In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: July 9, 2021

E.M.,	*	No. 14-753V
Petitioner,	*	Special Master Sanders
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Ruling on Entitlement; Influenza ("Flu") Vaccine; Small Fiber Neuropathy; Small Vessel Vasculitis; Molecular Mimicry.
Respondent.	*	

Scott B. Taylor, Urban & Taylor, S.C., Milwaukee, WI, for Petitioner.
Voris E. Johnson, United States Department of Justice, Washington, DC, for Respondent.

RULING ON ENTITLEMENT[1]

On August 19, 2014, E.M. ("Petitioner") filed a petition for compensation pursuant to the National Vaccine Injury Compensation Program.[2] Pet. at 1, ECF No. 1; 42 U.S.C. §§ 300aa-1 to -34 (2012). Petitioner alleges that the influenza ("flu") vaccine she received on August 23, 2011, caused her to suffer from small fiber neuropathy[3] and small vessel vasculitis.[4] Pet. at 1; *see also* Pet'r's Br. at 1, ECF No. 70.

[1] This Ruling shall be posted on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). In accordance with Vaccine Rule 18(b), a party has 14 days to identify and move to delete medical or other information that satisfies the criteria in § 300aa-12(d)(4)(B). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted ruling. If, upon review, I agree that the identified material fits within the requirements of that provision, such material will be deleted from public access.

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

[3] Small fiber neuropathy is "a type of neuropathy in which only the small sensory cutaneous nerves are affected." *Dorland's Illustrated Medical Dictionary* 1263, 1268 (32nd ed. 2012) [hereinafter "*Dorland's*"]. Neuropathy is "a functional disturbance or pathologic change in the peripheral nervous system, sometimes limited to noninflammatory lesions as opposed to those of neuritis; the etiology may be known or unknown." *Id.*

[4] Small vessel vasculitis is "any of a group of vascular diseases of the small vessels, including microscopic polyangiitis, Wegener granulomatosis, Churg-Strauss syndrome, and pauci-immune crescentic glomerulonephritis." *Dorland's* at 2026. Vasculitis is "inflammation of a blood or lymph vessel." *Id.*

After carefully analyzing and weighing all the evidence and testimony presented in this case in accordance with the applicable legal standards,[5] I find that Petitioner has met her legal burden with respect to her small fiber neuropathy. Petitioner has provided preponderant evidence that the flu vaccine she received on August 23, 2011, was the cause-in-fact of her small fiber neuropathy. Accordingly, Petitioner is entitled to compensation.

I. Procedural History

Petitioner filed her petition for compensation on August 19, 2014, including proof of vaccination and nine medical record exhibits. Pet. at 1; Pet'r's Exs. 1–9, ECF Nos. 1-2–1-18. Petitioner filed an affidavit from her treating physician Dr. Traci Purath on September 16, 2014. Pet'r's Ex. 10, ECF No. 7-1. The parties appeared for a status conference the same day. *See* Min. Entry, docketed Sept. 16, 2014. Following the conference, the presiding special master ordered Petitioner to file an affidavit regarding damages. Sched. Order, ECF No. 8. Petitioner filed her affidavit regarding damages on October 16, 2014. Pet'r's Ex. 11, ECF No. 9-1.

Respondent filed his Rule 4(c) report on November 14, 2014, recommending that compensation be denied. Resp't's Report, ECF No. 10. A status conference was held on November 25, 2014, to discuss Petitioner's damages affidavit. Sched. Order, ECF No. 11; *see also* Min. Entry, docketed Nov. 25, 2014. Following the conference, the presiding special master ordered Petitioner to decide whether she wanted to pursue an expert report or present a settlement demand to Respondent by the next status conference. Sched. Order at 1. Another status conference was held on January 8, 2015. Min. Entry, docketed Jan. 8, 2015. The case was subsequently referred to alternative dispute resolution ("ADR"). Order, ECF No. 12. The parties were unable to come to an agreement, and the case was removed from ADR on April 16, 2015. Order, ECF No. 15.

On April 24, 2015, Petitioner filed three additional medical record exhibits. Pet'r's Exs. 11[6]–13, ECF Nos. 19-1–19-3. The presiding special master ordered Petitioner to submit an expert report by June 8, 2015. Sched. Order, ECF No. 22. After one extension of time, Petitioner filed an expert report from Dr. David S. Younger on July 7, 2015, along with supporting medical literature and a supplemental affidavit authored by Petitioner. Pet'r's Exs. 14–20, ECF Nos. 25-1–25-7. Respondent filed his responsive expert report from Dr. Peter D. Donofrio on October 16, 2015, along with supporting medical literature. Resp't's Exs. A–H, ECF Nos. 29-1–29-8.

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[5] While I have reviewed all of the information filed in this case, only those filings and records that are most relevant to the decision will be discussed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision.") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.*, 527 F. App'x 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered.").

[6] Petitioner filed Exhibit 11 as her affidavit regarding damages on October 16, 2014. ECF No. 9-1. Petitioner also filed a medical records exhibit from Medical College of Wisconsin Plank Road Clinic as Exhibit 11 on April 24, 2015. ECF No. 19-1. For clarification, I will hereinafter refer to Petitioner's affidavit regarding damages as Petitioner's Exhibit 11a. I will refer to her medical records exhibit as Petitioner's Exhibit 11b.

The parties convened for a status conference on October 26, 2015, at which time the presiding special master ordered Petitioner to file a supplemental expert report from Dr. Younger. Sched. Order, ECF No. 30; *see also* Min. Entry, docketed Oct. 26, 2015. The presiding special master ordered Dr. Younger to address issues relating to diagnosis, medical theory, and timing. Sched. Order at 1. Petitioner filed a supplemental expert report and supporting medical literature on January 11, 2016. Pet'r's Exs. 21–38, ECF Nos. 35-1–35-18. Respondent filed a responsive supplemental expert report and supporting medical literature on March 21, 2016. Resp't's Exs. I–K, ECF Nos. 41-1–41-3.

On May 13, 2016, the presiding special master scheduled this matter for an entitlement hearing to take place on January 12–13, 2017. Sched. Order, ECF No. 47. However, on September 2, 2016, Petitioner filed a motion for relief to name a new expert neurologist, file new expert reports, and to adjourn the upcoming entitlement hearing in this matter. ECF No. 54. Petitioner indicated that the basis for her request was Dr. Younger's recent felony conviction involving a crime of dishonesty. *Id.* at 1. Petitioner "believe[d] that this conviction . . . may serve to seriously undermine Dr. Younger's credibility at the entitlement hearing and, as such, prejudice Petitioner's right to a fair hearing." *Id.* Petitioner's counsel submitted a personal declaration in support of Petitioner's motion. *See* ECF No. 55. The presiding special master granted Petitioner's motion and postponed the entitlement hearing "indefinitely." Order, ECF No. 56. The presiding special master ordered Petitioner to submit a status report on the progress of obtaining a new expert. *Id.*

On October 11, 2016, Petitioner filed a status report indicating she had retained Dr. Lawrence Steinman to opine in this matter and requested until January 31, 2017, to file a report. ECF No. 57. Prior to filing her expert report, on January 16, 2017, Petitioner submitted medical records from University Health Services at the University of Wisconsin Madison. Pet'r's Ex. 39, ECF No. 59-1. On January 31, 2017, Petitioner filed an expert report from Dr. Lawrence Steinman along with thirty-one pieces of medical literature. Pet'r's Exs. 40–72, ECF Nos. 60-1–60-33. Due to an error in filing, Petitioner re-filed her expert report from Dr. Steinman on June 3, 2019. Pet'r's Ex. 40, ECF No. 77-1; *see also* Pet'r's Mot. to Strike, ECF No. 76; Order, ECF No. 78. Respondent filed his responsive supplemental expert report from Dr. Donofrio along with supporting medical literature on April 20, 2017. Resp't's Exs. L–M, ECF No. 63-1–63-2.

This case was reassigned to me on October 10, 2017. ECF No. 65. On May 8, 2018, I contacted the parties regarding availability of dates for scheduling an entitlement hearing. Informal Comms., docketed May 8–15, 2018. This matter was subsequently set for an entitlement hearing on July 18–19, 2019. ECF No. 68. Petitioner filed her pre-hearing brief and pre-hearing reply brief with supporting medical literature on March 25, 2019 and June 3, 2019, respectively. Pet'r's Br., ECF No. 70; Pet'r's Reply Br., ECF No. 75; Pet'r's Exs. 73–77, ECF Nos. 74-1–74-5. Respondent filed his pre-hearing response brief on April 23, 2019. ECF No. 71. The entitlement hearing was held as scheduled on July 18–19, 2019. *See* Notice, ECF No. 80.

Following the entitlement hearing, I ordered Petitioner to file a supplemental expert report, supporting medical literature, and an opening post-hearing brief regarding the potential effect of steroid treatments on testing for antibodies by October 15, 2019. Sched. Order, ECF No. 84; *see also* Tr. 260:17–261:6. Petitioner filed a supplemental expert report and medical literature on October 14, 2019. Pet'r's Exs. 78–83, ECF Nos. 85-1–85-6. The same day, Petitioner filed her opening post-hearing brief. ECF No. 86. On November 15, 2019, Respondent filed his responsive

supplemental expert report along with his post-hearing response brief. Resp't's Ex. N, ECF Nos. 88–89. Petitioner submitted a rebuttal expert report and a post-hearing reply brief on January 6, 2020. Pet'r's Ex. 84, ECF Nos. 91–92.

This matter is now ripe for consideration.

II. Factual Background

A. Medical Records

Petitioner's pre-vaccination medical history is significant for Von Willebrand's disease,[7] dysmenorrhea,[8] asthma,[9] eosinophilic esophagitis,[10] and migraine headaches.[11] *See* Pet'r's Ex. 1 at 24–25. Petitioner's migraines began after she sustained a concussion in 2003. Pet'r's Ex. 2 at 49–62. In June 2010, Petitioner presented to neurologist Traci Purath, M.D., at the Comprehensive Headache Center to establish care and for treatment of occipital neuralgia[12] with underlying migraines. *Id.*

On August 23, 2011, Petitioner presented to her primary care physician ("PCP") Amy D. Cvengros, M.D., for her yearly physical examination. Pet'r's Ex. 1 at 27. During this visit, Petitioner reported that her migraines had worsened over the prior two weeks. *Id.* at 28. In response, Dr. Cvengros advised Petitioner to call Dr. Purath's office. *Id.* at 31. Petitioner received the flu vaccination during this visit. *Id.* At the time of vaccination, Petitioner was twenty-four years old. Pet. at 1.

Two days later, on August 25, 2011, Petitioner presented to Dr. Purath. Pet'r's Ex. 2 at 46. During this visit, Petitioner reported "that her headaches had been under great control until [two] weeks ago." *Id.* Dr. Purath noted that Petitioner indicated at that time, she "awoke with a severe

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[7] Von Willebrand's disease is "a congenital bleeding disorder caused by mutation in the *VWF* gene (locus: 12p13.3), resulting in deficiency of von Willebrand factor, with prolonged bleeding time and often impairment of adhesion of platelets on glass beads, associated with epistaxis and increased bleeding after trauma or surgery, menorrhagia, and postpartum bleeding. Several different types have been distinguished, ranging from mild to severe." *Dorland's* at 544, 2072.

[8] Dysmenorrhea is "painful menstruation." *Dorland's* at 578.

[9] Asthma is "recurrent attacks of paroxysmal dyspnea, with airway inflammation and wheezing due to spasmodic contraction of the bronchi. Some cases are allergic manifestations in sensitized persons []; others are provoked by factors such as vigorous exercise, irritant particles, psychological stresses, and others." *Dorland's* at 168.

[10] Eosinophilic esophagitis is "inflammation caused by eosinophilic infiltration of the esophageal mucosa; the etiology is unknown, although it sometimes accompanies gastroesophageal reflux disease and sometimes may be an allergic reaction." *Dorland's* at 629.

[11] Migraine headaches are "often familial symptom complex of periodic attacks of vascular headache, usually temporal and unilateral in onset, commonly associated with irritability, nausea, vomiting, constipation or diarrhea, and often photophobia. Attacks are preceded by constriction of the cranial arteries, often with resultant prodromal sensory (especially ocular) symptoms and the spreading depression of Leão; the migraines themselves commence with the vasodilation that follows." *Dorland's* at 1166.

[12] Occipital neuralgia is "pain in the distribution of the occipital nerves, due to pressure or trauma to the nerve. Called also occipital headache." *Dorland's* at 1262.

headache, and had this sporadic tingling in her face." *Id.* Petitioner stated this had been going on and off for the past two weeks, but "there was no inciting event, no trauma, no medication changes[.]" *Id.* However, Dr. Purath noted that the only change was that Petitioner had recently finished law school and was back at home with her parents. *Id.* Dr. Purath opined that "much of this may be just what we call the letdown headache where your body actually can start to rest." *Id.* Nonetheless, Dr. Purath noted that Petitioner stated "she ha[d] been having tingling in the left side of her face, both sides of her face, and into her hands. She feels that she feels off." *Id.* Petitioner also reported that she had a brief episode of sudden urinary incontinence, but it was not preceded by a loss of consciousness or any confusion. *Id.* Petitioner also reported feeling "somewhat nauseous." *Id.* Dr. Purath noted Petitioner was not on any medications for her headaches at that time. *Id.* Dr. Purath ordered an electroencephalogram ("EEG") and MRI "to rule out any possible seizure because of this episode of urinary incontinence and these vague feelings of being 'a bit off' and having trouble processing information." *Id.*

The next day, on August 26, 2011, Petitioner returned to Dr. Purath. *Id.* at 43. Upon further questioning regarding Petitioner's condition, Petitioner reported that "the dysesthesias[13] all started after Tuesday night [August 23, 2011] after she had a flu shot." *Id.* Dr. Purath noted Petitioner maintained "[t]hey did not occur before this." *Id.* Dr. Purath further indicated "[t]hey progressed to the point that today, Friday[,] August 26, 2011, she complain[ed] of complete numbness of the left face, dysesthesias in the left arm, swelling in the left leg, with weakness in the left hand." *Id.* Petitioner reported that the symptoms became progressively worse. *Id.* Dr. Purath wrote she was "concerned that this may all be related to the flu shot." *Id.* However, Dr. Purath noted she "d[id] not feel that [Petitioner] has encephalitis[14] symptoms but transverse myelitis[15] may be a possibility given the issues with the left side of the body." *Id.* Upon examination, Dr. Purath noted decreased sensation to pinprick in Petitioner's left arm and increased deep tendon reflexes ("DTRs")[16] in her left upper and lower extremities. *Id.* The MRI of Petitioner's brain and spine were normal. *Id.* However, Petitioner's antinuclear antibody ("ANA")[17] was elevated at 1.33 (range 0–0.89), and her creatinine kinase[18] was also elevated at 157 (range 26–140). *Id.* at 77–78. Petitioner also

[13] Dysesthesias is "1. distortion of any sense, especially of that of touch . . . 2. an unpleasant abnormal sensation produced by normal stimuli." *Dorland's* at 577.

[14] Encephalitis is "inflammation of the brain." *Dorland's* at 612.

[15] Transverse myelitis is "myelitis in which the functional effect of the lesions spans the width of the entire cord at a given level." *Dorland's* at 1218. Myelitis is "1. inflammation of the spinal cord, often part of a more specifically defined disease process. One group of diseases is named according to whether primarily white matter or gray matter is affected . . . ; another group is defined by whether there is coexistent disease of the meninges [] or the brain . . . . In practice, the term is also used to denote noninflammatory lesions of the spinal cord; [] 2. inflammation of the bone marrow[.]" *Id.*

[16] Deep tendon reflexes ("DTRs") are "involuntary contraction[s] of a muscle after brief stretching caused by percussion of its tendon; tendon reflexes include the biceps reflex, triceps reflex, quadriceps reflex, and others." *Dorland's* at 1881.

[17] Antinuclear antibodies ("ANA") are "directed against nuclear antigens; ones against a variety of different antigens are almost invariably found in systemic lupus erythematosus and are frequently found in rheumatoid arthritis, scleroderma (systemic sclerosis), Sjögren syndrome, and mixed connective tissue disease. Antinuclear antibodies may be detected by immunofluorescent staining. Serologic tests are also used to determine antibody titers against specific antigens." *Dorland's* at 101.

[18] Creatinine kinase is "an Mg^{2+}-activated enzyme of the transferase class that catalyzes the phosphorylation of creatine by ATP to form phosphocreatine. The reaction effectively stores the energy of ATP as

underwent a spinal tap which revealed negative oligoclonal bands,[19] negative Lyme disease DNA, negative myelin basic protein,[20] and an overall negative culture. *Id.* at 63–64. Dr. Purath prescribed a seven-day course of steroid treatment with Decadron,[21] two milligrams three times a day. *Id.* at 43.

On August 29, 2011, Petitioner returned to Dr. Purath for her complaints of paresthesias, weakness, and occipital headaches. *Id.* at 40. During this visit, Dr. Purath noted that Petitioner was experiencing different types of migraines compared to normal and that she had never experienced a migraine with aura before. *Id.* Upon examination, Dr. Purath indicated Petitioner's "[DTRs] were slightly brisk in the left upper extremity when compared to the right . . . there [we]re patchy sensory changes in the right face and arm when compared to the left[.]" *Id.* Dr. Purath reviewed Petitioner's recent lab work and noted that her basic chemistry was "essentially negative." *Id.* Dr. Purath noted that the positive ANA was likely a false positive. *Id.*

Three days later, on September 1, 2011, Petitioner returned to Dr. Purath with complaints of shooting back pain radiating down to the bilateral buttocks. *Id.* at 37. Dr. Purath had previously prescribed Percocet for this pain. *See id.* at 37, 40, 43–44. She also noted Petitioner "was to finish her course of Decadron." *Id.* at 37. Dr. Purath reiterated that the results of Petitioner's EEG conducted on August 25, 2011, were normal. *Id.* at 37. She also noted that Petitioner's dysesthesias and tingling "[we]re much improved." *Id.* Yet, "[i]t d[id] still have various locations, but it [wa]s overall not as severe or bilateral as it had been." *Id.* Dr. Purath again noted that "[a]ll these issues stem from having the flu shot . . . and this [wa]s certainly not a migraine." *Id.*

On September 16, 2011, Petitioner returned to Dr. Purath and reported an increase in numbness on the right side of her face and in her right upper and lower extremities. *Id.* at 34. At this time, Petitioner reported "no weakness in [her] right arm." *Id.* However, Petitioner indicated "[s]he d[id] feel that the right hand [wa]s weak, and she fe[lt] that there are some tremors to the right hand which [wa]s very sporadic." *Id.* Dr. Purath noted that Petitioner's complaints regarding

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phosphocreatine in muscle and brain tissue and holds the muscle concentration of ATP nearly constant during the initiation of exercise. It occurs as three isoenzymes, each having two components composed of M (muscle) and of B (brain) subunits. CK_1 (BB) is found primarily in brain, CK_2 (MB) primarily in cardiac muscle, and CK_3 (MM) primarily in skeletal muscle. Differential determination of isoenzymes is useful for clinical diagnoses." *Dorland's* at 429.

[19] Oligoclonal bands are "discrete bands of immunoglobulins with decreased electrophoretic mobility; their appearance in electrophoretograms of cerebrospinal fluid when absent in the serum is a sign of possible multiple sclerosis or other diseases of the central nervous system." *Dorland's* at 197.

[20] Myelin basic protein is "a basic protein (MW 18,000) that constitutes about 30 per cent of myelin proteins; elevated levels of MBP occur in acute exacerbation of multiple sclerosis and acute cerebral infarction. Immunization of laboratory animals with MBP produces encephalomyelitis by inducing T-cell activity that leads to demyelination and lymphoid infiltration." *Dorland's* at 1533. Myelin is "the substance of the cell membrane of Schwann cells that coils to form the myelin sheath []; it has a high proportion of lipid to protein and serves as an electrical insulator." *Dorland's* at 1218.

[21] Decadron is "trademark for preparations of dexamethasone." *Dorland's* at 474. Dexamethasone is "a synthetic glucocorticoid, 25 times as potent as cortisol; used topically on the skin and conjunctiva as an anti-inflammatory and administered orally in replacement therapy for adrenocortical insufficiency, as an anti-inflammatory and immunosuppressant in a wide variety of disorders, and as an antiemetic in cancer chemotherapy." *Id.* at 504.

her left side had completely resolved, her back pain had improved, and she was not having headaches. *Id.* During this visit, Dr. Purath noted that Petitioner "has been on Decadron, currently [two milligrams] daily[.]" *Id.* at 35. However, Dr. Purath was "weaning her off because [she was] concerned that it may be causing some [] jitteriness[.]" *Id.* Following this appointment, Dr. Purath wrote that she "still believe[d] that [Petitioner] has had a reaction to the flu shot, which [she] fe[lt wa]s slowly improving." *Id.* at 34.

