow on C and D. **B:** Abnormal signal hyperintensity within the anterior grey matter of the spinal cord at T7 level (yellow arrows on C and D). **C & D:** Abnormal signal is confined to the central cord, with an anterior distribution superiorly, and more diffuse central pattern inferiorly (orange arrow).

Zuconci Rep. at 3.

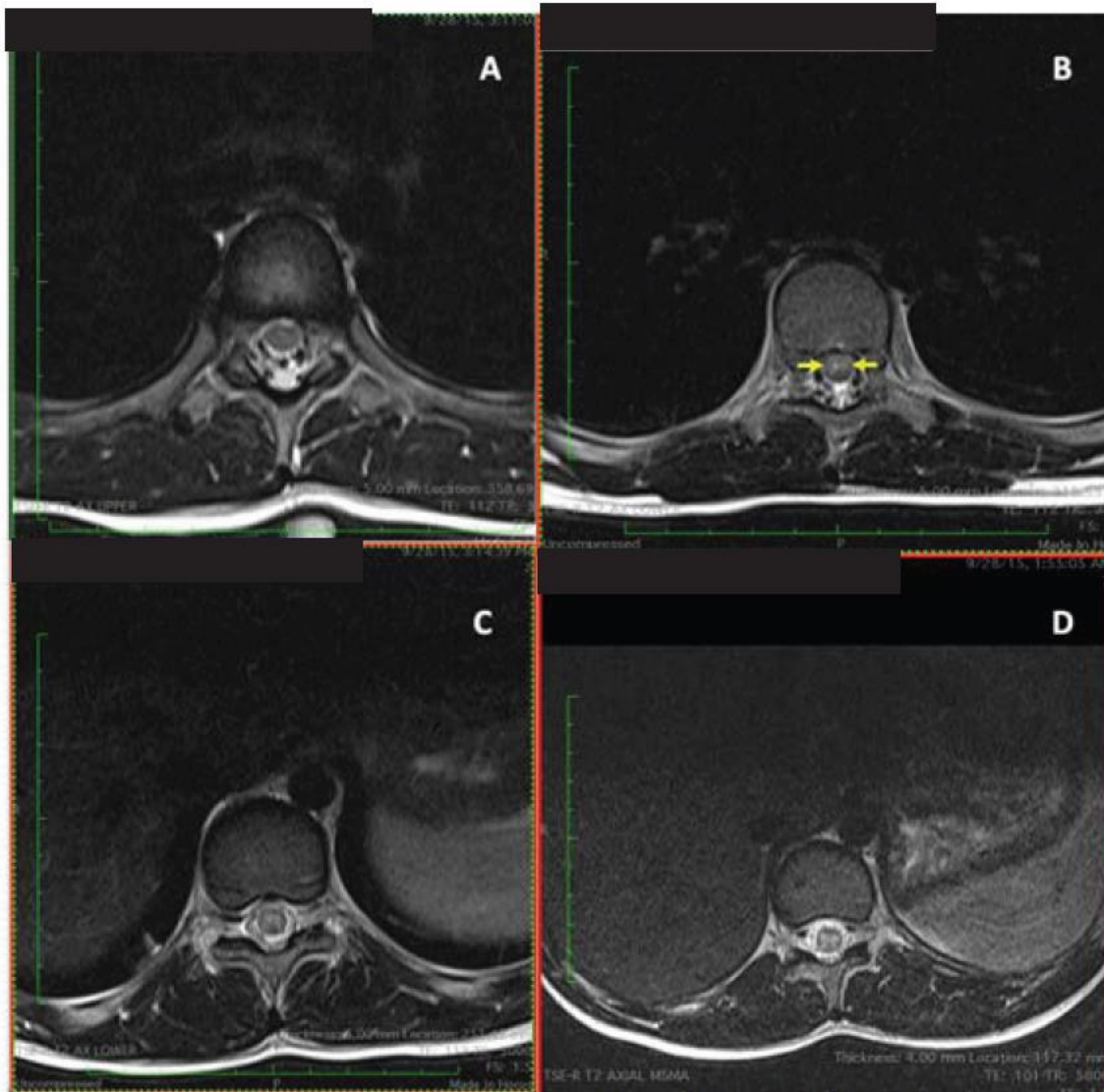


Figure 2, axial T2 weighted images of the spinal cord, 9/28/15. **A:** normal level for comparison. **B:** Lesion confined to the anterior gray matter (yellow arrows). **C and D:** Lower levels showing more diffuse abnormal signal confined to distribution of the central gray matter.

Zucconi Rep. at 4.

Dr. Zucconi noted that R.W.'s October 16, 2015 MRIs were performed with and without contrast and showed that the "T2 signal changes [remained] confined to the central cord" but had lengthened and become more diffuse. Zucconi Rep. at 4. He opined that the contrast enhanced images showed "prominent enhancement of the central gray matter, with anterior predominance, and conspicuous abnormal enhancement of the cauda equina, confined to the anterior roots." *Id.* In his view, the notation in the report that there was "patchy nodular enhancement along the ventral and dorsal aspects of the thoracic cord," which had not previously been observed, meant there was "enhancement in the ventral nerve roots, and dorsal horns of the central grey matter." *Id.* at 4-5.

Dr. Zucconi's annotated copy of the October 16, 2015 MRI is below:

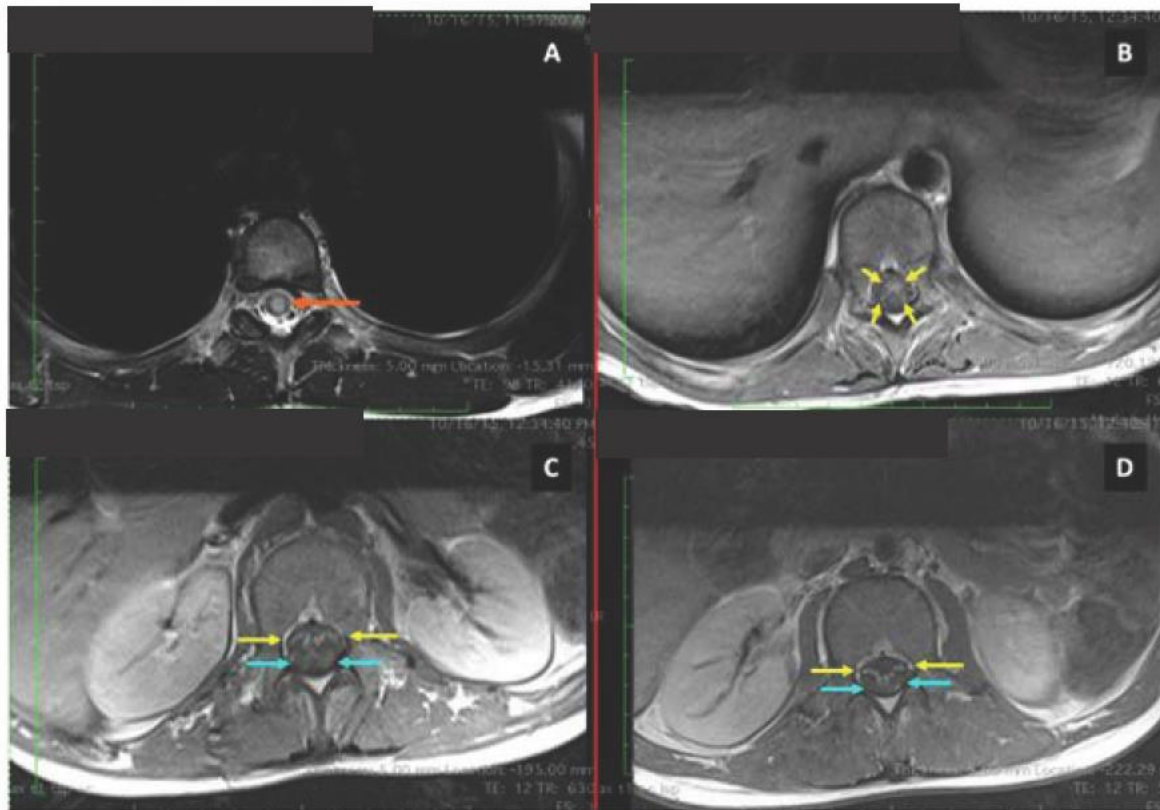


Figure 3, MRI of 10/16/15. A: Axial T2 shows more diffuse central signal abnormality. B: Central grey matter pattern of enhancement (yellow arrows). C & D: Exclusive ventral nerve root enhancement (yellow arrows). Dorsal nerve roots (blue arrows) are non-enhancing.

Zucconi Rep. at 5.

Dr. Zucconi disagreed with Dr. Wilson's conclusion that R.W.'s MRIs were atypical of AFM. Zucconi Rep. at 5. First, although there were no abnormalities observed in R.W.'s brainstem, the literature only documents brainstem lesions in AFM cases affecting the cervical spine, which did not apply here. *Id.* (citing Okumura). The thoracolumbar pattern of involvement seen in R.W.'s case was a common alternative presentation. *Id.* at 5-6.

Second, "[t]he case definition for AFM is not limited to cases with only gray matter involvement." Zucconi Rep. at 6. AFM includes cases with gray matter predominance, which was seen here. *Id.* Dr. Zucconi did acknowledge R.W.'s case differed from those documented in Okumura in that her T2 signal hyperintensity became more diffuse between the first and second scans, "rather than becoming more discrete or localized to the anterior gray matter." *Id.* However, "[n]otably the enhancing disease seen on later exam is confined to the central gray matter and anterior horns." *Id.*

Third, the Tartaglino paper cited by Dr. Wilson "pre-dated the 2002 work of the Transverse Myelitis Consortium Working Group, and the many developments that have since narrowed the definitions of IATM (Idiopathic Acute Transverse Myelitis)." Zucconi Rep. at 6 (citing Lisa M.

Tartaglino et al., *Idiopathic Acute Transverse Myelitis: MR Imaging Findings*, 201 RADIOLOGY 661 (1996) (Exs. H, 96) (“Tartaglino”).

Fourth, the combination of nerve root enhancement and gray matter lesions in the spinal cord is “exceedingly rare” in GBS, a “very unusual” feature of TM, but a common feature of AFM. Zucconi Rep. at 6 (citing Charidimos Tsagkas et al., *Acute Polyradiculomyelitis with Spinal Cord Gray Matter Lesions: A Report of Two Cases*, 12 FRONTIERS IN NEUROLOGY 1 (2021) (Ex. I) (“Tsagkas”); Okumura).

Dr. Zucconi opined that R.W. met the CDC diagnostic criteria for AFM, including the MRI finding of a “spinal cord lesion largely restricted to gray matter and spanning 1 or more spinal segments with or without ventral nerve root enhancement.” Zucconi Rep. at 6 (citing Eliza Gordon-Lipkin et al., *Comparative quantitative clinical, neuroimaging, and functional profiles in children with acute flaccid myelitis at acute and convalescent stages of disease*, 61 DEV. MED. CHILD NEUROLOGY 366 (2019) (Ex. J) (“Gordon-Lipkin”); Benjamin Greenberg et al., *Acute flaccid myelitis*, UPTODATE (last updated June 28, 2022) (Ex. K) (“Greenberg 2022”). T2 signal hyperintensity in the spinal cord gray matter, as was seen in R.W., is “the hallmark of AFM.” *Id.* (citing Olwen C. Murphy et al., *Acute flaccid myelitis: cause, diagnosis, and management*, 397 LANCET 334 (2021) (Exs. C, Tab 11 & L) (“Murphy”). Further, the delayed ventral nerve root enhancement is a well-documented sign of AFM but is very unusual in TM. *Id.* (citing Okumura). He concluded: “The imaging features of RWs case are highly suggestive of, and more likely to reflect a virally mediated AFM given the striking central gray matter involvement and accompanying characteristic anterior horn and ventral nerve root involvement.” *Id.* at 7.

IV. APPLICABLE LAW

A. Petitioner’s Burden in Vaccine Program Cases

Under the Vaccine Act, a petitioner may prevail in one of two ways. First, he may show that he suffered a Table injury within the time provided in the Table. § 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 in the Table, he may demonstrate that he suffered an “off-Table” injury that was caused-in-fact by his vaccination. § 11(c)(1)(C)(ii).

For both Table and non-Table claims, Vaccine Program petitioners bear a “preponderance of the evidence” burden of proof. § 13(a)(1). That is, a petitioner must offer evidence that leads the “trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact’s existence.” *Moberly v. Sec’y of Health & Hum. Servs.*, 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010); *see also* *Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). The petitioner must demonstrate that the vaccine was “not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury.” *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec’y of Health & Hum. Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999)); *Pafford v. Sec’y of Health & Hum. Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his

assertions; rather, the petition must be supported by either medical records or the opinion of a competent physician. § 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Secretary of Health and Human Services*. 418 F.3d 1274 (Fed. Cir. 2005). *Althen* requires a petitioner to establish by preponderant evidence that the vaccination caused his injury “by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury.” *Id.* at 1278.

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, a petitioner must provide a “reputable medical theory” demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citations omitted). To satisfy this prong, a petitioner’s theory must be based on a “sound and reliable medical or scientific explanation.” *Knudsen v. Sec’y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994) (citations omitted). Such a theory must only be “legally probable, not medically or scientifically certain.” *Id.* at 548-49; *Bunting v. Sec’y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991).

