In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Originally Filed: June 16, 2021
Refiled in Redacted Form: July 28, 2021

* * * * * * * * * * * * * * * * * * * *		
O.M.V.,	*	PUBLISHED
	*	
Petitioner,	*	No. 16-1505V
	*	
v.	*	Special Master Nora Beth Dorsey
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Entitlement; Influenza ("Flu") Vaccine; Acute Disseminated Encephalomyelitis ("ADEM"); Multiple Sclerosis ("MS"); Demyelinating Condition.
	*	
Respondent.	*	
	*	
* * * * * * * * * * * * * * * * * * * *		

Edward M. Kraus, Law Offices of Chicago Kent, Chicago, IL, for petitioner.
Laurie Wiesner, U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

I. INTRODUCTION

On November 14, 2016, O.M.V. ("petitioner") filed a petition under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42 U.S.C. § 300aa-10 et seq. (2012).[2] Petitioner alleges he suffers "permanent disabilities [and] permanent neurologic deficits" as a result of an influenza ("flu") vaccine administered on November 15, 2013. Petition at 1 (ECF No. 1). Respondent argued against compensation, stating that "this case is not

[1] Because this Decision contains a reasoned explanation for the action in this case, the undersigned is required to post it on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). **This means the Decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material from public access.

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 to -34 (2012). All citations in this Decision to individual sections of the Vaccine Act are to 42 U.S.C. § 300aa.

appropriate for compensation under the terms of the Act." Respondent's Report ("Resp. Rept.") at 2 (ECF No. 38).

After carefully analyzing and weighing the evidence presented in this case in accordance with the applicable legal standards, the undersigned finds petitioner is not entitled to compensation. Accordingly, petitioner's case must be dismissed.

II. ISSUES IN AGREEMENT AND IN DISPUTE

The parties agree that petitioner was generally healthy with no known neurological conditions prior to his flu vaccination on November 15, 2013. Joint Prehearing Submission, filed Oct. 22, 2020, at 1 (ECF No. 112). "[T]he appropriate diagnosis for [petitioner's] condition that began on November 16, 2013 and continues to the present day" is in dispute. Id. at 2. Additionally, the parties disagree as to whether the flu vaccine was a but-for cause and/or substantial factor in the development of petitioner's neurological illness. Id.

III. BACKGROUND

A. Medical Terminology

Acute disseminated encephalomyelitis ("ADEM") is "an acute or subacute encephalomyelitis[3] or myelitis[4] characterized by perivascular lymphocyte and mononuclear cell infiltration and demyelination."[5] Acute Disseminated Encephalomyelitis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=73033 (last visited Apr. 14, 2021). "It is believed to be a manifestation of an autoimmune attack on the myelin of the central nervous system [("CNS")]." Id.

[3] Encephalomyelitis is "inflammation involving both the brain and the spinal cord." Encephalomyelitis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=16191 (last visited May 4, 2021).

[4] Myelitis is "inflammation of the spinal cord." Myelitis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=32680 (last visited May 4, 2021).

[5] Demyelination is the "destruction, removal, or loss of the myelin sheath of a nerve or nerves." Demyelination, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=13092 (last visited May 4, 2021).

ADEM is a monophasic disease that is "usually triggered by an inflammatory response to viral infections and vaccinations." Pet. Ex. 98 at 1;[6] see also Pet. Ex. 28 at 3;[7] Pet. Ex. 99 at 1;[8] Pet. Ex. 102 at 5;[9] Pet. Ex. 103 at 1.[10] The monophasic nature of ADEM is "defined as a lack of recurrence (within 3 months) in the absence of treatment or while on appropriate treatment. Relapse occurring during cessation or tapering of therapy should be considered to belong to one monophasic episode." Pet. Ex. 102 at 5 (emphasis omitted). "A single clinical event of ADEM can evolve over a period of 3 months, with fluctuations in clinical symptoms and severity." Resp. Ex. H at 2.[11]

ADEM "is usually associated with multifocal neurologic symptoms and mental status change." Pet. Ex. 101 at 1.[12] Symptoms include "decreased level of consciousness varying from lethargy to coma, convulsions, and multifocal neurologic symptoms such as hemi-, para-, and tetraparesis, cranial nerve palsies, and movement disorders." Pet. Ex. 98 at 1. "[B]ehavioral changes varying from irritability, depression, delusions, and psychosis" dominate symptoms in some cases. Id. ADEM patients also "commonly have headache, vomiting, drowsiness, and meningism." Pet. Ex. 97 at 1-2.[13]

According to the Brighton Collaboration Working Group ("Brighton Collaboration"), "[t]he diagnostic hallmark of ADEM is the demonstration of scattered, focal or multifocal (disseminated) areas of inflammation and demyelination within cerebral subcortical and deep

---

[6] Jari Honkaniemi et al., Delayed MR Imaging Changes in Acute Disseminated Encephalomyelitis, 22 Am. J. Neuroradiology 1117 (2001).

[7] Xinqing Deng & Subramaniam Sriram, Role of Microglia in Multiple Sclerosis, 5 Current Neurology & Neuroscience Reps. 239 (2005).

[8] William Huynh et al., Post-Vaccination Encephalomyelitis: Literature Review and Illustrative Case, 15 J. Clinical Neuroscience 1315 (2008).

[9] James J. Sejvar et al., Encephalitis, Myelitis, and Acute Disseminated Encephalomyelitis (ADEM): Case Definitions and Guidelines for Collection, Analysis, and Presentation of Immunization Safety Data, 25 Vaccine 5771 (2007).

[10] S. Schwarz et al., Acute Disseminated Encephalomyelitis: A Follow-Up Study of 20 Adult Patients, 56 Neurology 1313 (2001).

[11] Lauren B. Krupp et al., Consensus Definitions Proposed for Pediatric Multiple Sclerosis and Related Disorders, 68 Neurology 87 (2007).

[12] Yann Mikaeloff et al., First Episode of Acute CNS Inflammatory Demyelination in Childhood: Prognostic Factors for Multiple Sclerosis and Disability, 144 J. Pediatrics 246 (2003).

[13] R C Dale & J A Branson, Acute Disseminated Encephalomyelitis or Multiple Sclerosis: Can the Initial Presentation Help in Establishing a Correct Diagnosis?, 90 Archives Disease Childhood 636 (2005).

cortical white matter." Pet. Ex. 102 at 5. The Brighton Collaboration developed the following diagnostic criteria for ADEM:[14]

Level 1 of Diagnostic Certainty	(a) Demonstration of diffuse or multifocal areas of demyelination by histopathology; **OR** (b) Focal or multifocal findings referable to the central nervous system, including one or more of the following: (1) Encephalopathy, (2) Focal cortical signs (including but not limited to: aphasia, alexia, agraphia, cortical blindness), (3) Cranial nerve abnormality/abnormalities, (4) Visual field defect/defects, (5) Presence of primitive reflexes (Babinski's sign, glabellar reflex, snout/sucking reflex), (6) Motor weakness (either diffuse or focal; more often focal), (7) Sensory abnormalities (either positive or negative; sensory level), (8) Altered deep tendon reflexes (hypo- or hyperreflexia, asymmetry of reflexes), or (9) Cerebellar dysfunction, including ataxia, dysmetria, cerebellar nystagmus, **AND** (c) Magnetic resonance imaging ("MRI") findings displaying diffuse or multifocal white matter lesions; **AND** (d) Monophasic pattern to illness (i.e., absence of relapse within a <u>minimum</u> of 3 months of symptomatic nadir).
Level 2 of Diagnostic Certainty	(a) Focal or multifocal findings referable to the central nervous system (as outlined in the Level 1 of diagnostic certainty section), **AND** (b) MRI findings displaying diffuse or multifocal white matter lesions, **AND** (c) Insufficient follow up time achieved to document absence of relapse within a minimum period of 3 months following symptomatic nadir.
Level 3 of Diagnostic Certainty	(a) Focal or multifocal findings referable to the central nervous system (as outlined in the Level 1 of diagnostic certainty section).
Level 3A	Insufficient information is available to distinguish case between acute encephalitis or ADEM; case unable to be definitively classified.
Exclusion Criteria for All Levels of Diagnostic Certainty	• Presence of a clear alternative acute infectious or other diagnosis for illness, • Recurrence or relapse of illness at any point following a 3 month period of clinical improvement from symptomatic nadir, or • If known, MRI findings or histopathologic data inconsistent with the diagnosis of ADEM.

[14] Pet. Ex. 102 at 8-9.

The Brighton Collaboration defined encephalopathy[15] as "depressed or altered level of consciousness, lethargy, or personality change lasting [more than] 24 h[ours]." Pet. Ex. 102 at 6. The Group recognized that "ADEM—or any other adverse event—which follows administration of an inactivated component or live vaccine may be temporally associated with, but is not necessarily the result of, administration of a vaccine." Id. at 5.

The International Pediatric Multiple Sclerosis Study Group ("MS Study Group") also set forth a list of findings that must all be present to render an ADEM diagnosis:

> ADEM (monophasic).
>
> - A first clinical event with a presumed inflammatory or demyelinating cause, with acute or subacute onset that affects multifocal areas of the CNS. The clinical presentation must be polysymptomatic and must include encephalopathy, which is defined as one or more of the following:
>   - Behavioral change, e.g., confusion, excessive irritability
>   - Alteration in consciousness, e.g., lethargy, coma
> - Event should be followed by improvement either clinically, on MRI, or both, but there may be residual deficits
> - No history of a clinical episode with features of a prior demyelinating event
> - No other etiologies can explain the event
> - New or fluctuating symptoms, signs, or MRI findings occurring within 3 months of the inciting ADEM event are considered part of the acute event
> - Neuroimaging shows focal or multifocal lesion(s), predominantly involving white matter, without radiologic evidence of previous destructive white matter changes:
>   - Brain MRI, with FLAIR or T2-weighted images, reveals large (>1 to 2 cm in size) lesions that are multifocal, hyperintense, and located in the supratentorial or infratentorial white matter regions; gray matter, especially basal ganglia and thalamus, is frequently involved
>   - In rare cases, brain MR images show a large single lesion (≥1 to 2 cm), predominantly affecting white matter
>   - Spinal cord MRI may show confluent intramedullary lesion(s) with variable enhancement, in addition to abnormal brain MRI findings above specified

Resp. Ex. H at 2. The Group's definition of ADEM requires both encephalopathy, defined as "mental status changes and/or behavioral alterations such as marked irritability," and multifocal involvement. Id. Additionally, an ADEM diagnosis "must rest on clinical features first," and

[15] Under the Vaccine Injury Table, an acute encephalopathy persists for at least 24 hours and is characterized by at least two of the following: "(1) a significant change in mental status that is not medication related (such as a confusional state, delirium, or psychosis); (2) [a] significantly decreased level of consciousness which is independent of a seizure and cannot be attributed to the effects of medication; and (3) [a] seizure associated with loss of consciousness." 42 C.F.R. § 100.3(c)(2)(i)(B).

"MRI findings alone are insufficient." Id. Although the Brighton Collaboration and MS Study Group differ on the requirement of encephalopathy for ADEM diagnosis, "[e]ncephalopathy . . . is considered mandatory for definite diagnosis." Pet. Ex. 35 at 2.[16]

Multiple sclerosis ("MS"), like ADEM, is a demyelinating and disseminated disease of the CNS. Pet. Ex. 97 at 1-2. MS is "a disease in which there are foci of demyelination throughout the white matter of the [CNS], sometimes extending into the gray matter." Multiple Sclerosis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=105130 (last visited Apr. 14, 2021). Symptoms "include weakness, incoordination, paresthesias, speech disturbances, and visual complaints," and disease course is usually prolonged, with "remissions and relapses that occur over a period of many years." Id. MS typically presents between 20 and 40 years of age. Resp. Ex. C at 4.[17] "A recent extensive review from the US Institute of Medicine did not find sufficient evidence to support a causal relationship between the onset of MS and various common vaccinations" including flu. Pet. Ex. 35 at 6.

The International Panel on Diagnosis of Multiple Sclerosis ("International Panel") developed the McDonald criteria, which combines clinical, imaging, and laboratory evidence, to aid in the diagnosis of MS. Resp. Ex. C at 1.

The 2017 McDonald Criteria:[18]

	Number of lesions with objective clinical evidence	Additional data needed for a diagnosis of multiple sclerosis
≥2 clinical attacks	≥2	None
≥2 clinical attacks	1 (as well as clear-cut historical evidence of a previous attack involving a lesion in a distinct anatomical location)	None
≥2 clinical attacks	1	Dissemination in space demonstrated by an additional clinical attack implicating a different CNS site or by MRI
1 clinical attack	≥2	Dissemination in time demonstrated by an additional clinical attack or by MRI **OR** demonstration of CSF-specific oligoclonal bands

[16] Dimitrios Karussis & Panayiota Petrou, The Spectrum of Post-Vaccination Inflammatory CNS Demyelinating Syndromes, 13 Autoimmunity Revs. 215 (2014).

[17] Alan J. Thompson et al., Diagnosis of Multiple Sclerosis: 2017 Revisions of the McDonald Criteria, 17 Lancet Neurology 162 (2018).

[18] Resp. Ex. C at 6 (emphasis added).

1 clinical attack	1	Dissemination in space demonstrated by an additional clinical attack implicating a different CNS site or by MRI **AND** Dissemination in time demonstrated by an additional clinical attack or by MRI **OR** demonstration of CSF-specific oligoclonal bands

The International Panel defined the first attack as a "clinically isolated syndrome," or "[a] monophasic clinical episode with patient-reported symptoms and objective findings reflecting a focal or multifocal inflammatory demyelinating event in the CNS, developing acutely or subacutely, with a duration of at least 24 h[ours], with or without recovery, and in the absence of fever or infection." Resp. Ex. C at 2. An objective finding consists of "[a]n abnormality on neurological examination, imaging . . . , or neurophysical testing . . . that corresponds to the anatomical location suggested by the symptoms of the clinically isolated syndrome." Id. The International Panel cautioned against "accepting symptoms accompanied only by patient-reported subjective alteration as evidence of a current or previous attack." Id.

"MS is characterized by discrete demyelinating events separated by at least 4 weeks" in time. Resp. Ex. H at 2. The dissemination in time requirement, described above, is met when new lesions have developed or appeared over time. Resp. Ex. C at 2. The dissemination in space requirement is met when lesions have developed in distinct anatomical locations within the CNS. Id. In certain situations when dissemination in space is met, but there is no dissemination in time, a finding of oligoclonal bands in the cerebrospinal fluid ("CSF") can substitute for the requirement of dissemination in time. Id. at 5. "Oligoclonal bands are present in the CSF of more than 85% of patients with clinically definite [MS]." Pet. Ex. 11 at 39. However, oligoclonal bands can be found in a variety of other diseases. Id.

"The pathological hallmark of MS is the demyelinated regions, referred to as plaques" or lesions. Pet. Ex. 28 at 1. "The lesions in MS are inflammatory in nature, and the underlying basis for the pathology is considered to be autoimmune and most likely mediated by activated T cells to the oligodendrocyte/myelin unit." Id. at 2. Demyelinated regions show "loss of oligodendrocytes and . . . variable inflammatory responses consisting of lymphocytes and macrophages," and contain activated microglia. Id. at 1. Additionally, "[m]icroglial cells express activation markers and are, therefore, presumed to play a key role in the disease." Id.

Although ADEM and MS are both demyelinating diseases of the CNS, they have many differences that aid in diagnosis. ADEM is more common in children, whereas MS is more common in adults. Pet. Ex. 97 at 1. Both ADEM and MS patients have lesions, however, lesions in ADEM patients completely or partially resolve, while new lesions are anticipated in MS patients. Id. at 2; Resp. Ex. H at 5. Unlike ADEM, encephalopathy is typically not associated with MS. Pet. Ex. 97 at 1-2; Resp. Ex. H at 2. Additionally, ADEM patients tend to have a polysymptomatic presentation, whereas MS patients have a monosymptomatic presentation. Pet. Ex. 97 at 2.

"[F]requently[,] patients originally diagnosed with ADEM relapse and are reclassified as MS." Pet. Ex. 97 at 3. The Brighton Collaboration recognized that "ADEM may fall along a

continuum of CNS demyelinating disorders that includes [MS]" and "a subset of patients with suspected ADEM will nonetheless progress to MS." Pet. Ex. 102 at 5. They found "[t]he absence of recurrence and monophasic nature of ADEM is useful as a distinguishing feature to discern ADEM from [MS]." Id. at 8 n.17. They "decided that recurrence of illness following a 3-month interval would be more likely representative of MS, and . . . such recurrence would be operationally considered MS, and thus 'not a case' of ADEM." Id. Others have found that when inflammation at an isolated CNS site is "followed by a further neurologic episode in another CNS site, [it] qualif[ies] for conversion to MS." Pet. Ex. 101 at 1.

B. Procedural History

Petitioner filed his petition requesting compensation under the Vaccine Act on November 14, 2016.[19] Petition at 1. Petitioner filed medical records in May, August, and October 2017. Petitioner's Exhibits ("Pet. Exs.") 1-18. On January 19, 2018, respondent filed his Rule 4(c) Report, arguing against compensation. Resp. Rept. at 2.

On June 11, 2018, petitioner filed an expert report of Dr. Marcel Kinsbourne. Pet. Ex. 25. Thereafter, petitioner filed additional medical records. Pet. Exs. 19-24. On November 7, 2018, respondent filed an expert report of Dr. Subramaniam Sriram. Resp. Ex. A. Petitioner filed additional medical records and a supplemental expert report of Dr. Kinsbourne on March 19, 2019. Pet. Exs. 45-59.

A status conference was held on April 11, 2019, where the undersigned ordered the parties to file additional expert reports further addressing the issues in petitioner's claim. Order dated Apr. 15, 2019 (ECF No. 61). In May and June 2019, petitioner filed additional medical records, a second supplemental expert report of Dr. Kinsbourne, and an expert report of Dr. M. Eric Gershwin. Pet. Exs. 60-69, 95. Respondent filed a supplemental expert report of Dr. Sriram on September 26, 2019. Resp. Ex. E.

A Rule 5 conference was held on October 22, 2019. The undersigned preliminarily concluded there was no firm diagnosis in this case although she noted that an exact diagnosis is not required to rule on causation. Rule 5 Order dated Oct. 24, 2019, at 1-2 (ECF No. 72) (citing Contreras v. Sec'y of Health & Hum. Servs., 107 Fed. Cl. 280, 293 (2012); Knudsen v. Sec'y of Health & Hum. Servs., 35 F.3d 543, 549-50 (Fed. Cir. 1994)). The undersigned encouraged the parties to resolve the case through settlement negotiations. Id. at 2-3.

Petitioner filed a third supplemental expert report of Dr. Kinsbourne on January 6, 2020, and respondent filed a second supplemental expert report of Dr. Sriram on July 8, 2020. Pet. Ex. 96; Resp. Ex. G. On October 2, 2020, petitioner filed a supplemental expert report from Dr. Gershwin. Pet. Ex. 107.

[19] Petitioner was pro se from November 14, 2016 until March 6, 2017, when a consented motion to substitute attorney was filed.

An entitlement hearing was held on November 5 and 6, 2020. Petitioner, Dr. Kinsbourne, Dr. Gershwin, and Dr. Sriram testified. Transcript ("Tr.") 3, 169. Thereafter, additional records were filed from both parties. Pet. Ex. 114; Resp. Ex. H.

This matter is now ripe for adjudication.

C. Factual History

1. Medical History Prior to Vaccination and Vaccination

Petitioner had no neurological symptoms prior to vaccination. Pet. Prehearing Memorandum, filed Sept. 17, 2020, at 1 (ECF No. 94); Joint Prehearing Submission at 1. On November 15, 2013, at thirty-nine years old, petitioner returned from a medical mission trip in Bolivia and received a flu vaccine. Pet. Ex. 1 at 1; Pet. Ex. 11 at 1.

2. Medical Treatment from November 16, 2013 to November 23, 2013

Post-vaccination, petitioner received medical diagnoses of acute severe migraine headache, weakness, and cerebrovascular accident ("CVA")[20] at different times.

On November 16, 2013, petitioner presented to Vista Medical Center East Emergency Department with a chief complaint of generalized weakness. Pet. Ex. 2 at 3. He stated his symptoms began at 2:00 PM that day and "came on gradually." Id. at 6. Petitioner reported he had "bilateral facial numbness [for 15-20 minutes] and left arm weakness. He fell asleep in his car today and woke up with a headache. Noted difficulty with speech. No trouble swallowing." Id. at 3. Review of systems was positive for headache and numbness and negative for altered mental status, confusion, weakness, and tingling. Id. at 5. Neurologic physical examination by Physician Assistant ("PA") Amee Patel revealed petitioner was awake and alert, intact, and had slightly decreased sensation to light touch in his left cheek, hand, and ankle. Id. at 3, 6. Motor examination was normal and symmetric. Id. at 6. Blood work was normal, and a computerized tomography ("CT") scan of the head showed no signs of acute disease. Id. at 6-7, 16-20. Petitioner was diagnosed with generalized weakness and an acute severe migraine headache. Id. at 7. He was discharged home. Id.

On November 22, 2013, petitioner presented to Community Healthcare System Emergency Department, complaining of left-sided weakness and drooping in face and left arm weakness. Pet. Ex. 5 at 2. Registered Nurse ("RN") Renee I. Thurman documented, "[petitioner's] speech [was] clear. [Moves all extremities] with equal strength. Pupils [equal and reactive to light and accommodation]. Ambulatory and steady. Smile symmetrical. Eyes close

[20] CVA, or stroke, is "a condition with sudden onset caused by acute vascular lesions of the brain, such as infarction from hemorrhage, embolism, or thrombosis, or rupturing aneurysm. It may be marked by any of a variety of symptoms . . . including hemiparesis, vertigo, numbness, aphasia, and dysarthria." Stroke Syndrome, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=111462 (last visited May 4, 2021).

normally, but [petitioner] state[d] it feels like his eye does not close normally and it 'waters' more than usual." Id. at 3.