Petitioner followed up with Dr. Purath on September 29, 2011. *Id.* at 32. During this visit, Petitioner reported that she felt that her symptoms were improving even though she was still experiencing some decreased sensation in her face and right arm. *Id.* She noted Petitioner was off Decadron completely as of September 17, 2011. *Id.* Dr. Purath characterized Petitioner's headaches as occipital neuralgia with episodic migraines. *Id.* Dr. Purath instructed Petitioner to follow-up in one month. *Id.*

Prior to her next appointment with Dr. Purath, Petitioner underwent a repeat brain MRI, which was normal. *Id.* at 83. During Petitioner's follow up visit with Dr. Purath on October 28, 2011, Dr. Purath noted Petitioner's lower back pain had completely resolved. *Id.* at 29. However, Petitioner reported having blurred vision in her right eye,[22] bilateral hand tremors, and numbness in various locations in her arms, legs, and face. *Id.* Dr. Purath noted Petitioner "fe[lt] that at times her right upper extremity feels heavy, and sometimes, her fingers 'droop.'" *Id.* Upon examination, Dr. Purath noted patchy, decreased sensation in Petitioner's arms and legs. *Id.* She again wrote her opinion that Petitioner's symptoms started after the flu injection. *Id.* However, Dr. Purath did not "find anything that [wa]s jumping out at [her] neurologically as a deficit[,]" so she referred Petitioner to another neurologist for further evaluation. *Id.*

On November 4, 2011, Petitioner presented to neurologist Jorge Marquez de Leon, M.D., for a second opinion. Pet'r's Ex. 4 at 535–43. Petitioner recited her medical history to Dr. Marquez de Leon and told him that her symptoms began after receiving the flu vaccine on August 23, 2011. *Id.* at 535. Petitioner reported that during the evening of August 23, 2011, she began experiencing "the onset of paresthesias[23] over the left side of [her] face with no true numbness or motor abnormalities." *Id.* However, Petitioner reported that her symptoms progressed to "the right side of [her] face and the whole left side ([f]ace, arm[,] and leg)." *Id.* Dr. Marquez de Leon noted Petitioner described her symptoms as "shooting pain and painful paresthesias" over the hands and feet. *Id.* Petitioner also reported a worsening of her vision. *Id.* Upon examination, Dr. Marquez de Leon noted Petitioner's sensation to light touch was decreased in her right forearm and shoulder blade. *Id.* at 538–39. Dr. Marquez de Leon conducted Quantitative Sudomotor Axon Reflex Tests ("QSARTs"),[24] which revealed decreased responses in the right foot, distal leg, and forearm. *Id.*

[22] On October 28, 2011, Petitioner presented to ophthalmologist John Conto, O.D., for an examination. Pet'r's Ex. 3 at 13–23. Petitioner reported a change in her vision within the previous two weeks. *Id.* at 19. Dr. Conto noted that his impression was that Petitioner experienced "sudden vision loss[.]" *Id.* at 20. However, the rest of Dr. Conto's notes are illegible and difficult to decipher. *See id.*

[23] Paresthesias is "an abnormal touch sensation, such as burning, prickling, or formication, often in the absence of an external stimulus." *Dorland's* at 1383.

[24] Quantitative Sudomotor Axon Reflex Tests ("QSARTs") also known as "quantitative sensory testing" involve "various tactile stimuli [] applied to the skin, such as light touch, heat, cold, and vibrations, and the

at 542, *see also* Pet'r's Ex. 9 at 46. The QSARTs also revealed normal sensation in Petitioner's right proximal leg. *See id.* Based on these results and Petitioner's medical history, Dr. Marquez de Leon opined that Petitioner's paresthesias and limb pain were "most likely secondary to a small fiber neuropathy." Pet'r's Ex. 4 at 542. He further noted that "[t]he possibility of a reaction to her vaccination appears to be the most likely etiology." *Id.* Dr. Marquez de Leon ordered Petitioner to undergo additional laboratory tests and an autonomic evaluation. *Id.*

Pursuant to Dr. Marquez de Leon's orders, Petitioner underwent an EMG, which revealed normal results, on November 4, 2011. Pet'r's Ex. 2 at 80. In response, Dr. Marquez de Leon noted "no significant electrophysiological changes to suggest the presence of a medium to small fiber polyneuropathy or a mononeuropathy." *Id.* Additionally, Dr. Marquez de Leon also ordered an extensive autoimmune work-up and a paraneoplastic autoantibody panel to rule out a neurological autoimmunity. Both yielded negative results. Pet'r's Ex. 4 at 725; *see also id.* at 521–26. Dr. Marquez de Leon further ordered a thermoregulatory sweat test, which revealed abnormalities including Petitioner's decreased, even absent, sweating from the knees down. Pet'r's Ex. 9 at 46–47. As a result, Dr. Marquez de Leon concluded that there were "changes indicative of mild autonomic neuropathy, which is affecting both the sudomotor and vasomotor sympathetic pathways.[25] The study suggests mostly a postganglionic[26] condition such as can be seen from multiple etiologies." *Id.* at 47.

On January 12, 2012, Petitioner presented to neuro-ophthalmologist Bernard F. Remler, M.D., for an evaluation of her intermittent blurred vision and eye pain. Pet'r's Ex. 6 at 8–11. Upon examination, Dr. Remler noted that Petitioner's symptoms occurred "in the context of a neurologic syndrome that evolved after a flu shot on 8/22/11 [sic]." *Id.* at 8. He also noted that Petitioner was previously diagnosed with an autonomic neuropathy. *Id.* Dr. Remler concluded that Petitioner showed abnormalities in her near vision including mild convergence insufficiency[27] and signs of stimulus hypersensitivity. *Id.* at 10. He saw no overt signs of sympathetic or parasympathetic denervation of the eyelids or pupils. *Id.* Dr. Remler also could not find structural abnormalities of Petitioner's eye to correlate with her right eye pain. *Id.* Dr. Remler stated he was "uncertain whether there is a casual relationship with a flu vaccination. This is only suggested by the temporal relationship." *Id.*

Four days later, on January 16, 2012, Petitioner returned to Dr. Purath for a follow-up of her small fiber neuropathy. Pet'r's Ex. 2 at 26. During this visit, Dr. Purath noted Petitioner saw Dr. Remler, "who felt that he could not find any etiology for these episodes which [Petitioner] described as blurry vision and retro-orbital eye pain." *Id.* Petitioner also reported that the numbness and pain in her arms had been better in the last three weeks but indicated that the eye exam and heavy exercise seemed to cause flare-ups of her symptoms. *Id.* Dr. Purath noted that "[t]his is not

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patient's responses are monitored and compared either with stimuli to the opposite side of the body or with the responses of a control subject known not to have impairment." *Dorland's* at 1903.

[25] The sudomotor sympathetic pathway relates to "stimulating the sweat glands." *Dorland's* at 1796. The vasomotor sympathetic pathway "affect[s] the caliber of a vessel, especially of a blood vessel." *Id.* at 2027.

[26] Postganglionic means "situated posterior or distal to a ganglion; said especially of autonomic nerve fibers so located." *Dorland's* at 1502.

[27] Mild convergence insufficiency is "in ophthalmic physiology, [is] the coordinated inclination of the two lines of sight toward their common point of fixation, or the point of fixation itself." *Dorland's* at 411.

uncommon with polyneuropathy that stress to the body can flare up the symptoms." *Id.* Petitioner indicated she was also experiencing some palpitations, but Dr. Purath suspected they were caused by nortriptyline hydrochloride,[28] a medication prescribed to Petitioner by Dr. Marquez de Leon. *Id.* Dr. Purath further noted that Petitioner's headaches had improved. *Id.* Upon examination, Petitioner showed some decreased sensation in her face and right-sided extremities. *Id.* Dr. Purath planned to monitor Petitioner's symptoms. *Id.* at 27.

On April 12, 2012, Petitioner presented to the emergency room with complaints of chest pain and shortness of breath. Pet'r's Ex. 4 at 603. Petitioner described her chest pain as "heavy" and stated that "[t]he pain d[id] not radiate[]" but was "aggravated by deep breathing." *Id.* Petitioner's past medical history noted small fiber neuropathy, migraines, and "vaccine reaction with vague neurologic symptoms since August." *Id.* Petitioner underwent an examination, including a chest x-ray and ventilation perfusion ("VQ") scan,[29] which were normal. *Id.* at 607, 628–29. Petitioner's white blood count ("WBC") was elevated at 29 (range 4.0–10.0), and her C-reactive protein was high at 12.1 (range 0–0.5). *Id.* at 622, 656. Petitioner was discharged home and diagnosed with elevated white blood cells and chest pain. *Id.* at 610.

Petitioner followed up with Dr. Cvengros on April 17, 2012, regarding her recent emergency room visit. Pet'r's Ex. 1 at 19. Petitioner reported that she had "feelings of dyspnea[30] and constant chest 'pressure[.]'" *Id.* Dr. Cvengros noted Petitioner described her pain as though she '"[f]eels like someone [wa]s sitting on [her] chest[.]'" *Id.* Dr. Cvengros noted that she reviewed Petitioner's case and elevated WBC findings with a pathologist, and "was told leukocytosis[31] appeared to be 'reactive' and there was 'no morphologic abnormalities.'" *Id*. Dr. Cvengros ordered a chest CT, which was notable only for a small pericardial cyst. *Id.* at 20. Upon evaluation of the cyst, the results were normal. *Id.* Petitioner's WBC also returned to normal. *Id.* Dr. Cvengros noted that she "wonder[ed] about possibility of lab error (wrong sample) given how quickly [Petitioner's] counts normalized." *Id.*; *see also* Pet'r's Ex. 4 at 675.

On April 20, 2012, Petitioner returned to Dr. Purath for a complaint of increased right eye pain and some chest pain. Pet'r's Ex. 2 at 23. At this time, Petitioner's DTRs were slightly increased, and she showed patchy sensation to pinprick in the left arm. *Id.* Dr. Purath noted that she found it "interesting" that Petitioner had a significantly elevated WBC but that it was normal the next day. *Id.* Dr. Purath indicated that she "wonder[ed] if there [wa]s some underlying inflammatory process." *Id*. During this visit, she again noted her impression was that Petitioner suffered from small fiber neuropathy. *Id.*

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[28] Nortriptyline hydrochloride is "a tricyclic antidepressant . . ., also used to treat panic disorder and to relieve chronic, severe pain; administered orally." *Dorland's* at 1291.

[29] A ventilation perfusion ("VQ") scan is "a scintigraphic technique for demonstrating perfusion defects in normally ventilated areas of the lung in the diagnosis of pulmonary embolism, consisting of the imaging of the distribution of an inhaled radionuclide followed by the imaging of the perfusion of the lungs by an injected radionuclide." *Dorland's* at 1673.

[30] Dyspnea is "breathlessness or shortness of breath; difficult or labored respiration." *Dorland's* at 582.

[31] Leukocytosis is "a transient increase in the number of leukocytes in the blood; seen normally with strenuous exercise and pathologically accompanying hemorrhage, fever, infection, or inflammation." *Dorland's* at 1028.

On April 24, 2012, Petitioner again presented to the emergency room for an abrupt onset of shortness of breath, fever, chest pain, headache, neck pain, and blurred vision. Pet'r's Ex. 4 at 714. Petitioner's main complaint was chest discomfort and she again stated it "[f]e[lt] like someone [wa]s sitting on her chest." *Id.* Petitioner underwent a full work-up, which was unrevealing except for another elevated WBC. *Id.* A repeat chest x-ray, ECG, and VQ were negative. *Id*. at 717. Petitioner was discharged home. *Id*.

On May 21, 2012, Petitioner presented for a follow-up with Dr. Marquez de Leon. Pet'r's Ex. 7 at 18. Petitioner reported that she continued to have a tingling sensation in both arms and legs but that it "[was] somewhat different from what it was six months ago." *Id.* at 19. Petitioner complained that "[i]t [was] more a sensation of coldness and numbness" which now only affected her right side; the "symptoms over the left side [were] almost not there." *Id.* Petitioner underwent a physical examination, which was normal. *Id.* Dr. Marquez de Leon did not prescribe any new medications during this visit. *Id.* at 20.

Petitioner presented to Dr. Purath for a follow-up on May 29, 2012. Pet'r's Ex. 2 at 20. During this visit, Petitioner reported that her headaches, tremors, and paresthesias had improved. *Id.* However, Petitioner reported she had seen a hematologist, pulmonologist, and cardiologist, all of whom could not determine a clear etiology for Petitioner's symptoms. *Id.* A physical examination revealed a decreased pinprick sensation in Petitioner's right upper extremity, right lower extremity, and left face. *Id.* Dr. Purath assessed Petitioner with a flare-up of her small fiber neuropathy. *Id.* Dr. Purath referred Petitioner to the Chair of Neurology at Froedtert Hospital for further evaluation. *Id.*

On June 8, 2012, Petitioner presented to pulmonologist Dr. Rade Tomic, M.D., with complaints of "shortness of breath and chest pains." Pet'r's Ex. 3 at 58. Petitioner described her chest pain as "very strong in intensity and lasts a few seconds, and it subsides by itself." *Id.* A full workup was normal except for an abnormal ANCA result. *Id.* at 59. The extensive workup revealed no indication of pulmonary disease. *Id.* Dr. Tomic suggested a repeat test in three months. *Id.* Later that month, on June 22, 2012, Petitioner presented to Dr. Eric Martin, M.D., a gastroenterologist. *Id.* at 73. Petitioner underwent an esophagogram,[32] which was normal. *Id.* at 82. Dr. Martin concluded that, because all other tests were normal, the "source of [Petitioner's] chest pain [wa]s likely secondary to [Petitioner's] small fiber neuropathy." *Id.* at 83.

Petitioner presented for her yearly physical with Dr. Cvengros on August 29, 2012. Pet'r's Ex. 1 at 8. Petitioner complained of daily chest discomfort. *Id.* She also reported that while moving to Chicago the previous week, she developed significant muscle fatigue in her arms. *Id.* Petitioner also reported she experienced "[b]urning of [her] bilateral arms and legs occasionally and most noticeabl[y] in the mornings when getting out of bed." *Id*. at 11. However, Petitioner's physical examination revealed normal results. *Id*. Under "health maintenance" Dr. Cvengros noted that Petitioner "will not get any further influenza vaccines – several neurologic [symptoms] occurred after 2011 vaccination." *Id*.

On September 4, 2012, Petitioner returned to Dr. Purath for a follow-up. Pet'r's Ex. 2 at 8. During this visit, Petitioner reported that her headaches were improving but that she was

[32] An esophagogram is "a radiograph of the esophagus." *Dorland's* at 648.

experiencing increased numbness and weakness in her extremities. *Id.* Petitioner further reported that she has been getting fatigued very easily. *Id.* Petitioner also complained of continued chest pain, vision issues in both eyes but more pronounced on the right, and difficulty swallowing. *Id.* Petitioner's physical exam revealed a decreased pinprick sensation in Petitioner's right arm and leg. *Id.* at 9.

On September 17, 2012, Petitioner returned to Dr. Marquez de Leon and reported having fatigue, chest pressure, and paresthesias of her arms and face. Pet'r's Ex. 2 at 15. Dr. Marquez de Leon conducted a physical examination, which yielded normal results. *Id*. at 16. He assessed Petitioner with small fiber neuropathy with both somatic[33] and autonomic[34] features. *Id*. at 17.

Petitioner returned to Dr. Purath for a follow-up on October 4, 2012. *Id.* at 12. During this visit, Petitioner indicated "[s]he found out whenever she [wa]s anxious[,] she [had] symptoms of either weakness, sometimes tremor, sometimes numbness and tingling, but most recently she had some burning in the bilateral hands." *Id.* Dr. Purath noted that "[a]ll of these symptoms are not uncommon for small fiber neuropathy." *Id.* Petitioner also reported that her headaches had improved. *Id.* Dr. Purath prescribed 100mg of Gabapentin[35] but noted that Petitioner was "going to wait to start this until she s[aw] how she [wa]s doing." *Id.* at 13.

On February 6, 2014, Petitioner presented to a new neurologist, Dr. Alexandru C. Barboi, M.D., to establish care. Pet'r's Ex. 9 at 9. When giving her medical history, Petitioner reported that "[a]bout [six] hours after the [f]lu shot [Petitioner] was putting makeup on using a brush and had a transient episode of right cheek pain that resolved." *Id.* Petitioner continued that "[a]bout [two] days later . . . [Petitioner] developed numbness in her left arm then right arm and then both legs." *Id.* Dr. Barboi noted that "[Petitioner] also started to have intermittent blurry vision and pain in her right eye which d[id] not adjust well to light." *Id.* Petitioner also reported that "[w]hen she g[ot] excited or in cold weather, [her] hands sh[ook] and she los[t] vision in [her] right eye." *Id.* Dr. Barboi conducted a physical examination, which revealed "inconsistent and patchy" sensory reactions in various areas including Petitioner's face and right and left extremities. *Id.* at 12. Dr. Barboi's impression was that Petitioner's "history would fit a small fiber neuropathy diagnosis but [her] physical examination d[id] not aid in the localization given the inconsistent nature of [her] sensory exam and non-dermatomal distribution." *Id.* at 13. Dr. Barboi indicated that Petitioner's "[m]ild hypermobility and [right] sided weakness [is] likely congenital." *Id.* Dr. Barboi also noted that "it is possible that [Petitioner] ha[d] some symptoms before her vaccination but this got worse after." *Id.* Dr. Barboi instructed Petitioner to follow-up in six weeks. *Id.*

Petitioner returned to Dr. Barboi for a follow-up on April 10, 2014. *Id.* at 224. During this visit, Petitioner reported that she no longer had pain in her right leg but did still suffer from bilateral wrist pain in the morning and shaking/pain in her hands when she got excited. *Id.* Petitioner also complained that she experienced pain in her feet at night that she treated with ice packs. *Id.*

[33] Somatic means "1. pertaining to or characteristic of the [] body. 2. pertaining to the body wall in contrast to the viscera." *Dorland's* at 1734.

[34] Autonomic means "self-controlling; functionally independent; [also affecting the] autonomic nervous system." *Dorland's* at 182.

[35] Gabapentin is "an anticonvulsant that is a structural analogue of γ-aminobutyric acid (GABA), used as adjunctive therapy in the treatment of partial seizures and the management of postherpetic neuralgia; administered orally." *Dorland's* at 753.

Petitioner further reported thigh burning and chest pain with exercise, and an "occasional choking feeling." *Id.* Dr. Barboi's impression was "1. [a]utonomic neuropathy, worse after flu vaccination or caused by it; 2. [m]ild hypermobility and r[ight] sided weakness likely congenital; 3. [m]igraine [headache] associated with vision blurring r[ight] eye; and 4. C[arpal] T[unnel] S[yndrome][36] mild bilateral." *Id*. at 227.

Petitioner submitted complete medical records from the University of Wisconsin-Madison, University Health Services, which includes a complete list of Petitioner's immunizations as of December 21, 2016. *See* Pet'r's Ex. 39 at 8–9. No other medical records have been submitted.

B. Petitioner's Affidavits and Fact Testimony

Petitioner submitted two affidavits in support of her petition and testified at the entitlement hearing. *See* Pet'r's Exs. 5, 14; Tr. 31–65. In her first affidavit, Petitioner averred that on the evening of August 23, 2011, following her receipt of the flu vaccine, she "experienced severe headaches and sporadic tingling in [her] face." Pet'r's Ex. 5 ¶ 3. Petitioner indicated that the tingling began in the left side of her face, spread to both sides of her face, and into her hands. *Id.* She asserted that she also began having trouble processing information soon thereafter. *Id*.

In her supplemental affidavit, Petitioner added that on August 23, 2011, around 4:00 p.m., she was putting on makeup and experienced a tingling sensation in her face when her makeup brush passed over a particular area. Pet'r's Ex. 14 ¶ 3. Petitioner noted this tingling resolved on its own and "lasted only a few seconds." *Id.* Petitioner also described that on Thursday, August 25, 2011, two days following the administration of the flu vaccine, she drove to visit her boyfriend and "recall[ed] feeling tingling and numbness in [her] face." *Id.* ¶ 4. She noted that during her return trip the following day, on August 26, 2011, she experienced worsening numbness in her face which was beginning to move to her arm. *Id.* ¶ 6. Petitioner indicated that she was alarmed and called her mother, who happened to be with Dr. Purath at the time. *Id.* Petitioner stated Dr. Purath instructed her to come to the office immediately. *Id.* Petitioner noted that upon arrival at Dr. Purath's office, she "had developed constant and complete numbness and tingling to the left side of [her] face, numbness in [her] left arm, swelling in [her] left leg, and weakness in [her] left hand." *Id.* ¶ 7; *see also* Pet'r's Ex. 5 ¶ 4.

Petitioner asserted that by October 28, 2011, her symptoms worsened to the point of "blurred vision in [her] right eye, fine tremors in both hands, bilateral numbness in [her] extremities and face[.]" Pet'r's Ex. 5 ¶ 5. By November 4, 2011, Petitioner further contended that she experienced "decreased sensation to touch on [her] right arm and forearm as well as [her] shoulder blades." *Id.* ¶ 6. At that time, Petitioner indicated that Dr. Marquez de Leon informed her that "the most likely cause of the small fiber neuropathy was an adverse reaction to the influenza vaccination[]" administered on August 23, 2011. *Id*. She stated that Dr. Marquez de Leon also told her "that [her] symptoms were likely associated with the autonomic dysfunction that occurred through the small fiber neuropathy, which began following the administration of the flu shot in August of 2011." *Id.* ¶ 12. Petitioner further stated that she continued to suffer from "the

[36] Carpal Tunnel Syndrome is "an entrapment neuropathy characterized by pain and burning or tingling paresthesias in the fingers and hand, sometimes extending to the elbow. Symptoms result from compression of the median nerve in the carpal tunnel." *Dorland's* at 1824.

residual effects or complications from the small fiber neuropathy." *Id.* ¶ 15. Such complications include "numbness and pain in both of [her] arms as well as intermittent loss of vision in [her] right eye." *Id.*

Petitioner also submitted an affidavit regarding damages in this matter. Pet'r's Ex. 11a.[37] In this affidavit, Petitioner described her pre- and post- vaccination lifestyles. *See generally id.* Petitioner indicated that before the flu vaccine at issue, she enjoyed playing various sports including soccer, basketball, tennis, skiing, and biking. *Id.* ¶¶ 2a, 2c. She noted that she typically exercised four to five times per week, including running outside and working out at a gym. *Id.* ¶ 2a. Petitioner noted that prior to the vaccine, she "was in law school, completed a summer associate program in [city] and accepted a job as an associate at [law firm] to begin after graduation[.]" *Id.* ¶ 5.