A petitioner may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec’y of Health & Hum. Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). Despite their expertise, special masters are not empowered by statute to conclusively resolve what are complex scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed “not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act’s preponderant evidence standard.” *Id.* at 1380. However, this does not negate or reduce a petitioner’s ultimate burden to establish his entitlement to compensation by preponderant evidence. *W.C. v. Sec’y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner’s medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326 (stating that “medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a ‘logical sequence of cause and effect show[s] that the vaccination was the reason for the injury’”) (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence because they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec’y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). However, the existence of medical records and/or statements of treating physician views does not require the special master to adopt their conclusions *per se*. § 13(b)(1) (providing that “[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court”); *Snyder v. Sec’y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 746 n.67 (2009) (“[T]here is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted.”). As with expert

testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence in the record—including conflicting opinions among such individuals. *Hibbard v. Sec’y of Health & Hum. Servs.*, 100 Fed. Cl. 742, 749 (2011) (it was not arbitrary or capricious for special master to weigh competing treating physicians’ conclusions against each other), *aff’d*, 698 F.3d 1355 (Fed. Cir. 2012); *Caves v. Sec’y of Health & Hum. Servs.*, No. 06-522V 2011 WL 1935813, *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den’d*, 100 Fed. Cl. 344, 356 (2011), *aff’d without opinion*, 475 Fed. App’x 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a “proximate temporal relationship” between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase “medically acceptable temporal relationship.” *Id.* Thus, a petitioner must offer “preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder’s etiology, it is medically acceptable to infer causation.” *de Bazan v. Sec’y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also be consistent with the theory for how the relevant vaccine can cause the alleged injury (*Althen* prong one’s requirement). *Id.* at 1352; *Shapiro v. Sec’y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand on other grounds*, 105 Fed. Cl. 353 (2012), *aff’d without op.*, 503 F. App’x 952 (Fed. Cir. 2013); *Koehn v. Sec’y of Health & Hum. Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *aff’d*, 773 F.3d 1239 (Fed. Cir. 2014).

B. Law Governing Analysis of Fact Evidence

The process for making factual determinations in Vaccine Program cases begins with analyzing the medical records, which are required to be filed with the petition. §11(c)(2). The special master is required to consider “all [] relevant medical and scientific evidence contained in the record,” including “any diagnosis, conclusion, medical judgment, or autopsy or coroner’s report which is contained in the record regarding the nature, causation, and aggravation of the petitioner’s illness, disability, injury, condition, or death,” as well as the “results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions.” §13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec’y of Health & Hum. Servs.*, 3 F. 3d 415, 417 (Fed. Cir. 1993) (it is within the special master’s discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given later, provided that such determination is based on a rational analysis).

Medical records created contemporaneously with the events they describe are generally trustworthy, because they “contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions,” where “accuracy has an extra premium.” *Kirby v. Sec’y of Health & Hum. Servs.*, 997 F.3d 1378, 1382 (Fed. Cir. 2021) (quoting *Cucuras*, 993 F.2d at 1528). Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *See generally Lowrie v. Sec’y of Health & Hum. Servs.*, No. 03-1585V, 2005 WL 6117475 at *19 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed,

contemporaneous medical records are often found to be deserving of greater evidentiary weight than oral testimony, especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also* *Murphy v. Sec’y of Health & Hum. Servs.*, 23 Cl. Ct. 726, 733 (1991), *aff’d per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den’d*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 396 (1947) (“[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.”)).

However, there are situations in which compelling oral testimony could be more persuasive than written medical records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec’y of Health & Hum. Servs.*, 69 Fed. Cl. 775, 779 (2006) (“[L]ike any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking.”); *Lowrie*, 2005 WL 6117475, at *19 (“Written records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent.”) (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, the special master should assess each witness’s credibility when determining the weight their testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec’y of Health & Hum. Servs.*, 991 F.2d 1570, 1575 (Fed. Cir. 1993).

In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person’s failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional’s failure to document everything reported to her or him; (3) a person’s faulty recollection of the events when presenting testimony; or (4) a person’s purposeful recounting of symptoms that did not exist. *LaLonde v. Sec’y of Health & Hum. Servs.*, 110 Fed. Cl. 184, 203-04 (2013), *aff’d*, 746 F.3d 1334 (Fed. Cir. 2014). In deciding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony, a rational analysis must be explicated. *Burns*, 3 F.3d at 417.

C. Analysis of 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). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594-96 (1993). *See Cedillo v. Sec’y of Health & 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)). “The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the

theory or technique enjoys general acceptance within a relevant scientific community.” *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592-95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do in other federal judicial proceedings. Those factors are employed by judges to exclude evidence that is unreliable and potentially confusing to a jury. In Vaccine Program cases, these factors are generally used to assess the reliability and weight of scientific evidence. *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[.]”). The flexible use of the *Daubert* factors to evaluate persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g., Snyder*, 88 Fed. Cl. at 743.

Respondent frequently offers one or more experts of his own to rebut a petitioner’s case. Where both sides offer expert testimony, a special master’s decision may be “based on the credibility of the experts and the relative persuasiveness of their competing theories.” *Broekelschen v. Sec’y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). Nothing requires the acceptance of an expert’s conclusion “connected to existing data only by the *ipse dixit* of the expert,” especially if “there is simply too great an analytical gap between the data and the opinion/ proffered.” *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)). 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. Weighing the relative persuasiveness of competing expert testimony, based on a particular expert’s credibility, is part of the overall reliability analysis special masters must employ in Vaccine Program cases. *Id.* at 1325-26 (“[a]ssessments as to the reliability of expert testimony often turn on credibility determinations”); *see also Porter v. Sec’y of Health & Hum. Servs.*, 663 F.3d 1242, 1250 (Fed. Cir. 2011) (“[T]his court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act”).

D. Consideration of Medical Literature

Finally, although this decision discusses some but not all the medical literature in detail, I have reviewed and considered all the medical records and literature submitted in this matter. *See 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).

V. ANALYSIS

The parties dispute both the relevant diagnosis and whether R.W.’s condition was vaccine caused. Mr. and Mrs. Williford contend R.W. suffered from TM and related sequela caused by her September 11, 2015 Tdap and meningococcal vaccinations. *Pets.’ Post-Hearing Br.* at 11.

Respondent argues that R.W. developed AFM, which was likely virally mediated and not caused by the subject vaccinations. Resp.’s Post-Hearing Br. at 24.

A. Diagnosis

As a threshold matter, a petitioner must establish that he suffered the injury for which he seeks compensation. *Broekelschen*, 618 F.3d at 1346. “[T]he function of a special master is not to ‘diagnose’ vaccine-related injuries, but instead to determine ‘based on the record as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the [petitioner]’s injury.’” *Andreu*, 569 F.3d at 1382 (quoting *Knudsen*, 35 F.3d at 549). “Although the Vaccine Act does not require absolute precision, it does require the petitioner to establish an injury – the Act specifically creates a claim for compensation for ‘vaccine-related injury or death.’” *Stillwell v. Sec’y of Health & Hum. Servs.*, 118 Fed. Cl. 47, 56 (2014) (quoting 42.U.S.C. § 300aa-11(c)). Accordingly, the Federal Circuit has concluded that it is “appropriate for the special master to first determine what injury, if any, [is] supported by the evidence presented in the record” before applying a causation analysis pursuant to *Althen*. *Lombardi v. Sec’y of Health & Hum. Servs.*, 656 F.3d 1343, 1351-53 (Fed. Cir. 2011).