Dr. Carrie Lynn Shaffer, in her physical examination, noted petitioner was alert, oriented to person, place, and time, and in no distress. Pet. Ex. 5 at 5. Her neurological physical examination found petitioner had normal gait and deep tendon reflexes, a sensory deficit, weakness in the left hip flexor and intrinsic muscles of the left hand, and abnormal heel to shin testing. Id. at 5-6. Dr. Shaffer diagnosed petitioner with weakness of left upper extremity. Id. at 6. She advised petitioner to follow up with Dr. Mark Alan Simaga, and discharged petitioner home. Id.

The following day, on November 23, 2013, petitioner presented to the Emergency Department at Porter Health System for continued weakness in his arm and difficulty grasping items, focusing, and putting together words. Pet. Ex. 5 at 8. Petitioner stated he was diagnosed with a CVA the previous Saturday and his "symptoms were much worse" then. Id. His nursing assessment placed his NIH stroke score[21] at 10. Id. at 9. Petitioner was seen by Dr. Vishnuvardhan Rao who documented petitioner's symptoms that began one week prior were "almost gone." Id. Physical examinations conducted by RN Tamara Barnes and Dr. Rao were inconsistent. Id.

> [Petitioner] was able to move his legs with strength when the ataxia exam was done by Dr. Rao, but [petitioner] [was] unable to hold the legs up during [Ms. Barnes'] exam. [Petitioner] also required re-focusing many times when he was getting undressed. He kept "forgetting" what he was doing, and was quick to apologize and restart the task, but became forgetful and needed to be asked again.

Id. During his physical examination, Dr. Rao found petitioner was well-developed, alert, and oriented to person, place, and time. Id. at 10. Neurological examination noted "Normal speech, ... Able to express self appropriately. Cranial nerves and [extraocular movements] are intact. Symmetrical smile. . . . Pupils equal round and reactive to light. Normal symmetric muscle strength and tone. Cerebellar exam grossly intact. Normal finger nose finger exam with overshooting." Id. Petitioner complained "pinprick [was] less sharp or [was] dull on the affected side[] or there [was] a loss of superficial pain with pinprick, but [petitioner] [was] aware of being touched." Id. Dr. Rao ordered labs, electrocardiogram ("EKG"), and brain MRI. Id. at 11. All tests were normal. Id. at 12, 18. The MRI showed no evidence of a demyelinating disorder. Id. at 18. Petitioner was diagnosed with paresthesia and stroke/CVA. Id. at 14-17. Petitioner was discharged home. Id. at 13.

[21] A stroke score is "any of various scoring systems that seek to characterize a patient's clinical state following a stroke." Stroke Score, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=105180 (last visited May 4, 2021); see also NIH Stroke Scale, Nat'l Insts. Health, https://www.stroke.nih.gov/resources/scale.htm (last visited May 4, 2021).

3. Medical Treatment from January 14, 2014 to May 6, 2014

During this time period, petitioner received diagnoses of transient ischemic attack ("TIA"),[22] hemiplegic migraine,[23] and CVA.

Petitioner next sought medical treatment on January 14, 2014 with neurologist, Dr. Simaga.[24] Pet. Ex. 6 at 1. Dr. Simaga diagnosed petitioner with TIA and hemiplegic migraine. Id. Numerous tests, including labs and MRIs, were ordered, and petitioner was prescribed Plavix.[25] Id.

Petitioner presented to Dr. Krista Molina on January 29, 2014 to establish care with a primary care physician for insurance purposes. Pet. Ex. 11 at 1; Pet. Ex. 6 at 3. Petitioner reported he returned from Bolivia in November and had a flu shot the same day.[26] Pet. Ex. 11 at 1. Petitioner repeated his history of developing confusion and weakness the day following vaccination, and complained of continued weakness. Id. Review of systems noted decreased coordination and residual weakness in left leg and foot. Id. On exam, petitioner was alert and oriented to person, place, and time. Id. at 1-2. He had a sensory deficit, normal coordination, decreased grip strength in left hand, and weakness in left lower extremity, hip flexors, and knee flexors. Id. at 2. He was diagnosed with TIA, left arm weakness, left leg weakness, and left facial numbness. Id. Dr. Molina was concerned for CVA and CNS vasculitis,[27] "especially given that his symptoms occurred the day after receiving a flu vaccine." Id. Tests, including

---

[22] TIA is "a brief attack (from a few minutes to an hour) of cerebral dysfunction of vascular origin, with no persistent neurologic deficit." Transient Ischemic Attack, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=59631 (last visited May 4, 2021).

[23] Hemiplegic migraine is a "migraine associated with varying degrees of transient hemiplegia or hemiparesis." Hemiplegic Migraine, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=89344 (last visited May 4, 2021).

[24] Petitioner testified that he did not have health insurance until January 2014, and this was the first available appointment. Tr. 16, 23-24.

[25] Plavix, a trademark of clopidogrel bisulfate, is "an inhibitor of platelet aggregation used as an antithrombotic." Plavix, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=39538 (last visited Apr. 14, 2021); Clopidogrel Bisulfate, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=10156 (last visited Apr. 14, 2021).

[26] According to petitioner's testimony at the hearing, he returned from Bolivia on November 11 and received the flu vaccine at issue on November 15, 2013. Tr. 12-13.

[27] Vasculitis is the "inflammation of a blood or lymph vessel." Vasculitis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=52617 (last visited May 4, 2021).

labs and MRIs, were re-ordered, petitioner was referred to neurology, and he was encouraged to start taking Plavix daily and continue Pravachol.[28] Id.; Pet. Ex. 6 at 3-4.

A duplex carotid doppler was conducted on January 29, 2014 and found no significant plaque or hemodynamically significant stenosis of the right or left carotid, and vertebral arteries showed normal antegrade flow. Pet. Ex. 6 at 12-13. An EKG was also conducted on January 29, 2014 and was normal. Id. at 36-37. Petitioner's symptoms were noted to have "started 1 day after flu shot, 2 days after a long plane trip."[29] Id. at 36.

On February 8, 2014, multiple tests were conducted. A brain MRI without contrast was done and compared to petitioner's November 23, 2013 brain MRI. Pet. Ex. 6 at 14. The MRI was normal, and no significant changes were noted. Id. at 14-15. A head magnetic resonance angiography ("MRA") without contrast showed "hypoplasia of the left anterior cerebral artery and right vertebral artery . . . which represent anatomic variants. The study [was] otherwise unremarkable." Id. at 16 (emphasis omitted). An MRA of the carotid arteries without contrast was conducted and was unremarkable. Id. at 18. Blood tests were normal, petitioner's ANA was negative, and petitioner's vitamin D level was low. Id. at 20-27.

Petitioner returned to Dr. Simaga on February 20, 2014, who reiterated the diagnoses of TIA and hemiplegic migraine. Pet. Ex. 6 at 6. Petitioner also saw Dr. Alexander Molina[30] at his primary care physician's office on February 20, 2014 for a follow-up exam. Pet. Ex. 11 at 4. Petitioner reiterated his complaints of left-sided weakness and added a complaint of neck pain that had been present for several months. Id. Dr. Molina added that petitioner was "[n]ot getting worse but not improving." Id. Dr. Molina found petitioner was alert and oriented to person, place, and time, and had a sensory deficit and normal coordination. Id. Physical examination revealed petitioner continued to have decreased grip strength in his left hand as well as weakness in his left lower extremity, hip flexors, and knee flexors. Id. at 5. Dr. Molina diagnosed petitioner with a CVA (cerebral infarction) and cervical pain (neck). Id.

On April 5, 2014, petitioner presented to Porter Regional Hospital Emergency Room complaining of "[s]udden onset of left parietal headache associated with left facial numbness and left upper extremity numbness and weakness with abnormal gait" that began at 4:00 AM that morning. Pet. Ex. 14 at 35. Petitioner reported that "this headache was much different than his usual migraine headache" and lasted until 8:00 AM. Id. Petitioner added that "his left face was feeling numb and had abnormal sensation associated with abnormal sensation in the left upper

[28] Pravachol, a trademark of pravastatin sodium, is an antihyperlipidemic agent. Pravachol, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=40665 (last visited Apr. 14, 2021); Pravastatin Sodium, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=40666 (last visited Apr. 14, 2021).

[29] Again, petitioner testified at the hearing that he returned from Bolivia on November 11 and was vaccinated on November 15, 2013. Tr. 12-13.

[30] This is the only visit to Dr. Alexander Molina. The remaining visits to a Dr. Molina were with Dr. Krista Molina.

extremity with left upper extremity feeling weak." Id. Petitioner reported that he was walking with a limp. Id. Petitioner reiterated his November 2013 symptoms and reported that he had "been fairly healthy" since then. Id.

Dr. Swati Singh documented petitioner was alert, oriented to person, place, and time, and in no distress. Pet. Ex. 14 at 36. Cranial nerves were intact. Id. Motor strength in left upper and lower extremity were decreased. Id. Petitioner exhibited decreased sensation to touch in left face and left upper extremity. Id. Cerebellar examination was within normal limits. Id. Urinalysis, blood work, CT, and MRI were normal. Id. An EKG showed sinus rhythm with early R-wave transition. Id. Dr. Singh diagnosed petitioner with left face numbness, left face and left-sided weakness and paresthesia, TIA versus complicated migraine, as well as borderline dyslipidemia. Id. at 36-37. Petitioner was admitted for observation. Id. at 37.

On the following day, April 6, 2014, petitioner underwent a neurology consult by Dr. Arkadiy Konyukhov. Pet. Ex. 14 at 38. Dr. Konyukhov noted that a repeat MRI of petitioner's brain conducted the day before was normal, "except possible very small FLAIR hyperintensity in the right parieto-occipital white matter." Id. Dr. Konyukhov, on physical examination, documented petitioner was in no acute distress, alert, and oriented to person, place, and time. Id. at 38-39. Petitioner's speech and language were normal. Id. at 39. Extraocular movements were intact, and he had normal tongue and shoulder movements. Id. Dr. Konyukhov noted decreased facial sensation in the V2 distribution on the left side, and slight weakness in left arm, leg, and intrinsic muscles of hand. Id. Left side sensory examination was normal. Id. Dr. Konyukhov's assessment was "[l]eft-sided weakness resolving as well as numbness." Id. An MRI of the cervical spine was recommended. Id. Petitioner's discharge diagnosis was "probable hemiplegic migraines" or dyslipidemia. Id. at 40.

MRIs of petitioner's thoracic and cervical spines with and without contrast were conducted on May 6, 2014. Pet. Ex. 7 at 30-33. The MRIs were unremarkable, and no lesions were seen. Id.

4. Medical Treatment from July 1, 2014 to December 23, 2014

Beginning in July 2014, petitioner's treating physicians considered a diagnosis of a demyelinating disease.

On July 1, 2014, petitioner returned to Porter Regional Hospital for a lumbar puncture. Pet. Ex. 7 at 3; Pet. Ex. 11 at 23. Petitioner's CSF showed normal protein at 32 (range 15-45), normal glucose at 63 (range 40-70), no cytomegalovirus, no growth or organisms on gram stain,

no white blood cells in the CSF, and five well-defined oligoclonal bands in the CSF that were not present in the corresponding serum sample.[31] Pet. Ex. 11 at 23-39.[32]

Petitioner returned to Dr. Konyukhov on July 14, 2014 to review his test results. Pet. Ex. 7 at 3. Petitioner reported episodes of tingling on left side of body and periodic tingling on right side of body. Id. Dr. Konyukhov's examination revealed normal facial sensation, no facial droop, and normal motor examination. Id. Petitioner's strength was normal in upper and lower extremities, "except [for] the subtle and [possibly] effort dependent" slight weakness in left arm and leg, and "very minimal" weakness in intrinsic muscles of the left hand. Id. at 3-4 (emphasis omitted). Sensory examination was normal except for decreased sensation in the left ulnar distribution. Id. at 4. Casual and tandem gait were normal. Id. Dr. Konyukhov noted "[petitioner's] age might indicate demyelinating disease. It could be clinically isolated syndrome. However[,] MRI[s] . . . were normal, as well as MRA." Id. Some test results from petitioner's lumbar puncture remained pending as of this visit. Id. Dr. Konyukhov diagnosed petitioner with disturbance of skin sensation and left hemiplegia. Id.

On July 24, 2014, petitioner saw Dr. Krista Molina with complaints of residual left-sided weakness and new complaints of left hip pain for the past two-to-three months. Pet. Ex. 11 at 6. Dr. Molina documented that petitioner's hip pain "does not radiate and is intermittent," but made worse when standing or walking. Id. "[Petitioner] wonder[ed] if he should see an immunologist since the neurologist told him he thinks his symptoms were due to an immunologic response to the flu vaccine." Id. Review of systems was positive for arthralgias and weakness. Id. Dr. Molina's physical examination revealed petitioner was alert and oriented to person, place, and time. Id. at 6-7. He had normal range of motion and no tenderness to palpitation in left hip. Id. at 6. Neurological examination was normal. Id. at 7. Dr. Molina diagnosed petitioner with hyperlipidemia, left-sided weakness and joint pain, left hip pain, and a vitamin D deficiency. Id. Petitioner was referred to physical therapy[33] and rheumatology, and labs were ordered. Id.

Petitioner presented to the emergency room at Advocate Sherman Hospital on July 30, 2014. Pet. Ex. 9 at 4. Petitioner reported feeling paresthesias, weakness, tingling, and loss of sensation on the left side of his body beginning at 5:00 AM. Id. at 21. Petitioner also reported difficulty speaking, driving, and walking. Id. Petitioner was admitted for further care and observation. Id.

---

[31] The test result comment regarding petitioner's five oligoclonal bands added, "[t]his finding is supportive evidence of [MS], but should be interpreted in conjunction with all clinical and laboratory data pertaining to this patient. Oligoclonal bands are present in the CSF of more than 85% of patients with clinically definite [MS]." Pet. Ex. 11 at 39. "Oligoclonal bands can however be observed in a variety of other diseases . . . . The data should be interpreted in conjunction with all pertinent clinical laboratory data for this patient." Id.

[32] Dr. Gershwin testified that petitioner tested positive for ANA antibodies in July 2014. Tr. 162. However, due to the way the records were scanned, the laboratory results are difficult to read and the undersigned was unable to find ANA results from July 2014.

[33] Petitioner did not use this referral to attend physical therapy. Pet. Ex. 11 at 8.

Dr. Gilbert Egekeze conducted a physical examination. Pet. Ex. 9 at 22-23. His examination revealed petitioner was awake, alert, oriented to person, place, and time, in no cardiopulmonary distress, but "a little bit unstable on his feet." Id. at 22. His neurologic examination revealed no focal deficits. Id. at 23.

While at the hospital, petitioner had a neurology consultation by Dr. Syed Munzir on July 30, 2014. Pet. Ex. 9 at 25. Dr. Munzir documented a neurologic examination that showed petitioner was awake, alert, and oriented to person, place, and time, and his speech was fluent. Id. at 26. "Motor examination of the extremities revealed poor effort on the left side with hand grasp. There was some give-way weakness affecting the proximal upper extremity, right shoulder abduction, but estimated strength was 5/5." Id. Additionally, "[l]ower extremity strength, left foot dorsiflexion and plantar flexion was 5/5. Hip flexion and knee flexion was at least 4/5, but demonstrated give-way weakness. Right-sided strength was normal. Deep tendon reflexes were 2+ bilaterally and symmetric and plantar responses were flexor bilaterally. Gait was slow but steady." Id. Musculoskeletal examination was unremarkable. Id. at 27. Dr. Munzir suspected petitioner had a complicated migraine and recommended a brain MRI. Id. MRI, CT, and EKG were normal. Id. at 21, 23.

On July 31, 2014, Dr. Munzir's neurologic examination revealed petitioner was awake, alert, and oriented to person, place, and time. Pet. Ex. 9 at 19. He found petitioner "was able to rise from the bed without any significant difficulty and he stood up on his feet." Id. "[Petitioner] walked lifting his left leg up and not dragging, and [Dr. Munzir did] see that he was able to dorsiflex his foot while walking. While walking, [petitioner] tend[ed] to complain of some feeling of weakness. Isometric strength testing showed give way weakness of the left lower extremity." Id. Dr. Munzir found petitioner was likely presenting with a complex migraine. Id.

On July 31, 2014, after Dr. Munzir's neurology consultation, Dr. Egekeze's diagnoses were left-sided paresthesias and weakness and possible hemiplegic migraine. Pet. Ex. 9 at 23. Petitioner was discharged home. Id. Dr. Egekeze wrote a note dated July 31, 2014, in which he stated petitioner's "etiology [was] currently unclear" and "recommend[ed] the [petitioner] abstain[] from vaccinations at this time until a clear diagnosis." Pet. Ex. 8 at 1.

On the following day, August 1, 2014, petitioner saw Dr. Konyukhov. Pet. Ex. 7 at 1. Petitioner reported his recent hospitalization. Id. Physical examination revealed normal facial sensation, no facial droop, and normal motor examination. Id. Again, Dr. Konyukhov found strength normal in upper and lower extremities except for subtle weakness in left arm, leg, and intrinsic muscles of hand. Id. at 1-2. Some crossing of the reflexes at the knees were noted. Id. at 2. Sensory examination was normal except for decreased sensation in the left ulnar distribution. Id. Normal coordination and ambulation were documented. Id. Dr. Konyukhov noted the presence of oligoclonal bands along with left-sided weakness. Id. at 2. He found the recent complaint of "right-sided weakness could be indication of 2 different attacks separated in time. Therefore, [MS], still in the differential. It is somewhat unusual that there is still no lesion[] present on the MRI." Id. (emphasis omitted). Diagnoses included disturbance of skin sensation, left hemiplegia, and MS. Id. Dr. Konyukhov recommended petitioner be evaluated at Indiana University. Id.

On August 18, 2014, petitioner presented to Dr. Jaison A. Grimes[34] at Indiana University due to concern for demyelinating illness. Pet. Ex. 45 at 1. Petitioner repeated his medical history. Id. Petitioner reported "[h]e continues to have significant issues with his left upper and lower extremity and . . . his right side has returned to baseline." Id. Petitioner stated his symptoms are worse when he is extremely overheated or fatigued. Id. Under review of systems, petitioner reported fatigue, energy loss, confusion, minor swallowing dysfunction, paresthesias and weakness in extremities, and occasional difficulties with gait. Id. at 2. Petitioner was alert, oriented to person, place, situation, and date, and in no acute distress. Id. Neurologic examination revealed slight weakness of left upper extremity, give way weakness on bilateral hip flexion, and mild weakness on left knee flexion. Id. "There was some very mild impairment to tandem gait." Id. Dr. Grimes reviewed petitioner's July 30, 2014 MRIs and MRA and found them unremarkable. Id. He further found petitioner's remaining testing unremarkable other than petitioner's July 1, 2014 CSF, which "note[d] the presence of 5 well-defined gamma restriction bands that are not present in the corresponding serum sample." Id. Dr. Grimes found "[i]t a bit atypical that the patient's symptoms are so severe without a corresponding lesion on imaging, but the presence of oligoclonal bands is suggestive that this could be an atypical presentation of demyelinating disease." Id. He recommended petitioner wean his corticosteroids and try an immunomodulating therapy, specifically Tecfidera.[35] Id. Dr. Grimes ordered evoked responses to assess for potential lesions "to aid in diagnosis of [MS], as it does appear that the [petitioner] has had at least 2 separate events," and repeat MRIs of brain and spine. Id. at 3.

On August 29, 2014, brainstem auditory, visual, and somatosensory evoked potentials[36] were normal. Pet. Ex. 7 at 35. On August 30, 2014, petitioner underwent MRIs of his lumbar, cervical, and thoracic spine with and without contrast. Pet. Ex. 62 at 13-17. The MRI of his lumbar spine showed degenerative disc disease at L5-S1. Id. at 14. The MRI of his cervical

[34] Dr. Jaison A. Grimes is an MS specialist at Indiana University. Tr. 35-36, 199.

[35] Tecfidera is a drug used to treat patients with MS. Tr. 92, 205-07.

[36] An evoked potential is "the electrical signal recorded from a sensory receptor, nerve, muscle, or area of the central nervous system that has been stimulated, usually by electricity." Evoked Potential, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=99671 (last visited May 4, 2021). A brainstem auditory evoked potential is "that portion of the auditory evoked potential which comes from the brainstem" and can be used "to support diagnosis of [MS]." Brainstem Auditory Evoked Potential, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=99675 (last visited May 4, 2021). A visual evoked potential looks at "changes in the evoked cortical potential when the eye is stimulated by light" and "variations are diagnostic for . . . neurologic disorders such as [MS]." Visual Evoked Potential, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=99729 (last visited May 4, 2021). Lastly, a somatosensory evoked potential looks at "waves recorded from the spinal cord or cerebral hemisphere after electrical stimulation or physiologic activation of peripheral sensory fibers" and "deviations in latency or amplitude can detect or characterize lesions." Somatosensory Evoked Potential, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=99723 (last visited May 4, 2021).

spine revealed a mild disc bulges with no focal disc protrusion or central canal stenosis, as well as bilateral foraminal narrowing in C6-7. Id. at 16. His thoracic spine MRI also showed minor disc bulges with no spinal canal stenosis. Id. at 17. There were no lesions characteristic of MS reported.

On October 1, 2014, petitioner was tested for neuromyelitis optica ("NMO")[37] antibodies, which were not detected. Pet. Ex. 7 at 43-44. It was noted that "seronegativity does not necessarily preclude a diagnosis of [NMO]." Id.