Petitioner asserted that after receiving the flu vaccine on August 23, 2011, she experienced difficulties attending [] law school. *Id.* ¶ 8a. She noted that she "missed classes and law school commitments for a variety of reasons all related to the vaccine." *Id.* Specifically, Petitioner indicated that "[i]t was difficult to study for long amounts of time due to vision issues and pain in [her] right eye . . . [and t]he pain and tremors in [her] hands and arms[.]" *Id.* Petitioner also noted she applied for and received accommodations, including extra time and reduced typing requirements for her law school and [state] bar exams. *Id.* She asserted that the accommodations helped "to decrease the stress on [her] body to help to lessen the pain [she] experienced." *Id.*

Petitioner noted that she began her position at [law firm] in October 2012. *Id.* ¶ 8b. She stated she "ha[d] not missed a significant amount of time from this job . . . but the symptoms [she] experience[d] from the small fiber neuropathy ha[d] made [her] job very difficult at times." *Id.* For example, she noted she experienced "pain in [her] right eyes, which often decreases the vision in [her] right eye." *Id.* ¶ 8bi. Petitioner indicated that the pain she experienced in her eyes, head, and extremities made it difficult to work for long hours. *Id.* ¶¶ 8bi–8biv. Petitioner also asserted that her pain and symptoms increased "at times of high stress, excitement, fatigue[,] or when [her] other symptoms are causing pain." *Id.* ¶ 8bii. Overall, Petitioner stated she was "finding it very difficult to maintain the pace [her] job requires." *Id.* ¶ 8bv.

During her testimony, Petitioner was asked about how she is able to keep up with her demanding job responsibilities despite her symptoms. Tr. 45:2–14. She indicated that she sometimes works remotely from home to better manage her symptoms and because of this, she can successfully handle her workload. Tr. 44:1–9. In larger moments, such as hearings or depositions, Petitioner stated she experiences numbness and pain in her arms, tremors in her hands, eye pain, blurred vision, and headaches. Tr. 60:6–19. She stated she works through the pain with very minimal accommodations. Tr. 61–64. Petitioner expressed that "in [her] mind, there is really no question, that [she] just need[s] to try and push forward and do the best [she] can and manage the symptoms in a way that would still allow [her] to do [her] job[.]" Tr. 45:8–11.

Petitioner noted that she no longer enjoys the same sport and outdoor recreational activities that she enjoyed prior to receiving the flu vaccine. *Id.* ¶¶ 10a–10c. For example, Petitioner asserted she "cannot exercise without experiencing extreme pain[]" including chest pain and burning in her

[37] *See supra* note 5.

thighs. *Id.* ¶ 10a. She noted that such severe symptoms deterred her from exercising or participating in team sports. *Id.* ¶¶ 10a, 10b. Petitioner wrote that "[t]he small fiber neuropathy cause[d her] hands and arms to shake uncontrollably in the cold." *Id.* ¶ 10c. She further explained that she can no longer cook or do common household tasks like vacuuming or washing dishes without assistance because of the severity of pain she experienced. *Id.* ¶¶ 10d, 10e.

During the hearing, Petitioner provided an account of the chronology of her symptoms that was consistent with her written affidavits and medical records. *See* Tr. 32–55. Petitioner testified that her progressing tingling symptoms on August 26, 2011, "were scary and something that [she] had not had before[.]" Tr. 38:2–3; 59:6–8. She described that the tingling and numbness began in her cheek and then "started to almost kind of wash over [her] body[]" from her face into her leg. Tr. 37:20–23. Petitioner testified that she did not recall being concerned about the tingling in her face until August 26, 2011. Tr. 59:24–25.

Petitioner also explained that she still experiences severe symptoms. Tr. 43:5–15. For example, Petitioner testified that her "symptoms usually get worse or appear when [she's] having times of high stress or anxiety, fatigue or during exciting moments[]" including exercise. Tr. 43:6–11. She also testified about her migraines in relation to her stress levels, including at times of high stress such as planning her wedding and finishing law school exams. Tr. 54:22–25; 57:17–19. She explained it was common for her to have "let-down headaches" during times like those. Tr. 57:7–9. Petitioner further expressed she has not found a medication that she can tolerate, so she does not take medication to manage her symptoms. Tr. 43:18–20. Instead, she stated that she uses ice packs and arm splints. Tr. 43:20–23.

Petitioner was also asked about her recollection of her QSARTs. Tr. 45–46. Petitioner testified that when she underwent any testing to confirm her diagnoses, including the QSARTs, "whatever instructions [that] would have been provided at that time, [she] would have made sure to follow . . . to make sure that we g[o]t an accurate test result to help identify and treat [her] symptoms." Tr. 45:25–46:1, 6–8. She further testified that she "highly doubt[ed]" that she would have taken antihistamines or decongestants in November 2011, during the time that her QSARTs were conducted because she only uses antihistamines during allergy season in the spring and fall. Tr. 46:21–25.

C. Dr. Traci Purath's Affidavit and Fact Testimony

In support of her petition, Petitioner offered an affidavit and the testimony of her treating neurologist, Dr. Traci Purath. Pet'r's Ex. 10. Dr. Purath noted that she was Petitioner's treating physician both before and after her receipt of the flu vaccine. *Id.* ¶ 1. Notably, Dr. Purath described Petitioner's symptom progression following her receipt of the flu vaccine on August 23, 2011. *See generally id.* ¶¶ 5–24. Specifically, Dr. Purath indicated that Petitioner presented to her on August 25, 2011, complaining of "increased headaches along with dysesthesias in both sides of her face and into her hands." *Id.* ¶ 6. She continued that the next day, Petitioner returned to her office and, upon further discussion, she noted that Petitioner's "symptoms had started in the evening of August 23, 2011, after she received the flu vaccination." *Id.* According to Dr. Purath, by August 26, 2011, Petitioner "was experiencing complete numbness of the left side of her face, dysesthesias in the left arm, swelling in the left leg[,] and weakness in her left hand." *Id.* ¶ 7. Dr. Purath noted that she ordered an MRI of Petitioner's brain and cervical spine on August 26, 2011, which yielded

normal results. *Id.* Repeat MRIs of the brain and cervical spine performed on October 27, 2011, showed no changes when compared to the June 16, 2010 and August 26, 2011 MRIs. *Id.* ¶¶ 7, 11.

Dr. Purath provided a complete account of the chronology of Petitioner's symptoms and treatment that was consistent with Petitioner's written affidavits and medical records. *See id.* Dr. Purath concluded that based on her comprehensive evaluations of Petitioner, she believed Petitioner suffered an autonomic small-fiber neuropathy. *Id.* ¶ 26. She further opined "that the administration of the influenza vaccination on August 23, 2011[,] caused the autonomic small-fiber neuropathy." *Id.* Dr. Purath averred that Petitioner has suffered from the residual effects of the neuropathy since the date of vaccination to the date of Dr. Purath's affidavit, August 15, 2014. *Id.*

During the hearing, Dr. Purath was called to testify as a fact witness regarding her treatment of Petitioner and to clarify her own notations in Petitioner's medical records. Tr. 9:8–9. Dr. Purath first noted Petitioner's history of migraines. Tr. 9:15–17. She initially testified that following receipt of the flu vaccine, Petitioner came into her office on August 25, 2011, with a change in her headache symptoms and some dysesthesias to her face and hands. Tr. 10:11–15. However, Dr. Purath's notes indicated she only learned of Petitioner's receipt of the flu vaccine on August 26, 2011. Tr. 12:4–9. Dr. Purath was asked to clarify her notes from these days. Tr. 10–12. Specifically, on cross-examination, Dr. Purath explained that at the time she evaluated Petitioner on August 25, 2011, she, in fact, did not know Petitioner had received a flu vaccine on August 23, 2011. Tr. 18:15–19. Dr. Purath highlighted that on August 25, 2011, she thought Petitioner's symptoms were caused by recently finishing law school and she was focused on the headache itself. Tr. 18:20–23, 19:1. Dr. Purath admitted that she did not learn about Petitioner's recent receipt of the flu vaccine until August 26, 2011, when Petitioner returned to her office yet again for her dysesthesias and extremity swelling and weakness. Tr. 19:2–12. Dr. Purath expressed that she then "wanted to know what else had changed recently," so she asked Petitioner further questions. Tr. 19:8–9, 27:10–15. Based on their discussion, she stated, "that was when the flu shot became apparent[.]" Tr. 19:9. Therefore, Dr. Purath's notation from August 25, 2011, was incorrect regarding the flu vaccine. Tr. 12:6–10. Dr. Purath further clarified that Petitioner told her that her increased headaches began two weeks prior to the flu vaccine she received on August 23, 2011. Tr. 11:20–22. However, she emphasized that Petitioner's "new symptoms," the dysesthesias, occurred only after her receipt of the flu vaccine. Tr. 11:23–25; 12:2–5.

On cross-examination, Dr. Purath was asked about her opinion that the flu vaccine was the cause of Petitioner's small fiber neuropathy, which she had put forth in her affidavit. Tr. 21:21–25. Dr. Purath noted she did not have any literature on hand to support this proposition but that there was nothing else in Petitioner's record, temporally speaking, to account for the change in her symptoms. Tr. 23:9–23.

D. P.E.'s Fact Testimony

Petitioner's mother P.E. testified during the entitlement hearing. Tr. 66–78. During the hearing, P.E. provided an account of the chronology of Petitioner's symptoms, focusing on the morning of August 26, 2011. Tr. 67–70. P.E. provided testimony that was consistent with both Dr. Purath's and Petitioner's testimony, written statements, and Petitioner's medical records. *See id.*

P.E. indicated that during Petitioner's emergency visit with Dr. Purath on August 26, 2011, Petitioner mentioned the flu shot "after a series of questions posed by Dr. Purath[.]" Tr. 69:20–23. P.E. further corroborated Petitioner's assertions and stated that Petitioner did not have tingling or numbness in her face and hands prior to the appointment with Dr. Purath on August 26, 2011. Tr. 71:2–10.

III. Experts

A. Expert Review

1. Petitioner's Expert, David S. Younger, M.D.

Dr. Younger received his medical degree from Columbia University in 1981. Pet'r's Ex. 16 at 1. At the time Petitioner filed this case, Dr. Younger was licensed to practice in New York and held board-certifications in internal medicine, clinical neurophysiology, electrodiagnostic medicine, and neurology and psychiatry. *Id.* Dr. Younger's clinical experience includes serving as an attending in neurology at Lenox Hill Hospital and New York University's ("NYU") Langone Medical Center, both in New York, New York, since 1994 and 1998, respectively. *Id.* He also served as the Chief of Neuromuscular Diseases at NYU Medical Center throughout 1998. *Id.* Since 2014, he has served as both the Co-Director of the Muscular Dystrophy Clinic and an attending in neurology at White Plains Hospital in White Plains, New York. *Id.* Dr. Younger also has academic experience, including serving as a Clinical Associate Professor of Neurology at NYU School of Medicine and as a member of the faculty at the Global Institute of Public Health at NYU. *Id.* Dr. Younger's curriculum vitae lists numerous books, book chapters, and research papers of which he is a listed author. *See id.* at 4–18.

Dr. Younger submitted two expert reports and a neurological summary of this case but did not testify at the hearing. Pet'r's Exs. 15, 21, 22. At Petitioner's request, Dr. Younger was not called to testify, as his recent felony conviction involving a crime of dishonesty would have undermined his credibility and prejudiced Petitioner's case. *See* ECF No. 55. His expert reports were not stricken and are still part of the record in this case. I will consider them for the limited purpose of his diagnoses of Petitioner as her treating physician. However, I will afford them considerably less weight, as Dr. Younger was not cross-examined. Instead, Petitioner proceeded with the testimony of Dr. Lawrence Steinman as her chief expert. Tr. 79–149.

2. Petitioner's Expert, Lawrence Steinman, M.D.

Dr. Steinman received his medical degree from Harvard University in 1973. Pet'r's Ex. 45 at 1. He completed his post-graduate training at Stanford University, where he completed an internship in surgery in 1973, a residency in pediatrics in 1974, and a residency in pediatric and adult neurology from 1977 to 1980. *Id.* He became board-certified in neurology in 1984. *Id.* at 2. He served as the Chairman of the Immunology Program at Stanford for approximately ten years from 2002 to 2011. *Id.* He currently serves as a Professor of Neurology, Pediatrics, and Genetics at Stanford University's Department of Neurology and Neurological Sciences. *Id.* Dr. Steinman's curriculum vitae includes over four-hundred and fifty published articles of which he is a listed author. *See id.* at 5–40. During the hearing, he noted that he "did a post-doctoral fellowship in

neuroimmunology[.]" Tr. 80:14. He explained that his clinical practice involves "see[ing] patients, both inpatients and outpatients . . . [with] neuroimmunological diseases." Tr. 80:20, 81:6. He also stated that he has testified many times in the Vaccine Program. Tr. 83–84.

Dr. Steinman submitted two expert reports and testified during the hearing. *See* Pet'r's Exs. 40, 78; Tr. 79:18–152:11. He also submitted one post-hearing supplemental report. Pet'r's Ex. 84. The parties stipulated that Dr. Steinman was qualified to render an expert opinion in neurology, and I recognized Dr. Steinman as such. Tr. 78:24–25, 79:1.

3. Respondent's Expert, Peter D. Donofrio, M.D.

Dr. Donofrio received his medical degree from the Ohio State University School of Medicine in 1975. Resp't's Ex. B at 1. He is licensed to practice medicine in several states and is board-certified in internal medicine, psychiatry and neurology, and electrodiagnostic medicine. *Id.* at 2. Dr. Donofrio has extensive academic and practical experience, including residencies in internal medicine and neurology, and a fellowship in neuromuscular medicine. *Id.* He has served as a Professor of Neurology at the Vanderbilt University School of Medicine from 2006 to present. *Id.* Prior to that, he served as first an Assistant Professor and then a Professor of Neurology at Wake Forest University School of Medicine from January 1986–July 2006. *Id.* at 2–3. His clinical experience includes serving as the Director of the Neuromuscular Division at Vanderbilt University School of Medicine from August 2006 through present and as Chief of the Neuromuscular Section at the Wake Forest University from July 1993–July 2006. *Id.* Dr. Donofrio has been appointed to numerous hospital committees throughout his career. *Id.* at 3–8. His curriculum vitae lists numerous publications and editorials of which he is a listed author. *See id.* at 12–58.

During the hearing, Dr. Donofrio explained that he, in addition to his other responsibilities as the Director of the Neuromuscular Division, is also "the Director of the EMT laboratory, Director of the Muscular Dystrophy Association Clinic, [] Director of the ALS Clinic[,] and Vice Chairman for Clinical Affairs[.]" Tr. 154:2–5. Dr. Donofrio testified that his "professional responsibilities are patient care, teaching, service, and research." Tr. 154:8–9. He stated he mainly sees patients "with diseases of the peripheral nerve muscle . . . so, [] people with spinal cord diseases." Tr. 154:12–15.

Dr. Donofrio submitted three expert reports and testified at the hearing. *See* Resp't's Ex. A, I, L; Tr. 153:5–174:3. He also submitted one post-hearing supplemental expert report. Resp't's Ex. N. The parties also stipulated that Dr. Donofrio was qualified to render an expert opinion in the field of neurology, and I recognized Dr. Donofrio as such. Tr. 155:9–22.

B. Expert Reports and Testimony

1. Petitioner's Expert, Dr. Younger

In his first expert report, Dr. Younger confirmed that based on Petitioner's medical records, Petitioner indeed suffered from small fiber sensory neuropathy. Pet'r's Ex. 15 at 7. Dr. Younger expressed that "[a]s an initial matter, every qualified treating neurologist . . . has determined that

[Petitioner] suffers from small fiber neuropathy." Pet'r's Ex. 21 at 4 (citing Pet'r's Ex. 4 at 542; Pet'r's Ex. 2 at 23–25; Pet'r's Ex. 9 at 12–13). Based on his own assessment of Petitioner, Dr. Younger noted that Petitioner demonstrated brisk reflexes, "convergence insufficiency, sensory loss to pinprick[,] and cold temperature with a gradient from distal to proximal." Pet'r's Ex. 21 at 6. Dr. Younger opined these symptoms were "consistent with a diagnosis of small fiber neuropathy." *Id.* Dr. Younger noted that none of Petitioner's complaints of "fatigue, tremor, and chest pain . . . are associated with small fiber neuropathy." *Id.* at 6. However, Dr. Younger concluded those symptoms resulted, instead, from Petitioner's "autonomic disorder and small vessel vasculitis, both associated with the influenza vaccination of August 23, 2011." *Id.*

As further support for his opinion regarding Petitioner's small fiber neuropathy diagnosis, Dr. Younger indicated that he met with Petitioner on December 28, 2015, and assessed her condition. Pet'r's Ex. 21 at 5. Dr. Younger revealed he performed an epidural nerve fiber density skin biopsy on Petitioner during their encounter on December 28, 2015.[38] *Id.*; *see also* Pet'r's Ex. 23 at 12–13, ECF No. 35-3). Dr. Younger explained he "performed a 3-mm punch skin biopsy and collected two skin specimens from [Petitioner] . . . one from her left thigh and one from her left calf." *Id.* He indicated the samples were sent to Dr. Kurenai Tanji, M.D., at Columbia-Presbyterian Hospital. *Id.* (citing Pet'r's Ex. 22 at 12–13). Dr. Tanji "concluded that both specimens exhibited 'significantly low epidermal nerve fiber density.'" *See id.* Dr. Younger stated "[b]ecause [Petitioner's] biopsy demonstrated a significant reduction in [e]pidermal [n]erve [f]iber density, her diagnosis of [s]mall [f]iber [n]europathy is therefore confirmed." Pet'r's Ex. 21 at 5.

Dr. Younger also diagnosed Petitioner with small vessel vasculitis. *Id.* at 7. He cited an article by Jennette et al.,[39] which noted that common symptoms associated with small vessel vasculitis include "fever, myalgias,[40] arthralgias,[41] and malaise[.]"[42] *Id.* (citing Pet'r's Ex. 26 at 5, ECF No. 35-6). He wrote that Petitioner's "epidermal nerve fibers were [] injured by influenza vaccination wherein the influenza vaccination led to an autoimmune response restricted to small nerve fibers in the skin with consequent sensory changes, including burning pain." Pet'r's Ex. 21 at 7. As support for his opinion, Dr. Younger cited to a case study by Blumberg et al.,[43] which described two patients suffering from autoimmune sequela in the form of small vessel vasculitis secondary to the influenza vaccination. *Id.* (citing Pet'r's Ex. 25 at 1, ECF No. 35-5). The authors noted that the first patient was a twenty-seven-year-old man "suffering from fever, arthralgias, and myalgias post-immunization, consisting of split-product virus a A-New Jersey Swine and A-Victoria influenza." *See id.* Dr. Younger indicated that "much like [Petitioner], this patient noted blurred vision." Pet'r's Ex. 21 at 7. He further noted that the second patient in the Blumberg study

[38] Petitioner submitted a letter from Dr. Younger describing their encounter on December 28, 2015, including a neurological summary of her condition. Pet'r's Ex. 22, ECF No. 35-2. During this appointment, he conducted a skin biopsy to assess Petitioner's epidermal nerve fiber densities in order to confirm Petitioner's small fiber neuropathy diagnosis. *Id.* at 2. Based on his findings, Dr. Younger indicated "[t]he findings were consistent with post-vaccination autoimmune small fiber neuropathy and dysautonomia with orthostatic intolerance." *Id.*

[39] J. Charles Jennette, et al., *Small-Vessel Vasculitis,* 337 N. ENG. J. MED. 1512–23 (1997).

[40] Myalgia is "pain in a muscle or muscles." *Dorland's* at 1214.

[41] Arthralgia is "pain in a joint." *Dorland's* at 150.

[42] Malaise is "a vague feeling of bodily discomfort and fatigue." *Dorland's* at 1097.

[43] Scott Blumberg, et al., *A Possible Association Between Influenza Vaccination and Small-Vessel Vasculitis,* 140 ARCH. INTERN. MED. 847–48 (1980).

was an eighty-seven-year-old man "that experienced onset systemic fever, malaise, generalized arthralgia, myalgia, and swelling in the face beginning hours after influenza vaccination." *Id.* (citing Pet'r's Ex. 25 at 1). The patient underwent a skin biopsy which revealed "cutaneous necrotizing venulitis localized to the papillary dermis." *See id.* He analogized this study to Petitioner's case and concluded that "[Petitioner] suffered [from] small vessel vasculitis as a result of the influenza vaccination on August 23, 2011." Pet'r's Ex. 21 at 7.

2. Petitioner's Expert, Dr. Steinman

Dr. Steinman submitted three expert reports in response to both Drs. Younger's and Donofrio's reports and testified during the hearing. Pet'r's Exs. 40, 78, 84; Tr. 79–152, 245–260. During his testimony, Dr. Steinman expanded upon the points he discussed in his first expert report regarding his opinion that the flu vaccine caused Petitioner's injuries. Tr. 79–152. As a preliminary matter, Dr. Steinman discussed the debate surrounding Petitioner's diagnoses. Pet'r's Ex. 40 at 17–18. First, he agreed with Dr. Younger and Petitioner's other treating physicians that Petitioner suffered from small fiber neuropathy. *Id.* (citing Pet'r's Ex. 4 at 542; Pet'r's Ex. 22 at 12–13). Dr. Steinman arrived at his own conclusion and testified that "by a preponderance of the evidence . . . [Petitioner] suffers from small fiber neuropathy." Tr. 87:20–22, 88:7–10. He stated that he based his opinion, in part, on Petitioner's treating physicians' notes indicating her symptoms showed "an inflammatory neuropathic condition[,]" and subsequent diagnosis of small fiber neuropathy. Tr. 91:2–3; *see also* Pet'r's Ex. 40 at 5 (citing Pet'r's Ex. 21 at 4; Pet'r's Ex. 4 at 542; Pet'r's Ex. 2 at 23–25; Pet'r's Ex. 9 at 12–13).