Petitioners argue that they do not have the burden to prove a specific injury, only that the subject vaccine(s) caused *an* injury. Pets.’ Post-Hearing Br. at 11. That is not in accordance with the Act, which “places the burden on the petitioner to make a showing of at least one defined and recognized injury.” *Lombardi*, 656 F.3d at 1353. This is a prerequisite to the causation analysis: in *Lombardi*, the Federal Circuit affirmed the special master’s decision that, because the petitioner had failed to prove she sustained any of the injuries alleged, there was no need to evaluate causation under *Althen*. *Id.*

Here, there are two diagnoses advanced: TM and AFM. Because the nature of R.W.’s injury itself is in dispute, I am charged with determining which injury is better supported by the record before turning to an *Althen* analysis. *Lombardi*, 656 F.3d at 1353.

1. Transverse Myelitis

TM is a rare syndrome involving “an immune-mediated process [that] causes neural injury to the spinal cord,” resulting in “varying degrees of weakness, sensory alterations and autonomic dysfunction.” Agmon-Levin at 1198; *see* Tr. at 84 (Dr. Steinman’s testimony). “The term *myelitis* refers to inflammation of the spinal cord; *transverse* refers to the pattern of changes in sensation.” NIH at 1 (emphases in original).

The symptoms of TM often include “pain, sensory problems, weakness in the legs and possibly the arms, and bladder and bowel problems.” NIH at 1. “A peak in incidence rates (the number of new cases per year) appears to occur between 10 and 19 years and 30 and 39 years.” *Id.* at 2.

Pediatric TM is a diagnosis of exclusion. Absoud at S47. It is important to differentiate TM from “other, rarer presentations of noncompressive myelopathy,” including those caused by infectious agents. *Id.* at S46-S47. “Multiple etiologies for myelitis can result in a similar clinical

presentation, including idiopathic transverse myelitis (TM), multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD) associated with anti-aquaporin 4 antibodies, MOG antibody-associated disease, and acute flaccid myelitis (AFM).” Wang & Greenberg at 1; *see also* F.S. Pidcock et al., *Acute transverse myelitis in childhood*, 68 NEUROLOGY 1474 (2007) (Exs. 18, 61) (“Pidcock”) (“The diagnosis requires both the presence of spinal cord inflammation, as defined by CSF pleocytosis, elevated CSF IgG index, or gadolinium enhancement on a spinal MRI, and the absence of an identified CNS infection. The diagnosis also requires exclusion of acute myelopathy secondary to a known underlying disease and from compressive myelopathies.”).

Dr. Wilson submitted the 2019 Helfferich paper, which set forth common signs, symptoms, results, and imaging findings in acute TM, AFM, and GBS. Helfferich at 1310 (Table 2). TM commonly is preceded by a febrile illness, with onset of weakness of days to weeks thereafter. *Id.* It usually involves symmetric weakness, which “may be asymmetric initially,” along with brisk reflexes, which “can be low initially.” *Id.* Sensory symptoms are common, “often with a sensory level.” *Id.* It does not involve cranial nerve deficits but commonly includes bowel and bladder dysfunction. *Id.* The course generally progresses over a period ranging from four hours to 21 days. *Id.* CSF findings will include “[s]light pleocytosis, raised protein, [but may] be completely normal.” *Id.*

In TM, the MRI of the spine will show a “[c]entral cord focal hyperintense lesion over multiple levels affecting white and gray matter.” Helfferich at 1310 (Table 2). Treatment of TM includes high-dose steroids, IVIG and/or PLEX, with partial recovery expected “over the course of months until years.” *Id.*

Another paper by Messacar (2016), submitted by Dr. Romberg, similarly compared the features of TM, AFM, GBS, and ADEM. Messacar at 17-18 (Tables 3 and 4). According to Messacar, idiopathic TM commonly is preceded by a prodrome of respiratory, gastrointestinal, or another systemic illness. *Id.* at 17 (Table 3). At onset, symptoms include dysesthesia and paresthesia, along with back pain. *Id.* Progression of symptoms proceeds over hours to days. *Id.* Weakness can be symmetric or asymmetric but is typically bilateral, below the level of the lesion. *Id.* Muscle tone is usually flaccid in the acute phase but later becomes spastic. *Id.* Reflexes can be decreased in the acute phase, then will be increased. *Id.* A sensory level is common, as are bowel and bladder dysfunction. *Id.* Cranial nerve deficits are uncommon. *Id.*

According to Messacar, in TM, the CSF will show pleocytosis in half of patients and elevated protein. Messacar at 18 (Table 4); *see also* Pidcock at 1476. On MRI, an enhancing, “often contiguous lesion involving multiple levels of the spinal cord” will be seen, involving the gray and white matter and accompanied by “associated edema.” Messacar at 18 (Table 4). Treatment of TM will produce a response to high-dose IV steroids, with IVIG and PLEX used as second-line therapies. *Id.* The prognosis is for “[p]artial recovery in most over months to years,” with some degree of residual disability expected in most cases. *Id.*

2. Acute Flaccid Myelitis

AFM is “a disabling, polio-like illness mainly affecting children.” Murphy at 334. The diagnosis is fairly recent. According to the 2021 Murphy paper, AFM was identified as a unique

form of myelitis after unusual clusters of a polio-like disease were seen in California in 2012 and Colorado in 2014. *Id.* AFM is now recognized globally, with “hundreds of cases reported across Europe, Asia, Australia, Africa, North America, and South America.” *Id.* “Epidemic enteroviral infection is believed to be the main driver of AFM in recent years, particularly enterovirus D68 infection.” *Id.*; *see also* Fatemi at 875 (Mayo Clinic paper reporting that epidemiology supports a temporal association between respiratory enteroviral illness, particularly with enteroviruses D68 and A71, and clustering of AFM cases, but causality has not been established); Aliabadi at 1 (studying 2014 cluster of cases in Colorado; of the 11 patients studied, four tested positive for D68 and three tested positive for a “variety of rhinoviruses”; the authors reported a statistically significant association between D68 and AFM but not with other enterovirus/rhinovirus subspecies).

The Messacar paper reported that AFM is commonly preceded by a “[f]ebrile respiratory or gastrointestinal illness,” with onset of symptoms occurring a median of seven days after the illness. Messacar at 17 (Table 3). At the time of onset, the patient will typically have fever, meningeal signs, and limb, back, and/or neck pain. *Id.* The progression of motor deficits occurs within hours to days. *Id.* Dr. Sweeney testified that pain will often be the “heralding sign” of weakness, and the onset of weakness will be markedly abrupt and rapid. Tr. at 196.

The distribution of weakness in AFM is often asymmetric, with upper limbs more often affected than lower limbs. Messacar at 17 (Table 3). Muscle tone remains flaccid in AFM, and deep tendon reflexes are decreased or absent. *Id.*; Tr. at 196. The persistence of absent/reduced reflexes and low muscle tone distinguishes AFM from TM, in which reflexes will become brisk and spasticity will develop. Tr. at 198-99.