On December 10, 2014, petitioner saw Dr. Molina for a follow up and complaints of continued left-sided weakness as well as new onset of right-sided weakness that began in July. Pet. Ex. 11 at 8. Review of systems was positive for arthralgias, myalgias, confusion, and weakness. Id. Petitioner reported "[r]ight arm and hand always feel colder than the left, occasional tingling on the left of the head." Id. Dr. Molina's physical examination noted petitioner was alert and oriented to person, place, and time. Id. Musculoskeletal examination noted petitioner had weakness of left upper and lower extremity. Id. Neurological examination was normal. Id. at 8-9. Dr. Molina diagnosed petitioner with left-sided weakness, history of TIA, hyperlipidemia, and a Vitamin D deficiency. Id. at 9. Upon request, Dr. Molina provided petitioner with a new referral to physical therapy. Id. at 8-9.

Dr. Molina provided a letter dated December 10, 2014, stating petitioner "had a severe reaction to the flu vaccine previously which resulted in long-lasting neurological deficits. Because of this, further [flu] vaccination is contraindicated." Pet. Ex. 8 at 2. Similarly, Dr. Gillespie provided a letter dated December 10, 2014, recommending petitioner "avoid any vaccines" at this time. Id. at 3.

On December 23, 2014, petitioner underwent an MRI of his cervical spine with and without contrast. Pet. Ex. 62 at 9. Mild degenerative disc disease at C4-5 and C5-6 was found, otherwise the MRI was normal. Id. A brain MRI with and without contrast was also conducted and was unremarkable. Id. at 11.

5. Medical Treatment in 2015

Petitioner returned to Dr. Gillespie on January 14, 2015, complaining of fatigue, joint pain, and back pain. Pet. Ex. 10 at 10. Petitioner had been off steroids for three weeks and stated he was at 90% of baseline and feeling generally well. Id. at 11. Petitioner was alert and in no acute distress. Id. Dr. Gillespie's assessment was weakness and pain in face, upper extremity, lower extremity, abnormal liver function tests, reactive arthritis, hypogammaglobulinemia, and back pain. Id. at 12. She recommended intermittent steroid dosing and a neurology follow up with Dr. Grimes. Id.

[37] NMO is the "combined, but not usually clinically simultaneous, demyelination of the optic nerve and the spinal cord; it is marked by diminution of vision and possibly blindness, flaccid paralysis of the extremities, and sensory and genitourinary disturbances." Neuromyelitis Optica, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=92610 (last visited May 4, 2021).

On February 5, 2015, petitioner followed up with Dr. Grimes. Pet. Ex. 52 at 6. Dr. Grimes noted petitioner started taking dimethyl fumarate (Tecfidera), but if he missed a dose, he had a recrudescence of his symptoms. Id. at 6-7. He reviewed petitioner's December 2014 MRIs and found the studies unremarkable. Id. at 7. Petitioner was in no acute distress, alert, and oriented to person, place, situation, and date. Id. Neurological examination revealed petitioner had "full power" in right extremities, and almost full strength in the left extremities.[38] Id. Dr. Grimes opined petitioner had "dysesthesias and transient weakness of unclear etiology." Id. He found petitioner did not meet criteria for MS. Id. If he did, it would likely be a progressive form. Id. He recommended petitioner see a neuromuscular specialist. Id.

Petitioner returned to Dr. Gillespie on March 20, 2015. Pet. Ex. 10 at 8. Petitioner continued to have "persistent" left-sided weakness. Id. Petitioner was "[w]orried about vascular causes" and vasculitis. Id. at 9. On examination, Dr. Gillespie noted petitioner was alert, in no acute distress, "able to rise from a seated position but more difficulty from low seated position," had no distal weakness, and some decreased range of motion at his left hip. Id. at 9. Her assessment was "neurologic symptoms of weakness and pain in face, [upper extremity], [lower extremity], abnormal [liver function tests], reactive arthritis, hypogammaglobulinemia now with features of myopathy and labs consistent with myopathy." Id. at 10. She noted that petitioner's ANA was positive. Id. Dr. Gillespie's plan included an MRI of left lower extremity and likely a muscle biopsy. Id.

An MRI of petitioner's left hip and thigh was conducted on March 23, 2015, and it was normal. Pet. Ex. 10 at 23-24. Incidentally, petitioner had an allergic reaction to the intravenous contrast used. Id. Petitioner underwent an EMG of the left arm and leg on April 24, 2015, which were both normal. Pet. Ex. 52 at 11-13.

On May 6, 2015, petitioner returned to Dr. Gillespie with complaints of persistent episodes of hip weakness, dorsiflexion weakness, persistent intermittent facial asymmetry, slower thought process, and feeling very sleepy. Pet. Ex. 10 at 6. Petitioner reported having pruritus and erythema prior to this episode of muscle weakness. Id. Petitioner had been taking prednisone for the past three days. Id. Dr. Gillespie's physical examination revealed petitioner was alert and in no acute distress. Id. at 7. Examination was normal other than slight facial asymmetry. Id. Assessment was "positive ANA, neuropathic symptoms, myopathic symptoms, oligoclonal bands." Id. Dr. Gillespie's gave petitioner a referral for a muscle biopsy, agreed with his prednisone use, ordered an ANA panel, and planned to follow up with EMG results. Id.

Petitioner next saw Dr. Gillespie on June 10, 2015. Pet. Ex. 10 at 3. Petitioner was "feeling generally well," but complained of "some persistent pain and weakness in left leg," "some [mild] residual weakness in left arm and legs," and "some decreased grip strength." Id. at 4. Petitioner was off prednisone for two months and was on propranolol for tremors. Id. Physical examination was normal. Id. at 5. Petitioner's muscle biopsy showed no evidence of inflammatory changes. Id. Dr. Gillespie believed petitioner had a "primary neurologic process." Id.

[38] Dr. Grimes' record stated, "[petitioner] has full power in the right upper and lower extremity. The left upper and lower extremity have grade diffusely as a 5/-5." Pet. Ex. 52 at 7.

On October 1, 2015, petitioner underwent a brain MRI that showed a 2 mm focus of signal abnormality within the periventricular white matter, which was noted to be an isolated finding and nonspecific. Pet. Ex. 62 at 8. The same day, a cervical spine MRI revealed no significant change from prior study and no signal alteration within the spinal cord to suggest a demyelinating process. Id. at 6-7. A thoracic spine MRI was also unremarkable. Id. at 5.

Petitioner saw Dr. Molina on October 29, 2015 for a follow up and medication refill. Pet. Ex. 11 at 10. Petitioner reported "recurrent episodes of muscle pain and weakness." Id. Petitioner stated he was taking Tecfidera for presumed MS even though Dr. Grimes' records indicated that they did not suspect MS. Id. Petitioner was also "taking propranolol for a question of hemiplegic migraines." Id. He reported going to the emergency room one week earlier for racing heart and a high heart rate, and all testing was normal. Id. Dr. Molina's physical examination was normal. Id. Diagnoses included hyperlipidemia; essential tremor; "[m]igraine without aura and without status migrainosus, not intractable;" palpitations; left-sided weakness; history of Vitamin D deficiency; and dyspnea on exertion. Id.

6. Medical Treatment in 2016

Petitioner returned to Dr. Gillespie on February 11, 2016, reporting that he started treatment for MS in the past six months with "some benefit." Pet. Ex. 10 at 1. He reported an episode of upper extremity weakness over Thanksgiving, which improved with steroids. Id. He complained of joint pain in hands and chronic neck pain. Id. Petitioner was alert and in no acute distress, he had no swollen joints, but was tender at the right 3-5 proximal interphalangeal joints. Id. at 2. Dr. Gillespie attributed petitioner's symptoms to an "[a]pparent response to MS treatment." Id. She recommended petitioner follow up with neurology and ordered more labs. Id.

On September 8, 2016, petitioner underwent repeat MRIs of his cervical and thoracic spine as well as his brain. Pet. Ex. 62 at 1-4. Petitioner's cervical spine MRI revealed C4-5 central disc protrusion, no evidence of central canal stenosis, and no abnormal signal within the cervical spinal cord. Id. at 2. MRI of his thoracic spine was normal. Id. at 3. Petitioner's MRI of his brain showed "nonspecific T2 flair signal hyperintensities within the frontal periventricular white matter regions bilaterally similar to the prior exam." Id. at 4 (emphasis omitted).

Petitioner presented to Dr. Konyukhov on October 20, 2016 for "possible MS follow up." Pet. Ex. 12 at 1. Petitioner reported the history of intermittent episodes of weakness, numbness, and tingling, mostly on the left side, which "[h]e originally attributed to the [flu] vaccination." Id. He reported getting better every time he was treated with steroids. Id. Dr. Konyukhov noted repeat MRIs did not show any abnormalities, and a MS specialist from Indiana University "considered possibility of [MS] even without any lesions and therefore placed [petitioner] on Tecfidera." Id. Dr. Konyukhov reviewed the September 2016 MRIs and did not see any nonspecific white matter lesions. Id. Petitioner was in no apparent distress, alert, and oriented to person, place, and time. Id. at 2-3. Dr. Konyukhov's neurological examination was normal except for mild decreased strength in left arm and leg. Id. at 3. In his assessment, Dr. Konyukhov wrote petitioner's "intermittent episodes of weakness and numbness . . . could be suggestive of some kind of problem in the brain (MS), but so far MRIs not showing any clear

lesions." Id. at 4. He recommended petitioner continue taking Tecfidera and have a repeat MRI in one year. Id.

7. Medical Treatment in 2017

On March 23, 2017, petitioner had a follow up visit with Dr. Konyukhov. Pet. Ex. 12 at 5. Petitioner reported an episode of weakness in his legs and problems swallowing in November 2016. Id. Petitioner was alert and oriented to person, place, and time during physical examination. Id. at 7. Neurologic examination performed by Dr. Konyukhov revealed mild weakness in the left arm and leg. Id. Dr. Konyukhov's assessment was unchanged since petitioner's last visit in October 2016. Id.

In May and June 2017, petitioner presented to the emergency room on multiple occasions for throat tightness and itching thought to be due to an allergic reaction. Pet. Ex. 15 at 5-6, 22-23, 69-70, 88-89.

On August 18, 2017, petitioner presented to Nurse Practitioner, Jennifer Davison. Pet. Ex. 16 at 1. Petitioner reported "he probably has MS after a flu vaccine and had a reaction and was paralyzed on the left side." Id. Petitioner also said that in the one to two years following vaccination, he developed allergies to everything, making breathing and swallowing difficult, and requested a referral to an allergist. Id. He reported difficulty breathing while sleeping. Id. Under review of symptoms, Ms. Davison noted "[petitioner] report[ed] MS" and petitioner was concerned that "MS flares also cause difficulty swallowing." Id. Physical examination was normal. Id. at 1-2. Diagnoses included history of allergic reactions, sleep apnea, and MS. Id. at 2.

On August 23, 2017, petitioner saw allergist Dr. Jatinder K. Kansal, who documented petitioner's report of onset of neurological symptoms one day after his flu vaccine in 2013, and added "[f]inal conclusion might be reaction to flu." Pet. Ex. 17 at 1. Allergy testing conducted on September 15, 2017 was negative for everything except histamine. Id. at 8.

Petitioner returned to Dr. Molina on September 18, 2017 "for medically necessary follow up of MS and with [complaints of] dysphagia/difficulty swallowing." Pet. Ex. 16 at 3. Petitioner reported his MS was bad over the summer. Id. Petitioner reported that he went to the emergency room a couple of times for "what he thought was due to some type of systemic allergic reaction" but "he was told that his symptoms were not due to allergies and more likely to be due to the MS." Id. Petitioner stated he had "several exacerbations of the MS where he has been unable to walk and has had to use a wheelchair." Id. He added that he was taking Tecfidera. Id. Dr. Molina, on examination, stated petitioner was oriented to person, place, and time. Id. Her neurologic examination revealed "[m]ildly decreased grip strength in left hand [and] mildly decreased flexor strength in legs bilaterally (R>L)." Id. at 4. Diagnoses included MS and dysphagia. Id. MRIs and labs were ordered, petitioner was referred to speech therapy and gastroenterology, and petitioner was prescribed Tecfidera. Id.

A brain MRI conducted on September 26, 2017 revealed "a few tiny faint punctate FLAIR hyperintense foci in the bifrontal periventricular white matter," but it was otherwise

unremarkable. Pet. Ex. 61 at 1. The impression was "[s]table brain MRI with very minimal nonspecific supratentorial white matter changes." Id. Petitioner's MRI of his cervical spine found no evidence of plaques in the spinal cord, and his thoracic spine MRI was unremarkable. Id. at 2-3. Petitioner began speech therapy on September 27, 2017. Pet. Ex. 25 at 11.

Petitioner returned to Dr. Gillespie on October 10, 2017 reporting a flare up in March, including difficulty swallowing and weakness in lower extremity and hands. Pet. Ex. 21 at 1. Petitioner reported persistent weakness in hands and worsening difficulty with swallowing. Id. Physical examination was normal. Id. at 2-3. Dr. Gillespie recommended petitioner follow up with neurology for "[a]pparent MS variant." Id. at 3.

On October 16, 2017, petitioner was seen by PA John S. Emmett at Indiana University for a follow up. Pet. Ex. 19 at 1. Mr. Emmett noted the "few nonspecific punctate white matter hyperintensities" on petitioner's September 26, 2017 MRI that were unchanged from petitioner's last MRI. Id. Petitioner reported taking Tecfidera for the past three years. Id. Petitioner reported several episodes of weakness over the past year as well as episodic swallowing difficulties. Id. Mr. Emmett's neurological examination of petitioner was normal, noting full strength in all extremities. Id. at 1-2. Mr. Emmett wrote petitioner has a "self reported [history] of relapsing MS," and "[w]hen Dr. Grimes saw him, MS was not suspected given lack of exam findings and relative lack of typical MRI changes." Id. at 2. He was concerned about the risk of progressive multifocal leukoencephalopathy ("PML"), and planned to test for John Cunningham ("JC") virus,[39] noting that the results may require petitioner to be taken off Tecfidera. Id. Mr. Emmett's assessment was weakness. Id. at 2.

Petitioner began physical therapy and occupational therapy in October 2017. Pet. Ex. 24 at 42, 45. Petitioner underwent a swallow study on October 31, 2017, which was normal. Pet. Ex. 23 at 15.

8. Medical Treatment from 2018 to 2019

On January 12, 2018, petitioner saw Dr. Gillespie, who noted that petitioner reported testing positive for the JC virus and thus, he was taken off Tecfidera. Pet. Ex. 95 at 5.

Petitioner visited Dr. Chad Glazer, an otolarynologist, on February 21, 2018 to establish care. Pet. Ex. 49 at 7. He requested an evaluation of dysphagia and difficulty breathing at night. Id. Petitioner underwent an esophageal motility study and the impression was ineffective esophageal motility. Id. Physical examination indicated bilateral small tonsil stones. Id. at 10. Dr. Glazer explained to petitioner that "MS can cause difficulty with swallowing as this takes the coordination of multiple muscles." Id. at 11. Dr. Glazer's assessment was dysphagia, sleep disorder breathing, tonsil stones, and MS. Id.

[39] JC virus "is the cause of progressive multifocal leukoencephalopathy," which has been known to occur in MS patients treated with Tecfidera. JC Polyomavirus, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=99364 (last visited Apr. 14, 2021); see Tecfidera, RxList, https://www.rxlist.com/tecfidera-drug.htm (last reviewed Mar. 13, 2020).

On March 12, 2018, petitioner visited Dr. Molina for a follow up examination of a recent hospitalization due to an allergic reaction. Pet. Ex. 48 at 19. Petitioner did not complain of any weakness. See id. Dr. Molina noted petitioner was not taking Tecfidera. Id. at 20.

Petitioner followed up with Dr. Glazer on April 18, 2018. Pet. Ex. 49 at 1. A flexible laryngoscopy was performed. Id. at 5. The post-operative diagnoses were dysphasia and paradoxical vocal cord motion. Id. Dr. Glazer's assessment was left tinnitus, dysphasia, sleep disorder breathing, and paradoxical vocal cord motion. Id. at 5-6.

Petitioner returned to Dr. Konyukhov on January 22, 2019 for a follow up. Pet. Ex. 53 at 5. Petitioner reported an MS flare up in February 2018 where he was hospitalized and had trouble walking, swallowing, and speaking. Id. On physical examination, Dr. Konyukhov found "some exaggerated physiological tremor . . . in both hands, [but] worse on the right side," and decreased strength in lower extremities with "somewhat poor effect." Id. at 7-8. He assessed petitioner with weakness. Id. at 8. Dr. Konyukhov noted "[n]o obvious diagnosis [so] far despite seeing multiple different physicians." Id.

The following day, on January 23, 2019, petitioner saw Dr. Molina. Pet. Ex. 48 at 1. Petitioner reported one relapse since February 2018 and complained of continued swallowing difficulty. Id. Physical examination was normal. Id. at 4-5. Under diagnoses, Dr. Molina listed hyperlipidemia, MS, muscle spasm, Vitamin D deficiency, osteoporosis of lumbar spine, and "[a]dverse reaction to [flu] vaccine, sequela." Id. at 5.

Dr. Molina authored a letter, dated January 23, 2019, stating, "[petitioner] should be excluded from routine required [flu] vaccination due to a previous history of adverse reaction to the vaccine. Shortly after receiving the seasonal [flu] vaccine in 2013[,] he developed significant neurologic symptoms, some of which are persisting even today." Pet. Ex. 48 at 63.

No more recent medical records were filed.

D. Petitioner's Affidavit and Testimony

Petitioner averred that prior to receiving the flu vaccine at issue, he "was in excellent health with no chronic health conditions and no neurological symptoms." Pet. Ex. 51 at ¶ 3. He was feeling well, strong, and energetic. Tr. 10-11. He had back pain, high cholesterol, possible allergies, elevated liver enzymes, "a couple [of] migraines in [his] life," and prior tendinitis and arthritis in his left shoulder. Tr. 11, 58-60. At the time of vaccination, he was working as a pediatric hospitalist and did not have health insurance. Tr. 9-10.

In November 2013, petitioner completed a medical mission trip to Bolivia. Tr. 11. While in Bolivia, he had no health issues. Tr. 12. He returned from Bolivia on November 11, 2013. Id. During his first shift at the hospital, on November 15, 2013, petitioner received a flu vaccine around 2:30 or 3:00 PM. Tr. 12-13, 60. He testified that he "probably" received a flu vaccine every year since 2000 and had never had an adverse reaction besides a sore arm. Tr. 13.

Around 24 hours later, on November 16, 2013, he "began to experience weakness and [paresthesia] on the left side of [his] body, including [his] hand, arm, leg, face[,] and scalp. [He] also had dysphonia and dysphagia, confusion, and problems with gait and balance." Pet. Ex. 51 at ¶¶ 4-5; see also Tr. 14. When his symptoms began, he was driving to meet his wife and daughter and stopped at a rest stop off the road for about 30 minutes. Tr. 14-15. He testified that everything was spinning, and he felt weak. Tr. 14. "[He] noticed the left side of [his] body was weak, but [his] right side was fine." Tr. 15. Once "[he] was feeling a little bit better," he drove to meet his wife at a hotel. Id.

Once he arrived at the hotel, "[his wife] immediately told [him] . . . that [his] left side of [his] face was kind of droopy." Tr. 15. He asked her to test his strength, and she noted his left side was weak. Tr. 15-16. Because he did not have health insurance, petitioner drove himself to the hospital. Tr. 16.

Petitioner arrived at Vista Medical Center and received an extensive work up to rule out stroke. Tr. 16; Pet. Ex. 51 at ¶ 5. Petitioner contended that he was never examined by the treating emergency room doctor, nor did he receive a follow up examination before discharge. Pet. Ex. 51 at ¶ 15; Tr. 17-18. On discharge, he stated "[his] symptoms had not improved." Pet. Ex. 51 at ¶ 15. He testified that he still had brain fog and weakness, and that he crashed his car on the way home from the hospital. Id.; Tr. 18-19, 64-65. He added that he did not remember how he got back to the hotel where he was staying. Tr. 19, 64. When he woke up the next morning, he still had weakness, which lingered for the next few days. Tr. 19.

From November 16 to November 22, 2013, petitioner did not return to work due to the lingering symptoms he was experiencing. Tr. 20. On November 22, 2013, he visited an urgent care clinic, where a doctor told him that he likely experienced a stoke and needed to see a neurologist. Tr. 19-20. The following day, on November 23, 2013, petitioner was having trouble using his arm and holding a fork and went to the emergency room at Porter Hospital. Tr. 21-22.

Petitioner submitted a Vaccine Adverse Event Reporting System ("VAERS") Report on November 26, 2013 when he returned to work. Pet. Ex. 3 at 1; Tr. 22. Petitioner wrote that one day after his flu vaccine, he had confusion; left-sided weakness in his face, arm, hand, and leg; tremors; dysphasia; dysphonia; and problems with his gait. Pet. Ex. 3 at 1. He indicated that all symptoms persisted. Id. His flu vaccination was noted to be administered on November 15, 2013 at 3:20 PM, and the adverse event onset was noted to have occurred at 3:00 PM on November 16, 2013. Id.

Petitioner saw neurologist, Dr. Simaga, on January 14, 2014. Tr. 23. He testified that this was the first available appointment he could make with a neurologist once he got health insurance. Tr. 23-24. On January 14, he was still experiencing weakness on his left side and decreased sensation on the left side of his face. Tr. 24. He was still working at this time, but it was hard to walk around the hospital and focus on a computer screen, and he felt he was not strong enough to hold a newborn baby. Tr. 25-26. Petitioner stated that after Dr. Simaga completed "a very thorough history and exam, . . . he told [petitioner] that [he] possibly [] had a small stroke" or a hemiplegic migraine. Tr. 24-25.