Dr. Steinman also based his opinion on Petitioner's symptoms. Tr. 88–89. During his testimony, Dr. Steinman explained small fiber neuropathy generally and stated that "[t]he fibers that are involved [with small fiber neuropathy] have a receptor called the alpha 3 acetylcholine receptor which the immune system targets[.]" Tr. 88:25–89:2. As a result, "the manifestations of small fiber neuropathy are highly variable . . . [and] include[] many of the features that [] Petitioner has faced, burning heat, pain, [tha]t comes and goes[.]" Tr. 89:2–5. Dr. Steinman was asked about Dr. Donofrio's assertion that small fiber neuropathy symptoms "typically don't fluctuate from one side to the other[,]" as they do in Petitioner's case. Tr. 93:13. He testified that he does not agree with Dr. Donofrio's characterization of these symptoms because "this type of illness, it's fibers that are associated with the autonomic nervous system and some of the symptoms are fleeting, some of them have to do with pain, some of them have to do with fatigue, which is a global symptom[.]" Tr. 93:20–24.

On cross-examination, Dr. Steinman maintained that Petitioner exhibited many of the common symptoms associated with small fiber neuropathy, as enumerated in the literature. Tr. 117:4–17; *see also* Pet'r's Ex. 19.[44] He cited the Lacomis et al.[45] study, to list several clinical features of small fiber neuropathy that Petitioner exhibited, including "tingling, burning, prickling, shooting pain, or aching." Tr. 117:22–25; Pet'r's Ex. 19 at 2. He testified that Petitioner's weakness and brisk reflexes can also be clinical features of her small fiber neuropathy. Tr. 118:7–8.

[44] David Lacomis, *Small-fiber neuropathy,* 26 MUSCLE NERVE 173–88 (2002).
[45] *See id.*

Dr. Steinman addressed Dr. Donofrio's argument that Petitioner must not suffer from small fiber neuropathy because "it would be particularly difficult for someone like [Petitioner], with small fiber neuropathy to maintain a demanding job[.]" Tr. 94:7–15. Dr. Steinman acknowledged that while Petitioner's job requires "a lot of hours[]" and "it's very high stressed," her ability to do it well does not have "any significance . . . in terms of making a diagnosis or deciding whether her diagnosis is small fiber neuropathy[.]" Tr. 94:10–15. He testified this is because he has "been repeatedly amazed by how driven people can overcome medical problems and do things at a [high functioning] level." Tr. 94:15–16.

Dr. Steinman testified that he also relied on Petitioner's biopsy results to support his opinion regarding Petitioner's small fiber neuropathy diagnosis. Tr. 91–92. Dr. Steinman cited an article by Lauria et al.,[46] in which the authors, like Dr. Younger, analyzed skin biopsies at the calf and "published epidermal nerve fiber density ["ENFD"] normative values for clinical use that are generally accepted within the scientific community." Pet'r's Ex. 40 at 18 (citing Pet'r's Ex. 55 at 3, ECF No. 60-16). Based on this study, Dr. Steinman determined the "ENFD normative values for Petitioner's age group and gender, . . . 10 cm. proximal to the lateral malleolus, would be 8.4 for the 5th percentile, with a median ENFD value per age span of 13.5." *See id.* Dr. Steinman noted the results of Petitioner's calf biopsy "yielded a mean of 2.8 (with a range of 1.3–3.0)." Pet'r's Ex. 40 at 18. Dr. Steinman therefore concluded that "these results indicate the presence of small fiber neuropathy." *Id.*; *see also id.* at 19–20. He opined that the low density of the nerve fibers revealed by the biopsy were "because of the immune attack that . . . is the basis for [Petitioner's] small fiber neuropathy." Tr. 92:7–9. He stated that Petitioner's biopsy results were "unmistakably . . . consistent with the diagnosis of small fiber neuropathy." Tr. 91:22–23.

Dr. Steinman was asked about Dr. Donofrio's concerns "that the skin biopsy was taken four years after the vaccination, so there's no contemporaneous proof that if she does suffer from small fiber neuropathy, that she suffered from [it] around the time of the vaccination." Tr. 92:14–18 (citing Resp't's Ex. L at 4). In response, Dr. Steinman testified that "in an ideal world, it would have been great to do the biopsy earlier, but . . . [the biopsy is] telling us that the pathology is small fiber neuropathy." Tr. 92:20–21, 93:2–3. Therefore, he "do[es]n't think that a separate diagnosis is viable, especially when all the doctors before that said anyway that she had small fiber neuropathy." Tr. 93:7–10.

Dr. Steinman also relied on the abnormal results of Petitioner's QSARTs from November 2011, to support his conclusion that Petitioner suffers from small fiber neuropathy. Tr. 94:24. He explained that QSARTs "trigger sweating in a local area and you can see the quantity." Tr. 95:3–4. He noted that the results of Petitioner's QSARTs revealed decreased responses in the right foot, distal leg, and forearm. Pet'r's Ex. 40 at 5 (citing Pet'r's Ex. 4 at 542); *see also* Pet'r's Ex. 9 at 46. These results indicated that Petitioner suffered from small fiber neuropathy. Pet'r's Ex. 40 at 5 (citing Pet'r's Ex. 21 at 4); Pet'r's Ex. 4 at 542; Pet'r's Ex. 2 at 23–25. However, Dr. Steinman testified that if a patient is using antihistamines such as allergy drugs at the time of this test, like Dr. Donofrio contended occurred in Petitioner's case, the antihistamine can interfere with the results. Tr. 95:4–5. However, he expressed that based on Petitioner's "testimony that she follows instructions [before laboratory tests] carefully, [and] only takes allergy drugs when it's allergy

[46] Giuseppe Lauria, et al., *Intraepidermal nerve fiber density at the distal leg: a worldwide normative reference study,* 15 J. PERIPHERAL NERVOUS SYS. 202–07 (2010).

season, and November is not her allergy season[,]" the abnormal results of Petitioner's QSARTs were not unreliable. Tr. 95:6–8, 12–15.

Dr. Steinman opined "that all other potential alternative neurologic explanations for Petitioner's condition have been excluded, and the diagnosis of small fiber neuropathy is the correct diagnosis." Pet'r's Ex. 40 at 18 (citing Pet'r's Ex. 2 at 43–44; Pet'r's Ex. 21 at 3). In fact, he stated that Petitioner "had a rather extensive evaluation for diseases that could masquerade or have similar manifestations [to small fiber neuropathy]. She was worked up for Lyme disease, lupus, various rheumatological disorders[,]" and all were negative. Tr. 89:18–21. Therefore, Dr. Steinman stated that "there's more than a preponderance of evidence with the QSART testing, [] skin biopsy, [] proper reference levels, [] the exclusion of other diagnoses, that we're dealing here with small fiber neuropathy." Tr. 95:15–19.

Dr. Steinman addressed whether Petitioner's small fiber neuropathy is autoimmune in nature. He opined that it is. Tr. 252:11. He based his opinion on Petitioner's elevated ANA and the density of the nerve fibers revealed by her biopsy. Tr. 252:13, 25, 253:1. In response to my questioning, Dr. Steinman posited that his theory of causation described below "fits better if [Petitioner's small fiber neuropathy] is autoimmune[,]" to account for the cross-reactivity from the flu vaccine that occurred in Petitioner's case. Tr. 257:2–7. He also explained that any reference he made to Petitioner having an "autonomic neuropathy" should be regarded as "a feature of her small fiber neuropathy[]" and "not a separate diagnosis[,]" as he is someone who "lumps" diagnoses together rather than "split[s]" them apart. Tr. 116:6–20.

Second, Dr. Steinman also agreed with Dr. Younger's conclusion that Petitioner suffered from small vessel vasculitis. Pet'r's Ex. 40 at 21. Dr. Steinman agreed that "none of [Petitioner's] treating physicians diagnosed her with small vessel vasculitis[,] other than Dr. Younger[.]" Tr. 116:1–5. He explained that his theory in this case, described below, "indicates how immune memory to components of the vaccine that mimic the alpha 3 nicotinic acetylcholine receptor are at the heart of the small fiber neuropathy. A vasculitic response would be involved in the penetrations of the autoimmune T cells." Pet'r's Ex. 40 at 21. Dr. Steinman cited a case study by Yang et al.,[47] which explained "the role of the nicotinic acetylcholine receptor α3 subtype (α3-nAChR) in vascular inflammation." *Id.* (citing Pet'r's Ex. 56 at 1, ECF No. 60-17). The authors of the study concluded that "α3-nAChRs play a pivotal role in regulating the inflammatory responses in endothelial cells and macrophages." *See id.* As a result, Dr. Steinman opined "[a]n immune response to alpha 3 nicotinic acetylcholine receptor would block a major suppressive pathway in the blood vessel wall, and predispose Petitioner to vasculitic inflammation and subsequently small-fiber neuropathy." Pet'r's Ex. 40 at 21.

Dr. Steinman testified regarding the criteria he relied on to support his opinion that Petitioner suffers from small vessel vasculitis. Tr. 96:1–18. He explained that "the way that the immune system attacks [the] peripheral nerve, the way it does in small fiber neuropathy, . . . [and] Guillain-Barr[é] . . . the immune cells and the antibodies go through the blood vessels, and it creates a small inflammatory response in the vessels." Tr. 96:9–15. Based on this, Dr. Steinman stated that Petitioner "has a vasculitis, which is, . . . concomitant with how the small fiber

[47] Cui Yang, et al., *Role of the nicotinic acetylcholine receptor a3 subtype in vascular inflammation,* 173 BR. J. PHARMACOL. 3235–47 (2016).

neuropathy pathophysiology works." Tr. 96:16–18. He explained that "[a]natomically, there is a relationship [between the two diseases] and the pathophysiology can link the two entities." Tr. 88:13–14. However, he acknowledged that a tissue sample was not tested in Petitioner's case that could have confirmed her small vessel vasculitis. Tr. 97:1–4. Dr. Steinman stated he did not know if Petitioner's skin biopsy "captured some small arterials and venules in the epidermal tissue[,]" which would also show the markings of small vessel vasculitis. Tr. 97:4–7. He also admitted that no laboratory studies were conducted to help confirm "abnormal values for markers of vasculitis[.]" Tr. 97:8–10. Dr. Steinman testified that even if those tests were conducted, "the confound in this case" was that Dr. Purath prescribed Decadron, a steroid, to Petitioner "which would reduce the possibility of detecting . . . th[e] antibody throughout the three acetylcholine receptor or some of the markers of vasculitis." Tr. 97:11–16.

Next, Dr. Steinman stated his theory was that Petitioner's August 23, 2011 flu vaccine triggered an immune response to her previous flu vaccines, resulting in her small fiber neuropathy and small vessel vasculitis. Tr. 109:3. Dr. Steinman stated that "one of the known immune responses associated with small fiber neuropathy is an antibody, an immune response directed to the alpha 3 acetylcholine receptor." Tr. 98:14–16. He explained that "[n]icotinic acetylcholine receptors ("AChRs") are a family of ligand-gated cation channels found throughout the central and peripheral nervous system. Every nicotinic AChR is formed by the association of five subunits of which at least two are α subunits. The α subunit contains important binding sites for acetylcholine." Pet'r's Ex. 40 at 6–7 (citing Pet'r's Ex. 69 at 1, ECF No. 60-30).[48] Based on this, Dr. Steinman theorized that Petitioner's "Fluarix vaccine in 2011 triggered a small fiber neuropathy[] based on the contents of the 2011 vaccine and their molecular mimicry with the alpha3 nicotinic AChR[]" contained in prior flu vaccines administered to Petitioner in 2005, 2008, 2009, and 2010. Pet'r's Ex. 40 at 13–17, 27; *see also* Pet'r's Ex. 39 at 8, 18, 37, 86.

Specifically, Dr. Steinman wrote that there were components in Petitioner's previous flu vaccines that "mimic[ked] the alpha3 AChR associated with vasculitis and small fiber neuropathy. A rapid recall response to those components following the 2011 Fluarix immunization triggered the immune cross-reaction to alpha 3 AChR, culminating in Petitioner's small fiber neuropathy." Pet'r's Ex. 40 at 26. Dr. Steinman explained that a "recall response" occurs when it is not the body's "first encounter" with that specific antigen, but rather "the immune system has seen this [antigen] before[.]" Tr. 102:8–9. Dr. Steinman cited an article by de St. Groth et al.,[49] which discusses the notion of recall response and shows that prior exposure to an antigen leads to an immune response when exposed to a subsequent, related antigen. Pet'r's Ex. 40 at 22 (citing Pet'r's Ex. 62 at 3, ECF No. 60-23). The authors of the study found "that there is a tremendous recall response that could be measured [eight] years later[]" following the original antigen exposure. *See id.* Dr. Steinman wrote that "[i]n parallel to these classic findings, Petitioner more likely than not carried antibodies to the alpha 3 nicotinic AChR from 2005 to the time of her vaccination in 2011." Pet'r's Ex. 40 at 23. He opined that "the earlier influenza immunizations documented in the record in 2005, 2008, 2009[,] and 2010 would have provided an ample immunological memory for a recall response [to the flu vaccine o]n [August 23,] 2011." *Id.* at 22.

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[48] Steven Vernino, et al., *Characterization of ganglionic acetylcholine receptor autoantibodies,* 197 J. NEUROIMMUNOL. 63–69 (2008).

[49] Fazekas de St. Groth, et al., *Disquisitions on Original Antigenic Sin,* 124(3) J. EXP. MED. 331–45 (1966).

Dr. Steinman indicated that, using the resources available at the National Institute of Health ("NIH") and the National Library of Medicine, he conducted a "filtration process" of running BLAST searches to discover if there was anything in Petitioner's 2011 flu vaccine, that would in fact, mimic, or share a "structural similarity with alpha 3 acetylcholine receptors." Tr. 98:24–25, 99:1. He testified that he targeted alpha 3 acetylcholine receptors because "one of the known immune responses associated with small fiber neuropathy is an antibody, an immune response directed to the alpha 3 acetylcholine receptor." Tr. 98:14–16. He wrote that the process involved "looking for [specific] homologies between the components of Fluarix and the alpha-3 subtype of nicotinic AChR." Pet'r's Ex. 40 at 7. Dr. Steinman indicated that this is a common practice. Tr. 106–107; *see also* Pet'r's Ex. 74, ECF No. 74-4.[50] To do so, he "enter[ed] a protein sequence, like alpha 3 nicotinic AChR . . . with one of the known components of Fluarix[.]" Pet'r's Ex. 40 at 7.

Dr. Steinman noted that the components of the 2011–2012 Fluarix vaccine include "A/California/7/09 (H1N1)-like virus (pandemic (H1N1) 2009 influenza virus), A/Perth/16/2009 (H3N2)-like virus, and B/Brisbane/60/2008-like virus[.]" *Id.* at 14 (citing Pet'r's Ex. 51 at 2, ECF No. 60-12).[51] He also noted the components of the other prior seasonal flu vaccines that Petitioner received. Pet'r's Ex. 40 at 13. The 2005 influenza vaccine contained "A/New Caledonia/20/99 (H1N1)-like virus; A/California/7/2003 (H3N2)-like virus; and B/Shanghai/361/2002-like virus." *Id.* (citing Pet'r's Ex. 70 at 2, ECF No. 60-31). The FluMist 2008 contained "A/Brisbane/59/2007 (H1N1)-like virus; an A/Brisbane/10/2007 (H3N2)-like virus; and B/Florida/4/2006-like virus." Pet'r's Ex. 40 at 14 (citing Pet'r's Ex. 51 at 2). The components of the 2009–2010 flu vaccine include A/Brisbane/59/2007 (H1N1)-like virus, A/Brisbane/10/2007 (H3N2)-like virus, and B/Brisbane/60/2008-like virus, a component also in the 2011 Fluarix vaccine. Pet'r's Ex. 40 at 16 (citing Pet'r's Ex. 71 at 1, ECF No. 60-32). The 2010–2011 flu vaccine contained "A/California/7/09 (H1N1)-like virus (pandemic (H1N1) 2009 influenza virus), A/Perth/16/2009 (H3N2)-like virus, B/Brisbane/60/2008-like virus." Pet'r's Ex. 40 at 16 (citing Pet'r's Ex. 72 at 1, ECF No. 60-33).

Once he generated the computerized results, Dr. Steinman demonstrated that there "are homologies between alpha 3 nicotinic AChR and the hemagglutinin in B/Brisbane/60/2008 in the 2011 Fluarix vaccine that Petitioner received[.]" Pet'r's Ex. 40 at 10–11. He wrote that he considered "a run of [five] or more of [twelve] amino acids that are identical in the Fluarix components and the alpha-3 subtype of nicotinic AChR[,]" to be a "'meaningful molecular mimic[.]'" *Id.* at 7–8 (citing Pet'r's Exs. 58–60, ECF Nos. 60-19–60-21).[52] As support, Dr. Steinman relied on his own research and posited that it revealed the "identity of [five] of [twelve]

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[50] Robert Root-Bernstein, *Rethinking molecular mimicry in rheumatic heart disease and autoimmune myocarditis: laminin, collagen IV, CAR, and B1AR as initial targets of disease,* 2 FRONTIERS IN PEDS. 1–17 (2014).

[51] *Influenza Virus Vaccine for the 2008–2009 Season,* U.S. FOOD & DRUG ADMIN. (original URL not available).

[52] Anand Gautam, et al., *A Viral Peptide with Limited Homology to a Self Peptide Can Induce Clinical Signs of Experimental Autoimmune Encephalomyelitis,* 161 J. IMMUNOL. 60–64 (1998); Anand Gautam, et al., *Minimum structural requirements for peptide presentation by major histocompatibility complex class II molecules: Implications in induction of autoimmunity,* 91 J. IMMUNOL. 767–71 (1994); Anand Gautam, et al., *A Polyalanine Peptide with only Five Native Myelin Basic Protein Residues Induces Autoimmune Encephalomyelitis,* 176 J. EXP. MED. 605–09 (1992).

amino acids, not even consecutive amino acids, was sufficient to trigger experimental encephalomyelitis[]" in mice. Pet'r's Ex. 40 at 8 (citing Pet'r's Ex. 58 at 5).[53] He also cited two studies, in which he is listed author, that found that "a [six] amino acid peptide with identity at [five] amino acids was sufficient to trigger neuroinflammation[]" in mice, and "a peptide with [four] of [eleven] amino acids induced neuroinflammation[.]" Pet'r's Ex. 40 at 8 (citing Pet'r's Ex. 59 at 4, Pet'r's Ex. 60 at 3).[54] Based on this, Dr. Steinman noted that he found "two ABSOLUTELY REMARKABLE sequence homologies[.]" Pet'r's Ex. 40 at 11 (emphasis in original). The first, Dr. Steinman described was "[five] amino acids in a row PLIGE with the sixth amino acid representing a small change from leucine to isoleucine[.]"[55] *Id.* Dr. Steinman indicated "this degree of molecular mimicry is sufficient to trigger clinically relevant clinical neuroinflammation." *Id.* The second, was "a [five] of six identity PSWVKT, again sufficient to trigger clinically relevant neuroinflammation." *Id.* (citing Pet'r's Exs. 58–60).[56]

Dr. Steinman performed a second BLAST search "directed to the hemagglutinin found in the 2011 Fluarix component, known as hemagglutinin [Influenza A virus (A/California/07/2009(H1N1))]." Pet'r's Ex. 40 at 12. Dr. Steinman found "[o]ther relevant homologies [] between components of the 2011 Fluarix vaccine and alpha 3 nicotinic AChR." *Id.* Specifically, Dr. Steinman identified "from DKAKIDLVLIG, a stretch with a [seven] of [eleven] amino acid identity between a component of the 2011 Fluarix vaccine and alpha3 nicotinic AChR, . . . [which] has shown to be sufficient to trigger clinical relevant neuroinflammation in animal models." *Id.*

Dr. Steinman conducted a third round of BLAST searches comparing the 2005–2006 flu vaccine to the 2011 Fluarix. *Id.* at 13. He "blasted the hemagglutinins from B/Brisbane/60/2008 and B/Shanghai/361/2002 . . . [and found] over a 90% identity in their protein sequences[.]" *Id.* at 13–14. Dr. Steinman noted that "[t]he homologies between the 2005–2006 influenza vaccine received by Petitioner and the Fluarix she received in 2011 cover the region with PLIG and PIWVKT that share homology with alpha 3 nicotinic AChR." *Id.* at 14.

Dr. Steinman conducted the same analysis between the 2008 FluMist and the 2011 Fluarix. *Id.* He found that "[t]he hemagglutinin sequences are nearly identical between B/Brisbane/60/2008 in Fluarix and B/Florida/4/2006 in FluMist . . . [and] cover the region with PLIGE and PIWVKT that share homology with alpha 3 nicotinic AChR." *Id.* at 14–16. Dr. Steinman conducted the same assessment of the 2009–2010 and 2010–2011 flu vaccines compared to the Fluarix 2011, respectively. *Id.* at 16–17. He noted that all three seasonal flu vaccines contain

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[53] Anand Gautam, et al., *A Viral Peptide with Limited Homology to a Self Peptide Can Induce Clinical Signs of Experimental Autoimmune Encephalomyelitis,* 161 J. IMMUNOL. 60–64 (1998).

[54] Anand Gautam, et al., *Minimum structural requirements for peptide presentation by major histocompatibility complex class II molecules: Implications in induction of autoimmunity,* 91 J. IMMUNOL. 767–71 (1994); Anand Gautam, et al., *A Polyalanine Peptide with only Five Native Myelin Basic Protein Residues Induces Autoimmune Encephalomyelitis,* 176 J. EXP. MED. 605–09 (1992).

[55] Leucine is "an essential amino acid, 2-amino-4-methylpentanoic acid, necessary for optimal growth in infants and for nitrogen equilibrium in human adults. It is obtained by the digestion or hydrolytic cleavage of protein." *Dorland's* at 1026. Isoleucine is "an essential amino acid, α-amino-β-methylvaleric acid, produced by the hydrolysis of fibrin and other proteins; necessary for optimal growth in infants and for nitrogen equilibrium in human adults." *Id.* at 964.

[56] *See supra* note 52.