Sensory deficits in AFM can be “variably present in [the] affected limb.” Messacar at 17 (Table 3). Like TM, bowel and bladder dysfunction are possible. *Id.* Cranial nerve deficits are common. *Id.* CSF generally reveals mild pleocytosis and normal to mildly elevated protein levels. *Id.* at 18 (Table 4). Imaging generally shows “[c]onfluent, longitudinally extensive, nonenhancing lesions in gray matter of spinal cord; cranial nerve motor nuclei lesions in brainstem; nerve root enhancement later in course.” *Id.* Most patients do not respond to treatment with IVIG, PLEX, or steroids, and residual weakness and muscle atrophy in affected limbs is expected. *Id.*

Helffferich reported similar characteristics of AFM, specifically cases associated with D68. There is typically a prodromal illness, with onset of weakness thereafter usually within one week. Helffferich at 1310 (Table 2). Weakness is generally asymmetric and affects upper limbs more prominently, with weakness occurring more proximally than distally. *Id.* Reflexes are usually reduced or absent, and sensory deficits are typically not seen. *Id.* Cranial nerve deficits are common, including bulbar weakness and asymmetric facial palsy. *Id.* Weakness will progress over hours to days. *Id.* CSF will often reveal slight pleocytosis and mildly elevated protein but may be normal. *Id.*

Spinal MRI of an AFM patient will be characterized by a “[l]ongitudinally extensive diffuse slightly hyperintense central cord lesion, usually most pronounced in the cervical region,” and sometimes cauda equina root enhancement. Helffferich at 1310 (Table 2). Brain MRI often shows a T2 hyperintense region in the dorsal pons, sometimes in the caudate nuclei, as well as

possible cranial nerve enhancement. *Id.* There is no effective treatment for AFM, though IVIG might have a “positive effect.” *Id.* The patient is likely to have significant residual weakness and muscle atrophy. *Id.*

AFM is classified as “definite,” “probable,” “possible,” or “uncertain,” depending on which features are present. Murphy at 339 (Fig. 2); *see also* Fatemi at 876 (“The case definition of confirmed AFM from the CDC since 2014 includes acute flaccid weakness of one or more limbs in individuals of any age and magnetic resonance imaging (MRI) showing a spinal cord lesion largely restricted to gray matter secondary to anterior myelitis (anterior horn cell/spinal cord involvement) and spanning one or more spinal segments.”).

3. R.W.’s case was more consistent with AFM than TM.

There is substantial overlap among the symptoms and signs of AFM and idiopathic TM, as described in the literature and as acknowledged by both parties’ experts. This can make distinguishing between these conditions challenging, a fact that is highlighted by the extensive workup and numerous consultations R.W. underwent. Although R.W.’s case had some ambiguities, the overall record preponderantly favors AFM over TM. The most important factors underlying this conclusion, taken collectively, are (1) her imaging; (2) her acute onset, the pain she had at onset, and the quick progression of her symptoms; (3) the persistent absence of reflexes and low muscle tone in her affected limbs; (4) her failure to meaningfully respond to any type of immunotherapy; (5) her positive test for rhinovirus A69; and (6) the opinions of her treating physicians at Duke, who had the benefit of a comprehensive set of images and test results and a relatively complete view of her clinical course.

a. Imaging

Both Dr. Wilson and Dr. Zucconi were well qualified to opine on the characteristics of R.W.’s neuroimaging. Dr. Wilson commented:

In AFM, the classical MRI feature is a longitudinally extensive slight T2-hyperintense signal in the central cord, affecting the central gray matter, often most pronounced in the cervical regions. Initially, there is usually more diffuse spinal cord edema, evolving over several days to T2-hyperintensity that is restricted to the anterior horn. Enhancement of the caudal roots and sometimes of the cranial nerves can be seen.

Wilson Rep. at 2-3 (quoting Helfferich). Dr. Wilson opined that instead of showing a lesion of the central cord in the cervical region, R.W.’s images showed a process of the distal thoracic cord, including the conus medullaris, as well as the cauda equina nerve roots. *Id.* at 3. The lesion did worsen over time, but the T2 hyperintensity did not localize to the anterior horn. *Id.* Dr. Wilson also read the T2 signal abnormality as somewhat patchy and diffuse and noted that it affected both gray and white matter. *Id.* at 6.

Dr. Wilson did see clear enhancement of the ventral cauda equina nerve roots. Wilson Rep. at 6. This is characteristic of GBS and can be seen in AFM, but it is not typical of TM.⁸ *Id.* Dr. Wilson then searched the UCSF mPower database and did not retrieve any AFM cases with cauda equina enhancement. *Id.* He acknowledged, however, that “some published studies in the literature describe a high rate of cauda equina enhancement in AFM.” *Id.*

Ultimately, Dr. Wilson did not flatly rule out AFM, but he felt R.W.’s case was not “characteristic” of AFM and that an autoimmune process such as TM or GBS was more likely. Wilson Rep. at 6.

Dr. Zucconi persuasively responded that R.W.’s imaging was, in fact, consistent with AFM cases described in the literature. Zucconi Rep. at 6-7. As the Okumura study found, a lesion in the lower spinal cord, as opposed to the cervical spine, is a common presentation of AFM. *Id.* at 6; Okumura at 447 (Table 1) (reporting nine of 26 AFM patients had thoracolumbar lesions). Also, AFM can include lesions involving both gray and white matter, with gray matter involvement predominant (as was the case with R.W.). Zucconi Rep. at 6; Okumura at 446 (noting that “a majority of children with AFM had both gray and white matter lesions in our study”).

Dr. Zucconi acknowledged that R.W.’s presentation was unusual in that the T2 signal abnormality did not localize to the anterior gray matter by the time of her second set of MRIs, which were taken about 18 days after her first set. Zucconi Rep. at 6. However, he pointed out that the enhancement seen on the later images was limited to the central gray matter and anterior horns. *Id.* Okumura reported that in AFM, nerve root/cauda equina enhancement frequently appeared in a delayed fashion after the onset of limb weakness, consistent with R.W.’s case. Okumura at 449 (Table 3) (reporting appearance of cauda equina/nerve root enhancement up to 55 days after onset of weakness).

Dr. Zucconi also was persuasive in rebutting Dr. Wilson’s opinion that R.W.’s MRIs were consistent with GBS. He noted that the combination of nerve root enhancement and gray matter lesions in the spinal cord is “exceedingly rare” in GBS and “very unusual” in TM, but common in AFM. Zucconi Rep. at 6; *see* Tsagkas at 1 (reporting first two cases of acute polyradiculomyelitis involving lesions of the gray matter of the lower thoracic spinal cord). Moreover, neither party’s experts argued R.W.’s clinical presentation was consistent with GBS, nor was GBS suspected by her treating physicians.

In sum, Dr. Zucconi persuasively opined that R.W.’s case bore many of the imaging hallmarks of AFM, including T2 signal hyperintensity of the spinal cord lesion with predominantly gray matter involvement, along with the later appearance of cauda equina/nerve root and spinal cord gray matter enhancement. Zucconi Rep. at 6-7. The delayed ventral nerve root enhancement seen on the imaging was not typical of TM. *Id.* at 6.