On January 29, 2014, petitioner began seeing Dr. Molina as his primary care physician. Tr. 26. Dr. Molina noted "concern for CNS vasculitis, especially given that [petitioner's] symptoms occurred the day after receiving a flu vaccine." Tr. 28. Petitioner returned to Porter Hospital on April 5, 2014 and was admitted. Tr. 29, 31. He testified that he had a sensation on the left side of his face, and despite what the medical records state, he contended it was not a headache or migraine. Tr. 29-31. While admitted to the hospital, Dr. Konyukhov, a neurologist, examined petitioner. Tr. 31-32. Petitioner testified that Dr. Konyukhov has been his treating neurologist since April 2014. Tr. 32.

Petitioner averred that based on his symptoms, medical treatment, and testing, it is "[his] understanding from [his] doctors [] that [he] [is] suffering from a form of [MS]." Pet. Ex. 51 at ¶ 8. Petitioner testified that beginning in July 2014, he began to experience periodic weakness on his right side that began in his legs. Tr. 33. Dr. Konyukhov ordered a lumbar puncture, which showed oligoclonal bands. Tr. 34. Dr. Konyukhov told petitioner that he could have MS, but because petitioner's MRIs did not show any findings consistent with MS, he referred petitioner to MS specialist Dr. Grimes. Tr. 35-36. Dr. Konyukhov explained to petitioner that he "based his diagnosis of MS [] on the McDonald[] criteria . . . since [his] clinical picture included more than 2 different episodes, in more than 2 different areas of [his] body (which accounts for dissemination in space and time), presence of specific oligoclonal bands, and excluding a very extensive list of neurological conditions." Pet. Ex. 51 at ¶¶ 8-9. Additionally, Dr. Konyukhov, along with Dr. Gillespie, found no other diagnostic possibilities. Id. at ¶ 9; Tr. 40-41.

Petitioner saw Dr. Grimes on August 18, 2014. Tr. 36. Petitioner testified that Dr. Grimes told him he most likely had a demyelinating disease, most similar to primary progressive MS. Tr. 36-37. Petitioner was "recommended Tecfidera, a medication specific to treat MS, which [he] took for about 3 years and which helped [him] by reducing the number of relapses from 6-7 per year to 2-3 relapses per year." Pet. Ex. 51 at ¶ 10; see also Tr. 37-38, 41-42. On February 5, 2015, at petitioner's next visit to Dr. Grimes, Dr. Grimes told petitioner he did not meet the criteria for MS. Tr. 39.

At the end of 2017, petitioner tested positive for the JC virus, and therefore, Dr. Grimes recommended petitioner stop taking Tecfidera. Pet. Ex. 51 at ¶ 11; Tr. 46-47. After he stopped taking Tecfidera, he averred that "all of [his] symptoms began to worsen." Pet. Ex. 51 at ¶ 12. The right side of his body started getting weak and had poor grip strength. Tr. 47. In February 2018, petitioner experienced a relapse that left him unable to work until June 2018. Id.; Pet. Ex. 51 at ¶ 12. Thereafter, Dr. Konyukhov recommended high dose Biotin,[40] which improved petitioner's symptoms and which petitioner was still taking at the time of the hearing. Pet. Ex. 51 at ¶ 12; Tr. 47-48. Petitioner testified that Dr. Konyukhov explained that "many neurologists now consider the McDonald[] criteria to be outdated, as there is constantly new knowledge on MS." Pet. Ex. 51 at ¶ 13.

[40] Biotin is "a water-soluble dicyclic monocarboxylic acid considered to be part of the vitamin B complex." Biotin, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=6292 (last visited May 4, 2021). Deficiencies in humans can manifest as "dermatologic, neurologic, and ocular disorders." Id.

Petitioner's symptoms, which he averred have persisted since November 2013 and "many of which have waxed and waned at different times," include

> 1) weakness on the left side of [his] body, including weakness of [his] left arm, hand, gluteal area, leg, and foot; 2) weakness on the right side of [his] body, including [his] right gluteal area, quadriceps, and ankle; 3) decreased grip strength in both hands; 4) tingling on the scalp, left arm and left leg, tingling on other areas, and electricity sensation down [his] spine; 5) numbness on [his] extremities, loss of sensation on the left side of [his] face and left arm; 6) tremors; 7) loss of coordination and balance; 8) confusion or brain fog, including slowed thought process at times and problems with memory; 9) double vision and difficulty focusing vision; 10) face drop and drooling, initially on the left side of the mouth, but now mostly drooling on the right side; 11) paresthesia on left side of the scalp and face; 12) difficulty swallowing and advancing food past the stomach (gastroparesis, decreased esophageal motility and uncoordinated swallow demonstrated in Motility study); 13) difficulty with speech at times, both in pronouncing words and getting words out; 14) problems dropping things; 15) episodes of dizziness; 16) tinnitus; 17) sudden pain in my legs; 18) spasticity in legs and toes; 19) fluctuating blood pressure and tachycardia (referred to by neurologist as dysautonomia); 20) episodes of tiredness and fatigue; 21) heat intolerance/sensitivity, worsening weakness and other symptoms when exposed to heat, for example, having to use cooling bands and a cooling vest to deal with heat and prevent symptoms in the Summer time; 22) difficulty walking to the bathroom at night; 23) frequent urinary tract infections and frequent urinating at night; 24) difficulty breathing at night at times; 25) vocal cord dysfunction (also related to dysautonomia); 26) intermittent constipation alternated with inability to hold it; 27) hypotonic bladder; 28) problems with erection; 29) difficulty climbing stairs, walking long distances, running, prolonged standing, exercising, and participating in sports; 30) difficulty with hand writing and typing at times; 31) difficulty with handling silverware and other small objects; and 32) difficulty sleeping well (lack of sleep also makes all symptoms worse).

Pet. Ex. 51 at ¶ 7. As of the hearing, petitioner testified that he continues to experience paresthesia, weakness, problems with balance and gait, difficulty focusing, slurred speech, issues swallowing, and issues with his memory. Tr. 48-50.

Petitioner averred that his condition has had a significant impact on his life. Pet. Ex. 51 at ¶ 17. He described having difficulty getting through the day, requiring cooling bands and vests in the summer to prevent symptoms from worsening, and experiencing fatigue, weakness, and overheating in the winter. Id. Because he gets tired easily and has difficulty handling stress, he has had to decrease his hours at work because his symptoms interfered with his job. Id.; Tr. 51-52. He testified that he also has not been able to care for his daughter properly or participate fully in her life. Tr. 53.

Petitioner contended that many of his medical records, particularly those at Vista Medical Center, Sherman Hospital, and Porter Hospital, inaccurately documented his symptoms. Pet. Ex. 51 at ¶ 14. He further asserted that on many visits, doctors or nurses "failed to examine [him] or improperly or inadequately examined [him]." Id.; see also Tr. 61-62. He asserted that he never had a headache during his relapses, despite many medical records stating this fact. Pet. Ex. 51 at ¶ 16.

Petitioner testified that he has not visited Dr. Konyukhov since January 2019. Tr. 55. And since March 2020, the start of the Covid-19 pandemic, he has not seen any of his treating physicians. Tr. 55-56.

E. Expert Reports

1. Petitioner – Dr. Marcel Kinsbourne[41]

a. Background and Qualifications

Dr. Kinsbourne earned his B.A. from Christ Church at Oxford University in 1952, his Bachelor of Medicine (B.M.) and Bachelor of Surgery (B.Ch.) from Oxford University Medical School in 1955, his M.A. and Doctor of Medicine (D.M.) from Oxford University in 1956 and 1963, and his M.D. from State of North Carolina in 1967. Pet. Ex. 44 at 1. From 1955 to the early 1990s, he regularly treated patients. Tr. 74. Throughout his career, Dr. Kinsbourne has also held teaching positions at various institutions. Pet. Ex. 44 at 2-3. Dr. Kinsbourne has held medical licenses in the United Kingdom, Canada, North Carolina, Massachusetts, and Virginia. Id. at 2. He has been bestowed numerous honors and awards, has served and is currently serving on a number of editorial boards, and has authored or co-authored more than 400 publications. Id. at 3-39.

b. Opinion

i. Diagnosis

Based on petitioner's testimony and medical records, Dr. Kinsbourne opined that petitioner "has an inflammatory autoimmune encephalopathy"[42] that is most like MS with an ADEM-like onset, and with symptoms consistent with a demyelinating disorder. Tr. 99-100, 102; see also Pet. Ex. 25 at 4. Dr. Kinsbourne found petitioner "most likely . . . began with an ADEM-like presentation which morphed into [a] [MS]-like disorder." Tr. 78; see also Pet. Ex. 96 at 1-3.

[41] Petitioner filed four expert reports authored by Dr. Kinsbourne. Pet. Exs. 25, 54, 63, 96.

[42] Dr. Kinsbourne clarified that "inflammatory autoimmune encephalopathy" is a description of his condition that "encompasses a number of entities." Tr. 102, 129. Dr. Kinsbourne did not enumerate the "number of entities" or otherwise define them.

At the hearing, Dr. Kinsbourne testified that he would not have diagnosed petitioner with MS or ADEM, and that petitioner's condition is most like a cross between MS and ADEM. Tr. 78, 102. However, on cross-examination, Dr. Kinsbourne testified that as a practical matter, he would have diagnosed petitioner with MS, as his treating physicians did. Tr. 129. And in his fourth expert report, he wrote, "there is no question that the subsequent course was that of MS." Pet. Ex. 96 at 3.

Prior to vaccination, petitioner was generally in good health with no record or history of any neurological illness. Tr. 78-79. Looking at petitioner's medical records from November 2013, Dr. Kinsbourne testified that he most likely would have thought petitioner suffered a stroke. Tr. 80-81. He found petitioner's complaint of difficulty focusing would not be unlikely with a stroke. Tr. 82. Additionally, petitioner complained of difficulty speaking due to the numbness and weakness in the left side of his face. Tr. 82-83. Dr. Kinsbourne did not believe that petitioner had a TIA or a hemiplegic migraine. Tr. 83, 88, 103; Pet. Ex. 25 at 4. However, he did think that CNS vasculitis was a reasonable possibility in early 2014. Tr. 85-87.

Although he agreed that petitioner had symptoms of a stroke, Dr. Kinsbourne testified that it would have been appropriate to consider a diagnosis of ADEM at onset. Tr. 131-32. Dr. Kinsbourne opined that petitioner's presentation at onset was polysymptomatic, a feature "typical of ADEM, which develops acutely with multiple symptoms appearing at the same time." Pet. Ex. 96 at 1-2; see also Tr. 108. He opined that petitioner's "disease onset conformed to ADEM, as an encephalopathy that featured headache and confusion." Pet. Ex. 96 at 2. For support that petitioner suffered from ADEM at onset, Dr. Kinsbourne pointed to petitioner's November 2013 complaints of numbness and tingling in his left face and arm, trouble walking on his left leg, and cognitive issues. Tr. 108.

Dr. Kinsbourne opined that MRI evidence is not required for a diagnosis of ADEM. Tr. 110. He also stated that there is a delay between ADEM symptoms and associated MRI changes, and thus, petitioner's MRI would not reflect lesions typically identified in ADEM. Pet. Ex. 96 at 2; Tr. 110.

However, Dr. Kinsbourne believed the remainder of petitioner's clinical course, after onset, conformed to MS. Pet. Ex. 96 at 2; see also Tr. 78. Dr. Kinsbourne opined that petitioner's clinical manifestations at onset relapsed and conformed to the McDonald criteria, specifically, episodes differing in time and space. Pet. Ex. 25 at 4. Additionally, petitioner had heat sensitivity, five oligoclonal bands in his CSF, a positive response to steroids, and positive ANA antibodies, which Dr. Kinsbourne opined supported a diagnosis of MS. Id. Because petitioner's treating physicians started petitioner on Tecfidera, Dr. Kinsbourne assumed they believed petitioner had MS. Id. Although petitioner was taken off Tecfidera, he found it appropriate to discontinue the medication due to petitioner's positive test result for the JC virus. Tr. 96.

Dr. Kinsbourne opined that it is appropriate to consider a diagnosis of MS after three months, and that a diagnosis is clear once there is dissemination in space—here, when petitioner first reported symptoms on the right side of his body in July 2014. Tr. 132.

He also argued that a brain MRI is often normal when clinical diagnostic criteria for MS are first met. Pet. Ex. 25 at 4. He conceded that "normal-appearing white matter on MRI of the MS brain can be quite abnormal." Pet. Ex. 63 at 1. However, he asserted that advanced MRI techniques were not used on petitioner that could have revealed underlying pathology. Pet. Ex. 54 at 1-2; Tr. 116. He opined that in petitioner's case, his normal-looking white matter would likely have been abnormal if appropriate advanced techniques had been used. Tr. 116.

Further, Dr. Kinsbourne argued that "MRI abnormalities are not essential for the diagnosis for MS if there are oligoclonal bands." Pet. Ex. 54 at 1. In fact, 90-95% of MS patients have oligoclonal bands according to Dr. Kinsbourne. Id. at 2; Tr. 117. David Keren[43] wrote, "examination of the CSF for the presence of [oligoclonal]-bands is still the best single laboratory test providing support for the diagnosis of MS because many of the non-MS conditions in which they appear can be distinguished clinically from MS." Pet. Ex. 65 at 1. Keren added that "[i]n the appropriate clinical setting, the presence of the [oligoclonal]-bands provides powerful supportive evidence for the diagnosis." Id.

Additionally, Dr. Kinsbourne testified that "if these oligoclonal bands occur only in the CSF and not in the serum, that is probably convincing evidence of an inflammatory autoimmune . . . or infectious condition of the brain." Tr. 89. Dr. Kinsbourne noted petitioner's CSF showed five oligoclonal bands, which is "strong evidence of inflammatory disease of his brain." Id.; see also Pet. Ex. 54 at 1. He conceded that other conditions can exhibit oligoclonal bands, but opined that there is no evidence that petitioner has any of those conditions. Tr. 117. He reiterated that it is "very possible" for someone to suffer from a CNS demyelinating condition even when there are no visible lesions on MRI. Tr. 118-20.

And at petitioner's most recent visit to Dr. Konyukhov in January 2019, Dr. Konyukhov documented symptoms that Dr. Kinsbourne opined are consistent with someone who is suffering from a demyelinating illness. Tr. 98-100.

In summary, Dr. Kinsbourne concluded that petitioner has a primary inflammatory CNS white matter demyelinating disease. Tr. 106. He opined it is primary because there is no evidence that his condition is secondary to any systemic disease. Tr. 106, 112-13. It is inflammatory because there is no evidence that petitioner had an infection, nor is there any evidence of any other cause. Tr. 106.

ii. Althen Prong One

Dr. Kinsbourne opined that petitioner's November 15, 2013 flu vaccination more likely than not caused petitioner's demyelinating illness. Tr. 103; Pet. Ex. 25 at 8. At the hearing and in his expert reports, Dr. Kinsbourne opined as how the flu vaccine can cause or trigger the innate immune system and lead to a demyelinating condition.

[43] David F. Keren, Optimizing Detection of Oligoclonal Bands in Cerebrospinal Fluid by Use of Isoelectric Focusing with IgG Immunoblotting, 120 Am. Soc'y for Clinical Pathology 649 (2003).

He opined generally that vaccinations can cause demyelinating disorders, like ADEM, but deferred to Dr. Gershwin as to the mechanism. Pet. Ex. 96 at 2-5; Tr. 104; see also Pet. Ex. 99 at 2; Pet. Ex. 102 at 5; Pet. Ex. 104 at 2, 3 tbl.1.[44]

Dr. Kinsbourne next opined that ADEM can "morph" into MS. Tr. 78; Pet. Ex. 96 at 1-3. He did not explain the process or mechanism by which ADEM can morph into MS other than to say it can happen. He did, however, cite to medical literature in support of this opinion.

In Schwarz et al., for example, the authors conducted a long-term follow-up study of 40 adults originally diagnosed with ADEM to determine possible diagnostic criteria to distinguish ADEM from MS. Pet. Ex. 103 at 1. Those originally diagnosed with ADEM had (1) "[a]cute neurologic symptoms without a history of previous, unexplained neurologic symptoms," (2) one or more lesions on MRI, and (3) "exclusion of CNS infection, vasculitis, or other autoimmune disease with CSF analysis." Id. at 2. A final diagnosis of ADEM was established only if "there was no evidence of a second clinical episode of CNS demyelination." Id. The authors found 14 of the 40 patients (35%) originally diagnosed with ADEM had a second clinical episode within one year of initial presentation and thus, were ultimately diagnosed with MS.[45] Id. at 3. They determined "the presence of oligoclonal bands of IgG did not discriminate ADEM from MS." Id. All 40 patients exhibited at least one lesion on MRI, and 13 of the 14 patients with definite MS developed additional lesions. Id. Schwarz et al. concluded that "[m]any patients initially diagnosed with ADEM develop clinically definite MS upon long-term follow-up." Id. at 1. They "found no useful diagnostic criteria for the differentiation of a first episode of MS from monophasic ADEM." Id. The authors did not hypothesize as to whether ADEM "morphs" into MS, nor did the authors provide a mechanism by which ADEM can "morph" into MS. But the authors demonstrated that an original diagnosis of ADEM can change to a diagnosis of MS based on long-term follow-up.

Mikaeloff et al. conducted a study of 296 children with a first episode of acute inflammatory demyelination of the CNS. Pet. Ex. 101 at 2. Those who received a diagnosis of ADEM at presentation had "a polysymptomatic onset with mental status change and [a] suggestive brain MRI." Id. Diagnosis of definite or probable MS was made using the Poser criteria,[46] with MRI suggestive of MS when multiple lesions were seen in periventricular and/or subcortical locations. Id. Suspected MS diagnosis was given to those who met the MRI criteria and had compatible clinical criteria. Id. Children with ADEM at onset who had a second attack were reclassified as clinically definite MS. Id. Initial diagnosis was suggestive of MS in 96 patients (33%) and suggestive of ADEM in 119 patients (40%). Id. at 4. At the end of the follow-up period, the authors found 168 of 296 of the patients (57%) met the criteria for a final diagnosis of MS, 34 (20%) of which had ADEM at onset, but when they experienced a second

[44] A. Shoamanesh & A. Traboulsee, Acute Disseminated Encephalomyelitis Following Influenza Vaccination, 29 Vaccine 8182 (2011).

[45] The authors used the outdated Poser criteria for diagnosing MS.

[46] The authors note they did not use the McDonald criteria because it is not recommended for those below the age of 10. Pet. Ex. 101 at 2.

attack, their final diagnosis was modified to MS. Id. Again, the authors did not opine as to whether ADEM can "morph" into MS, nor did they opine to the mechanism by which this could occur. Mikaeloff et al. showed that after a follow-up period, an initial diagnosis of ADEM can change to MS once there is a second flare or attack.

As for the mechanism of causation, Dr. Kinsbourne opined that the flu vaccine can cause MS through the innate immune system. Pet. Ex. 25 at 6. Although he noted that "MS is thought frequently to involve molecular mimicry between the infectious antigen and self-antigens," Dr. Kinsbourne expressly rejected the mechanism of molecular mimicry in this case and opined that molecular mimicry would not occur within 24 hours. Id.

Dr. Kinsbourne testified that when the flu vaccine is administered, it elicits the development of pro-inflammatory cytokines that stimulate inflammatory changes. Tr. 77-78. For a vaccine to be effective, it must activate the innate immune system, which responds within a few hours. Tr. 103. He asserts that the innate immune system produces pro-inflammatory cytokines that pass the blood-brain barrier and activate inflammation, which can subsequently result in demyelination. Id.; Pet. Ex. 25 at 6.

Specifically, he opined that the flu vaccine "prompt[s] activation of the macrophages of the innate immune system within minutes." Pet. Ex. 25 at 6. Subsequently, lymphocytes travel to key sites, resulting in the production of proinflammatory cytokines that "cause endothelial damage and activate intra-cranial astrocytes and microglial cells. These immune cells of the [CNS] release more proinflammatory cytokines intracranially . . . causing demyelination." Id. Dr. Kinsbourne added that "innate immunity is also characterized by memory of previous immune reaction to similar antigens, resulting in anamnestic responses by [toll-like receptors ("TLRs")] and an enhanced cytokine-initiated cascade." Id. at 7.

Dr. Kinsbourne cited to Deng and Sriram[47] to support the premise that an innate as opposed to an adaptive autoimmune etiology is favored for MS because according to Dr. Kinsbourne, "Deng and Sriram [] favored an autoimmune etiology for MS other than molecular mimicry." Pet. Ex. 25 at 6. However, his characterization of the article is misleading. Deng and Sriram did not state that an innate immune etiology is the favored mechanism for MS. Instead, they stated that "lesions in MS are inflammatory in nature, and the underlying basis for the pathology is considered to be autoimmune and most likely mediated by activated T cells to the oligodendrocyte/myelin unit."[48] Id. at 2. Within that frame of reference, Deng and Sriram examined the role of microglia in the development of demyelination. They hypothesized that

[47] The Deng and Sriram article is co-authored by Dr. Sriram, the respondent's expert in this case.

[48] T cells, or lymphocytes, are "cells primarily responsible for cell-mediated immunity." T Lymphocytes, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition? id=87562 (last visited May 4, 2021). "When activated by antigen, T lymphocytes proliferate and differentiate into T memory cells and the various types of regulatory and effector T cells." Id. Adaptive, not innate, immunity is "mediated by B and T lymphocytes following exposure to a specific antigen." Illustrated Dictionary of Immunology 18 (3d ed. 2009).