B/Brisbane/60/2008, and "[t]he homologies with PLIGE and PIWVKT that share homology with alpha 3 nicotinic AChR are contained in [all three] vaccines." *Id.* Based on his findings, Dr. Steinman opined that through the "numerous examples of molecular mimicry between the alpha 3 nicotinic acetylcholine receptor and the Fluarix vaccine, and between earlier seasonal influenza vaccines given to Petitioner[,]" he has demonstrated "that the Fluarix vaccine can trigger an autoimmune response to the alpha3 nicotinic acetylcholine receptor via molecular mimicry." *Id.* at 17.

Regarding Petitioner's small vessel vasculitis, Dr. Steinman posited that "the immune response to alpha 3 nicotinic acetylcholine receptor triggered by molecular mimicry would block a major suppressive pathway in the blood vessel wall, and predispose [] Petitioner to vasculitic inflammation, and then subsequently to small-fiber neuropathy." *Id*. In response to my questioning, Dr. Steinman admitted that the inflammation caused by small vessel vasculitis would be necessary for molecular mimicry to occur in Petitioner's case. Tr. 149:10–14. However, he stated that "the traditional use of the word vasculitis . . . isn't critical for the theory." Tr. 149:8–9. But the way he used "vasculitis" in Petitioner's case is to refer to inflammation generally, which is "necessary for molecular mimicry to work in her particular case[.]" Tr. 149:10–14. Thus, Dr. Steinman concluded that Petitioner's August 23, 2011 flu vaccine caused her small fiber neuropathy and small vessel vasculitis. Pet'r's Ex. 40 at 26. He held his conclusion "to a reasonable degree of medical and scientific probability[.]" *Id.* at 27.

Dr. Steinman admitted that he could not say for sure that the presence of these sequences in Petitioner "prove[d] that Fluarix [sic] cross-react[ed] with alpha 3 acetylcholine receptor[,]" as establishing computerized homologies between proteins is only the first step in proving molecular mimicry. Tr. 101:16–17, 128:15–17. The next step would be to show "cross-reactivity between the homologous proteins and that the cross-reactivity actually leads to damage[,]" but that experiment cannot be done in humans, as "it would be unethical." Tr. 99:25, 128:17–21.

On cross-examination, Dr. Steinman agreed that neither animal nor human studies have been conducted with respect to the specific homologies he found between the flu vaccine and the acetylcholine receptor to see if they, in fact, result in disease. Tr. 130:5–18. He testified that he was "not surprised" that his search did not yield any experimental models. Tr. 150:12–13. However, he pointed out that "[t]here is an association between alpha 3 acetylcholine receptor and [small fiber neuropathy,]" but "not the flu vaccine as the cause of the molecular mimicry with acetylcholine receptors leading to small fiber neuropathy." Tr. 132:6–7, 10–14. Dr. Steinman testified that he did not know of "any epidemiol[ogical] actual [sic] studies that support a causal association between the flu vaccine and small fiber neuropathy[]" or small vessel vasculitis, in general, or via molecular mimicry, specifically. Tr. 118:9–14, 125:5–8. Dr. Steinman acknowledged that the suspected relationship between the flu vaccine and small fiber neuropathy has been documented, but it is not "widely reported[.]" Tr. 107:7. While he maintained that the cause of small fiber neuropathy is unknown in 30% of cases, he "certainly, through the strategies that [he] used in the theory, s[aw] how [the flu vaccine] could cause it." Tr. 109:13–14.

Dr. Steinman conceded that an issue with his theory on causation is "that we don't have evidence that [an] alpha 3 immune response was actually detected[]" in Petitioner. Tr. 108:1–2. He admitted that the only time Petitioner was tested, the presence of this antibody could have been

blocked by her use of Decadron, a corticosteroid, near the time of her antibody test. Tr. 108:1–3. He opined that Petitioner's use of Decadron may have influenced her negative antibody test. Tr. 248–249. Dr. Steinman stated that while Dr. Donofrio opined that Decadron therapy would not have blocked a positive antibody test, Dr. Steinman "believe[s he is] correct[.]" Tr. 249:3. Dr. Steinman supported his opinion by explaining the pharmacokinetics and pharmacodynamics of Decadron. Tr. 249. He stated that pharmacokinetics refers to "how long it takes for [the drug] to be out of your system[,]" Tr. 249:7, while "[p]harmacodynamics is how long the effects of the drug are lasting." Pet'r's Ex. 84 at 1. Based on this, Dr. Steinman explained that Decadron is "gone from the system in a matter of days in most people[because i]t's a fat[-]soluble drug." Tr. 249:10–11. But, "it depletes your T cells and B cells and they come back very slowly. It takes weeks and months for, particularly the B cells that are the antibody lineage to come back." Tr. 249:19–22. Therefore, he opined Petitioner's antibody "may have been below the level of detection." Tr. 250:2–3. He stated that he "would be really close to certainty about linking the molecular mimicry with the alpha 3 acetylcholine receptor, had they been positive[]" in Petitioner. Tr. 250:4–6.

To address this issue, Dr. Steinman submitted a second expert report and supporting medical literature following the entitlement hearing regarding how Decadron "could suppress the immune system, and how it therefore may have suppressed an antibody response to ganglionic AChR[]" in Petitioner. Pet'r's Ex. 78 at 1; *see also* Pet'r's Exs. 79–83, ECF Nos. 85-2–85-6. In this report, Dr. Steinman cited The Advisory Committee on Immunization Practices for the CDC[57] to support his assertion that corticosteroids, such as Decadron and its generic form dexamethasone, are immune suppressive. Pet'r's Ex. 78 at 4 (citing Pet'r's Ex. 82 at 42, ECF No. 85-5). He wrote that "The Advisory Committee on Immunization Practices for the CDC states that '[s]evere immunosuppression can be caused by congenital immunodeficiency, leukemia, lymphoma, . . . or **large amounts of corticosteroids**.'" Pet'r's Ex. 78 at 4 (citing Pet'r's Ex. 82 at 42) (emphasis in original).

Dr. Steinman maintained that "Petitioner has shown that there are molecular mimics between ganglionic AChR and the influenza vaccines that Petitioner received[]" even though "the only time that the ganglionic AChR antibody test was measured, on 11/4/2011[,] it was negative." Pet'r's Ex. 78 at 1. Dr. Steinman opined that "the 22-day[58] course of Decadron reduced Petitioner's capacity to mount a ganglionic AChR antibody response that was negative when actually measured." *Id.* As support, Dr. Steinman cited a study by Baris et al.[59] to explain how long the cells that make antibodies are "suppressed after cessation of treatment with corticosteroids." *Id.* at 2 (citing Pet'r's Ex. 79). Dr. Steinman wrote that the authors of the study found "that the prolonged

[57] Center for Disease Control, Immunization of health-care workers: recommendations of the Advisory Committee on Immunization Practices (ACIP) and the Hospital Infection Control Practices Advisory Committee (HICPAC), MMWR 1997;46 (No. RR-18).

[58] Dr. Steinman wrote that "it is an established fact that Petitioner was on Decadron immunosuppressive therapy for 22 days (8/26/11–9/17/11)." Pet'r's Ex. 78 at 2. As support, he indicates that Petitioner was initially placed on Decadron on 8/26/11. *Id.* at 1 (citing Pet'r's Ex. 2 at 43). Dr. Steinman noted that on 9/16/11, Dr. Purath wrote that she was "weaning [Petitioner] off [Decadron]…" and she "will be off of Decadron tomorrow (9/17)." Pet'r's Ex. 78 at 1 (citing Pet'r's Ex. 2 at 35). He further noted that Dr. Purath wrote that Petitioner was off of Decadron "completely" by 9/29/11. Pet'r's Ex. 78 at (citing Pet'r's Ex. 2 at 32).

[59] Hatice E. Baris, et al., *The effect of systemic corticosteroids on the innate and adaptive immune system in children with steroid responsive nephrotic syndrome,* 175 EUR. J. PEDIATR. 685–93 (2016).

effect on the antibody producing cells after cessation of corticosteroids is notable[.]" Pet'r's Ex. 78 at 2. He explained that "[t]he cells that make antibod[ies] are in the B cell class and include plasma cells and memory cells." *Id.* In fact, the authors of the Baris et al.[60] study found that "[t]he change of B cells and B cell subtypes (CD27+ memory) shows prolonged effect of CSs [CSs=corticosteroids] on B cells which may alter antibody production even after [three] months of CSs cessation." Pet'r's Ex. 79 at 2.

The authors of the Baris et al.[61] study examined patients with kidney disease who were treated with prednisolone, a corticosteroid. *Id.* at 1. These patients were started on 2mg/kg/daily prednisolone therapy for one month and then were weaned the following month to prednisolone therapy every other day. *Id.* By the end of the third month, the treatment had tapered and ceased completely. *Id.* The authors noted that, "[i]t is widely accepted that 2 mg/kg/day prednisolone causes immunosuppression after [fourteen] days of continuous administration." Pet'r's Ex. 79 at 2. Specifically, the authors found that

> [a]fter the cessation of CS, . . . a progressive decline was observed, reaching a statistical significance at first month (41 ± 22/mm³) compared to the baseline (131 ± 128/mm³) . . . . This effect continued until third month of CS cessation (50 ± 26/mm³) . . . . The same pattern was seen in the un-class switched memory B cell compartment ($CD19^{+}CD27^{+}IgD^{+}$).

Id. at 6, Fig. 3b. Based on these findings, the authors concluded that "patients receiving CSs might be deemed immunosuppressed even earlier in course of therapy and immunological alterations may last as long as [three] months following the cessation of CS treatment." *Id.* at 8. Dr. Steinman therefore concluded that "[t]he suppressive effect of corticosteroids like Decadron on antibody production can last for a month or more after cessation[.]" Pet'r's Ex. 78 at 4. He opined that "these alterations in the cell population responsible for making antibodies, even a month or more after cessation of corticosteroids, more probably than not, impaired the ability to measure an anti-ganglionic AChR response [in Petitioner] on 11/4/11 [sic]." *Id.*

Dr. Steinman conceded that "[t]here are issues in generalizing from [the Baris et al.[62] study] . . . as [] the population studied were children with kidney disease, not an adult with small fiber neuropathy[, and] . . . a different steroid was used[,]" with different dosages. Pet'r's Ex. 78 at 3 (citing Pet'r's Ex. 79). To remedy the dosage discrepancy between Petitioner's case and the Baris et al. study, Dr. Steinman submitted a corticosteroid dose comparison chart. *See id.* (citing Pet'r's Ex. 80 at 1).[63] He highlighted that Petitioner's "dose of 2 mg dexamethasone is equivalent to a dose of 20mg prednisolone." *See id.* In the Baris et al.[64] study, the child patients received a 2mg/kg dose of prednisolone. Pet'r's Ex. 78 at 3 (citing Pet'r's Ex. 79).

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[60] *See id.*
[61] *See* Baris, et al., *supra* note 59, at 685–93.
[62] *Id.*
[63] *Adrenal Cortical Steroids,* In Drug Facts and Comparisons, 5th ed. St. Louis, Facts and Comparisons, Inc., 122–28 (1997).
[64] *See* Baris, et al., *supra* note 59, at 685–93.

In his rebuttal report, Dr. Steinman stated that Dr. Donofrio "fail[ed] to differentiate the pharmacokinetic effect of Decadron (days) to the pharmacodynamic effect (weeks) when [he] writes, . . . 'Decadron is a long acting form of corticosteroids whose duration of action is 36–54 hours . . . Decadron blood levels would no longer be detectable and would not be expected to interfere with antibody detection.'" Pet'r's Ex. 84 at 1 (citing Resp't's Ex. N at 1). Instead, Dr. Steinman wrote that "Decadron has long-lasting effects on the immune system far beyond when it is out of the blood stream, because of its effects in depleting and sequestering different populations of immune cells." Pet'r's Ex. 84 at 1. He again relied on the Baris et al.[65] study to "support that [twenty-two] days of oral Decadron could suppress an antibody response measured [seven] weeks later, after Decadron treatment was discontinued." *Id.* at 2 (citing Pet'r's Ex. 79). The authors of the study found that "the prolonged effect of corticosteroids was demonstrated, with the corticosteroids having an effect on antibody producing cells until the third month after cessation." *See id.* In fact, the authors noted that "it has been shown that even low dose CS therapy may lead to extended suppression of humoral immunity, only to resolve over time, which may take as long as [two] years." Pet'r's Ex. 79 at 2. Therefore, Dr. Steinman opined that "Petitioner's 22-day course of Decadron immunosuppressive therapy could have suppressed antibody levels at the time of testing, based on an application of [p]harmacodynamic principles." Pet'r's Ex. 84 at 2.

Dr. Steinman also stated that another "confound" with the negative results of Petitioner's antibody test is that "even when [this antibody] is detected [in other patients], it's only about 50[%] of the time . . . even detected." Tr. 98:21–23, 213:19–25. Dr. Steinman cited an article by Vernino et al.[66] and reiterated that "'[a]ntibodies that specifically bind to the ganglionic AChR are detectable in about 50% of patients[.]'" Pet'r's Ex. 78 at 1 (citing Pet'r's Ex. 69). He therefore opined that "it is not surprising that [Petitioner's test] was negative, from the steroid treatment done already on a background where in general 50% of cases are negative anyway in autoimmune autonomic ganglionopathy[.]" Pet'r's Ex. 78 at 2 (citing Pet'r's Ex. 69 at 3).

Dr. Steinman addressed the timing and onset of Petitioner's symptoms. Pet'r's Ex. 40 at 21–26. He opined the "sentinel sign" of Petitioner's symptoms was between four- to- six- hours post vaccination. Tr. 104:13, 135:2–3, 144:22–24. Dr. Steinman opined that her rather immediate response to the flu vaccine is based on the notion of "recall response." Pet'r's Ex. 40 at 21. Based on his purported medical theory and the notion that Petitioner received several flu vaccines in the past, Dr. Steinman wrote "there [was] an immense recall response to influenza[.]" *Id.* at 22. Dr. Steinman elaborated that under the notion of "recall response," once one receives a subsequent dose of a vaccine that the body has seen before, it "work[s]" fast" because "you have immune memory[.]" Tr. 104:7. He noted that "a rapid recall response can begin even on the day of immunization." Pet'r's Ex. 40 at 21. Dr. Steinman explained that this was possible because "[t]he immune system, once it has memory, is trigger happy . . . to stop things like polio[,]" or whichever disease the vaccine is designed to defend against. Tr. 103:25–104:1. Dr. Steinman stated that regardless of whether the onset of Petitioner's symptoms occurred around 4:00 p.m. on the day of her flu vaccine, or [forty-eight] hours later when the tingling started manifesting into her hands, "it would still go along with [] how the immune system works[,]" and was a sufficient amount of time to generate an immune response under his theory. Tr. 104:13–14, 110:1–6.

[65] *Id.*

[66] *See* Vernino, et al., *supra* note 48, at 63–69.

Dr. Steinman relied on several articles in his report and testimony, which noted "that recall responses to specific antigens can be read within [twenty-four] hours of vaccination." *Id.* (citing Pet'r's Exs. 63–65, ECF Nos. 60-24–60-26[67]; *see also* Tr. 110–113). Dr. Steinman cited the Serane et al.[68] study to demonstrate that a recall response to a tuberculin test can be read as positive and produce a reaction in children after twenty-four hours. Pet'r's Ex. 63 at 1. He also cited the Kardjito et al.[69] study, which found that the first reaction elicited by a tuberculin test can occur within thirty minutes. Pet'r's Ex. 65 at 1. Dr. Steinman relied on an article by Lai et al.,[70] to show that during a recall response reaction, memory cells can react "within six hours [of the vaccine], . . . not just days[.]" Tr. 113:15–19; *see also* Pet'r's Ex. 77, ECF No. 74-5. He wrote that a study by Schonberger et al.[71] "described an increased incidence of [GBS] . . . even within 0–1 day" of vaccination. Pet'r's Ex. 40 at 24 (citing Pet'r's Ex. 67 at 8, ECF No. 60-28). Dr. Steinman equated the onset interval of GBS to Petitioner's small fiber neuropathy and small vessel vasculitis and opined that the onset of Petitioner's symptoms fits within the acceptable timeframe for the onset of GBS. Pet'r's Ex. 40 at 25. He testified that the Schonberger et al. article is an example of how the "inflammatory response can trigger something real [sic] quickly." Tr. 111:18.

On rebuttal, Dr. Steinman reiterated his preference for the Schonberger et al. article over the Langmuir et al.[72] article relied on by Dr. Donofrio. Tr. 246–248. He maintained that the Schonberger et al. article is better because "it's much more incisive about what's happening, at least within [forty-eight] hours [of vaccination,]" whereas the Langmuir et al. article "does not wipe away the issue of what can happen in a shorter interval than a seven day interval." Tr. 247:19–20, 248:16–17. Dr. Steinman noted that the authors of the Langmuir et al. study found there were no patients who developed onset symptoms of GBS on the same day as the swine flu vaccine. Resp't's Ex. G at 15. Dr. Steinman addressed this conclusion and stated that, in accepting this conclusion, Dr. Donofrio "does not understand figure one[.]" Tr. 246:14 (citing Resp't's Ex. G at 15, Fig. 1). Dr. Steinman explained that the horizontal axis contained seven-day intervals, representing a weekly analysis. Tr. 246:16. He noted that the authors of the article drew "each dot . . . right in the middle of the interval, as if something happened on day three-and-a-half." Tr. 246:25, 247:1–2. But, since the analysis is on a weekly basis, "it cannot tell you anything about what's happening in anything less than the interval of a week[]" and "[t]here are no places where it's zero." Tr. 247:7–8, 254:22.

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[67] Tiroumourougane Serane, et al., *Tuberculin Test can be Read after 24 hours in Adolescent Children,* 60:2 J. TROP. PEDS. (2014); Lin Fan, et al., *Variation of Mycobacterium tuberculosis Antigen-Specific IFN-γ and IL-17 Responses in Healthy Tuberculin Skin Test (TST)-Positive Human Subjects,* 7:8 PLoS ONE (2012); T. Kardjito, et al., *Immunological and Clinical Features of Smear-Positive Pulmonary Tuberculosis in East Java,* 61 TUBERCLE 231–38 (1980).

[68] Tiroumourougane Serane, et al., *Tuberculin Test can be Read after 24 hours in Adolescent Children,* 60:2 J. TROP. PEDS. (2014).

[69] T. Kardjito, et al., *Immunological and Clinical Features of Smear-Positive Pulmonary Tuberculosis in East Java,* 61 TUBERCLE 231–38 (1980).

[70] Wendy Lai, et al., *Transcriptional Control of Rapid Recall by Memory CD4 T Cells,* 187 J. IMMUNOL. 133–40 (2011).

[71] Lawrence Schonberger, et al., *Guillain-Barré Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976–1977,* 110:2 AM. J. EPIDEMIOL. 105–24 (1979).

[72] Alexander D. Langmuir, et al., *An Epidemiologic and Clinical Evaluation of Guillain-Barré Syndrome Reported in Association with the Administration of Swine Influenza Vaccines,* 119:6 AM. J. EPIDEMIOL. 841–80 (1984).

On cross-examination, Dr. Steinman was asked how memory T cells "travel through the circulatory system to the site and then cross-react to cause the damage" so quickly. Tr. 122:15–17. In response, Dr. Steinman stated that "the heart [is] pumping [the memory cells] around all the time, . . . the same way that we need oxygenation of all of our tissues, . . . nourishment of even a nerve is second to second, within a minute, . . . [and] the cross-reaction can take place in nanoseconds." Tr. 122:18–21, 123:3. Therefore, he maintained the onset of Petitioner's symptoms fit within the appropriate timeframe in which to ascribe causation to the flu vaccine. Tr. 109–110.

Dr. Steinman was also asked on cross-examination to explain why, if Petitioner already had an immune memory to the flu vaccine, she did not have a reaction to any of the prior flu vaccines she received between 2005 and 2011. Tr. 137:1. He opined that the occurrence of Petitioner's reaction after several flu vaccines "is not unusual." Pet'r's Ex. 40 at 25. He analogized Petitioner's reaction with patients who suffer from food allergies. *Id.* He noted that "[p]eople with food allergies often do not have clinical manifestations until multiple encounters." *Id.* Dr. Steinman relied on a case study by Kappos et al.,[73] to demonstrate that the onset of hypersensitivity reactions via a "molecular mimic of a nervous system component" following subcutaneous injections in MS patients ranged from two to twenty-seven injections. Tr. 136:18–25, 137:1–6; Pet'r's Ex. 68 at 3, ECF No. 60-29. Dr. Steinman could not proffer a better explanation for why this reaction varied from patient to patient or why Petitioner did not have a reaction to earlier flu vaccines. Tr. 136–137. Therefore, he opined this explanation is a "work in progress[]" because "[he]'d like to know the answer as much as anyone[.]" Tr. 137:2–6.

However, in response to my questioning, Dr. Steinman elaborated on this point and stated that the innate and adaptive immune systems work differently. Tr. 139:13. He agreed that the adaptive immune system is more efficient than the innate immune system. Tr. 139:16–17. Nonetheless, he noted that we have the innate immune system "for when our responses are naïve. Once we have memory, fortunately, we . . . get to fight it with adaptive immunity which comes on really fast." Tr. 139:18–21. Dr. Steinman testified that each time one receives a flu vaccine, it could contain different strengths and iterations of the virus. Tr. 140:1–5. He agreed that memory cells, while they have seen the flu vaccine or flu virus before, may create new memory cells every time they are introduced to a new strain of the virus. Tr. 140:6–11. He stated that "the memory of our immune system to influenza is really complicated by our first or second encounters with influenza. And even with [subsequent] seasonal flu vaccines, the memory cells revert[] to that original antigenic exposure." Tr. 140:16–21. Dr. Steinman testified that this could explain why this particular flu vaccine iteration triggered Petitioner's immune response. Tr. 140:22–25. However, he conceded that this explanation "cuts against the assertion that the T cells are already primed and immediately ready to go for cross-reaction . . . in nanoseconds." Tr. 141:1–4, 20–21. Dr. Steinman qualified his statement that the cross-reaction can occur in "nanoseconds." Tr. 141:13–23. He explained that the use of this term was merely "fodder" in his testimony and that the cross-reaction does not occur in actual "nanoseconds," but still very quickly. Tr. 141:20–23.