⁸ Dr. Wilson cited the 1996 Tartaglino study for the proposition that cauda equina enhancement can sometimes be seen in idiopathic TM. Wilson Rep. at 6 (citing Tartaglino). But as Dr. Zucconi persuasively countered, Tartaglino was published before the TM diagnostic criteria were updated and before “many developments that have since narrowed the definitions of [TM].” Zucconi Rep. at 6.

b. Onset and progression of symptoms

In TM, the progression of symptoms from onset to nadir generally occurs from four hours to 21 days. Helfferich at 1310 (Table 2). AFM is characterized by a sudden onset and rapid progression over hours to days, often combined with a “heralding sign” of pain. Tr. at 196, 200-01; Murphy at 336 (“In many patients, limb weakness is heralded by pain in the affected limb(s), neck, or lower back.”); *id.* at 339 (Fig. 2) (all classifications of AFM require a progression of limb weakness from onset to nadir of hours to 10 days). Fever can also occur at the time of onset. Fatemi at 376.

Here, R.W. had been experiencing some low back pain and fatigue in the few days prior to her hospitalization, without other symptoms. Ex. 2 at 156. She became noticeably sluggish and tired on September 27, 2015. *Id.* She developed a low-grade fever. Ex. 5 at 11. That afternoon, at about 3 p.m., she began feeling pain in her right posterior thigh. Ex. 4A at 116; Ex. 5 at 11. About 30 minutes later, she began experiencing progressive weakness and numbness of the right thigh, causing her to fall when she got out of bed. Ex. 5 at 11. By about 8 p.m., when she arrived in the emergency room, the “decreased sensation and weakness had spread to her left leg and lower abdomen and she was febrile to 100.5F.” *Id.* She experienced bladder incontinence in the emergency room. *Id.* The entire course, from onset of pain to profound weakness of both legs, took about five hours, which Dr. Sweeney persuasively explained was characteristic of AFM. Tr. at 200 (“So walking through [R.W.’s] presentation that’s documented from the Wake records and from the Duke records, she had rapid onset of weakness. So I think in her own testimony she discussed how she went to the bathroom, was able to walk there, and then shortly thereafter from coming back to her bed, she was unable to walk or to get up from the bed, to stand or even get dressed to go to the hospital. That is a very fast onset.”).

c. Persistently absent/reduced reflexes and low tone

As Dr. Sweeney explained, in TM and other classic demyelinating illnesses, although initially the patient may have absent reflexes and reduced muscle tone, over time they will develop brisk reflexes and spastic tone. Tr. at 198-99; *see also* Helfferich at 1310 (Table 2); Messacar at 17 (Table 3). R.W.’s lower extremity reflexes were absent at the time of her initial presentation, and they remained absent or diminished throughout her hospitalization. *See, e.g.*, Ex. 4A at 3, 118, 123; Ex. 5 at 4, 15. Similarly, R.W. had flaccid lower limbs throughout her course and did not develop spasticity.⁹ *See, e.g.*, Ex. 4A at 62, 77, 118; Ex. 5 at 19 (October 7, 2015 consultation with Dr. Gallentine that noted “flaccid tone, no spontaneous movement; mild response to pain [stimulation]” in R.W.’s bilateral lower extremities); 6 (October 12, 2015 discharge exam by Dr.

⁹ Petitioners state that R.W. developed “increased spasticity” in her hips, which required treatment with Botox. Pets.’ Post-Hrg. Br. at 4; Ex. 16 at 1. Dr. Sweeney was persuasive, however, in explaining that this occurred only after “she had instrumentation of her spinal cord, so after she had surgery for her scoliosis.” Tr. at 259. Further, because it is “very unusual to develop spasticity in only one muscle group,” it is more likely that R.W. developed contractures, meaning the “shortening of a muscle group because of disuse,” rather than true spasticity. *Id.* at 260.

Ming that noted “flaccid legs, normal upper extremity tone and bulk”); 1800 (April 12, 2016 follow-up visit with Dr. Smith at which R.W. still had “absent” lower-extremity reflexes).

Dr. Steinman surmised that the reason R.W. did not develop brisk reflexes and spasticity was because her disease involved inflammation of both the posterior and anterior aspects of the lower spinal cord. Tr. at 381. He testified he had seen that presentation in about 15-20% of his TM cases. *Id.* He did not dispute that persistently flaccid limbs and absent reflexes are characteristic of AFM, as set forth in the literature.

d. Lack of response to immunotherapy

R.W. was treated at WakeMed with IVIG and high-dose steroids, beginning within one day of the onset of her symptoms. Ex. 4A at 4. These treatments did not significantly improve her condition, prompting her physicians to recommend transfer to Duke for PLEX treatment. *Id.* at 18. A five-day course of PLEX and repeat courses of IVIG and high-dose steroids also failed to produce improvement, leading the team at Duke to suspect that she had a viral condition rather than an antibody-mediated disease. See Ex. 5 at 205 (pediatric rheumatologists Drs. Dvergsten and Balevic noting that they “would expect plasmapheresis to rapidly improve any antibody mediated inflammatory process”); *id.* at 5-6 (Duke discharge summary stating that R.W. did not respond to five days of PLEX, repeat IVIG, or additional high-dose methylprednisone treatment; the team ultimately concluded her condition was virally mediated).

Dr. Sweeney opined that R.W.’s failure to respond to these treatments signified her condition was not likely autoimmune, pulling against TM as the appropriate diagnosis. Sweeney Rep. at 4 (noting that TM is generally responsive to immunotherapies, and about 50% of pediatric TM patients will fully recover within two years of onset, though outcomes can vary); Tr. at 216-17. Conversely, it would not be surprising to see a lack of response to immunotherapy in AFM, because the disease destroys the anterior horn cells in the spinal cord, making recovery of motor function unlikely. *Id.* at 217.

Dr. Steinman replied that some patients with TM will not have a meaningful response to steroids or IVIG. Tr. at 351, 355-56. Thus, R.W.’s lack of response to immunotherapies did not rule out TM. *Id.* In the CAPTURE study, the investigators compared the outcomes in 90 pediatric patients with TM or AFM over a period of five years. CAPTURE at 1. The study did find that some percentage of both TM and AFM patients reported “no improvement” or “minimal improvement” with steroids/IVIG. *Id.* at 8 (Table 4). A greater percentage of TM patients than AFM patients reported “some improvement” or “mostly recovered” in response to steroid treatment. *Id.* On the other hand, none of the TM patients reported more than minimal improvement in response to IVIG. *Id.*; see also NORD at 3 (about one-third of TM patients have “virtually no recovery and [are] left severely functionally disabled. Most show good to fair recovery.”); Absoud at S49 (children with TM have better outcomes than adults, with nearly one-half making a complete recovery within two years).¹⁰

¹⁰ Dr. Sweeney explained that although a few AFM patients in the CAPTURE study reported improvement with IVIG, most “mixed” AFM patients with both white and gray matter involvement (like R.W.) had no or minimal improvement with either steroids or IVIG. Tr. at 432; CAPTURE at 8 (Table 4) (37% of

Notably, the CAPTURE study did not assess the response to PLEX in either TM or AFM patients. As discussed above, R.W.'s rheumatologists believed that had her condition been antibody mediated, PLEX treatment would likely have been successful. Ex. 5 at 205. Overall, R.W.'s failure to improve with multiple types and courses of immunotherapy, while not dispositive, pulls in favor of a virally mediated condition, as her treating physicians concluded.

e. Positive result for Rhinovirus A29

R.W.'s rapid test for enterovirus/rhinovirus at WakeMed was positive. Ex. 4A at 104. Further nasopharynx studies for viral speciation were negative for Enterovirus D68 and Human Parechovirus but positive for Rhinovirus A29. *Id.* at 185.