"microglia may play a role in both presentation of an autoantigen and in secretion of proinflammatory cytokines." Id. They proposed three models of demyelination in inflammatory disorders, "where microglial activation is evident and [] an important feature of the pathologic process." Id. at 1, 3-5.

The first model described by Deng and Sriram implicates "antibody-mediated destruction of the myelin unit." Pet. Ex. 28 at 4 fig.1A, 3, 5. This model fits the paradigm of molecular mimicry and/or the adaptive immune system. The second model contemplates "activation of microglia as the primary event leading to secondary recruitment of lymphocytes and damage to myelin." Id. at 4 fig.1B, 5. This model does not include activation of T cells. Id. However, it does require "[a]ctivation of microglial by [lipopolysaccharides], toll receptor agonists, [or] super antigens." Id. at 4 fig.1B. Dr. Kinsbourne did not suggest that the flu vaccine at issue contained lipopolysaccharides, a toll receptor agonist, or a super antigen.

The third model proposed by Deng and Sriram is "characterized by oligodendrocyte death." Pet. Ex. 28 at 4 fig.1C, 5. "All other immunological . . . processes that follow, including the development of an immune response to myelin antigens, are secondary events following oligodendrocyte death." Id. at 5. In this model, "activation of microglia [is] an unintended consequence of extensive myelin destruction." Id. Therefore, this model does not suggest that microglia or the innate immune system causes demyelination.

To support his opinion that cytokines play a role in triggering the inflammation seen in MS, Dr. Kinsbourne also cited to Graber et al.,[49] whom Dr. Kinsbourne found "attribute MS lesions to inflammation triggered by cytokines" and "demonstrated that the levels of proinflammatory cytokine IL-6 are increased in the CSF of MS patients." Pet. Ex. 25 at 6. In Graber et al., the authors investigated the role of IL-17 and its possible link with IL-6 in autoimmune inflammation of the CNS by examining IL-17 and other cytokine levels in peripheral blood mononuclear cells. Pet. Ex. 32 at 2. The authors determined that IL-17 and IL-6 production were increased in the peripheral blood mononuclear cells of patients with transverse myelitis ("TM") compared to the control group and those with MS. Id. at 5. Notably, there were limitations to the study in that all MS patients in the study had clinically definite relapsing-remitting MS at the time of participation in the study. Thus, it was impossible to determine cytokine levels at the time of onset because they were not tested. Regardless, the authors stated that IL-17 is made by activated memory CD4+ cells, and that "IL-17 in turn stimulate[d] macrophage production of IL-6, TNF α and IL-1B." Id. at 2, 8. While they speculated that, it is "possible that IL-17 is an early triggering event in autoimmune CNS diseases," this possibility appears to be put into the context of the adaptive immune response. See id. at 7. They recommended additional studies to address the "temporal relationships between the cytokines studied and disease activity." Id.

[49] Jerome J. Graber et al., Interleukin-17 in Transverse Myelitis and Multiple Sclerosis, 196 J. Neuroimmunology 124 (2008).

iii. Althen Prong Two

Dr. Kinsbourne opined that, in petitioner's case, "[t]he flu vaccination caused an outpouring of pro-inflammatory cytokines, which stimulated inflammatory change in the microglia in [petitioner's] brain, and caused him to have an acute polysymptomatic neurological disorder, which was more like what happens in ADEM than in any other alternative condition." Tr. 77-78. However, Dr. Kinsbourne testified that over time, petitioner had multiple relapses, which were most similar to a form of MS, and his condition morphed into MS. Tr. 78; Pet. Ex. 96 at 3. Dr. Kinsbourne maintained petitioner's current condition is most like MS because petitioner has experienced dissemination in space and time. Tr. 102, 132; Pet. Ex. 25 at 4. However, it is not essential to his theory of causation that petitioner's condition fits neatly into the technical definition of MS. Tr. 104-05.

Dr. Kinsbourne conceded that petitioner's condition is atypical because there is no MRI confirmation of MS. Tr. 124. However, he opined that it is "very possible" for someone to suffer from a CNS demyelinating condition even when there are no visible lesions on MRI. Tr. 118-20.

First, Dr. Kinsbourne opined that MRI evidence is not required for a diagnosis of ADEM. Tr. 110. He argued there is a delay between ADEM symptoms and associated MRI changes, and thus, MRIs do not always reflect lesions typically identified in ADEM. Pet. Ex. 96 at 2; Tr. 110. He cited to Honkaniemi et al., which examined MRIs of four adult patients with ADEM from a few days of onset for up to eight months. Pet. Ex. 98 at 1. The authors found "a delay of about 1 to 6 weeks between the onset of clinical symptoms and the appearance of the lesions in MR images." Id. at 7. Additionally, new lesions appeared during the recovery period. Id. at 6-7. However, this article does not address the situation were MRIs are done over a period of years, and still do not show evidence of lesions.

In Dale et al.,[50] another article cited by Dr. Kinsbourne, the authors noted "[h]istological studies of patients with ADEM [performed] at various intervals up to a month after clinical onset have shown that microscopic lesions are very numerous, appear within days of clinical presentation[,] and do not increase in size or number." Pet. Ex. 27 at 12.

Next, Dr. Kinsbourne opined that MS patients can have normal MRIs, and cited Thorpe et al.,[51] which looked 170 patients with possible, probable, or definite MS who had undergone brain and spinal cord MRIs. Pet. Ex. 42 at 2. Of the 170 patients, 20 had minimal or no abnormalities on their brain MRIs and abnormal spinal MRIs. Id. at 1. Eight patients, three of which were diagnosed with MS, had completely normal brain MRIs. Id. at 3, 3tbl.1. The authors "conclude[d] that the finding of a normal brain MRI, although rare, is nevertheless quite compatible with a diagnosis of [MS]." Id. at 5. However, all eight patients exhibited at least one

[50] R. C. Dale et al., Acute Disseminated Encephalomyelitis, Multiphasic Disseminated Encephalomyelitis and Multiple Sclerosis in Children, 123 Brain 2407 (2000).

[51] J. W. Thorpe et al., Spinal MRI in Patients with Suspected Multiple Sclerosis and Negative Brain MRI, 119 Brain 709 (1996).

spinal cord lesion. Id. at 3, 3tbl.1. Thus, while patients may have normal brain MRIs, their spinal cord MRIs may show cord lesions, which aid in the diagnosis of MS. Id. at 5.

The authors in Healy et al.[52] discussed the dissociation between clinical symptoms and MRI findings in MS patients. Pet. Ex. 55 at 1. The authors separated their subjects into three groups: (1) low lesion load/high disability; (2) high lesion load/low disability; and (3) non dissociated.[53] Id. at 1-2. They found 13.5% of patients had a clinical/MRI dissociation, with 4.1% having a low lesion load and high disability and 9.4% having a high lesion load and low disability. Id. at 4. The low lesion load group was more likely to have progressive MS and cervical cord lesions, while all but one patient in the high lesion group had relapsing MS. Id. at 3-4. The authors noted that their study did not use high resolution and higher field MRI to measure lesions, which they acknowledged "might show important differences between the dissociation groups." Id. at 5.

Additionally, Dr. Kinsbourne argued "MRI abnormalities are not essential for the diagnosis for MS if there are oligoclonal bands," and petitioner's CSF showed five oligoclonal bands. Pet. Ex. 54 at 1. At the hearing, Dr. Kinsbourne cited Thompson et al., an article from respondent's expert, where the International Panel recommended that when dissemination in space is met and there is "no better explanation for the clinical presentation," oligoclonal bands in CSF can fulfill the dissemination in time requirement, meeting the criteria for a diagnosis of MS. Resp. Ex. C at 5.

Because petitioner had been exposed to the flu vaccine before, Dr. Kinsbourne opined that petitioner's innate immune memory was accelerated and amplified by the flu vaccine which initiated activation of TLRs.[54] Pet. Ex. 25 at 5, 7. He asserted that the flu vaccine activated TLRs that "stimulate[d] immunity by triggering the release of proinflammatory cytokines . . . capable of triggering an autoimmune cascade against the white matter of the brain." Id. at 7.

Lastly, Dr. Kinsbourne opined that there were no other triggers other than vaccination that could have caused petitioner's condition. Pet. Ex. 25 at 7.

---

[52] Brian C. Healy et al., Characterizing Clinical and MRI Dissociation in Patients with Multiple Sclerosis, 27 J. Neuroimaging 481 (2017).

[53] Individuals placed into the low lesion load/high disability group were patients with less than 2 ml in T2 hyperintense lesion volume and more than or equal to 3 on the Expanded Disability Status Scale. Pet. Ex. 55 at 2. High lesion load/low disability patients were those with more than 6 ml in T2 hyperintense lesion volume and less than 2 on the Expanded Disability Status Scale. Id.

[54] TLRs are "[a] type of pattern recognition receptor that recognizes unique structures derived from microorganisms. [Signaling] through TLRs promotes inflammatory immune responses, cytokine production[,] and cell activation in response to microorganisms." Pet. Ex. 89 at 1 (Serge Rivest, Regulation of Innate Immune Responses in the Brain, 9 Nature Revs. Immunology 429 (2009)).

iv. Althen Prong Three

Dr. Kinsbourne opined that petitioner's neurological symptoms appeared 24 hours after his flu vaccination. Tr. 124. He attributed such rapid onset "to an anamnestic response involving the innate immune system, induced by frequent prior exposure to [flu] vaccination." Pet. Ex. 25 at 7. Based on his proposed mechanism involving the innate immune system, he found the time frame to be medically reasonable. Id.

He opined petitioner's "clinical presentation one day following vaccination closely approximated the clinical characteristics of a[n] onset of ADEM." Pet. Ex. 96 at 3.

For support of a 24-hour onset in ADEM, Dr. Kinsbourne cited Huynh et al., who examined ADEM cases and noted that "[d]epending on the inciting agent, the onset of symptoms may vary . . . from 1 to 14 days." Pet. Ex. 99 at 5. The authors examined a 61-year-old male who received a flu vaccine three weeks prior to symptom onset and found his "clinical presentation was most likely due to post-[flu] vaccination." Id. at 7-8. The authors also noted "[a] 14-year-old female developed ADEM 2 weeks after [a flu] vaccination, while 2 adult males, ages 62 and 70, were diagnosed with ADEM and TM with acute motor axonal neuropathy respectively within 1 week of vaccination," but did not discuss these cases in more detail. Id. at 3. Mechanisms for these specific cases were not noted. However, the authors did briefly discuss the pathogenesis of ADEM, specifically noting molecular mimicry.[55] Id. at 4.

Shoamanesh and Traboulsee examined an ADEM case with an onset of two days following flu vaccination. Pet. Ex. 104 at 1. The authors also examined 10 cases of encephalomyelitis or ADEM following flu vaccination and found "neurological symptoms typically developed within 3 weeks of vaccination." Id. at 2, 3 tbl.1. A mechanism was not discussed by the authors.

Dale and Branson noted a mean onset period of two weeks in 51-74% of ADEM patients with a history of a precipitating infection. Pet. Ex. 97 at 1. The authors did not note the mechanism by which ADEM is thought to be caused.

In Schwarz et al., the authors noted that one patient, who was originally diagnosed with ADEM and later diagnosed with MS, "experienced the first symptoms a few days after active immunization against diphtheria and tetanus." Pet. Ex. 103 at 3. The authors indicated the length of time their patients experienced symptoms before admission, but did not otherwise indicate onset. Id. at 3, 3 tbl.1. The authors wrote that "[a]lthough the pathophysiology of

[55] The authors also discussed the immuno-inflammatory model. Pet. Ex. 99 at 4. The immuno-inflammatory model combines molecular mimicry with an inflammatory cascade process. Id. Under this model, "[a] 'first hit' is experienced after an antecedent infection with a virus that expresses determinants allowing molecular mimicry. . . . A second infection with an unrelated virus results in sufficient reactivation of the primed autoreactive T cells to eventuate in demyelination of the CNS. This constitutes the 'second hit.'" Id. Petitioner's experts have not asserted this theory characterized by two unrelated viral infections.

ADEM is not known, an autoimmune response to myelin basic protein triggered by infection or immunization is considered to be a possible etiologic factor." Id. at 1.

Of the 296 children studied by Mikaeloff et al., 94 had an infection during the month preceding onset and 16 had a vaccination during the six months preceding onset. Pet. Ex. 101 at 3 tbl.1. The authors did not otherwise discuss onset after an inciting event. Nor did the authors discuss a mechanism by which ADEM occurs.

Dr. Kinsbourne cited to an article from Karussis and Petrou. See Pet. Ex. 35. Karussis and Petrou conducted a PubMed search from 1979 to 2013 and found 71 cases of a temporal association between an inflammatory CNS demyelinating disease and the administration of a vaccine. Id. at 2. Of these 71 cases, 21 were associated with the flu vaccine. Id. For those cases of ADEM post-flu vaccination, onset was between 8 days and 3 weeks. Id. at 4 tbl.2. The authors noted "[t]he current pathogenetic hypothesis in post-vaccination ADEM is that antigens of viral origin cross-react with myelin components (molecular mimicry) and in a secondary manner induce a hyperergic reaction, that leads to the development of disseminated demyelination."[56] Id. at 3.

With regard to a 24-hour onset of MS after flu vaccination, Dr. Kinsbourne deferred to an immunologist. Pet. Ex. 54 at 3. He testified that it would have been appropriate to consider a diagnosis of MS three months after onset, once there is dissemination in time and space. Tr. 132. According to Dr. Kinsbourne, dissemination in petitioner's case occurred in July 2014 when he first reported right-sided weakness and five oligoclonal bands were found in his CSF. Id.

2. Petitioner – Dr. M. Eric Gershwin[57]

a. Background and Qualifications

Dr. Gershwin is board-certified in internal medicine, rheumatology, and allergy and clinical immunology. Pet. Ex. 94 at 2. He received his A.B., summa cum laude, from Syracuse University in 1966 and his M.D. from Stanford University in 1971, and holds various honorary degrees and special awards for his work in immunology. Id. at 1. Thereafter, he completed his internship and residency at Tufts-New England Medical Center. Id. at 2. Since 2003, Dr.

[56] The authors further hypothesized "that vaccination may activate in a non-specific way distinct clones of antimyelin T-cells and that suppressor or regulatory cells that are aimed to control this abnormal reactivity are compromised or malfunctioning." Pet. Ex. 35 at 3. The authors noted "[t]he inflammatory process in MS is propagated by an autoimmune cascade, involving mainly T-cells that target myelin self antigens, possibly mediated by mechanisms of molecular mimicry (cross-reactive antigens expressed by viruses or other microorganisms and myelin components)." Id. Alternatively, "'naturally' existing myelin-specific T-cells, especially of the Th17 phenotype, may expand to critical pathogenic quantities due to malfunctioning immunoregulatory mechanisms." Id.

[57] Petitioner filed two expert reports authored by Dr. Gershwin. Pet. Exs. 69, 107.

Gershwin has been a Distinguished Professor of Medicine with the University of California, Davis, where he currently holds a chaired professorship in honor of Jack and Donald Chia. Id. at 1. Throughout his career, he has been presented various honors and awards, served as an editor and reviewer on journals and publications, and authored or co-authored articles, papers, editorials, and books. Id. at 3-134.

b. Opinion

Dr. Gershwin opined that petitioner's November 15, 2013 flu vaccine more likely than not caused his demyelinating neurological condition. Tr. 139. He deferred to Dr. Kinsbourne as to petitioner's diagnosis, and thus, did not provide an opinion other than that petitioner suffers from a neurologic disease. Tr. 139, 275; Pet. Ex. 69 at 1. His opinion focused on "whether inflammation in the [CNS] can occur within 24 hours of an antigen challenge." Pet. Ex. 69 at 1.

i. Althen Prong One

Dr. Gershwin opined that the underlying mechanism at play is inflammatory in nature. Tr. 139. He explained that the immune system is divided into innate and adaptive responses. Tr. 141. The innate immune system acts as a first responder to anything that is foreign in the body. Id. He also testified that there must be an innate response before an adaptive response occurs. Tr. 142; Pet. Ex. 69 at 2.

Dr. Gershwin testified that the flu vaccine is a "heat-killed vaccine" containing both an adjuvant and polysorbate 80. Tr. 140. He opined that the vaccine caused a rapid release of cytokines and other mediators upon administration.[58] Tr. 140, 145; Pet. Ex. 107 at 1. The mediators, which peak 24 hours after vaccination, go from the lymph node, to the blood, and then into the brain, and produce an inflammatory response. Tr. 140; Pet. Ex. 107 at 1. He opined that the "activated cells can cross the blood brain barrier, even in the absence of neuroinflammation." Pet. Ex. 69 at 2.

Dr. Gershwin described the brain as a lymphoid organ with innate immune cells, including microglia and astrocytes, that can respond to and produce cytokines. Tr. 144, 149; Pet. Ex. 69 at 2. Specifically, the brain contains mononuclear-like cells that are capable of cytokine production and other inflammatory mediators that lead to inflammation. Tr. 140. "In some organs, these changes in innate immunity may not be clinically apparent, but in the case of the brain, they would have more profound clinical implications." Pet. Ex. 69 at 2.

[58] Dr. Gershwin testified that the flu vaccine here contained an adjuvant and polysorbate 80, however, the petitioner did not file any evidence to support this testimony. Petitioner filed a package insert for the Fluzone vaccine for 2020-2021, not the formula administered to petitioner. See Pet. Ex. 114. The insert describes how the vaccine was prepared, and lists the ingredients. See id. at 20-22. No adjuvants are listed or otherwise identified. Id. at 22. Polysorbate 80 is also not identified in the list of ingredients. Id.

To support the premise that both antigens and cytokines are involved in the immune response, Dr. Gershwin cited to Hervé et al.[59] Pet. Ex. 107 at 1-2; Tr. 146-47. Hervé et al. explained, "[v]accine antigens and immune enhancers (as adjuvants) injected into the muscle are [recognized] by the body as potential pathogens and/or danger signals." Pet. Ex. 108 at 3 fig.1. This "leads to the stimulation of local cells, followed by the recruitment of blood immune cells to the local site and the production of different soluble factors including vasodilators and cytokines, which may trigger the development of signs and symptoms of local inflammation." Id. Those factors, like cytokines, travel into the bloodstream and "may contribute to the development of general symptoms (fever, myalgia, headache etc) in the vaccinee." Id.

Hervé et al. further explained that after vaccination, TLRs recognize and bind antigens and potential immune enhancers in the vaccine to trigger inflammation. Pet. Ex. 108 at 4 fig.2. "Resident immune cells, mast cells, monocytes[,] and macrophages are activated within minutes of injection and release soluble factors" such as proinflammatory cytokines. Id. "These newly recruited immune cells, mainly composed of blood-born neutrophils, monocytes[,] and T lymphocytes, also contribute to pain sensation by releasing soluble factors, such as cytokines, . . . that can directly interact with local sensory receptors." Id. Once cytokines are produced, they "act both locally . . . and may act systemically at distant organs." Id. "Several immune-to-brain signaling pathways may propagate an inflammatory response to the [CNS] after peripheral activation of the innate immune system . . . leading to the development of fever and sickness [behaviors]." Id.

To further support his argument that cytokines may be present in the brain after vaccination, Dr. Gershwin cited Wendeln et al.[60] Pet. Ex. 69 at 2. In Wendeln et al., the authors gave mice low dose injections of lipopolysaccharides[61] on four consecutive days, leading to mild sickness and temporary weight loss. Pet. Ex. 88 at 1. They found that three hours after the first injection, "there was a pronounced increase in blood cytokine levels, but only modest increases in brain cytokines." Id. After the second injection, blood levels of certain pro-inflammatory cytokines reduced, while brain cytokines markedly increased, "indicating a brain-specific training effect induced by the first [injection]." Id. A change in microglia occurred after the second injection, while astrocytes increased only after the third injection. Id. Their results "indicat[ed] the immune memory in the brain is predominantly mediated by microglia." Id. at 1,

[59] Caroline Hervé et al., The How's and What's of Vaccine Reactogenicity, 39 NPJ Vaccines 1 (2019).

[60] Ann-Christin Wendeln et al., Innate Immune Memory in the Brain Shapes Neurological Disease Hallmarks, 556 Nature 332 (2018).

[61] Lipopolysaccharide is "a major component of the cell wall of gram-negative bacteria, a type of endotoxin and important group-specific antigen (O antigen). The lipopolysaccharide molecule consists of three parts: lipid A, a glycolipid responsible for the endotoxic activity, which is covalently linked to a heteropolysaccharide chain." Lipopolysaccharide, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=28471 (last visited May 4, 2021).

6. The authors also "found that individual cytokines applied peripherally may also elicit immune memory effects in the brain." Id. at 6.

The Wendeln et al. study, however, does not appear to be relevant here, since there is no evidence that petitioner's vaccine contained lipopolysaccharides.[62] See Pet. Ex. 114 at 22, 40-41. Dr. Gershwin testified that the reaction described in Wendeln et al. can apply to "other instigators" or "generic materials," and is not specific to lipopolysaccharides. Tr. 148. But he did not describe what he meant by "other instigators" or "generic materials."[63]

On cross-examination, Dr. Gershwin reiterated that inflammation that causes neurologic diseases are caused by a combination of innate immune responses. Tr. 156. He testified that for most people, cytokines developed after vaccination do not cause demyelination. Id. But he emphasized that microglia and mononuclear cells can be actors in demyelination. Tr. 270. Th1 cytokines, for example, are inflammatory cytokines, and "the more inflammatory the cytokine is, the more likely it is to produce neurotoxicity." Tr. 156-57.