Dr. Steinman also testified that there was no "alternative trigger, in [his] opinion for small fiber neuropathy." Tr. 109:2–3. He explained that a "battery of tests" were performed on Petitioner

[73] Ludwig Kappos, et al., *Induction of a non-encephalitogenic type 2 T helper-cell autoimmune response in multiple sclerosis after administration of an altered peptide ligand in a placebo-controlled, randomized phase II trial,* 6 NATURE MED. 1176–83 (2000).

and none of them yielded positive for other causes of her symptoms. Tr. 108:20–23. However, on cross-examination, he stated prior to Petitioner's mother's testimony regarding her diagnosis of rheumatoid arthritis, an autoimmune disease, he was unaware of Petitioner's genetic predisposition for autoimmune disease. Tr. 145:5–6. Dr. Steinman noted that while a genetic predisposition could have contributed to Petitioner's development of small fiber neuropathy, this fact did not change his opinion that the flu vaccine caused Petitioner's small fiber neuropathy and small vessel vasculitis. Tr. 145:2–10.

3. Respondent's Expert, Dr. Donofrio

Dr. Donofrio filed his first expert report in response to Dr. Younger's original report. Resp't's Ex. A. Dr. Donofrio opined that "more likely than not, [P]etitioner did not develop a small fiber neuropathy as a result of the flu vaccination of August 23, 2011." *Id.* at 13. First, Dr. Donofrio began his analysis by explaining Petitioner's diagnoses. *Id.* at 8. He opined that Petitioner does not suffer from "a small fiber neuropathy or autonomic neuropathy." *Id.* Dr. Donofrio considered Petitioner's symptoms and indicated that contrary to Dr. Younger's findings, "[p]atients with small fiber neuropathy would not have weakness, loss of deep tendon reflexes or problems with balance or walking[,] as the fibers for those functions are large fibers." *Id.* (citing Pet'r's Ex. 18, ECF No. 25-5; Pet'r's Ex. 19, ECF No. 25-6; Resp't's Ex. F, ECF No. 29-6).[74] He explained "[b]ecause small fiber neuropathy is a relatively permanent process affecting the small fibers, one would not expect fluctuations of symptoms and movement from one side of the body to the other or improvement followed by worsening." Resp't's Ex. A at 8.

Dr. Donofrio testified that Petitioner's shifting symptoms are not related to or features of her small fiber neuropathy. Tr. 243:5–12. In fact, Dr. Donofrio stated that Petitioner's "shifting" symptoms from one side of her body to the other did not fit the pattern for small fiber neuropathy as described by Lacomis et al.,[75] in which the authors noted the typical symmetric symptoms of small fiber neuropathy include "tingling, burning, prickling, shooting sensation, [which are] often worse at night." Tr. 157:21–22, 158:21. Dr. Donofrio described that "[t]he typical presentation of small fiber neuropathy . . . begins in the toes, . . . works its way through the feet and ankles, remaining symmetrical." Tr. 156:4–7. The symptoms then "move[] up between the ankles and [] knees[,] and [] by that time, patients often have numbness, tingling, and burning pain in their fingertips . . . hands[,] and [] forearms." Tr. 156:7–10. Dr. Donofrio stated that this "evolution can be anywhere from days to weeks, but it's commonly measured in months and years." Tr. 156:11–12. Dr. Donofrio relied on an article by Tavee et al.,[76] to support his assertion that small fiber neuropathy symptoms present symmetrically and are length-dependent, meaning the symptoms appear more predominantly in the point that is furthest away from the axis of the body (the fingertips and toes). Tr. 158:8–18 (citing Resp't's Ex. C at 4, ECF No. 29-3). However, the authors of the Tavee et al. study noted that "[i]n rare cases, small fiber neuropathy follows a non-length-

[74] Jinny Tavee, et al., *Small fiber neuropathy: A burning problem,* 76:5 CLEV. CL. J. MED. 297–305 (2009); David Lacomis, *Small-fiber neuropathy,* 26 MUSCLE NERVE 173–88 (2002); Alexandra Hovaguimian, et al., *Diagnosis and Treatment of Pain in Small Fiber Neuropathy,* 15(3) CURR. PAIN HEADACHE REP. 193–200 (2011).
[75] *See* Lacomis, *supra* note 44, at 173–88.
[76] Jinny Tavee, et al., *Small fiber neuropathy: A burning problem,* 76:5 CLEV. CL. J. MED. 297–305 (2009).

dependent distribution in which symptoms may be manifested predominantly in the arms, face, or trunk." Resp't's Ex. C at 2.

Dr. Donofrio considered the neurologic examinations following Petitioner's vaccination and noted she exhibited "brisk reflexes in the arms and legs." Resp't's Ex. A at 8 (citing Pet'r's Ex. 2 at 23, 40, 43). He wrote "[b]risk reflexes are not a feature of a small fiber or autonomic neuropathy . . . [i]n most neuropathies, reflexes are diminished or absent." Resp't's Ex. A at 8 (citing Pet'r's Exs. 18, 19; Resp't's Exs. E, F).[77] He noted Petitioner exhibited "normal sensation or an inconsistent loss of sensation[]" following the vaccination. Resp't's Ex. A at 8 (citing Pet'r's Ex. 2 at 38; Pet'r's Ex. 7 at 11, 19; Pet'r's Ex. 4 at 316; Pet'r's Ex. 9 at 10). He also explained that Petitioner's "[f]atigue, tremor[,] and chest pain" symptoms are not "considered symptoms associated with small fiber neuropathy." Resp't's Ex. A at 8 (citing Pet'r's Ex. 2 at 35; Pet'r's Exs. 18, 19; Resp't's Exs. E, F).[78] He argued that Dr. Steinman ignored these facts in determining that Petitioner suffers from small fiber neuropathy. Resp't's Ex. L at 1–4. However, Dr. Donofrio could not offer an alternative diagnosis for her fatigue, tremors, or shifting symptoms. Tr. 244:19–22.

Dr. Donofrio indicated that instead, patients with small fiber neuropathy typically "complain of dry eyes and mouth, orthostasis (drop of blood pressure when the patient stands up), constipation, sexual dysfunction, daily urinary incontinence, impaired sweating[,] and red or white discoloration of the feet and hands." Resp't's Ex. A at 8 (citing Pet'r's Exs. 18, 19; Resp't's Exs. E, ECF No. 29-5, F).[79] Dr. Donofrio concluded that "[l]ittle proof exists in the medical records that [Petitioner] truly had an autonomic neuropathy[,]" or small fiber neuropathy as "[Petitioner] did not have common symptoms one associates with an autonomic neuropathy[,]" such as orthostasis, bradycardia, tachycardia, impaired sweating, or a tonic pupil. Resp't's Ex. A at 9.

Dr. Donofrio wrote that Dr. Younger stated, and Dr. Steinman agreed, that '"every qualified treating neurologist diagnosed [P]etitioner with a small fiber neuropathy."' Resp't's Ex. L at 1 (citing Pet'r's Ex. 21 at 4; Pet'r's Ex. 40 at 1). However, Dr. Donofrio indicated this was inaccurate, as it was not true for each of Petitioner's other treating physicians. Resp't's Ex. L at 1. For example, he noted that Dr. Purath's office note from October 28, 2011, states "that she had no reasonable explanation for [P]etitioner's symptoms." *Id.* (citing Pet'r's Ex. 2 at 30). Dr. Donofrio also noted that Dr. Remler's office note from January 12, 2012, indicates that he was unable to render a diagnosis for Petitioner's symptoms. Resp't's Ex. L at 1 (citing Pet'r's Ex. 6 at 8). He further highlighted that Dr. Barboi, one of Petitioner's treating neurologists and a specialist in autonomic neuropathy, "gave a weak endorsement for a small fiber neuropathy." Resp't's Ex. L at 1 (citing Pet'r's Ex. 9 at 10). In fact, Dr. Barboi stated Petitioner's "history would fit with a small fiber neuropathy but her physical examination did not aid in localization because of the inconsistent nature of her sensory loss and non-dermatomal distribution." *See id.*

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[77] Jinny Tavee, et al., *Small fiber neuropathy: A burning problem,* 76:5 CLEV. CL. J. MED. 297–305 (2009); David Lacomis, *Small-fiber neuropathy,* 26 MUSCLE NERVE 173–88 (2002); Christopher Gibbons, *Small Fiber Neuropathies,* 20 CONTINUUM 1398–1412 (2014); Alexandra Hovaguimian, et al., *Diagnosis and Treatment of Pain in Small Fiber Neuropathy,* 15(3) CURR. PAIN HEADACHE REP. 193–200 (2011).
[78] *See id.*
[79] *Id.*

Dr. Donofrio considered Petitioner's "typical workday as a trial lawyer[,]" specifically her long hours. Resp't's Ex. A at 9 (citing Pet'r's Ex. 11a at 3). Based on Petitioner's affidavit, Dr. Donofrio opined that patients like Petitioner "with a significant painful small fiber neuropathy would not be able to work the prolonged hours of a trial lawyer." Resp't's Ex. A at 10. Dr. Donofrio wrote that Dr. Steinman failed to "comment about the remarkable ability of [P]etitioner to work very long hours . . . [which] would be highly unusual for someone with the number and severity of her [small fiber neuropathy] symptoms." Resp't's Ex. L at 4. Dr. Donofrio also wrote that "[Petitioner] states that she cannot exercise, walk, or play sports because of the heightened pain she experiences. She is unable to cook for herself." Resp't's Ex. A at 7. He opined that "[Petitioner's] inability to exercise, walk, or play sports are incongruent with her long hours of work." *Id.* at 10. He opined that "[i]t seems unusual for [P]etitioner to be able to work [eleven] to [eighteen] hours per day in a busy law practice and, yet, be unable to cook for herself." Resp't's Ex. I at 2 (citing Pet'r's Ex. 11a at 2–5). As a result, Dr. Donofrio maintained Petitioner could not suffer from small fiber neuropathy. *See id.* However, on cross-examination, Dr. Donofrio admitted he "overstated" Petitioner's inabilities to exercise or cook for herself. Tr. 192:23–25, 193:1. He conceded that Petitioner stated that she merely had difficulties doing those activities. Tr. 193:4–9 (citing Pet'r's Ex. 11a ¶ 10a).

As further support of his opinion that Petitioner does not suffer from small fiber neuropathy, he noted that this diagnosis was confirmed by "indirect evidence," abnormal results of QSARTs, which according to Dr. Donofrio, could have been "influenced by [Petitioner] taking Allegra[.]" Resp't's Ex. A at 9; Resp't's Ex. I at 2. Dr. Donofrio testified that "[he] noticed that when the [QSARTs] w[ere] done on November 4th, 2011, that the medical records lists that [Petitioner] was taking Allegra, which is a[n] antihistamine. Whether she was taking it or not that day or for several days, it cannot be determined in [Petitioner's] chart." Tr. 162:1–5. Dr. Donofrio therefore concluded this test was not determinative of Petitioner's small fiber neuropathy diagnosis because the results may have been influenced by her use of Allegra. Resp't's Ex. A at 9. However, Dr. Donofrio admitted that he "had no means to determine whether she was taking the medication within [forty-eight] hours of the testing." Resp't's Ex. I at 2.

Dr. Donofrio also indicated that, at the time of his first report, neither a skin nor peroneal sensory biopsy was ever performed to confirm Petitioner's diagnosis of small fiber neuropathy. Resp't's Ex. I at 2; *see also* Resp't's Ex. A at 9. However, in his second report, pursuant to the presiding special master's order, Dr. Donofrio addressed the skin biopsy performed on Petitioner by Dr. Younger on December 28, 2015, which revealed the diagnosis of small fiber neuropathy. Resp't's Ex. I at 2, 6; *see also* Sched. Order, ECF No. 36. Accordingly, Dr. Donofrio reviewed the results and wrote that the evaluator of Petitioner's biopsy recorded an "epidural nerve fiber density consistent with the diagnosis of a small fiber neuropathy." Resp't's Ex. I at 6. At the time of his second report, Dr. Donofrio noted that he attempted to review and opine as to the meaning of the results of Petitioner's skin biopsy but, "[t]he reference values for [Petitioner's] age and gender were not reported, so [he] c[ould not] interpret the data himself." *Id.* at 2, 4, 5. Based on this, he opined Petitioner's results "may have been low, but not abnormal." *Id.* at 2. However, during his testimony, Dr. Donofrio admitted that he had since received the reference values from Petitioner's biopsy. Tr. 160:7–8. After repeated questioning, he conceded that "clearly there was evidence for a small fiber neuropathy . . . . " Tr. 160:8–9.

While Dr. Donofrio admitted that Petitioner's biopsy revealed evidence of small fiber neuropathy, he continued to question the results as conclusive evidence of her small fiber neuropathy diagnosis in 2011. Resp't's Ex. L at 4; *see also* Tr. 160:16–18. Dr. Donofrio noted that the biopsy was performed "more than [four] years after the flu vaccination." *Id.*; *see also* Tr. 160:18–19. He argued "[t]he presence of a small fiber neuropathy by skin biopsy at that time cannot be unequivocally related to a year 2011 vaccination . . . because of the [four] year lag between the biopsy and the vaccination." *See id.* Therefore, he opined that the skin biopsy showing small fiber neuropathy did not explain Petitioner's symptoms in 2011. Tr. 160:16–18. Nonetheless, Dr. Donofrio opined that "the fact that the skin biopsy was abnormal four years later shows pathologic . . . evidence for a small fiber neuropathy." Tr. 160:21–24. On cross-examination, Dr. Donofrio conceded that by "pathologic evidence" of small fiber neuropathy within Petitioner's biopsy results, he meant that "the pathology report demonstrated a significant reduction in epidermal nerve fiber density[,]" which is conclusive evidence of small fiber neuropathy. Tr. 200:22–25, 201:1. But, he still opined that the results are unreliable evidence of her small fiber neuropathy in 2011 because "in th[ose] four years, other things may have happened to her life. She may have developed some illnesses that were not diagnosed or uncovered . . . . " Tr. 160:24–24, 161:1.

However, Dr. Donofrio admitted that "[he] didn't find any[]" evidence in Petitioner's medical records that she suffered an underlying or subsequent illness, "but she may not have had any new symptoms that would have led to ordering further testing that would be necessary to evaluate her small fiber neuropathy." Tr. 195:9–13. He stated if he had received Petitioner's biopsy results without an explanation for the evidence of small fiber neuropathy, he would have ran tests for the "eight or nine illnesses that were not ruled out" among the "approximately [twenty-five]" illnesses known to cause small fiber neuropathy including, "[H]epatitis C, Sjogren's [disease], . . . family history for neuropathy, . . . HIV[,] . . . sarcoidosis, . . . B-6 [sic] level, [but] probably not [] Lyme . . . . " Tr. 167:23, 196:15–16, 199:9–15; *see also* Resp't's Ex. A at 8; Resp't's Ex. L at 1–2. Yet, he admitted he was speculating that Petitioner may have had any of these other illnesses during that time. Tr. 196:1–4. Based on the pathologic evidence in Petitioner's skin biopsy, he conceded "it's more likely than not that [Petitioner] suffers from small fiber neuropathy[.]" Tr. 201:11–12; *see also* Tr. 203:16 (indicating Dr. Donofrio stated "[Petitioner] has a small fiber neuropathy."). Dr. Donofrio also admitted that in light of Petitioner's biopsy and his conclusion that she suffered from small fiber neuropathy Petitioner's "atypical" symptom presentation carried less weight in his opinion. Tr. 207:1–15.

He further opined that Petitioner's small fiber neuropathy is not autoimmune in nature. Dr. Donofrio argued that for him to conclude Petitioner's small fiber neuropathy was autoimmune, he would have to see significant biomarkers, such as an elevated ANA. Tr. 223:25–224:2. He also argued that he "would have extremely low suspicion that [Petitioner's small fiber neuropathy] was autoimmune[]" if she does not already have a pre-existing autoimmune disease. Tr. 225:5–19. Yet, on re-cross-examination, Dr. Donofrio conceded that on August 29, 2011, Petitioner *did* have a positive ANA with an index of 1.33, but he opined that it "has no meaning[, as i]t's a test that can be positive in normal people[.]"[80] Tr. 240:17–18, 242:6–7, 16–18 (emphasis added).

[80] On rebuttal, Dr. Steinman noted that Dr. Purath wrote this "must be false positive." Tr. 252:14. But he opined he did not "know what her mindset was that she said it must be [a false positive]." Tr. 252:15–16. Dr. Steinman agreed that her notation could have been an interpretation of the fact that the rest of

Dr. Donofrio elaborated on the relationship between autonomic neuropathy and small fiber neuropathy, as both diagnoses had been proposed to describe Petitioner's symptoms. Tr. 156:14–25, 157:1. Dr. Donofrio testified that "small fibers constitute the peripheral aspect of the autonomic nervous system." Tr. 156:17–18. He stated that "the autonomic nervous system [] begins in the brain stem and the spinal cord, but then gives rise to one series of nerve fibers that go to ganglions[,] and then [] a second order goes to [] many places, hands, skin, heart, gut." Tr. 156:18–22. Dr. Donofrio explained that patients can have a small fiber neuropathy without autonomic involvement and vice versa, but that patients "commonly [] have both." Tr. 156:24–25, 157:1. He noted that patients with autonomic neuropathy exhibit "difficulty with pupillary reactions, . . . they don't sweat well[,] . . . they may have skin changes . . . their feet and hands may feel colder or too warm." Tr. 163:2–3, 16–20. Dr. Donofrio testified that Petitioner underwent autonomic testing, which yielded normal results and she did not exhibit many of the purported symptoms. Tr. 162:12–22, 163:22. He maintained that Petitioner did not have autonomic involvement or suffer from an autonomic neuropathy. Tr. 156–157, 162–163.

Regarding Petitioner's small vessel vasculitis diagnosis, Dr. Donofrio opined that neither Petitioner's medical records nor skin biopsy revealed evidence of a small vessel vasculitis. Resp't's Ex. L at 2. He indicated "tissue is necessary to confirm the presence of a small vessel vasculitis. There was no comment by the pathologist reading the skin biopsy of changes consistent with a small fiber vasculitis or a vasculitis of any size blood vessel." *Id.* Dr. Donofrio testified that "[i]f blood vessels were present in the skin biopsy . . . [he] th[ought] the pathologist would have commented on the [] presence of vasculitis in the small arterials of the skin." Tr. 164:6–9. Dr. Donofrio highlighted none of Petitioner's laboratory tests "showed abnormal values for markers of vasculitis." Resp't's Ex. L at 2. Therefore, he opined Petitioner could not be suffering from small vessel vasculitis. *Id.*

Dr. Donofrio considered Dr. Steinman's "theory and hypothesis about how [the] Fluarix [vaccine] triggered an autoimmune response to the alpha-3 nicotinic acetylcholine receptor via molecular mimicry." Resp't's Ex. L at 2 (citing Pet'r's Ex. 40 at 6). Dr. Donofrio noted that Dr. Steinman "discusse[d] the concept of molecular mimicry and its application to the flu vaccination of 2011 and those from previous years . . . [but h]e doesn't discuss how long it takes to develop antibodies against those amino acid homologs." Resp't's Ex. L at 2. He pointed out that Dr. Steinman's theory and filtration process has not been published or subjected to peer-review. Tr. 173:17–18.

Dr. Donofrio testified that based on available data, he is not convinced by Dr. Steinman's theory that the flu vaccine more likely than not caused Petitioner's small fiber neuropathy. Tr. 164:15–18. He explained that "if it did, [he] would expect [] the neurologic literature to be replete with either a very large number of case reports or even some epidemiologic data to support that. And that is just not the case." Tr. 164:20–23. However, in response to my questioning, Dr. Donofrio conceded that epidemiological studies are not the only way to associate a theory of molecular mimicry with causation of an injury; but he stated that the presence of epidemiological studies would be the only way to convince *him.* Tr. 227:24–25, 228:4–7 (emphasis added). Dr.

Petitioner's testing was normal, but he could not speculate regarding whether that interpretation was accurate. Tr. 259:10–15.

Donofrio argued that Petitioner's literature wholly fails to mention vaccination as a possible cause of small fiber neuropathy. Resp't's Ex. A at 11 (citing Pet'r's Exs. 18, 19, 20).[81]

Dr. Donofrio wrote that Dr. Steinman's "analysis makes logical sense as a theory and hypothesis, but its application to [P]etitioner . . . is speculative." Resp't's Ex. L at 2. Dr. Donofrio argued Dr. Steinman could not show the homologies he identified resulted in the production of autoantibodies against acetylcholine receptors resulting in small fiber neuropathy. *See id.* As support for his opinion, Dr. Donofrio noted that Petitioner "underwent serum testing for antibodies against the ganglionic acetylcholine receptor and none were detected." *Id.* He testified that the presence of the ganglionic acetylcholine receptor antibody would have been the best indicator of antibodies but was negative. Tr. 166:2–3. Dr. Donofrio concluded that "[t]his result refute[d] the presence of an autoimmune response against the ganglionic acetylcholine receptors." Resp't's Ex. L at 2. Dr. Donofrio responded to Dr. Steinman's assertions that Petitioner's use of Decadron could have suppressed her immune response, resulting in a negative test. Tr. 166–167. He noted that Petitioner received a seven-day course of Decadron on August 26, 2011, and the antibody test was performed in November. Tr. 167:2–3. Therefore, he opined that "any steroid effect would have been long gone to suppress the antibodies[]" by the time the test was performed. Tr. 167:4–6.