As Dr. Romberg explained, rhinoviruses and enteroviruses are genetically related. Tr. at 305-06. Rhinoviruses are part of the genus *Enterovirus* and the family *Picornaviridae*. RED BOOK: REPORT OF THE COMMITTEE ON INFECTIOUS DISEASES (Am. Acad. of Pediatrics, 2018) (Ex. A, Tab 2) at 1. At least one study has reported a statistically significant association between Enterovirus D68 and AFM. Aliabadi at 1.

Some patients with AFM test positive for rhinoviruses, though a statistical association has not been reported with rhinoviruses generally or any subtype thereof. For example, in Messacar, the authors reported characteristics of AFM cases occurring between 2012 and 2015. Messacar at 16 (Table 2). Of the 117 patients whose respiratory specimens were tested, 21 were positive for either a non-D68 enterovirus or a rhinovirus. *Id.* Ayers reported positive rhinovirus tests for AFM cases from 2015-2017, though none of those patients were positive for A29. Ayers at 5 (Table 3) (of the 90 AFM patients whose respiratory specimens were tested, 10 were positive for non-D68 enteroviruses or rhinovirus subtypes). Similarly, the CDC reported on a series of AFM cases in 2018, several of which were positive for rhinovirus subtypes or unspecified rhinoviruses/enteroviruses; again, none were positive for A29. McKay at 1274 (Table).

Notably, before 2015, rhinoviruses and enteroviruses could not be distinguished from one another through standard testing methods. Tr. at 306 (Dr. Romberg's testimony). As Duke infectious disease specialist Dr. Drucker commented: "Rhinovirus is of the same family as the enterovirus (picornaviridae) and for many years Rhinovirus wasn't diagnosed . . . thus the literature and data that have been published state enterovirus and *it isn't clear how many of these were actually rhinovirus since rhinovirus has been mistaken for enterovirus.*" Ex. 5 at 208 (emphasis added).

Dr. Steinman argued that R.W.'s positive test for A29 did not necessarily suggest she had AFM, because rhinoviruses are very commonly present in children's noses. Tr. at 109-10. He

"mixed" AFM patients had no improvement with steroids; 42% had minimal improvement; 11% were mostly recovered, and 5% had full recovery; none of the "mixed" AFM patients reported any more than minimal improvement with IVIG). Thus, R.W.'s lack of response to IVIG or steroids was consistent with AFM.

downplayed the findings in Messacar and Ayers, noting that the rates of rhinovirus positivity in those studies were low, making it difficult to assess potential causality. Second Steinman Rep. at 2. But given the genetic relationship between enteroviruses and rhinoviruses, the data showing enterovirus and rhinovirus positivity in AFM patients, and the recency of the technology capable of detecting rhinoviruses, I am persuaded that R.W.'s positive A29 result was clinically relevant and weighs in favor of an AFM diagnosis.

f. Treating physician opinions

R.W.'s team of physicians at Duke engaged in extensive discussions after her thorough workup, ultimately concluding that R.W.'s condition was virally mediated, though they did not specifically identify A29 as the cause. Ex. 5 at 5-6. The discharge summary indicated the case was reported to the CDC and the state health department as one of "unexplained" AFM.¹¹ *Id.* at 6. This determination was made after the series of MRIs was completed and after R.W.'s disease had been ongoing for more than one month. At that time, therefore, the Duke team had a fairly complete view of R.W.'s clinical course and a comprehensive set of images. The team's conclusion was based on her imaging showing inflammatory progression, negative tests for a number of infectious and autoimmune causes, and her lack of response to immunotherapies or other treatments. *Id.*

Petitioners correctly point out that the physicians at both WakeMed and Duke repeatedly used the term "transverse myelitis" to describe R.W.'s case. *See* Pets.' Post-Hrg. Br. at 12; Ex. 4A at 100, 118, 126; Ex. 5 at 34, 39, 68-69, 183, 3910. But as Dr. Sweeney explained, in his experience "myelitis" is often used in practice as an overarching descriptor of a paralytic condition. Tr. at 230. This use of the term should not be confused with the more precise diagnosis of idiopathic autoimmune TM. *Id.*

The Duke team also used the term "acute flaccid paralysis." *See, e.g.,* Ex. 5 at 5-6, 39, 88, 3910. Respondent's experts pointed out that term was a precursor to the more modern "acute flaccid myelitis," and those terms are effectively synonymous, with the only distinction being that "AFM" refers to acute flaccid paralysis with a specific viral cause. Tr. at 242-43 (Dr. Sweeney's testimony); Romberg Rep. at 4; *but see* Xiang Fang & Ruksana Huda, *Acute Flaccid Myelitis: Current Status and Diagnostic Challenges*, 16 J. CLIN. NEUROL. 376 (2020) (Exs. 54, 83) ("Fang") ("AFM is a subset of AFP that is also characterized by a limb paralytic condition, but it has certain distinct features such as lesions in magnetic resonance imaging of the spinal cord gray matter."). Importantly, at the time of discharge, the Duke team specifically characterized her condition as "acute flaccid myelitis." Ex. 5 at 6.

I do note that Dr. Honeycutt, the physician who treated R.W. in the PICU at WakeMed, has continued to opine that R.W. had TM, not AFM. *See* Ex. 10 at 1; Ex. 84 at 1. It is unclear whether Dr. Honeycutt reviewed the complete set of medical records and/or imaging.

¹¹ It is odd that Duke was apparently unable to locate a copy of the letter sent to the CDC regarding R.W.'s case. Ex. 53 at 1. It is unclear whether the letter to the state health department was located. Still, the Duke team's diagnosis of AFM is clearly documented in the medical records. Ex. 5 at 6.