Dr. Gershwin agreed with Dr. Sriram that innate immunity is not T-cell mediated, but disagreed with Dr. Sriram that T cells are required for demyelination to occur. Tr. 271. He testified that innate immunity can cause demyelination. Tr. 157. However, petitioner provided a number of medical articles that supported Dr. Sriram's opinion that the adaptive immune system, and T-cell mediated processes, are involved in the pathogenesis of MS. See, e.g., Pet. Ex. 87 at 29-32;[64] Pet. Ex. 91 at 11-13.[65]

[62] See Pet. Ex. 114 at 22 (noting the ingredients for the 2020-2021 Fluzone vaccine); Pet. Status Rept., filed Dec. 7, 2020, at 1 (stating "petitioner's counsel [was] unable to locate the ingredient list or package insert for the 2013 Fluzone vaccine by Sanofi").

[63] Petitioner also cited an animal study where lipopolysaccharide was used to activate microglia, resulting in the release of pro-inflammatory cytokines. See Pet. Ex. 29 (Alessandra di Penta et al., Oxidative Stress and Proinflammatory Cytokines Contribute to Demyelination and Axonal Damage in a Cerebellar Culture Model of Neuroinflammation, 8 PLoS ONE e54722 (2013)). The activation was "associated with demyelination and axonal damage" within 24 hours in mouse brain tissue in the in vitro study. Id. at 1, 10-11.

[64] Scott S. Zamvil & Lawrence Steinman, The T Lymphocyte in Experimental Allergic Encephalomyelitis, 8 Ann. Rev. Immunology 579 (1990).

[65] Antoine Lamprone et al., Innate Immunity in the CNS: Redefining the Relationship Between the CNS and Its Environment, 78 Neuron Rev. 214 (2013).

Additional articles supporting Dr. Sriram's opinion were provided by petitioner's other expert, Dr. Kinsbourne. See, e.g., Pet. Ex. 35 at 3, 7; Pet. Ex. 38;[66] Pet. Ex. 41.[67] For example, petitioner cited Karussis and Petrou, a 2014 article, which stated that "[t]he current pathogenetic hypothesis in post-vaccination ADEM is that antigens of viral origin cross-react with myelin components (molecular mimicry) and in a secondary manner induce a hyperergic reaction, that leads to the development of disseminated demyelination." Pet. Ex. 35 at 3. Molecular mimicry is "the molecular similarity between the proteins of the viruses used for the vaccination and self-antigens." Id. at 7. In the context of vaccinations, "[it] also represents one of the main immunopathogenetic mechanisms in post-vaccination CNS demyelination." Id.

Dr. Gershwin also discussed the theory of trained immunity.[68] Tr. 152-54; Pet. Ex. 107 at 3. He explained that trained immunity "implies that previous exposure to an infection or a vaccine can accelerate innate immune responses." Pet. Ex. 107 at 5; see also Tr. 153. Thus, "the more things you're exposed to, the faster your response is." Tr. 153.

Netea et al.[69] defined trained immunity as "an enhanced innate immune response to different pathogens after an initial challenge, such as vaccination or infection." Pet. Ex. 112 at 5. The innate immune cells "display adaptive characteristics after certain infections or vaccines, a property that is functionally similar to building immunological memory." Id. at 3. This "[g]reater protection against reinfection . . . has also been reported in plants and invertebrates, which lack an adaptive immune system." Id.

ii. Althen Prong Two

Dr. Gershwin opined that petitioner did not have an aberrant local response, but that he did have an aberrant response in his brain to the flu vaccine. Tr. 142-43; Pet. Ex. 107 at 1. In petitioner's case, after vaccination, the "antigen is processed and there is a rapid release of cytokines and other mediators" that "enter the blood and spread throughout the body, including the brain." Pet. Ex. 107 at 1. The microglial cells, which are components of innate immunity, led to the inflammation seen in petitioner. Id.; Tr. 149.

Even assuming that petitioner's flu vaccine did not contain an adjuvant, Dr. Gershwin opined there would still be a cytokine response, albeit less vigorous. Tr. 159. However, because

[66] D Matusevicius et al., Interleukin-17 mRNA Expression in Blood and CSF Mononuclear Cells Is Augmented in Multiple Sclerosis, 5 Multiple Sclerosis 101 (1999).

[67] Siddharama Pawate & Subramaniam Sriram, The Role of Infections in the Pathogenesis and Course of Multiple Sclerosis, 13 Annals Indian Acad. Neurology 80 (2010).

[68] Dr. Gershwin testified that the theory of trained immunity "[is not] necessary for [his] opinions, meaning [his] opinion will be the same with or without trained immunity." Tr. 152.

[69] Mihai G. Netea et al., Trained Immunity: A Tool for Reducing Susceptibility to and the Severity of SARS-CoV-2 Infection, 181 Cell 969 (2020).

his vaccine is a "heat-killed vaccine," Dr. Gershwin testified that it would have contained an adjuvant.[70] Tr. 158-59.

On November 16, 2013, when petitioner first went to the emergency room, he reported cognitive impairment (confusion), which Dr. Gershwin opined was evidence of swelling and inflammation in his brain. Tr. 157, 159. Dr. Gershwin added that some patients with swelling in the brain have normal MRIs. Tr. 159-61. Dr. Gershwin found "the development of the oligoclonal bands [to be] biomarkers of an inflammatory response." Tr. 144. He also testified that petitioner's positive ANA antibodies in July 2014[71] was a nonspecific indicator of an inflammatory response. Tr. 162.

Dr. Gershwin, relying on the theory of trained immunity, opined that petitioner's "multiple previous [flu] vaccines would prime or accelerate future immune responses." Pet. Ex. 107 at 3. Petitioner would be "likely to have a more brisk innate immune response" because of his prior vaccinations. Tr. 153-54.

In response to respondent's expert's position that a vaccine injury was unlikely because petitioner had had many prior flu vaccines without experiencing any adverse reaction, Dr. Gershwin opined that the flu vaccine changes every year and immune systems change with age. Tr. 150; Pet. Ex. 107 at 2. For support, he cited Simon et al.,[72] who reviewed the development of the immune response through life, from neonatal to old age. Pet. Ex. 109 at 1. They explained that as individuals age, the immune system remodels and declines. Id. at 5. Individuals "develop[] an expanding repertoire comprising memory T and B cells triggered by previous infections and vaccinations." Id. Simon et al. added that "the immune responses of any single adult vary considerably." Id.

[70] After the hearing, petitioner was ordered to file the ingredients of the flu vaccine administered to petitioner. Order dated Nov. 6, 2020, at 1 (ECF No. 113). On December 7, 2020, petitioner filed a status report indicating petitioner's counsel was unable to locate the ingredient list or package insert for the flu vaccine administered to petitioner. Pet. Status Rept., filed Dec. 7, 2020, at 1 (ECF No. 119). Petitioner asserted "the vaccine ingredients are not vital to the outcome of this matter." Id.

[71] The undersigned was unable to find ANA test results from July 2014.

[72] A. Katharina Simon et al., Evolution of the Immune System in Humans from Infancy to Old Age, 282 Proc. Royal Soc'y B 1 (2015).

Dr. Gershwin opined that "[w]ithout qualification," petitioner did not have Chagas disease.[73] Tr. 270. Nor are there "other viable clinical explanations" other than the November 2013 flu vaccination to explain petitioner's condition. Tr. 154.

iii. Althen Prong Three

Dr. Gershwin agreed with Dr. Kinsbourne that a 24-hour onset "is plausible and compatible with contemporary literature." Pet. Ex. 69 at 2. He testified that an onset of a neurological condition within 24 hours after vaccination is immunologically sound. Tr. 154. After vaccination, there is a rapid release of cytokines and other mediators that peak within 24 hours. Tr. 140; Pet. Ex. 107 at 1. Because these mediators mostly peak at 24 hours after vaccine administration, Dr. Gershwin opined that this means that such cytokine production begins sooner. Tr. 146 (citing Pet. Ex. 108 at 3).

3. Respondent – Dr. Subramaniam Sriram[74]

a. Background and Qualifications

Dr. Sriram currently works as a Physician Scientist, Professor of Neurology and Immunology, and Director of the Multiple Sclerosis Clinic at Vanderbilt Medical Center. Tr. 172-73. He received his M.B. and B.S. from University of Madras in India in 1973. Resp. Ex. B at 1. Thereafter, he was an intern and internal medicine resident at Wayne State University in Michigan, as well as a neurology resident, chief neurology resident, and post-doctoral fellow in neuroimmunology at Stanford University. Id. Dr. Sriram is board certified in internal medicine and psychiatry and neurology, and is licensed to practice in California, Vermont, and Tennessee. Id. He had authored or co-authored over 150 publications. Id. at 6-18.

[73] The question of whether petitioner suffered from Chagas disease came up during the hearing. See Tr. 241-43, 269-70; see also Resp. Ex. A at 9. Chagas disease is a disease seen widely in Central and South America that is transmitted by bug bites. Chagas Disease, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=70173 (last visited May 4, 2021). "The acute form, prevalent in children, is characterized by an erythematous nodule (chagoma) at the site of inoculation, high fever, Romaña sign (swelling on one side of the face), regional lymphadenopathy, hepatosplenomegaly, and meningoencephalic irritation." Id. The subacute form may last for several months or years and is characterized by mild fever, severe asthenia, and generalized lymphadenopathy. The chronic form, which may or may not be preceded by an acute episode, is characterized by cardiac manifestations . . . as well as gastrointestinal manifestations . . . ." Id. Neither expert opined that more likely than not, petitioner suffered from the condition. Thus, the undersigned does not make any finding relative to Chagas disease.

[74] Respondent filed three expert reports authored by Dr. Sriram. Resp. Exs. A, E, G.

b. Opinion

i. Diagnosis

Dr. Sriram opined that petitioner's condition is unknown, but the evidence does not support a diagnosis of MS, ADEM, or a demyelinating condition. Resp. Ex. A at 12; Tr. 178, 204, 207, 227. Dr. Sriram opined that petitioner's diagnosis remains ill-defined and unclear. Resp. Ex. A at 6; Tr. 204. He found insufficient evidence to support a diagnosis of MS, ADEM, or a demyelinating condition. Resp. Ex. A at 7; Resp. Ex. E at 4; Resp. Ex. G at 5; Tr. 204, 207, 227.

First, Dr. Sriram opined that petitioner did not meet the criteria for diagnosis of ADEM. Resp. Ex. G at 3-4; Tr. 207-08. ADEM is "polysymptomatic, that is, different parts of the nervous system might be involved;" however, petitioner was not polysymptomatic. Tr. 208-09. Petitioner's November 16, 2013 complaints were subjective bilateral facial numbness and left arm weakness, and his facial numbness resolved. Resp. Ex. G at 4. On November 23, 2013, petitioner complained of transient weakness that resolved by discharge. Id. at 4-5.

Patients with ADEM also have "abnormalities on cognition and arousal." Tr. 208. Dr. Sriram explained that patients with cognition abnormalities have an encephalopathy, defined as "a reduction in the cognitive awareness of the individual." Id. Although petitioner complained of confusion, his cognitive examination was documented as normal; petitioner was awake, alert, and talking, and he was able to recite his medical history. Tr. 209, 212-13; Resp. Ex. G at 4. Dr. Sriram found it "highly unusual" that an individual with encephalopathy could drive himself to the emergency room like petitioner did. Tr. 209. Dr. Sriram opined that petitioner did not exhibit behavioral changes at onset, which is critical for an ADEM diagnosis, nor did petitioner exhibit clinical features that could be identified as encephalopathy. Resp. Ex. G at 3-4. Petitioner had normal arousability, drove his car, did not have seizures, and answered questions appropriately. Tr. 228. Dr. Sriram opined that these "are not the mental capabilities of an individual who is encephalopathic." Id.

Moreover, Dr. Sriram emphasized that patients with ADEM have abnormalities on MRI, which petitioner did not have. Tr. 210. Lastly, none of petitioner's treating physicians at the time thought he had ADEM. Id. Thus, Dr. Sriram opined that petitioner does not meet the criteria for ADEM. Resp. Ex. G at 3-5; Tr. 207, 210.

In response to Dr. Kinsbourne's opinion that petitioner had ADEM[75] which then morphed into MS, Dr. Sriram asserted that "ADEM does not 'evolve into MS.'" Resp. Ex. G at 3; see also Tr. 215. "ADEM and MS are two entirely different diseases, clinically, radiologically, and immunologically." Resp. Ex. G at 3. In the cases where an individual had an ADEM-like presentation at onset but was subsequently diagnosed with MS, Dr. Sriram explained that "the initial presentation was MS albeit with atypical features which was misdiagnosed as ADEM." Resp. Ex. G at 3; see also Tr. 221-22.

[75] Dr. Sriram opined that Dr. Kinsbourne relied on outdated diagnostic criteria for ADEM. Tr. 212.

Dr. Sriram explained that ADEM and MS are "inflammatory diseases in the nervous system" known to be "T cell mediated diseases involving the white matter and myelin." Tr. 214. The distribution in ADEM is very similar to MS, but ADEM and MS have different clinical phenotypes. Tr. 208, 214. ADEM is an "explosive disease at onset," associated with encephalopathy, and patients usually respond well to steroids. Tr. 207-08, 214. It is rarely seen in adults. Tr. 208. Further, it is monophasic, "one-time one-off process." Tr. 214. On the other hand, MS is a chronic, lifelong disease that usually presents slowly and evolves over time. Id.

Although causes of MS remain an area of research, it is thought to be an autoimmune disorder where "auto reactive lymphocytes target the proteins on the cells and the membranes that wrap around the axons." Resp. Ex. A at 6. At the hearing, Dr. Sriram testified that the current prevailing view is that MS is a T cell inflammatory disease to an undetermined antigen. Tr. 176-77.

To diagnose an individual with MS, Dr. Sriram testified that physicians use the 2017 McDonald criteria. Tr. 179-80; see also Resp. Ex. C at 6. There must be "delineation of lesions involving the white matter, which are separated in space and time." Resp. Ex. A at 7; see also Tr. 182, 186-88. In the absence of lesions, other abnormalities on MRI or other studies can identify subclinical lesions. Resp. Ex. A at 7. Dr. Sriram acknowledged that on rare occasions, MRIs can be normal, especially during the initial phase of the disease, but he argued there must be other objective clinical evidence to warrant a diagnosis of MS. Resp. Ex. E at 1. Dr. Sriram noted that the authors of the McDonald criteria cautioned against acknowledging symptoms reported only by the patient as evidence of a current MS flare or attack. Id. at 2 (citing Resp. Ex. C at 2).

Applying the McDonald criteria, Dr. Sriram opined that petitioner did not meet the criteria for a diagnosis of MS because his left-sided weakness was waxing and waning, there were no abnormalities in reflex testing, electrical studies were all normal, and multiple MRIs of the brain and spinal cord failed to show any lesions. Resp. Ex. A at 8-9. Dr. Sriram argued petitioner's clinical records do not show objective evidence, as required by the McDonald criteria, of a clinical attack. Resp. Ex. E at 2. Dr. Sriram defined "attack" as a clinical event with a discrete onset, progression, and resolution, lasting greater than one day, with "objective clinical abnormalities." Tr. 189-90. When there is a MS attack, corticospinal fibers, which are fibers that come from the brain to the spinal cord, "are disrupted because of an immune activation somewhere along the axis." Tr. 195-96. Certain deficits would be present, and petitioner did not have these deficits. Tr. 196.

Specifically, Dr. Sriram explained that petitioner's initial presentation on November 16, 2013 did not support a diagnosis of MS. Resp. Ex. E at 2; Resp. Ex. G at 3. Petitioner complained of generalized weakness and confusion, as well as facial weakness and numbness lasting for 15-20 minutes. Resp. Ex. E at 2; Tr. 189. However, Dr. Sriram found "[o]bjective evidence of weakness was lacking and the sensory exam failed to show any sensory abnormalities on repeat evaluation." Resp. Ex. E at 2.

Moving forward to November 22, 2013, petitioner's evaluation was documented as follows: "Speech clear. Moves all extremities with equal strength. Pupils are equal and reactive to light and accommodation. Ambulatory and steady. Smile symmetrical. Eyes close normally, but patient states it feels like his eye does not close normally and it waters more than usual." Resp. Ex. E at 2 (quoting Pet. Ex. 5 at 3). On physical exam, "[petitioner] had normal finger to nose, abnormal heel to shin, negative pronator drift, weakness in the left hip flexors, weak[ness] in the left hand, [and] incomplete markers." Tr. 192 (citing Pet. Ex. 5 at 6). Given petitioner's weakness in his left arm and leg, Dr. Sriram testified that in MS there should be asymmetry in reflexes and a positive pronator drift. Tr. 192-93. Also, the weakness in petitioner's left hip flexors should have been associated with changes in his reflexes. Tr. 193. On November 23, 2013, a neurologic evaluation conducted by Dr. Rao was normal, but petitioner was unable to hold his legs during the nurse's exam. Resp. Ex. E at 2 (citing Pet. Ex. 5 at 9); Tr. 193-95. Dr. Sriram opined that these records are evidence of an "inconsistent neurological event." Tr. 194.

In summary, Dr. Sriram opined that the November 2013 neurological events "failed to meet the clinical evidence of an attack due to [MS]." Resp. Ex. E at 2. Petitioner's neurologic examination did not reveal deficits in pyramidal or sensory pathways, his brain MRI was normal, and his weakness was "transient, lasting less than 24 hours." Id. at 2-3. Petitioner's November 23, 2013 brain MRI was conducted eight days after vaccination, which Dr. Sriram found was a sufficient amount of time for immune activation to have occurred and show lesions on MRI. Resp. Ex. G at 5. The fact that petitioner's weakness was transient was "important because if the cause of the clinical deficits [were] due to inflammatory lesions in the brain and spinal cord, they [would have been] unlikely to resolve within 24 hours." Resp. Ex. E at 3.

Further, Dr. Sriram opined that there was "no evidence that there was an abnormality on the right side of his body" in July 2014 to support a finding of a clinical attack. Tr. 188. Additionally, 90% of MS patients exhibit visual changes in conduction pathways, and petitioner's conduction velocities, which were tested in July 2014, were all normal. Tr. 229.

For further support that petitioner does not have MS, Dr. Sriram noted that headaches are not a feature of MS. Resp. Ex. A at 10. Nor is heat sensitivity a diagnostic criteria for MS. Id. Dr. Sriram explained that complaints of symptoms worsening in hot weather is not exclusive of MS and is seen in many neurological conditions. Id.

Dr. Sriram added that none of petitioner's MRIs were abnormal. Resp. Ex. A at 10-11; Tr. 196. His MRIs showed "nonspecific white matter changes" that can be attributed to petitioner's age and/or high cholesterol. Tr. 196. In response to Dr. Kinsbourne's opinion that MS patients sometimes have normal MRIs, Dr. Sriram opined it is "highly unusual" and "very rare to see a patient with clinically definite MS [with] a normal MRI." Tr. 199-200. On cross-examination, Dr. Sriram conceded that it could be possible for a MS patient to have normal MRIs, although he has never seen it in his 1,500 patients. Tr. 246-47.

Dr. Sriram noted that although petitioner was prescribed Tecfidera, a drug used for the treatment of MS, several neurologists questioned the need for petitioner to be taking Tecfidera. Resp. Ex. A at 9. At the hearing, Dr. Sriram testified that neither he nor the Food and Drug

Administration require patients to stop taking Tecfidera if they test positive for the JC virus antibody. Tr. 205-06.

Another important factor contributing to Dr. Sriram's opinion is that Dr. Grimes' February 5, 2015 record documents that petitioner did not meet the criteria for MS. Resp. Ex. E at 3 (citing Pet. Ex. 52 at 6-8). Moreover, a diagnosis of MS was never confirmed. Resp. Ex. G at 5; Tr. 199.

With regard to the presence of oligoclonal bands in petitioner's CSF, Dr. Sriram opined that this finding is not conclusive. Resp. Ex. A at 9; Tr. 201. He explained that "[o]ligoclonal bands are abnormal immunoglobulins that are present in the spinal fluid but not in the serum. These antibodies are not specific for [MS] and are seen in many other infectious and autoimmune conditions." Resp. Ex. A at 9; see also Tr. 201-02. Thus, "[t]he presence of oligoclonal bands does not indicate that [petitioner] has [MS]." Resp. Ex. A at 9; see also Tr. 205. Because petitioner showed "no clinical evidence of either a relapse or progression of neurological symptoms" or "supportive radiological evidence of inflammatory changes in the white matter, the mere presence of oligoclonal bands does not meet the criteria sufficient to warrant the diagnosis of MS." Resp. Ex. E at 3.

On cross-examination, Dr. Sriram agreed that petitioner is most likely suffering from a neurological condition. Tr. 235. However, the records from November 2013 do not show that his condition is inflammatory. Tr. 236-37. The first evidence that petitioner's condition may be inflammatory was in July 2014. Tr. 237. However, it was not clear to Dr. Sriram whether the "July [2014] event that led to increased oligoclonal bands was part of [the] whole picture [or] separate from the whole picture." Id. Dr. Sriram believed that an infectious or inflammatory process in the CNS caused petitioner's oligoclonal bands. Tr. 244. With regard to petitioner's positive ANA in May 2015, Dr. Sriram opined that this is not evidence of inflammation especially when there is no corresponding titer. Tr. 245-56 (citing Pet. Ex. 10 at 2).

Dr. Sriram concluded that "something abnormal in [petitioner's] nervous system is going on, but it's not MS [and] it's not ADEM," nor is it a demyelinating condition. Tr. 226-27. Further, Dr. Sriram opined that whatever the condition, it was not caused by petitioner's flu vaccine. Tr. 227, 232. Alternatively, Dr. Sriram questioned whether petitioner contracted a chronic illness in Bolivia in 2011, which was then reactivated in 2013 when he returned to Bolivia. Resp. Ex. A at 9; Tr. 241. Dr. Sriram also testified that it is not inconceivable that petitioner has a chronic infection that has not been uncovered that could explain his condition. Tr. 243.

ii. Althen Prong One

Dr. Sriram opined that there is no evidence of a causal relationship between petitioner's November 15, 2013 flu vaccine and the onset of his symptoms 24 hours later on November 16, 2013. Resp. Ex. A at 12.