On cross-examination, Dr. Donofrio acknowledged that he failed to consider Dr. Purath's notation from September 16, 2011, indicating that "as of tomorrow [September 17, 2011], she will be off the Decadron completely[.]" Tr. 215:20–25. Dr. Donofrio corrected his impression that Petitioner was only on a seven-day course of Decadron and stated he had "no reason to dispute that[]" Petitioner was on a 22-day course of Decadron through September 17, 2011. Tr. 216:17. He also had no reason to dispute that the antibody test was performed on November 4, 2011, approximately fifty days later. Tr. 216:18–25. However, he maintained that "it takes about a full month of [using] any steroid before [it] interfere[s] with the pituitary adrenal access and suppressive," so Petitioner's period of Decadron use "would not be long enough to interfere with the [antibody] testing [fifty] days after discontinuation of use[.]" Tr. 217:2–14. He opined that even if Petitioner was on Decadron on November 4, 2011, the antibody testing "would have still uncovered the problem of the antibody, had it been there." Tr. 217:23–24. However, Dr. Donofrio could not cite to any literature to support this position. Tr. 218:2–7.

In his final report filed after the entitlement hearing, Dr. Donofrio revisited Dr. Steinman's "argument that corticosteroids in the form of Decadron eliminated the antibody production and for that reason the ganglionic AChR antibodies were not measured in [P]etitioner." Resp't's Ex. N at 1. As support for his opinion, Dr. Donofrio attacked Dr. Steinman's reliance on the Baris et al.[82] study, as figure one "shows the dynamic function of lymphocytes CD19 and lymphocyte proliferation in children with renal failure. The figure does not show antibody levels[,] which is the data reported in . . . [P]etitioner's medical records (not lymphocyte activity)." *Id.* (citing Pet'r's Ex. 79 at 3). Dr. Donofrio opined that "[e]ven if figure one indirectly inferred antibody levels, the figure[] did not show complete suppression of CD19 function that would be necessary to achieve unrecordable antibody levels." Resp't's Ex. N at 1 (citing Pet'r's Ex. 79 at 3). He also attacked Dr.

[81] Jinny Tavee, et al., *Small fiber neuropathy: A burning problem,* 76:5 CLEV. CL. J. MED. 297–305 (2009); David Lacomis, *Small-fiber neuropathy,* 26 MUSCLE NERVE 173–88 (2002); Phillip Low, et al., *Autonomic Dysfunction in Peripheral Nerve Disease,* 27 MUSCLE NERVE 646–61 (2003).
[82] *See* Baris, et al., *supra* note 59, at 685–93.

Steinman's use of a corticosteroid comparison chart to equate the Baris et al. study with Petitioner's case. Resp't's Ex. N at 1 (citing Pet'r's Ex. 80). Dr. Donofrio noted that this comparison is ineffective because "Decadron is a long acting form of corticosteroids whose duration of action is 36 to 54 hours." Resp't's Ex. N at 1. Therefore, he opined that based on the number of days between Petitioner's last dose of Decadron on September 17, 2011, and the date of her testing for the titer of ganglionic acetylcholine receptor antibodies on November 4, 2011, "Decadron blood levels would no longer be detectable and would not be expected to interfere with antibody detection." *Id.* Dr. Donofrio maintained his opinion that "the absence of antibodies against the ganglionic acetylcholine receptor is due to their absence in the blood stream of [P]etitioner[,]" not by her taking a 22-day course of Decadron weeks before the study. *Id.*

Dr. Donofrio wrote that Petitioner's treating physicians "who judged the vaccine causal to her condition do not appear to have known that the symptoms predated her vaccination, and they too offer no explanation as to how the flu vaccine could cause her condition." Resp't's Ex. A at 12. For example, Dr. Donofrio noted "Dr. Purath does not explain why, other than a temporal relationship, she believes the vaccine caused [P]etitioner's condition." *Id.* Additionally, Dr. Bernard Remler "mentioned his uncertainty regarding a causal relationship between [Petitioner's] symptoms and the flu vaccination." *Id.* (citing Pet'r's Ex. 6 at 9). Thus, Dr. Donofrio opined "there is no reliable evidence showing that flu vaccine causes small fiber neuropathy[,]" or that it did so in Petitioner's case. Resp't's Ex. A at 11, 13.

Next, Dr. Donofrio discussed his opinion regarding the onset of Petitioner's condition. *Id.* at 11. Dr. Donofrio felt it was "clear from the medical records that [P]etitioner had tingling for almost [two] weeks before the vaccination of August 23, 2011." *Id.* at 11–12 (citing Pet'r's Ex. 2 at 46); *see also* Resp't's Ex. L at 1, 4. He also indicated his conclusion is contrary to Dr. Steinman's theory that the onset of Petitioner's symptoms was the "numbness and tingling in [her] face [that] occurred within hours of the vaccination." Resp't's Ex. L at 1 (citing Pet'r's Ex. 40 at 4).

As support for his opinion, Dr. Donofrio noted that during Petitioner's visit with Dr. Purath on August 25, 2011, "she specifically complained of severe headaches and sporadic tingling in the face off-and-on for [two] weeks." Resp't's Ex. A at 11–12 (citing Pet'r's Ex. 2 at 46); *see also* Resp't's Ex. L at 1, 4. He maintained that "[t]he tingling of the face described in [Petitioner's] first affidavit was not taken out of context." Resp't's Ex. I at 1. Rather, he stated that "[Petitioner's] affidavit does not acknowledge [her] symptoms [] beginning [two] weeks before the flu vaccination." *Id.* (citing Pet'r's Ex. 5). During his testimony on cross-examination, Dr. Donofrio admitted that Dr. Purath made a "corrective entry" on August 26, 2011, indicating Petitioner's "symptoms of paresthesia did not begin until . . . August 23, 2011." Tr. 220:15, 22–24. He then agreed that Petitioner's "paresthesia and the numbness and tingling *did not* occur before August 23, 2011[.]" Tr. 221:21–24 (emphasis added). Instead, he stated that Petitioner's symptoms "all started after Tuesday night after she had a flu shot." Tr. 221:5–6, 222:3–10. Dr. Donofrio further agreed that in order to maintain his conclusion that Petitioner's symptoms began two weeks prior to August 2011, he would have to "disbelieve the testimony of Dr. Purath, . . . [Petitioner], . . . [and] [Petitioner's] mother[,]" who is also an attorney. Tr. 222:3–10.

Dr. Donofrio further noted that Petitioner's theory relating to timing "is not scientifically sound because the breakdown of immune tolerance requires several days to evolve[,]" not hours.

Resp't's Ex. A at 10. Dr. Donofrio testified that the four- to- six-hour timeframe proposed by Dr. Steinman is inconsistent with what is known about how long it takes for the development of autoimmunity. Tr. 170:17–21. Dr. Donofrio reiterated that "the immune system must process a foreign antigen and slowly develop the signal for the antibodies to form . . . [t]his takes several days and usually 7–10 days . . . [up] until 2–3 weeks after the vaccination." Resp't's Ex. A at 10 (citing Resp't's Ex. G).[83] Dr. Donofrio opined that Petitioner's "manifestation of symptoms within a few hours [of the flu vaccine] would be too rapid in onset for the vaccine to have been the cause." Resp't's Ex. A at 12.

Dr. Donofrio expanded on Petitioner's GBS comparison and explained "most patients with [GBS] do not develop the initial features of the illness until 7–10 days after a prior respiratory or gastrointestinal infection." *Id.* (citing Resp't's Ex. G).[84] He continued that "[t]he immune system must process a foreign antigen and slowly develop the signal for the antibodies to form that attack the myelin that surrounds the nerves." Resp't's Ex. A at 10. Dr. Donofrio cited the Langmuir et al.[85] article, which "did not identify patients who developed symptoms of GBS on the same day as the flu vaccination." *Id.* (citing Resp't's Ex. G). The authors of the study noted that the onset of GBS after the swine flu vaccine showed a neurological response "most commonly at [seven] days and never within hours" of vaccination. Resp't's Ex. I at 4 (citing Resp't's Ex. G). Dr. Donofrio wrote this article "does not support the concept that neurologic symptoms begin within hours of a flu vaccine." Resp't's Ex. I at 3. Based on this, Dr. Donofrio concluded that "it is inconceivable for [Petitioner] to receive a flu vaccination on August 23, 2011, and to have her first symptom from the flu vaccination by 4[:00] pm on the same day, if one uses the theory of immunopathogenesis of the condition." Resp't's Ex. A at 10. Therefore, Dr. Donofrio opined that based on Dr. Steinman's purported theory regarding timing, it is "highly unlikely that [Petitioner's] now proven small fiber neuropathy relates to the [flu] vaccine." Tr. 173:24–25, 174:1.

Dr. Donofrio addressed Dr. Steinman's explanation of rapid onset and noted that Dr. Steinman instead relied on an article by Schonberger et al.,[86] "to support the concept that neuro-inflammation of the peripheral nervous system can begin within 0–1 days after a flu vaccination." Resp't's Ex. L at 3 (citing Pet'r's Ex. 67 at 8; Resp't's Ex. M, ECF No. 63-2). The authors of the article analyzed patients who developed GBS following the 1976–1977 flu vaccination. Pet'r's Ex. 67 at 1. However, Dr. Donofrio explained that the issue with this study is that the authors of the Schonberger article lumped one thousand patients together with presumed GBS following the swine flu vaccination. Tr. 171:11–15 (citing Resp't's Ex. M). Dr. Donofrio testified that the Langmuir et al.[87] study re-examined the data because the authors were concerned that each patient in the Schonberger study did not, in fact, suffer from GBS. Tr. 171:19–20 (citing Resp't's Ex. G). Instead, the authors of the Langmuir et al. study focused on patients with "extensive muscle weakness, which is what you should have if you have [GBS]." Tr. 171:22–23. Dr. Donofrio explained that when the authors of the Langmuir et al. study re-examined the data from the Schonberger et al. study, the data failed to reveal "any cases of [GBS] developing in the first [three] days following the vaccination." Resp't's Ex. L at 3 (citing Resp't's Ex. G at 15; Pet'r's Ex. 67 at

[83] *See* Langmuir, et al., *supra* note 72, at 841–80.
[84] *See id.*
[85] *Id.*
[86] *See* Schonberger, et al., *supra* note 71, at 105–24.
[87] *See* Langmuir, et al., *supra* note 72, at 841–80.

8). Rather, the Langmuir et al. study found "the interval of vaccination to onset of symptoms in days and [seven] day intervals." Resp't's Ex. G at 15. He explained the authors found that "[t]here were no patients reported on day one, two[,] or three developing the onset of the illness after the vaccination." Tr. 172:4–5 (citing Resp't's Ex. G at 15, Fig. 1). Instead, the authors found the reported cases of GBS following a flu vaccination "did not occur until either day three or day four." Tr. 231:22–23. Dr. Donofrio opined that the Langmuir et al. article "is a stronger paper because it intended to collect only people with strong evidence of GBS." Tr. 172:8–10. Therefore, Dr. Donofrio concluded that "if one uses this model of flu vaccination and onset of [GBS], it is not possible to support the onset of a small fiber neuropathy within hours of a flu vaccination[]" and Dr. Steinman's argument must fail. Resp't's Ex. L at 3. However, in response to my questioning, Dr. Donofrio testified that assuming Petitioner's small fiber neuropathy was autoimmune in nature (which he does not believe), the onset of symptoms could occur within a matter of hours after a vaccine, although it is "highly unlikely" to occur. Tr. 237:18–23.

Finally, Dr. Donofrio addressed Dr. Steinman's assertion that he did not proffer an alternative neurologic explanation for Petitioner's symptoms. Resp't's Ex. L at 1 (citing Pet'r's Ex. 40 at 5). Dr. Donofrio explained that in his first report, he "mentioned the possibility that [P]etitioner's symptoms might integrate with her long history of migraines." Resp't's Ex. L at 1 (citing Resp't's Ex. A at 10). He reiterated that "patients with complicated migraines can have numbness and tingling, weakness, gait imbalance, dizziness, vertigo, and even loss of consciousness." *See id.* In response to my questioning, he stated he "believe[s] there is a higher incidence of migraine[s] in autoimmune diseases," but the correlation is not strong. Tr. 226:14–18. He further noted that "all [other] potential alternative causes have not been eliminated[]" for "the causes or associations of [Petitioner's] small fiber neuropathy[.]" Resp't's Ex. L at 3. In fact, Dr. Donofrio indicated that Petitioner was never tested for other possible explanations for her small fiber neuropathy including "Sjogren's syndrome, [H]epatitis C, inherited neuropathies, thyroid disease, Fabry's disease or Tangiers disease." Resp't's Ex. L at 2. He cited to several articles which mentioned other "causes or associations of small fiber neuropathy[,]" for which Petitioner was never tested such as "diabetes, connective tissue disorders such as lupus, HIV infection, sarcoidosis, thyroid disease, vitamin B1, B6, [] B12 deficiency, . . . celiac disease, . . . amyloidosis, erythromelalgia, hypertriglyceridemia, Lyme disease, leprosy, [and] restless leg syndrome[.]" *Id.* at 3 (citing Pet'r's Exs. 18, 19; Resp't's Exs. E, F).[88] Therefore, Dr. Donofrio opined that "alternative explanations might be uncovered if those conditions are investigated . . . [t]hus all potential alternative causes have not been eliminated." Resp't's Ex. L at 2–3.

On cross-examination, he maintained that while these alternate explanations are very "unlikely," they are still possibilities. Tr. 198:9, 200:1–9. However, he would not opine that any of those conditions caused her small fiber neuropathy because they have not been tested for. Tr. 198:19–22. On re-direct, Dr. Donofrio clarified that he was not insinuating that Petitioner suffered from any of the other conditions, simply that such conditions have not been ruled out. Tr. 234:16–20. Still, he could not identify a definitive alternative cause for Petitioner's small fiber neuropathy. Tr. 203:17–20. He maintained "there's a cause out there somewhere," but it has not been identified yet. Tr. 204:14–18.

[88] *See supra* note 77.

IV. Applicable Legal Standards

To receive compensation under the Vaccine Act, a petitioner must demonstrate either that: (1) the petitioner suffered a "Table injury" by receiving a covered vaccine and subsequently developing a listed injury within the time frame prescribed by the Vaccine Injury Table set forth at 42 U.S.C. § 300aa-14, as amended by 42 C.F.R. § 100.3; or (2) that petitioner suffered an "off-Table injury," one not listed on the Table, as a result of his receiving a covered vaccine. *See* 42 U.S.C. §§ 300aa-11(c)(1)(C); *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1319-20 (Fed. Cir. 2006). Petitioner does not allege a Table injury in this case; thus, she must prove that her injury was caused-in-fact by a Table vaccine.

To establish causation-in-fact, a petitioner must demonstrate by a preponderance of the evidence that the vaccine was the cause of the injury. 42 U.S.C. § 300aa-13(a)(1)(A). A petitioner is required to prove that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321–22 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)).

In the seminal case of *Althen v. Sec'y of the Dept. of Health & Hum. Servs*, the Federal Circuit set forth a three-pronged test used to determine whether a petitioner has established a causal link between a vaccine and the claimed injury. *See* 418 F.3d 1274, 1278–79 (Fed. Cir. 2005). The *Althen* test requires petitioners to set forth: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id.* at 1278. To establish entitlement to compensation under the Program, a petitioner is required to establish each of the three prongs of *Althen* by a preponderance of the evidence. *See id.*

A petitioner who satisfies all three prongs of the *Althen* test has established a prima facie showing of causation. *Hammitt v. Sec'y of Health & Hum. Servs*., 98 Fed. Cl. 719, 726 (2011). A petitioner who demonstrates by a preponderance of the evidence that he suffered an injury caused by vaccination is entitled to compensation unless the respondent can demonstrate by a preponderance of the evidence that the injury was caused by factors unrelated to the vaccination. *See Althen*, 418 F.3d at 1278; *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 547 (Fed. Cir. 1994). Consequently, when and if Petitioner establishes a prima facie case, the burden then shifts to the government to prove that an alternative cause, unrelated to the administration of the vaccine, was the "sole substantial factor" in causing the alleged injury. *de Bazan*, 539 F.3d at 1354; *see also Hammitt*, 98 Fed. Cl. at 726 (explaining that the respondent's burden is to show that the "factor unrelated" was the "sole substantial factor" in causing the injury). Additionally, a factor unrelated "may not include 'any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness or condition.'" 42 U.S.C. § 300aa-13(a)(2); *see also Doe v. Sec'y of Health & Hum. Servs.*, 601 F.3d 1349 (Fed. Cir. 2010) (opining that an idiopathic diagnosis cannot be a "factor unrelated," as it is idiopathic).

V. Discussion

A. Petitioner's Diagnoses

As a factual predicate to proving vaccine-causation, it is Petitioner's burden to demonstrate that she actually suffers from the injuries alleged to have been caused by the August 23, 2011 flu vaccination. *See Hibbard v. Sec'y of Health & Hum. Servs.*, 698 F.3d 1358, 1364-65 (Fed. Cir. 2012); *Lombardi v. Sec'y of Health & Hum. Servs.*, 656 F.3d 1343, 1353 (Fed. Cir. 2011); *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1346 (Fed. Cir. 2010) (finding that in a case where the injury itself is in dispute, it is appropriate for the special master to "first determine which injury was best supported by the evidence presented in the record before applying the *Althen* test so that the special master could subsequently determine causation relative to the injury."). The Vaccine Act provides that a treating physician's diagnosis "shall not be binding on the special master or court," but that the special master should consider the "entire record and the course of the injury" when evaluating how much weight to afford a treating physician's diagnosis. 42 U.S.C. § 300aa-13(b)(1). In this case, Petitioner must show by preponderant evidence that she suffers from small fiber neuropathy and small vessel vasculitis. *See Broekelschen*, 618 F.3d at 1349; *see also Lombardi*, 656 F.3d at 1353.

I. Small Fiber Neuropathy

Petitioner has established by preponderant evidence that she suffers from small fiber neuropathy. A majority of Petitioner's treating physicians diagnosed her with small fiber neuropathy. For example, Dr. Marquez de Leon's notes from November 4, 2011, indicate that he originally diagnosed Petitioner with small fiber neuropathy. Pet'r's Ex. 4 at 542. Drs. Purath and Barboi agreed with Dr. Marquez de Leon's diagnosis of small fiber neuropathy and individually arrived at the same conclusion. Dr. Purath noted on January 16 and April 20, 2012, that Petitioner suffered from small fiber neuropathy. Pet'r's Ex. 2 at 23–26. Dr. Purath indicated that Petitioner's numbness and pain in the arms, which flared with stress, "is not uncommon with polyneuropathy[.]" *Id.* at 26. Dr. Barboi noted on February 6, 2014, that Petitioner's "history would fit a small fiber neuropathy diagnosis[,] but physical examination does not aid in localization given the inconsistent nature of her sensory exam and non-dermatomal distribution." Pet'r's Ex. 9 at 13. Nonetheless, Dr. Barboi agreed with Dr. Marquez de Leon's diagnosis. *Id.*

Petitioner's experts, Drs. Younger and Steinman, agreed with Petitioner's treating physicians' diagnosis of small fiber neuropathy. Indeed, Dr. Steinman maintained this opinion throughout his reports and testimony. While Respondent's expert, Dr. Donofrio, originally opined that Petitioner's symptoms were not consistent with the diagnosis of small fiber neuropathy, he later conceded that there is pathologic evidence showing that Petitioner suffers from small fiber neuropathy. Tr. 200:22–25, 201:1. In fact, he stated that her abnormal symptom presentation "carried less weight" in light of Petitioner's other evidence supporting her small fiber neuropathy diagnosis. Tr. 207:1–15. Therefore, an extensive discussion regarding Petitioner's symptom presentation is unnecessary for the diagnosis analysis.

Petitioner's small fiber neuropathy diagnosis was also confirmed by direct evidence. Following Dr. Donofrio's criticism regarding the lack of a biopsy performed on Petitioner, she

underwent a skin biopsy to confirm her small fiber neuropathy diagnosis. The results of Petitioner's biopsy showed a low ENFD consistent with small fiber neuropathy. Dr. Steinman relied on the reference values contained in the Lauria et al.[89] study, which stated that, for a biopsy at the calf, the ENFD normative values for Petitioner's age group and gender would be 8.4 for the 5th percentile, with a median ENFD value of 13.5. He explained that Petitioner's results yielded a mean of 2.8. Pet'r's Ex. 40 at 18. Based on this, he concluded that "these results indicate the presence of small fiber neuropathy." *Id.* Dr. Steinman credibly testified that Petitioner's biopsy results were "unmistakably . . . consistent with the diagnosis of small fiber neuropathy." Tr. 91:22–23.

Despite Dr. Donofrio's conclusion that Petitioner's biopsy revealed clear, pathologic, evidence of small fiber neuropathy, he argued that just because there was evidence of small fiber neuropathy when the biopsy was performed in 2015, it does not mean she suffered from it in 2011 following her flu vaccine. Tr. 160:8–9, 16–24, 201:6–13. He argued that "other things may have happened to her life[]" over those four years which could explain Petitioner's symptoms and biopsy results. Tr. 160:24–25, 161:2. I am not persuaded by Dr. Donofrio's argument that these results are unreliable evidence of Petitioner's small fiber neuropathy in 2011 because they were taken four years after her flu vaccine. In fact, Dr. Donofrio admitted that there is no evidence in Petitioner's medical records to indicate that she suffered from any other disease that could cause small fiber neuropathy or any of her manifested symptoms, in between the time of her flu vaccine on August 23, 2011, and her biopsy performed on December 28, 2015, that could explain why her biopsy results in 2015 showed small fiber neuropathy. *See, e.g.,* Pet'r's Exs. 2, 4; *see also* Tr. 195:7–24.