Furthermore, Dr. Honeycutt's specialty is in critical care, and he has not explained the basis of his expertise in distinguishing AFM from TM. Accordingly, I do not find his opinion more persuasive than that of the Duke team or Respondent's experts.

g. Other factors

Petitioners point out that R.W. had sensory symptoms, which are not characteristic of AFM but are common in TM. Pets.' Post-Hrg. Br. at 13-15. Shortly after the onset of weakness, R.W. experienced diminished sensation over her affected limbs. *See* Ex. 4A at 3 (noting that in the hospital on September 27, 2015, R.W. had absent reflexes and decreased sensation to light touch across the distal right thigh but no clearly defined sensory level); *id.* at 106; 118. She also reported tingling sensations in her legs. *Id.* at 60. At Duke, she continued to report sensory symptoms, including decreased sensation, in her affected limbs. Ex. 5 at 4, 19, 183. On October 9, 2015, neurologist Dr. Neuhaus observed a sensory level at the T6-7 level. *Id.* at 39. Dr. Sweeney testified that R.W. appeared to have a sensory level at the level of her lower abdomen. Tr. at 422.

Dr. Sweeney agreed that sensory loss and a sensory level are not typical symptoms of AFM. Sweeney Rep. at 5. The filed literature does, however, describe a subset of cases with sensory loss and other sensory symptoms. *See* Messacar at 4 (noting that CDC surveillance of AFM reported numbness in affected limbs in 24% of patients, and California Department of Public Health surveillance reported that 44% of patients had sensory deficits, including 31% with pain/temperature deficits and 22% with fine touch/vibration deficits); Bove at 23 (Table 1) (about 35% of parents of AFM patients reported their child had sensory symptoms at the time of nadir); CAPTURE at 3-4 (Table 1) (30% of AFM patients in the CAPTURE study reported numbness at onset). Dr. Sweeney persuasively explained that R.W.'s sensory symptoms could have been secondary to her spinal lesion, which was causing swelling in the spinal cord. Tr. at 233. He also pointed out that, on some exams during her hospitalization, R.W. had some degree of sensation. *Id.* at 421-22.

R.W.'s CSF results were not characteristic of classic AFM, in that she did not exhibit pleocytosis. Ex. 4A at 107. Dr. Sweeney explained that this caused him to classify her case as "probable" rather than "definite" AFM. Tr. at 206. This characterization of her diagnosis is consistent with the literature and does not pull against AFM as the appropriate diagnosis. Murphy at 339 (Fig. 2).

In sum, I conclude that the preponderant evidence, including the imaging, test results, medical records, treating physician opinions, and literature, preponderate in favor of a diagnosis of AFM, not idiopathic autoimmune TM.

B. *Althen* Analysis

Because Petitioners have not proven the diagnosis alleged, it is not necessary for me to resolve the question of whether R.W.'s condition was caused by the subject vaccines. *Lombardi*, 656 F.3d at 1353. I also find, however, that Petitioners have failed to prove the *Althen* prongs with respect to a claim that the subject vaccines caused R.W. to develop AFM.

As discussed, Petitioners' burden under *Althen*'s first prong is to provide a sound and reliable medical theory causally connecting the vaccination and the injury. *Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019); *Langland v. Sec'y of Health & Hum. Serv.*, 109 Fed. Cl. 421, 441 (2013). Dr. Steinman did not opine that either of the subject vaccines could cause AFM, nor did he propose a mechanistic theory by which that could occur. To the contrary, as Dr. Romberg stated:

[T]here is very little epidemiologic data on vaccines and acute flaccid paralysis. A 2016 MMWR study described cases of ten acute flaccid paralysis patients from Washington State, all were <14 years old. The study's authors noted that all but one patient was fully immunized which suggested to them that the standard CDC vaccination schedule does not offer protection against this disease. The authors also noted that the median interval between symptom onset and last vaccination was 1.9 years (range 2 months to 7 years). ***Hence, a vaccine could not be a cause of acute flaccid paralysis in most of the described patients.*** The CDC has also informally reported that of the acute flaccid paralysis cases reviewed in 2018, approximately 85% had no recorded vaccinations in the 30 days prior to the onset of limb weakness.

Romberg Rep. at 5 (emphasis added); see Bonwitt at 826. Dr. Romberg also persuasively explained that AFM is caused by a virus, but “[t]he Tdap or DTaP, both of them, and Menactra are killed or dead vaccines. They are not living. They cannot reproduce, and therefore, I cannot imagine a scenario in which they can cause AFM.” Tr. at 302. Only a living pathogen could damage the anterior horn cells and produce the damage seen in AFM. *Id.* at 307. This opinion was not rebutted by Dr. Steinman. Thus, I conclude *Althen* prong one is not met.

Under *Althen*'s second prong, a petitioner must “prove a logical sequence of cause and effect showing that the vaccination was the reason for the injury.” *Althen*, 418 F.3d at 1278. The sequence of cause and effect must be “‘logical’ and legally probable, not medically or scientifically certain.” *Id.* A petitioner is not required to show “epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect.” *Id.* (internal citations omitted); *Capizzano*, 440 F.3d at 1325. Instead, circumstantial evidence and reliable medical opinions may be sufficient. *Isaac v. Sec'y of Health & Hum. Servs.*, No. 08-601V, 2012 WL 3609993, *24 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review den'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. App'x 999 (Fed. Cir. 2013). Furthermore, special masters are expected to consider the views of treating doctors on this prong. *Capizzano*, 440 F.3d at 1326. The views of treating doctors can be persuasive because they have direct experience with the patient. See *McCulloch v. Sec'y of Health & Hum. Servs.*, No. 09-293V, 2015 WL 3640610, *20 (Fed. Cl. Spec. Mstr. May 22, 2015).

Because Petitioners have failed to satisfy prong one, they also cannot show a logical sequence of cause and effect between the subject vaccines and R.W.'s AFM. Also, R.W.'s treating physicians at Duke concluded, after “extensive discussions” and a full workup, that R.W. had a virally mediated condition, not a vaccine-caused injury. Ex. 5 at 5-6. Although the WakeMed

physicians, including Dr. Honeycutt, disagreed, concluding R.W. had vaccine-caused TM, the opinion of the multidisciplinary Duke team was more persuasive, because it was based on a more complete picture of R.W.'s course. Ex. 10 at 1; Ex. 84. Thus, Petitioners failed to satisfy prong two.

To satisfy *Althen* prong three, a petitioner must establish the “timeframe for which it is medically acceptable to infer causation” and that the onset of her claimed injury occurred within that period. *Shapiro v. Sec’y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542-43 (2011), *recons. denied after remand on other grounds*, 105 Fed. Cl. 353 (2012), *aff’d without op.*, 503 F. App’x 952 (Fed. Cir. 2013). Respondent’s experts did not dispute that the onset of R.W.’s condition about 16 days after vaccination was medically appropriate. Thus, prong three has been satisfied.

VI. CONCLUSION

Again, I extend my heartfelt sympathies to R.W. and her family for their ordeal. However, upon careful evaluation of all the evidence submitted in this matter, including the medical records, affidavits, expert reports, testimony, and medical literature, I conclude that Petitioners have failed to prove by preponderant evidence that they are entitled to compensation under the Vaccine Act. **Their petition is therefore DISMISSED. The clerk shall enter judgment accordingly.**¹²

IT IS SO ORDERED.

s/ Jennifer A. Shah
Jennifer A. Shah
Special Master

¹² Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by each filing (either jointly or separately) a notice renouncing their right to seek review.