Dr. Sriram opined that ADEM and MS are two separate diseases that are both T cell mediated diseases. Tr. 214; see also Resp. Ex. D at 1.[76] ADEM cannot turn into MS. Tr. 214. "The prevailing opinion is that MS is a disorder of an adaptive immune response to an as yet unrecognized self antigen." Resp. Ex. A at 11. Dr. Sriram testified there is no scientific evidence linking the flu vaccine to the development of MS, nor is there evidence that innate immunity is responsible for the development of MS. Id.; Tr. 215.

Dr. Sriram explained that when an individual receives a vaccine in their deltoid muscle, antigens are activated in the lymph nodes. Tr. 279. The T cells then proliferate in the lymph nodes, which takes at least one to two days. Tr. 279-80. The T cells amplify and leave the lymph node system into general circulation, and subsequently enter the brain. Tr. 280. Once the T cells are in the brain, the T cells "meet[] its cognate antigen [] and divide[] even more before the clinical symptoms become apparent." Id.

Dr. Sriram agreed with Dr. Gershwin that "the [flu] vaccines are antigenic, and they are part of a pathogenic protein, and therefore, the immune system will recognize they are foreign and mediate a response," which "is due to the production of cytokines." Tr. 230. However, he maintained that lymphocytes, not cytokines, in the brain cause demyelination. Id. "[I]n the absence of these lymphocytes, there may be some tissue damage from all these cytokines, but you won't have demyelination." Tr. 231.

In response to Dr. Kinsbourne's opinion that petitioner had ADEM which then morphed into MS, Dr. Sriram argued "ADEM does not 'evolve into MS.'" Resp. Ex. G at 3; see also Tr. 215. "ADEM and MS are two entirely different diseases, clinically, radiologically, and immunologically." Resp. Ex. G at 3. When an individual exhibits ADEM-like presentation at onset and is subsequently diagnosed with MS, "the initial presentation was MS albeit with atypical features which [were] misdiagnosed as ADEM." Id.; see also Tr. 221-22.

iii. Althen Prong Two

Dr. Sriram opined that the evidence does not support a causal relationship between petitioner's flu vaccine and the petitioner's condition. Resp. Ex. A at 12; Tr. 227, 232.

Dr. Sriram opined that an individual can have a primary inflammatory disorder of the CNS that does not fit neatly into one of the categories (ADEM, MS, optic neuritis ("ON"), acute TM, and NMO). Tr. 258-59. He testified that petitioner did not have ADEM or encephalopathy. Tr. 266-67. None of petitioner's MRIs were abnormal and "there are no cases to [his] knowledge in which you have a normal MRI and you diagnose that person with ADEM." Tr. 267.

[76] Gareth Pryce & David Baker, Oligoclonal Bands in Multiple Sclerosis; Functional Significance and Therapeutic Implications. Does the Specificity Matter?, 25 Multiple Sclerosis & Related Disorders 131 (2018).

On cross-examination, Dr. Sriram testified that "when [] patients are symptomatic, the MRI is usually forwardly evident." Tr. 253. In ADEM, it would be "highly unusual for a person to have significant neurological deficits . . . and have a normal MRI, [of] either brain, spinal cord[,] or optic nerves." Tr. 254. Lesions seen on MRI normally resolve within four to six weeks, depending on their size. Id. Depending on the size of the lesions and how destructive they are, one may not be able to tell that the patient ever had an event once the lesions resolve. Tr. 255.

As for MS, Dr. Sriram testified that there is no objective evidence of dissemination in space in petitioner's case. Tr. 266. Oligoclonal bands "can satisfy the dissemination in time when you have evidence for dissemination in space." Tr. 260. That is, oligoclonal bands "do not demonstrate dissemination in time per se but can substitute for requirements when dissemination in space has been demonstrated." Tr. 266. There was an eight-month gap between petitioner's onset and his spinal fluid being drawn. Tr. 228. Thus, it is not known when the abnormalities first appeared in the spinal fluid. Id.

With regard to the clinical course/MRI dissociation discussed by Dr. Kinsbourne, Dr. Sriram explained that clinical disability relates to spinal cord disease and is driven by spinal cord lesions. Tr. 223. In the brain and brainstem there are eloquent lesions. Id. There can be "a lot of lesions in the brain and the patient [can] be asymptomatic . . . because the tracts that occur in the brain . . . don't produce clinical symptoms." Id. Thus, Dr. Sriram opined that it is not unusual for a patient to have a lot of lesions in the brain and no clinical disability "because they have sparing of the spinal cord to a large extent." Tr. 224. "Some people have few lesions and big disability . . . because the spinal cord is involved." Id.

Dr. Sriram opined that Dr. Gershwin's "references of activation of lymphocytes by innate immune pathways . . . have no bearing on the [petitioner]" because the vaccine he received "did not [contain] activators of innate immunity such as lipopolysaccharide, which is a bacterial cell wall component with the capacity to activate the innate immune pathway." Resp. Ex. E at 4.

Although Dr. Molina and Dr. Gillespie wrote letters stating petitioner should not receive a flu vaccine in the future, Dr. Sriram noted there was no record attributing petitioner's symptoms to the flu vaccine. Tr. 217.

Dr. Sriram agreed that petitioner's neurologist, Dr. Grimes, treated petitioner in the same or similar way to how he would treat a patient with MS, as evidenced by the Tecfidera prescription. Tr. 263. However, Dr. Sriram probably would not have prescribed Tecfidera to petitioner. Id. Further, he did not agree that Tecfidera should be discontinued if a patient, like petitioner, tested positive for the JC virus. Tr. 264-65.

iv. Althen Prong Three

Dr. Sriram agreed that petitioner's symptoms began one day after vaccination. Resp. Ex. A at 9. He opined that if petitioner "suffer[s] from an immune-mediated demyelinating neurological condition," then "an onset of one day after vaccination is too short of an interval for the vaccine to have been the cause." Id.

He opined a 24-hour onset is not immunologically sound for a T-cell mediated disease. Tr. 231. After vaccination, antigens are activated in the lymph nodes, where T cells then proliferate. Tr. 279-80. This process takes at least one to two days, after which the T cells leave the lymph node system and subsequently enter the brain. Id. Thus, it is not possible "to produce a demyelinating inflammatory disease of T cells in the brain within 24 hours." Tr. 220; see also Tr. 280.

Dr. Sriram agreed that innate immunity has a rapid onset and that a cytokine response can occur within 24 hours. Tr. 219, 231. However, he maintained that T cells must be in the brain for demyelination to occur. Tr. 220. He found no evidence that "immune injury following activation of the innate immune pathways result[s] in a T cell response with the temporal time frame of under 24 hours in MS." Resp. Ex. E at 3; see also Tr. 219-20.

Additionally, Dr. Sriram testified that the literature does not support an onset of MS within 24 hours of vaccination. Resp. Ex. E at 4. For support, Dr. Sriram cited animal models, which have defined the time from activation of antigens to the development of inflammatory injury, the most common of which is an experimental autoimmune encephalitis model. Resp. Ex. E at 4 (citing Resp. Ex. F, Tab 2;[77] Resp. Ex. F, Tab 3).[78] In an experimental autoimmune encephalitis model, "sensitization with brain antigens in susceptible strains of mice lead[] to activation of T lymphocytes which go to the brain and induce a pathological picture which resembles [MS]." Id.; see also Tr. 216. "In all these models[,] the average time between the sensitization of the animal to the brain protein and the development of paralysis and brain inflammation [was] between 10-14 days." Resp. Ex. E at 4; Tr. 216. "Even when you flood the whole vascular system with T cells that are recognizing myelin, it takes about . . . three to five days for the animals to show paralysis." Tr. 216. Based on these studies, Dr. Sriram concluded that it is "highly impossible" and unlikely that inflammatory demyelination can be induced 24 hours after vaccination. Resp. Ex. E at 4; Tr. 217.

Dr. Sriram noted that "there are no animal models of CNS demyelination which are induced by the activation of innate immune pathways in the peripheral immune system" that are similar to a pathological picture resembling MS. Resp. Ex. E at 4.

In response to Dr. Kinsbourne's opinion that a one day onset of ADEM is reasonable, Dr. Sriram found Dr. Kinsbourne misinterpreted the article from Huynh et al. Tr. 224-25. Dr. Sriram stated that Huynh et al. found "neurological presentation varied from an acute explosive onset with the maximum neurological deficit that came within one day or more to an indolent progression." Tr. 225. The article did not state when the inciting event occurred. Id. And thus,

[77] Markus Kipp et al., Experimental in Vivo and in Vitro Models of Multiple Sclerosis: EAE and Beyond, 1 Multiple Sclerosis & Related Disorders 15 (2012).

[78] Caigan Du et al., Administration of Dehydroepiandrosterone Suppresses Experimental Allergic Encephalomyelitis in SJL/J Mice, 167 J. Immunology 7094 (2001).

it is not clear whether the inciting event also occurred on day one, or whether only symptoms began on day one. Id.

Although Dr. Sriram testified that he is not familiar with the theory of trained immunity, he opined that the process cannot happen in 12 to 24 hours. Tr. 218.

IV. LEGAL STANDARDS

A. Standards for Adjudication

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Hum. Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, petitioner must prove 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, 1352-53 (Fed. Cir. 1999)); see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner who satisfies this burden is entitled to compensation unless respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B).

B. Factual Issues

A petitioner must prove, by a preponderance of the evidence, the factual circumstances surrounding his claim. § 13(a)(1)(A). To resolve factual issues, the special master must weigh the evidence presented, which may include contemporaneous medical records and testimony. See Burns v. Sec'y of Health & Hum. Servs., 3 F.3d 415, 417 (Fed. Cir. 1993) (explaining that a special master must decide what weight to give evidence including oral testimony and contemporaneous medical records).

Medical records generally "warrant consideration as trustworthy evidence." Cucuras v. Sec'y of Health & Hum. Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). However, greater weight is typically given to contemporaneous records. Vergara v. Sec'y of Health & Hum. Servs., No. 08–882V, 2014 WL 2795491, at *4 (Fed. Cl. Spec. Mstr. May 15, 2014) ("Special Masters frequently accord more weight to contemporaneously-recorded medical symptoms than those recorded in later medical histories, affidavits, or trial testimony."). Contemporaneous medical records are presumed to be accurate. See Cucuras, 993 F.2d at 1528. The weight afforded to

contemporaneous records is due to the fact that they "contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium." Id. To overcome the presumptive accuracy of medical records, a petitioner may present testimony which is "consistent, clear, cogent, and compelling." Sanchez v. Sec'y of Health & Hum. Servs., No. 11–685V, 2013 WL 1880825, at *3 (Fed. Cl. Spec. Mstr. Apr. 10, 2013) (citing Blutstein v. Sec'y of Health & Hum. Servs., No. 90–2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)), mot. for rev. denied, 142 Fed. Cl. 247 (2019), vacated on other grounds & remanded, 809 F. App'x 843 (Fed Cir. 2020).

There are situations in which compelling testimony may be more persuasive than written 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 v. Sec'y of Health & Hum. Servs., No. 03–1585V, 2005 WL 6117475, at *19 (Fed. Cl. Spec. Mstr. Dec. 12, 2005) ("[W]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent." (quoting 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))). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1379 (Fed. Cir. 2009); Bradley v. Sec'y of Health & Hum. Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

Despite the weight afforded medical records, special masters are not bound rigidly by those records in determining onset of a petitioner's symptoms. Valenzuela v. Sec'y of Health & Hum. Servs., No. 90–1002V, 1991 WL 182241, at *3 (Fed. Cl. Spec. Mstr. Aug. 30, 1991); see also Eng v. Sec'y of Health & Hum. Servs., No. 90–1754V, 1994 WL 67704, at *3 (Fed. Cl. Spec. Mstr. Feb. 18, 1994) (Section 13(b)(2) "must be construed so as to give effect also to § 13(b)(1) which directs the special master or court to consider the medical records (reports, diagnosis, conclusions, medical judgment, test reports, etc.), but does not require the special master or court to be bound by them").

C. Causation

To receive compensation through the Program, petitioner must prove either (1) that petitioner suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that he received, or (2) that petitioner suffered an injury that was actually caused by a vaccination. See §§ 11(c)(1), 13(a)(1)(A); Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1319-20 (Fed. Cir. 2006). Because petitioner does not allege that he suffered a Table Injury, he must prove that a vaccine he received caused his injury. To do so, he must establish, by preponderant evidence: (1) a medical theory causally connecting the vaccine and his injury ("Althen Prong One"); (2) a logical sequence of cause and effect showing that the vaccine was the reason for his injury ("Althen Prong Two"); and (3) a showing of a proximate temporal relationship between the vaccine and his injury ("Althen Prong Three"). § 13(a)(1); Althen v. Sec'y of Health & Hum. Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005).

The causation theory must relate to the injury alleged. The petitioner must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen, 35 F.3d at 548-49. Petitioner cannot establish entitlement to compensation based solely on his assertions; rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether petitioner is entitled to compensation, the special master shall consider all material in the record, including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in petitioner's favor when the evidence weighs in his favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in petitioner's favor).

"Expert medical testimony which merely expresses the possibility—not the probability—of the occurrence of a compensable injury is insufficient, by itself, to substantiate the claim that such an injury occurred." LaCour v. Sec'y of Health & Hum. Servs., No. 90–316V, 1991 WL 66579, at *5 (Fed. Cl. Spec. Mstr. Apr. 15, 1991); accord Burns v. Sec'y of Health & Hum. Servs., No. 90–953V, 1992 WL 365410, at *6 (Fed. Cl. Spec. Mstr. Nov. 6, 1992), aff'd, 3 F.3d 415. The Federal Circuit has likewise made clear that the mere possibility of a link between a vaccination and a petitioner's injury is not sufficient to satisfy the preponderance standard. Moberly, 592 F.3d at 1322 (emphasizing that "proof of a 'plausible' or 'possible' causal link between the vaccine and the injury" does not equate to proof of causation by a preponderance of the evidence); Waterman v. Sec'y of Health & Hum. Servs., 123 Fed. Cl. 564, 573-74 (2015) (denying petitioner's motion for review and noting that a possible causal link was not sufficient to meet the preponderance standard); Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019). While certainty is by no means required, a possible mechanism does not rise to the level of preponderance. Moberly, 592 F.3d at 1322; see also de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1351 (Fed. Cir. 2008).

V. ANALYSIS

A. Diagnosis

As Federal Circuit precedent establishes, in certain cases it is appropriate to determine the nature of an injury before engaging in the Althen analysis. Broekelschen v. Sec'y of Health & Hum. Servs., 618 F.3d 1339, 1346 (Fed. Cir. 2010). Since "each prong of the Althen test is decided relative to the injury[,]" determining facts relating to the claimed injury can be significant in a case like this, where petitioner's diagnosis is not clear. Id. Thus, before determining if petitioner has met each prong of Althen, the undersigned addresses whether petitioner has established, by a preponderance of the evidence, that petitioner suffers from

ADEM, MS, or any other demyelinating disease.[79]

1. ADEM

First, the undersigned finds petitioner did not suffer from ADEM for three reasons: (1) petitioner did not have signs and symptoms consistent with encephalopathy; (2) his MRIs were normal; and (3) his treating physicians did not consider ADEM as a possible diagnosis.

The Brighton Collaboration and the MS Study Group developed diagnostic criteria to aid in the diagnosis of ADEM. Under the MS Study Group criteria, encephalopathy is required for diagnosis. Although the Brighton Collaboration criteria does not require encephalopathy, Dr. Kinsbourne and Dr. Sriram both agreed that encephalopathy is a feature of ADEM. See Pet. Ex. 96 at 2; Resp. Ex. G at 3-4; Tr. 108, 208-13; see also Pet. Ex. 35 at 2.

The undersigned finds that there is no evidence to suggest that petitioner was encephalopathic at any time in November 2013. Petitioner visited three different emergency rooms in November 2013. On the first visit, on November 16, 2013, physical examination revealed that petitioner was awake and alert. On November 22, 2013, petitioner's speech was clear, he was alert, in no acute distress, and oriented to person, place, and time. On November 23, 2013, Dr. Rao performed a physical examination and documented that petitioner was alert and oriented to person, place, and time. Therefore, three different assessments done by three different health care providers at three different times consistently documented that petitioner was alert and oriented. No change in mental status or objective symptoms of encephalopathy were documented at any of these visits.

Petitioner testified that he experienced confusion and brain fog on November 16, 2013. However, the objective physical examination by health care providers did not document any cognitive issues. Petitioner was noted to be awake and alert during examination. He was able to provide a history, and the history he provided to each different provider was generally consistent. Additionally, petitioner was able to drive himself to the hospital and back to his hotel room on November 16. The undersigned agrees with Dr. Sriram that the objective evidence in the medical records does not support a finding of encephalopathy.

[79] Petitioner's pleadings and expert reports are not entirely consistent as to what diagnosis the petitioner alleges is vaccine-related. See Petition at 1 (neurologic deficits); Pet. Ex. 25 at 7-8 (MS); Pet. Ex. 54 at 3 (MS); Pet. Ex. 63 at 1-2 (MS); Pet. Ex. 95 at 3 (ADEM that became MS); Joint Prehearing Submission at 2 (neurological illness); Pet. Prehearing Submission, filed Sept. 17, 2020, at 16 (ECF No. 94) (describing petitioner's condition as a "demyelinating neurological disease . . . , which could be viewed as an 'atypical presentation of MS,' or perhaps an 'MS-like' condition"); Tr. 78 (ADEM-like that morphed into MS-like); Tr. 99-100 (symptoms consistent with a demyelinating disorder); Tr. 102 (cross between ADEM and MS). Dr. Kinsbourne's testimony and expert reports read together consistently stated that petitioner had ADEM that became MS. Thus, the undersigned will analyze whether there is preponderant evidence of ADEM, MS, or any other demyelinating condition, as well as whether petitioner has proven by preponderant evidence that he sustained a different vaccine-related neurological condition.

To the extent that petitioner's affidavit and testimony are inconsistent with and contradicted by the contemporaneous medical records, it is reasonable to give greater weight to the contemporaneous medical records. See Cucuras, 993 F.2d at 1528 (noting that "the Supreme Court counsels that oral testimony in conflict with contemporaneous documentary evidence deserves little weight"); Doe/70 v. Sec'y of Health & Hum. Servs., 95 Fed. Cl. 598, 608 (2010); Stevens v. Sec'y of Health & Hum. Servs., No. 90–221V, 1990 WL 608693, at *3 (Cl. Ct. Spec. Mstr. Dec. 21, 1990) (noting that "clear, cogent, and consistent testimony can overcome such missing or contradictory medical records"); Vergara, 2014 WL 2795491, at *4 ("Special Masters frequently accord more weight to contemporaneously-recorded medical symptoms than those recorded in later medical histories, affidavits, or trial testimony.").

Next, the undersigned finds petitioner's MRIs do not support a diagnosis of ADEM. Although MRI evidence of demyelination is not required by the Brighton Collaboration, they noted evidence of inflammation or demyelination is a "diagnostic hallmark." Pet. Ex. 102 at 5. The MS Study Group requires at least one lesion for an ADEM diagnosis. Dr. Kinsbourne opined that MRI evidence is not required for an ADEM diagnosis, while Dr. Sriram opined ADEM patients have abnormalities on MRI.

Dr. Kinsbourne relied on Honkaniemi et al., who found "a delay of about 1 to 6 weeks between the onset of clinical symptoms and the appearance of the lesions in MR images." Pet. Ex. 98 at 7. However, lesions did appear in their patients. Here, petitioner's MRI done on November 23, 2013, seven days after onset on November 16, 2013 and within the time frame found in Honkaniemi et al.,[80] showed no evidence of a demyelinating disorder. Additionally, none of petitioner's subsequent MRIs showed evidence of demyelination. Therefore, the undersigned finds that the MRIs do not support a diagnosis of ADEM.

Third, none of petitioner's treating physicians opined that petitioner was suffering from ADEM. In November 2013, petitioner received diagnoses of acute severe migraine headache, weakness, and CVA. In January and February 2014, petitioner received diagnoses of TIA, hemiplegic migraine, and CVA. ADEM was not considered as a possible diagnosis by any treating physician at any point in petitioner's clinical course. See Capizzano, 440 F.3d at 1326.

Overall, the undersigned finds no evidence to support a diagnosis of ADEM.

2. MS

Next, based on the record as a whole, the medical records, the opinions and diagnoses of petitioner's treating neurologists, and the parties' respective experts, the undersigned finds there is not preponderant evidence that petitioner suffers from MS.

Both Dr. Kinsbourne and Dr. Sriram used the McDonald criteria to evaluate whether petitioner suffers from MS. Dr. Kinsbourne opined that petitioner has MS because he had

[80] Dale et al. noted "[h]istological studies of patients with ADEM dying at various intervals up to a month after clinical onset have shown that microscopic lesions are very numerous, appear within days of clinical presentation and do not increase in size or number." Pet. Ex. 27 at 12.

episodes differing in time and space, a heat sensitivity, five oligoclonal bands in his CSF, a positive response to steroids, and positive ANA antibodies. He also opined that it can be inferred that petitioner's treating physicians believed petitioner had MS because they prescribed him Tecfidera. On the other hand, Dr. Sriram opined petitioner does not meet the diagnostic criteria for MS because petitioner's left-sided weakness was waxing and waning, there were no abnormalities in reflex testing, electrical studies were all normal, multiple MRIs of the brain and spinal cord failed to show any lesions, and there is no objective evidence of a clinical attack.

A review of the records reveals that petitioner was not diagnosed with MS post-vaccination. On November 16, 2013, petitioner was diagnosed with generalized weakness and an acute severe migraine headache. Petitioner was diagnosed with weakness of left upper extremity on November 22, 2013. On November 23, 2013, petitioner was diagnosed with paresthesia and stroke/CVA.

Petitioner's treating physicians did not consider a diagnosis of a demyelinating disease until July 2014, more than seven months after vaccination, when petitioner's CSF showed five oligoclonal bands and petitioner reported weakness on his right side. When petitioner presented to Dr. Grimes in August 2014, Dr. Grimes found the presence of oligoclonal bands suggestive of demyelinating disease, but he did not diagnose petitioner with MS at this visit. Instead, he ordered additional testing. By February 2015, Dr. Grimes determined petitioner did not meet the criteria for MS.

The undersigned finds that the opinion of petitioner's treating neurologist, Dr. Grimes, is persuasive, and that petitioner does not meet the criteria for a diagnosis of MS. She also agrees with the opinions of Dr. Sriram, which appear to be consistent with those of Dr. Grimes, that oligoclonal bands alone are insufficient to support a diagnosis of MS. Further, a prescription for Tecfidera, a drug used to treat MS, does not provide preponderant evidence to support a diagnosis, given that Dr. Grimes affirmatively stated that petitioner did not meet the criteria for diagnosis and the medication was discontinued, albeit only after he tested positive for the JC virus.

Additionally, none of petitioner's numerous MRIs have shown lesions in his brain or spinal cord. Under the McDonald criteria, at least one lesion is required for diagnosis. Further, petitioner's treating physicians often commented on the fact that even after the passage of time, no lesions were found on serial MRI studies.[81] See, e.g., Pet. Ex. 7 at 2; Pet. Ex. 12 at 4; Pet. Ex. 45 at 2. The undersigned again finds petitioner's treating physician Dr. Grimes and Dr. Sriram more persuasive on this point.

3. Miscellaneous Demyelinating or Neurological Conditions

In his pleadings, petitioner alleges that he sustained a "neurological condition," caused

[81] Thorpe et al. suggests that Dr. Sriram is correct that in MS, a normal brain MRI is rare. Pet. Ex. 42 at 5. The authors found that in patients with normal brain MRIs, a spinal cord MRI may show cord lesions, aiding in the diagnosis of MS. Id. All eight patients in Thorpe et al. with normal brain MRIs had at least one spinal cord lesion. Id. at 3, 3tbl.1.

by vaccination. Petitioner's experts define what he means by "neurological condition" in their reports and testimony. Dr. Kinsbourne defines the condition as ADEM, ADEM-like, MS, or MS-like. See Tr. 78, 102, 108; Pet. Ex. 25 at 4; Pet. Ex. 96 at 1-3. Dr. Kinsbourne also uses the phrase "inflammatory autoimmune encephalopathy," which he states encompasses a "number of entities." Tr. 129. Dr. Kinsbourne does not otherwise explain or define the entities he references. Lastly, Dr. Kinsbourne uses the phrase, "primary inflammatory CNS white matter disease." Tr. 106. Use of these various phrases is somewhat confusing, in that it is difficult to analyze the condition at issue when it is not well-defined. Regardless of the phrase Dr. Kinsbourne uses to describe petitioner's diagnosis, the totality of Dr. Kinsbourne's opinions boil down to one category of neurological conditions—a demyelinating illness of the CNS. Thus, regardless of the name or phrase used, the undersigned finds that petitioner has alleged that he suffered a demyelinating neurological condition of the CNS. Further, the undersigned finds that the petitioner has not established by preponderant evidence that he suffered a demyelinating illness post-vaccination.

Petitioner's post-vaccination medical records also reference a number of other non-demyelinating conditions, including stroke (CVA), hemiplegic migraine, and CNS vasculitis. But petitioner has not alleged, nor have his experts opined, that his alleged vaccine-related diagnosis is stroke, hemiplegic migraine, or vasculitis.[82] Thus, the undersigned finds that there is insufficient evidence of any other neurological condition or diagnosis to support petitioner's claim for compensation.

B. Causation

1. Althen Prong One

Under Althen Prong One, petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu, 569 F.3d at 1375; Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by a "sound and reliable" medical or scientific explanation. Boatmon, 941 F.3d at 1359; see also Knudsen, 35 F.3d at 548; Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioner relies upon a medical opinion to support his theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen, 618 F.3d at 1347 ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better than the soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

The undersigned finds that petitioner has not offered a sound and reliable medical theory in support of his claim. Based on the undersigned's experience, current medical literature, and Dr. Sriram's testimony, the prevailing mechanism causally associated with a demyelinating CNS

[82] Additionally, there is no evidence that these diagnoses constitute demyelinating illnesses.

illness is a T cell mediated adaptive immune response, not an innate immune response.

First, based on the undersigned's experience and cases in the Program, molecular mimicry,[83] an adaptive immune system response, is the prevailing mechanism implicated in CNS demyelinating conditions. See, e.g., Palattao v. Sec'y of Health & Hum. Servs., No. 13–591V, 2019 WL 989380, at *35-37 (Fed. Cl. Spec. Mstr. Feb. 4, 2019) ("[M]any of the existing Program decisions in which TM has been found to be caused by a vaccine rely on a mechanism [of] []molecular mimicry . . . ."); Caruso v. Sec'y of Health & Hum. Servs., No. 15–200V, 2017 WL 5381134, at *14, *14 n.19 (Fed. Cl. Spec. Mstr. Oct. 18, 2017) (finding petitioner satisfied Althen Prong One under a theory of molecular mimicry in a flu/ADEM case); Reinhardt v. Sec'y of Health & Hum. Servs., No. 17–1257V, 2021 WL 1851491, at *16-18 (Fed. Cl. Spec. Mstr. Apr. 2, 2021) (determining petitioner established Althen Prong One in a flu/bilateral ON case under the theory of molecular mimicry).

In addition to the Program case support, the mechanism of molecular mimicry is also supported by numerous medical literature articles filed in this case, including many articles filed by the petitioner. See, e.g., Pet. Ex. 35 at 3 ("The current pathogenesis hypothesis in post-vaccination ADEM is that antigens of viral origin cross-react with myeline components . . . . The inflammatory process in MS is propagated by an autoimmune cascade, involving mainly T-cells that target myelin self antigens . . . ."); Pet. Ex. 36 at 4 (noting molecular mimicry as a potential mechanism in acute TM);[84] Pet. Ex. 99 at 4 (documenting molecular mimicry as a mechanism for the pathogenesis of ADEM); Pet. Ex. 102 at 2 (listing molecular mimicry as a mechanism to explain the demyelination and etiology of ADEM). Dr. Kinsbourne agreed that "MS is thought frequently to involve molecular mimicry between the infectious antigen and self-antigens." Pet. Ex. 25 at 6. However, he did not implicate molecular mimicry in this case, and instead opined that the innate immune system was the mechanism at play. He specifically rejected molecular mimicry because onset here was within 24 hours.[85] See id.

[83] Molecular mimicry is "a model of autoimmunity in which an immune response to a foreign antigen containing a peptide region that mimics a self epitope provokes cross-reactivity to a self protein." Molecular Mimicry, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=89392 (last visited May 4, 2021).

[84] Douglas A. Kerr & Harold Ayetey, Immunopathogenesis of Acute Transverse Myelitis, 15 Current Op. Neurology 339 (2002).

[85] Additionally, petitioner, in his prehearing submission, stated that in a case of a demyelinating injury "where the onset of symptoms occurs over the course of several days or weeks, the mechanism of injury is generally thought to involve molecular mimicry, whereby homology between a foreign antigen and self-antigen leads to the development of tissue damage and clinical disease from antibodies and T-cells directed initially against the exogenous agent that also react against self-antigen." Pet. Prehearing Submission at 18-19. Petitioner added that "in cases where the onset is more acute, as here, the likely mechanism is an abrupt innate immune response that starts shortly after vaccination and involves the production of proinflammatory cytokines that pass the blood brain barrier and ultimately lead to demyelination." Id. at 19.

The innate immune system as the causal mechanism in a demyelinating condition is a novel theory to the undersigned, although it has been used unsuccessfully in this context in the Program in the past. See, e.g., Palattao, 2019 WL 989380, at *34-37 (rejecting petitioner's theory that the innate immune system produces cytokines that can cause a demyelinating condition like TM); Samuels v. Sec'y of Health & Hum. Servs., No. 17–071V, 2020 WL 2954953, at *20 (Fed. Cl. Spec. Mstr. May 1, 2020) (finding petitioner's theory of "generalized inflammation promoted by an innate immune response . . . not scientifically/medically reliable" in an ADEM/MS case). The undersigned agrees with the reasoning in the above cases where special masters have rejected the theory of innate immunity as a sound and reliable mechanism in CNS demyelinating conditions.

Here, petitioner asserted that cytokines are released after vaccination and that cytokines cause inflammation. Dr. Gershwin made a compelling argument that cytokines play a role in the pathological process of ADEM and MS. While cytokines may be part of the process, petitioner did not provide sound and reliable evidence that the innate immune system cytokine-induced inflammation explains CNS demyelination.[86]

Merson and Binder[87] appear to best characterize the role of microglial activation and the cytokine response in contributing to the pathogenesis CNS demyelinating conditions. See Pet. Ex. 39.

> The range of activities exhibited by microglia during inflammatory demyelination can be broadly classified into four categories: inflammation, phagocytosis, immuno-modulation[,] and the promotion of neural repair. . . . Although the nature of the inflammatory response is influenced by the specific pattern recognition receptor (e.g. [TLRs]) that a given pathological stimulus activates in microglia, the response is by nature generic and relatively non-specific compared to the exquisite specificity of an adaptive immune response.

Id. at 2.

It is the adaptive immune response that conducts the orchestra of various instruments that together play a role to cause CNS demyelination. This conclusion is supported by the medical literature, which explains the role played by T cells in the adaptive immune system in causing demyelinating conditions like MS. See, e.g., Pet. Ex. 35 at 3 ("The inflammatory process in MS is propagated by an autoimmune cascade, involving mainly T-cells that target myelin self antigens, possibly mediated by mechanisms of molecular mimicry . . . ."); Pet. Ex. 39 at 3 fig.1

[86] The medical literature supporting a finding of cytokines in clinically definite MS patients did not address whether cytokines caused or initiated the demyelinating disease; instead, the articles found cytokines present in individuals who were already diagnosed with clinically definite MS. See, e.g., Pet. Ex. 32; Pet. Ex. 38.

[87] Tobias D. Merson & Michele D. Binder, Role of Cytokines as Mediators and Regulators of Microglial Activity in Inflammatory Demyelination of the CNS, 12 Neuromolecular Med. 99 (2010).

(illustrating that microglia, activated by T cells, release pro-inflammatory cytokines that can lead to demyelination); Pet. Ex. 72 at 5-7 (discussing the impact of T cells);[88] Pet. Ex. 86 at 1 ("Neuroinflammatory diseases, such as [MS], are characterized by invasion of the brain with autoreactive T cells.");[89] Pet. Ex. 87 at 31 ("Histologic evidence also suggests that T cells participate in MS."); Pet. Ex. 89 at 1 ("[A]daptive immune responses have been described mainly in the context of autoimmune diseases of the CNS, such as [MS]."); Pet. Ex. 91 at 11-13;[90] Pet. Ex. 93 at 4 ("The presence of inflammation driven by the adaptive immune system in absence of infectious pathogens . . . strongly suggest[s] an autoimmune origin [in MS].").[91]

The undersigned finds Dr. Sriram's testimony more persuasive because his testimony is consistent with the undersigned's experience, the medical literature, and prevailing case law. Dr. Sriram testified that after vaccination, antigens are activated in lymph nodes where T cells proliferate. Thereafter, the T cells amplify and subsequently enter the brain. Again, this implicates the adaptive immune response.

Next, the undersigned finds Dr. Kinsbourne did not fully explain the mechanism by which ADEM can "morph" into MS. After a review of the record as a whole, it most likely appears that those originally diagnosed with ADEM were rediagnosed with MS once they had a second attack and fit the criteria for MS. The condition did not morph, but instead the diagnosis was refined.

With regard to trained immunity, the undersigned finds that it may accelerate an innate response, but it does not explain how an innate response can cause demyelination.

Accordingly, the undersigned finds petitioner has not offered a sound and reliable medical theory in support of his claim. Thus, petitioner has not met the preponderant evidentiary standard with respect to Althen Prong One.

---

[88] Antoine Louveau et al., Revisiting the Concept of CNS Immune Privilege, 36 Trends Immunology 569 (2015).

[89] Antoine Louveau et al., CNS Lymphatic Drainage and Neuroinflammation Are Regulated by Meningeal Lymphatic Vasculature, 21 Nature Neuroscience 1380 (2018).

[90] In Lamprone et al., the authors wrote "inflammatory innate immune processes are clearly detrimental in the pathophysiology of MS;" however, "mechanisms by which T and B cells migrate through endothelial cells are key steps in the pathogenesis of MS." Pet. Ex. 91 at 11-12. The authors further explained that "MS is a complex chronic disease involving a host of cells with deregulated roles," with "[t]he main culprits [being] autoreactive T cells" that "infiltrate massively into the CNS and induce demyelination." Id. at 13 fig.5. They also acknowledged that "[m]onocytic cells (monocytes, macrophages, microglia, etc.) are also very important in the development of the disease." Id.

[91] Miriam Hernangómez et al., Brain Innate Immunity in the Regulation of Neuroinflammation: Therapeutic Strategies by Modulating CD200-CD200R Interaction Involve the Cannabinoid System, 20 Current Pharmaceutical Design 4707 (2014).

2. Althen Prong Two

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

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical 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 trustworthy evidence since they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528. The petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, petitioner may satisfy his burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

Since petitioner failed to prove Althen Prong One, it follows that he cannot prove Althen Prong Two. However, even if petitioner had proven a sound and reliable causal mechanism, he failed to prove by preponderant evidence a logical sequence of cause and effect, showing his flu vaccine caused his condition.

Petitioner asserts that after his flu vaccination, an innate immune response consisting of a release of cytokines occurred and led to inflammation in his brain within 24 hours. However, the undersigned finds no evidence of inflammation until July 2014.

As discussed in the diagnosis analysis above, the treating physicians found no evidence of inflammation in November 2013. Petitioner was alert and oriented during three hospital visits in November 2013 and showed no change in mental status during this time. Additionally, petitioner's November 2013 MRI showed no evidence of demyelination.

The only evidence of inflammation was found in July 2014, more than seven months after vaccination, when five oligoclonal bands were found in petitioner's CSF. However, the undersigned agrees with the McDonald criteria, Dr. Sriram, and Dr. Grimes that oligoclonal bands alone are insufficient for a diagnosis. As Dr. Sriram explained, the McDonald criteria allows oligoclonal bands to fulfill the dissemination in time requirement only if dissemination in space is met. Dissemination in space is met when one or more lesions are present. Here, petitioner's numerous MRIs since November 2013 have never shown lesions. According to Dr. Grimes, petitioner's oligoclonal bands were only suggestive of a demyelinating disease. He ordered additional testing and thereafter confirmed petitioner did not suffer from MS. The undersigned also agrees with Dr. Sriram that because of the more than seven month gap between

vaccination and the discovery of oligoclonal bands, the evidence of inflammation is not temporarily associated with vaccination.

Although some of petitioner's treating physicians provided letters stating petitioner should not receive a future flu vaccination, the undersigned does not find these letters to be preponderant evidence that petitioner's flu vaccination caused a demyelinating condition 24 hours later. Dr. Egekeze, on July 21, 2014, only "recommend[ed] the [petitioner] abstain[] from vaccinations at this time until a clear diagnosis." Pet. Ex. 8 at 1. Likewise, Dr. Gillespie, on December 10, 2014, only recommended petitioner "avoid any vaccines" at this time. Id. at 3. Neither Dr. Egekeze nor Dr. Gillespie opined as to causation.

Dr. Molina provided two letters. In her December 10, 2014 letter, she stated petitioner "had a severe reaction to the flu vaccine previously which resulted in long-lasting neurological deficits. Because of this, further [flu] vaccination is contraindicated." Pet. Ex. 8 at 2. Dr. Molina's January 23, 2019 letter stated, "[petitioner] should be excluded from routine required [flu] vaccination due to a previous history of adverse reaction to the vaccine. Shortly after receiving the seasonal [flu] vaccine in 2013[,] he developed significant neurologic symptoms, some of which are persisting even today." Pet. Ex. 48 at 63. The undersigned again finds these letters do not amount to preponderant evidence that the flu vaccine caused petitioner's symptoms. Read together, Dr. Molina does not opine that petitioner's "neurologic symptoms" were caused by the flu vaccine in her letters; she merely notes the temporal association between vaccination and symptom onset. Her letters alone are not sufficient evidence to reach the preponderant evidentiary standard required.

For all of the reasons described above, the undersigned finds that petitioner has failed to provide preponderant evidence of a logical sequence of cause and effect required under Althen Prong Two.

3. Althen Prong Three

Althen Prong Three requires petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That term has been equated to mean a "medically acceptable temporal relationship." Id. The petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disease's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352. The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen Prong One). Id.; Koehn v. Sec'y of Health & Hum. Servs., 773 F.3d 1239, 1243 (Fed. Cir. 2014); Shapiro v. Sec'y of Health & Hum. Servs., 101 Fed. Cl. 532, 542 (2011), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 503 F. App'x 952 (Fed. Cir. 2013).

The parties and experts agree that petitioner's onset was 24 hours after vaccination. The experts agree that an innate immune reaction occurs before an adaptive immune reaction. A 24-hour innate immune response is not disputed.

The issue here is that there is no evidence that an innate immune response can cause a demyelinating condition in 24 hours.

Huynh et al. noted that in ADEM, "[d]epending on the inciting agent, the onset of symptoms may vary . . . from 1 to 14 days." Pet. Ex. 99 at 5. However, they did not state the date of the inciting agent. The authors did note patients who developed ADEM between one and three weeks after flu vaccination. Huynh et al. discussed mechanisms of ADEM, including molecular mimicry and immuno-inflammatory model. An innate immune response was not listed.

Shoamanesh and Traboulsee examined an ADEM case with an onset of two days following flu vaccination. Dale and Branson noted a mean onset period of two weeks in most ADEM patients. Neither article discussed a mechanism at play.

Schwarz et al. found onset in one patient with MS "a few days" after diphtheria and tetanus vaccination. Pet. Ex. 103 at 3. The authors noted "an autoimmune response to myelin basic protein triggered by infection or immunization . . . to be a possible etiologic factor," similar to an experimental autoimmune encephalitis model. Id. at 1. Karussis and Petrou found onset between 8 days and 3 weeks in patients with ADEM post-flu vaccination. Similarly, Karussis and Petrou noted [t]he current pathogenetic hypothesis in post-vaccination ADEM is that antigens of viral origin cross-react with myelin components (molecular mimicry)" or that vaccination activates T cells. Pet. Ex. 35 at 3. And with MS, the authors also found the mechanism at play to be "an autoimmune cascade, involving mainly T-cells that target myelin self antigens, possibly mediated by mechanisms of molecular mimicry," or alternatively, T cells "expand to critical pathogenic quantities due to malfunctioning immunoregulatory mechanisms." Id. Innate immune responses were not discussed in either article as a mechanism by which a demyelinating disease can occur.

Taken together, the medical literature provided does not support a 24-hour onset. None of these articles on onset discussed an innate immune response mechanism. The articles that did discuss onset as well as mechanisms that could be at play consistently mentioned an adaptive T cell response and molecular mimicry. Additionally, petitioner did not provide medical literature to support a T cell response within 24 hours.

The undersigned finds Dr. Sriram's testimony regarding onset more persuasive. In summary, he testified that it takes at least one to two days for T cells to proliferate in the lymph node system before they subsequently enter the brain. And according to experimental autoimmune encephalitis models, demyelination cannot occur within 24 hours.

Lastly, the undersigned notes other decisions from other special masters where a petition alleging a demyelinating injury in the Program has been dismissed for a similar onset that was found too close in time to vaccination to be medically reasonable. See, e.g., Palattao, 2019 WL 989380, at *35 (citing dismissals of cases with 24-hour onset for vaccine-related TM and finding a 30- to 36-hour onset to not be medically acceptable); Samuels, 2020 WL 2954953, at *20-21 (finding a 24-hour onset "entirely too short a timeframe to be medically acceptable" because petitioner failed to show how "proinflammatory cytokines upregulated by a vaccine could begin

to cause autoimmune-mediated demyelinating injuries" within 24 hours). The undersigned agrees with the reasoning in these decisions as to the appropriate onset given the mechanism at issue here.

Based on a review of all of the evidence, the undersigned finds that petitioner has failed to prove by preponderant evidence that an onset of symptoms occurring approximately 24 hours after vaccination is an appropriate time frame. Therefore, petitioner has failed to provide preponderant evidence to satisfy Althen Prong Three.

VI. CONCLUSION

It is clear that petitioner has had a very difficult struggle with his health since November 2013, and the undersigned extends her sympathy to him. The undersigned's decision, however, cannot be decided based upon sympathy, but rather on the evidence and law.

For all of the reasons discussed above, the undersigned finds that petitioner has not established by preponderant evidence that vaccination caused his condition. Therefore, petitioner is not entitled to compensation and his petition must be dismissed. In the absence of a timely filed motion for review pursuant to Vaccine Rule 23, the Clerk of Court **SHALL ENTER JUDGMENT** in accordance with this Decision.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master