Furthermore, the four-year gap between Petitioner's flu vaccine and skin biopsy loses its significance because Petitioner's small fiber neuropathy diagnosis is also confirmed by the abnormal findings from her QSARTs performed in November 2011. The results of Petitioner's QSARTs revealed decreased responses in the right foot, distal leg, and forearm, a finding consistent with small fiber neuropathy. Pet'r's Ex. 40 at 5; *see also* Pet'r's Ex. 4 at 542; Pet'r's Ex. 9 at 46. Dr. Donofrio notes that such testing can be influenced by a patient's use of antihistamines such as Allegra. However, Petitioner provided credible testimony that she always follows the instructions prior to testing and that the instructions for this test were to refrain from taking antihistamines. I am persuaded by Petitioner's testimony that, as the QSARTs were performed in November, they were not conducted within her active allergy season. Therefore, I am convinced that Petitioner was not taking Allegra at the time of this testing. As a result, the evidence revealed by Petitioner's QSARTs was more likely than not unaffected by an antihistamine such as Allegra. I find that Petitioner has shown by preponderant evidence that she suffers from small fiber neuropathy.

The experts disagree regarding whether Petitioner's small fiber neuropathy is autoimmune in nature. Dr. Steinman opined that Petitioner's small fiber neuropathy is autoimmune in nature based, in part, on her August 26, 2011 elevated ANA with an index of 1.33, and the low density of the nerve fibers revealed by her biopsy. *See, e.g.*, Pet'r's Ex. 2 at 77–78; Tr. 252:11–13, 25, 253:1–8. He admitted that his theory "fits better" if Petitioner's small fiber neuropathy is autoimmune in nature because it explains how cross-reactivity and damage occurred in Petitioner's

[89] *See* Lauria, et al., *supra* note 46.

case. Tr. 257:2–7. He testified that after listening to testimony from Petitioner's mother regarding her own diagnosis of rheumatoid arthritis, an autoimmune condition, he found it even more likely that Petitioner's small fiber neuropathy is autoimmune in nature because Petitioner may have a genetic pre-disposition for autoimmune disease. *See* Tr. 89:21–24, 145. Dr. Steinman found this fact to be convincing evidence there was "some kind of autoimmune reaction" that triggered Petitioner's small fiber neuropathy. Tr. 90:2. Petitioner's test results, coupled with her family medical history, is persuasive evidence that her small fiber neuropathy is autoimmune.

Dr. Donofrio argued that he could not conclude Petitioner's small fiber neuropathy was autoimmune in nature because she did not have significant biomarkers like an elevated ANA or a pre-existing autoimmune disease. Tr. 223:25–224:2, 225:5–19. However, I am not influenced by Dr. Donofrio's argument because he conceded that Petitioner did have an elevated ANA. Tr. 242:6–7. In fact, I must afford Dr. Donofrio's arguments regarding the nature of Petitioner's small fiber neuropathy less weight in light of his apparent opinion reversal and eventual admission that Petitioner suffered from small fiber neuropathy, in general. Therefore, I find that Petitioner has shown by preponderant evidence that her small fiber neuropathy is autoimmune in nature.

There was some discussion between the experts regarding autonomic neuropathy and whether Petitioner's condition has an autonomic component. *See* Tr. 116:18–20, 163:2–3, 16–20. Although both experts referenced autonomic neuropathy in passing, Petitioner failed to elaborate on the significance of this argument so that I could properly consider it. In fact, neither expert sufficiently explained the relevance of this discussion to a determination of whether Petitioner's small fiber neuropathy was vaccine-caused. While I considered all of the evidence presented in this case, to the extent that an opinion or argument is inadequately explained with supporting literature or medical records, it is less helpful to my analysis of the ultimate issue. Therefore, I will not further discuss the brief mention of autonomic neuropathy by the experts.

II. Small Vessel Vasculitis

Petitioner has failed to establish by preponderant evidence that she suffers from small vessel vasculitis. Petitioner's expert, Dr. Younger, diagnosed Petitioner with small vessel vasculitis, but he was the only one of Petitioner's treating physicians to do so. *See* Pet'r's Ex. 21 at 7. Dr. Younger was not available to testify at the hearing, and therefore was not subjected to cross-examination. However, Respondent did not object to the use of his reports. As Dr. Younger's opinion relates to Petitioner's diagnosis as her physician, I will consider it as I would the opinion of any other treater. But as his opinion relates to vaccine causation, to the extent that it has been rebutted by testifying experts, I will afford his opinion considerably less weight.

As support for his opinion, Dr. Younger relied on medical literature to show instances where the flu vaccine led to small vessel vasculitis. Pet'r's Ex. 21 at 7. Dr. Younger cited to a case study by Blumberg et al.,[90] which described two patients suffering from small vessel vasculitis secondary to the influenza vaccination. *Id.* (citing Pet'r's Ex. 25 at 1). Both patients in the study noted post-vaccine reactions indicative of small vessel vasculitis including fever, malaise, generalized arthralgias and myalgias, and swelling in the face. Pet'r's Ex. 25 at 1. One patient in the study underwent a skin biopsy which revealed "cutaneous necrotizing venulitis localized to the

[90] *See* Blumberg, et al., *supra* note 43, at 1.

papillary dermis." *See id.* Dr. Younger analogized this study to Petitioner's case and concluded that Petitioner suffered from small vessel vasculitis. Pet'r's Ex. 21 at 7. He wrote that her "epidermal nerve fibers were [] injured by influenza vaccination wherein the influenza vaccination led to an autoimmune response restricted to small nerve fibers in the skin with consequent sensory changes, including burning pain." *Id.* However, Dr. Younger could not rely on Petitioner's medical records to demonstrate that she suffered from other post-vaccine reactions indicative of small vessel vasculitis as enumerated in the Blumberg study, such as fever, malaise, arthralgias and myalgias, or swelling in the face. *See id.*

In fact, Dr. Younger failed to point to *any* notation in Petitioner's medical records to support his opinion that Petitioner suffers from small vessel vasculitis. This omission is critical to my finding that Petitioner does not suffer from small vessel vasculitis. In addition, unlike the patient in the Blumberg study, who underwent a skin biopsy revealing cutaneous necrotizing venulitis and a diagnosis of small vessel vasculitis, Petitioner's skin biopsy did not reveal the same. *See, e.g.*, Resp't's Ex. L at 2. Dr. Donofrio highlighted that "[t]here was no comment by the pathologist reading Petitioner's skin biopsy of changes consistent with a small fiber vasculitis or a vasculitis of any size blood vessel." *See id.*; *see also* Pet'r's Ex. 22 at 2. Dr. Donofrio provided credible testimony that "[i]f blood vessels were present in the skin biopsy . . . [he] th[ought] the pathologist would have commented on the [] presence of vasculitis in the small arterials of the skin." Tr. 164:6–9. I find this interpretation of Petitioner's skin biopsy results to be persuasive evidence that her biopsy did not reveal the presence of small vessel vasculitis.

It is even more convincing that Dr. Steinman also could not point to a single medical record or evidence from Petitioner's biopsy to show the presence of small vessel vasculitis. In fact, his criteria for agreeing that Petitioner suffered from small vessel vasculitis was merely rooted in his medical theory connecting the flu vaccine to her small fiber neuropathy. Dr. Steinman stated that the way the immune system "attacks [the] peripheral nerve, the way it does in small fiber neuropathy, . . . the immune cells and the antibodies go through the blood vessels, and it creates a small inflammatory response in the vessels." Tr. 96:9–15. Based on this, he stated that Petitioner's vasculitis is "concomitant with how the small fiber neuropathy pathophysiology works." Tr. 96:16–18. Still, Dr. Steinman was unable to rely on Petitioner's medical records or biopsy results as support.

He did not provide medical literature that establishes vasculitis as a necessary condition for autoimmune neuropathy generally, or small fiber neuropathy specifically. Instead, the literature Petitioner submitted demonstrates that small vessel vasculitis is not a disease in and of itself, but rather is an umbrella diagnosis that encompasses several other categories or versions of small vessel vasculitis, including Wegener's granulomatosis, Churg-Strauss syndrome, microscopic polyangiitis, Henoch-Schönlein purpura, essential cryoglobulinemic vasculitis, and cutaneous leukocytoclastic angiitis. Pet'r's Ex. 26 at 2.[91] Based on the literature, other features of small vessel vasculitis, such as the presence of cryoglobulins in the blood and vessels, ANCA in the blood, necrotizing granulomas, and asthma and eosinophilia, provide differential diagnostic criteria unique to each subcategory of small vessel vasculitis. *Id.* at 6. Each subcategory of small vessel vasculitis can be distinguished by, among other things, the presence of additional prerequisite features such as necrotizing vasculitis or inflammation affecting the small-to-medium sized

[91] *See* Jennette, et al., *supra* note 39, at 2.

vessels, resulting in pain. *Id.* at 2, 5. As supported by the literature, the pain caused by necrotizing inflammation in the small vessels manifests in fever, myalgias, arthralgias, and malaise. *Id.* at 5; *see also* Pet'r's Ex. 25 at 1.[92] Petitioner's medical records and biopsy results do not contain evidence that is consistent with the clinical presentation of small vessel vasculitis as described in the Blumberg and Jennette et al. articles. Therefore, I find Petitioner has failed to show by preponderant evidence that she suffers from small vessel vasculitis.

B. *Althen* Prong One

Under the first prong of *Althen*, a petitioner must offer a scientific or medical theory that answers in the affirmative the question: "can the vaccine[] at issue cause the type of injury alleged?" *See Pafford v. Sec'y of Health & Hum. Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004), *mot. for rev. denied*, 64 Fed. Cl. 19 (2005), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2006). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen*, 35 F.3d at 548; *see also Andreu v. Sec'y of Health & Hum. Servs.*, 569 F. 3d 1367, 1375, 1379 (2009) (ruling that the petitioners had satisfied *Althen* prong one where their expert witness had "presented a 'biologically plausible' theory"). Such a theory must only be "legally probable, not medically or scientifically certain." *Knudsen*, 35 F.3d at 548–49. A petitioner is not required to identify "specific biological mechanisms" to establish causation, nor are they required to present "epidemiologic studies, rechallenge[] the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities." *Capizzano,* 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280). However, as the Federal Circuit has made clear, "simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof." *LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) (citing *Moberly*, 592 F.3d at 1322). Rather, "[a] petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case." *Moberly*, 592 F.3d at 1322. In general, "the statutory standard of preponderance of the evidence requires a petitioner to demonstrate that the vaccine more likely than not caused the condition alleged." *LaLonde,* 746 F.3d at 1339.

Furthermore, establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of her claim. *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). The Supreme Court's opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), requires that courts determine the reliability of an expert opinion before it may be considered as evidence. "In short, the requirement that an expert's testimony pertain to 'scientific knowledge' establishes a standard of evidentiary reliability." *Id*. at 590 (citation omitted). Thus, for Vaccine Act claims, a "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly*, 592 F.3d at 1324. The *Daubert* factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen*, 618 F.3d at 1347 (citing *Lampe*, 219 F.3d at 1362). And nothing requires the

[92] *See* Blumberg, et al., *supra* note 43, at 1.

acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder v. Sec'y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 743 (2009) (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)).

Petitioner has met her burden under *Althen* prong one. Petitioner's expert, Dr. Steinman, has posited a reliable medical theory showing that the flu vaccine can cause small fiber neuropathy. Dr. Steinman opined that the 2011 Fluarix vaccine triggered an autoimmune response to the alpha 3 nicotinic acetylcholine receptor via molecular mimicry, resulting in small fiber neuropathy. *See* Pet'r's Ex. 40 at 6. Dr. Steinman based his theory, in part, on the notion of "recall response." Dr. Steinman provided credible testimony that a recall response occurs because it is not the body's "first encounter" with that specific antigen, but rather "the immune system has seen this [antigen] before[.]" Tr. 102:8–9. He explained that earlier doses of flu vaccines provide "ample immunological memor[ies] for a recall response" to occur following receipt of a subsequent flu vaccine. *Id.* at 22. His reliance on the article by de St. Groth et al.,[93] is persuasive. The authors found that prior exposure to an antigen, such as a vaccine, leads to an immune response when exposed to a subsequent, related antigen. In fact, the authors found that this recall response to the original antigen can be measured eight years later. Pet'r's Ex. 62 at 3. Dr. Steinman effectively used this article to opine that when the body is confronted with a subsequent flu vaccine, an immune response can occur based on the body's immunological memory created in response to a flu vaccine received up to eight years earlier. While he does not say how many times the body needs to be exposed before a recall response occurs, he did submit literature saying why one would not have a reaction after the first exposure. *See, e.g.*, Pet'r's Ex. 68 at 3.[94] Like people with food allergies who "often do not have clinical manifestations until multiple encounters," he explained that the body's recall response reaction occurs only after multiple encounters with an antigen. Pet'r's Ex. 40 at 25.

Dr. Steinman researched his theory by running BLAST searches through the protein databases of the National Library of Medicine and the NIH to look for homologies between the components of the Fluarix vaccine that Petitioner received in 2011 and the alpha3 subtype of nicotinic AChR, which is known to be associated with small fiber neuropathy. Pet'r's Ex. 40 at 7. Dr. Steinman entered the sequence of alpha3 nicotinic AChR, with one of the known components of the 2011 Fluarix and flu vaccines from previous years. *Id.* at 7, 16. Dr. Steinman performed this process for several rounds of BLAST searches. During the first round, Dr. Steinman found two homologies between the alpha3 nicotinic AChR and the hemagglutinin in B/Brisbane/60/2008 in the 2011 Fluarix. *Id.* at 11–12. The first, was "[five] amino acids in a row PLIGE with the sixth amino acid representing a small change[.]" *Id.* The second, was "a [five] of six identity PSWVKT[.]" *Id.* Based on the Gautam et al. articles,[95] Dr. Steinman opined that the stretch of these sequence homologies was sufficient to trigger clinically relevant neuroinflammation.

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[93] *See* de St. Groth, et al., *supra* note 49.

[94] *See* Kappos, et al., *supra* note 73.

[95] *See supra* note 52 (indicating the "identity of [five] of [twelve] amino acids . . . was sufficient to trigger experimental encephalomyelitis[;]" a "[six] amino acid peptide with identity at [five] amino acids was sufficient to trigger neuroinflammation[;]" and "a peptide with [four] of [eleven] amino acids induced neuroinflammation[.]"). Pet'r's Ex. 40 at 8 (citing Pet'r's Exs. 58 at 5; 59 at 4; 60 at 3).

Dr. Steinman performed a second BLAST search "directed to the hemagglutinin found in the 2011 Fluarix component, known as hemagglutinin [Influenza A virus (A/California/07/2009(H1N1))]." *Id.* at 12. Dr. Steinman found "[o]ther relevant homologies [] between components of the 2011 Fluarix vaccine and alpha 3 nicotinic AChR[,]" including "from DKAKIDLVLIG, a stretch with a [seven] of [eleven] amino acid identity between a component of the 2011 Fluarix vaccine and alpha3 nicotinic AChR, . . . [which] has shown to be sufficient to trigger clinical relevant neuroinflammation in animal models[,]" based on the literature.[96] *Id.* Dr. Steinman provided evidence that there are numerous examples of sequences in the 2011 Fluarix vaccine and between earlier seasonal flu vaccines, that share similar homologies with the alpha3 nicotinic AChR, which is associated with small fiber neuropathy. *See, e.g.*, *id.* at 10–11.

Dr. Steinman conducted a third round of BLAST searches comparing the 2005–2006 flu vaccine to the 2011 Fluarix. *Id.* at 13. He "blasted the hemagglutinins from B/Brisbane/60/2008 and B/Shanghai/361/2002 . . . [and found] over a 90% identity in their protein sequences[.]" *Id.* at 13–14. Dr. Steinman noted that "[t]he homologies between the 2005–2006 influenza vaccine received by Petitioner and the Fluarix she received in 2011 cover the region with PLIG and PIWVKT that share homology with alpha 3 nicotinic AChR." *Id.* at 14. Dr. Steinman conducted the same analysis between the 2008 FluMist and the 2011 Fluarix. *Id.* He found that "[t]he hemagglutinin sequences are nearly identical between B/Brisbane/60/2008 in Fluarix and B/Florida/4/2006 in FluMist . . . [and] cover the region with PLIGE and PIWVKT that share homology with alpha 3 nicotinic AChR." *Id.* at 14–16.

Dr. Steinman conducted the same assessment of the 2009–2010 and 2010–2011 flu vaccines compared to the Fluarix 2011, respectively. *Id.* at 16–17. He noted that all three seasonal flu vaccines contain B/Brisbane/60/2008, and "[t]he homologies with PLIGE and PIWVKT that share homology with alpha 3 nicotinic AChR are contained in [all three] vaccines." *Id.* Based on his findings, Dr. Steinman asserted that through the "numerous examples of molecular mimicry between the alpha 3 nicotinic acetylcholine receptor and the Fluarix vaccine, and between earlier seasonal influenza vaccines given to Petitioner[,]" he has demonstrated "that the Fluarix vaccine can trigger an autoimmune response to the alpha3 nicotinic acetylcholine receptor via molecular mimicry." *Id.* at 17. Based on Dr. Steinman's theory, it is probable that given the number of components in prior seasonal flu vaccines that mimic the alpha 3 AChR associated with small fiber neuropathy, the body's recall response to the components of the subsequent 2011 Fluarix could trigger the immune cross-reaction to alpha3 AChR, resulting in small fiber neuropathy.

Dr. Steinman's reliance on his own studies in animals to demonstrate the criteria he used for considering homologies to be a "meaningful molecular mimic," is persuasive. He indicated that "meaningful," to him, means capable of producing neuroinflammation. Pet'r's Ex. 40 at 8. Dr. Steinman argued his research showed "a run of [five] or more of [twelve] amino acids that are identical in the Fluarix components and the alpha3 subtype of nicotinic AChR[]" to be a meaningful molecular mimic sufficient to activate an autoimmune response in mice. *Id.* (citing Pet'r's Exs. 58–60).[97] In fact, he argued his research showed that a run of five or more of twelve amino acids, "not even consecutive amino acids," was sufficient to trigger experimental

[96] *See id.*
[97] *See supra* note 52.

encephalomyelitis and neuroinflammation. Pet'r's Ex. 60 at 1.[98] He also cited two studies, in which he is listed author, that found that "a [six] amino acid peptide with identity at [five] amino acids was sufficient to trigger neuroinflammation[]" in mice, and "a peptide with [four] of [eleven] amino acids induced neuroinflammation[.]" Pet'r's Ex. 40 at 8 (citing Pet'r's Ex. 59 at 4, Pet'r's Ex. 60 at 3).[99] Dr. Steinman also relied on the Root-Bernstein et al.[100] study, in which the authors determined that similarities of sequences of five out of ten amino acids were significant enough to show that molecular mimicry occurred. Pet'r's Ex. 74 at 1. Dr. Donofrio did not provide evidence to refute this fact.

Notably, Dr. Donofrio did not present evidence demonstrating that the sequence homologies revealed by Dr. Steinman were insufficient to show a degree of molecular mimicry capable of triggering neuroinflammation. Instead, Dr. Donofrio's main contention was that there is a lack of epidemiological studies that associate the flu vaccine with small fiber neuropathy, in general, or via molecular mimicry, specifically. Tr. 164:15–23. However, after extensive questioning, Dr. Donofrio conceded that epidemiological studies are not the only way to associate a theory of molecular mimicry with causation of an injury. Tr. 227:24–25, 228:4–7. Despite his concession, he vehemently maintained that the presence of epidemiological studies would be the only way to convince him. *See id.* Dr. Donofrio's refusal to acknowledge any other ways to show an association between the flu vaccine and small fiber neuropathy via molecular mimicry or otherwise undercuts the credibility of his remaining testimony. Indeed, the presence of epidemiological studies is not the standard in the Program. Therefore, a lack of epidemiological studies establishing a causal connection between the flu vaccine and small fiber neuropathy is not dispositive, [101] and I will not hold the lack of studies against Petitioner.

Respondent criticizes Dr. Steinman's molecular mimicry theory because it has been rejected by other special masters in the Program. *See* Resp't's Br. at 15; *see also Forrest v. Sec'y of Health & Hum. Servs.*, No. 14-1046V, 2019 WL 925495 (Fed. Cl. Jan. 28, 2019) (finding that Dr. Steinman's theory that a flu vaccine caused TM via molecular mimicry was not sufficiently developed to meet Petitioner's burden under *Althen* prong one because Dr. Steinman had "not investigated his hypothesis[,]" other than through computerized homologies revealing "some overlap in sequences of amino acids[.]"). In that case, the special master discredited Dr. Steinman's theory in part, because he "appear[ed] to have made errors in proclaiming the degree of similarity [in the homologies] that he found[.]" *Forrest,* 2019 WL 925495, at *4. However, Dr. Steinman's theory involving molecular mimicry has been accepted in numerous Program cases as an accepted scientific or medical theory in the context of targeted BLAST searches. For example, in *White v.*

[98] Anand Gautam, et al., *A Polyalanine Peptide with only Five Native Myelin Basic Protein Residues Induces Autoimmune Encephalomyelitis,* 176 J. EXP. MED. 605–09 (1992).
[99] *See* Gautam, et al., *supra* note 54.
[100] *See* Root-Bernstein, *supra* note 50, at 1–17.
[101] While Petitioner has not provided medical literature ascribing small fiber neuropathy to the flu vaccine, she has provided literature documenting several cases of small fiber neuropathy whose etiology is suspected to have been induced by the human papillomavirus vaccine. *See* Pet'r's Ex. 75, ECF No. 74-3. The Kafaie et al. study analyzed a fourteen-year-old girl who presented with "[b]urning dysesthetic pain beg[inning] in the lower back and progress[ing] to all extremities [nine] days following human papillomavirus vaccination[.]" Jafar Kafaie, et al., *Small Fiber Neuropathy Following Vaccination,* 18 J. CLIN. NEUROMUSC. DIS. 37–40 (2016). The authors found that the patient's small fiber neuropathy was "potentially related to human papillomavirus vaccine administration." *See id.*

Sec'y of Health & Hum. Servs., the special master credited Dr. Steinman's molecular mimicry theory and supporting BLAST searches and determined that there were "sufficient homologies between the basic myelin protein and two of the strains of the HPV L1 strains . . . and between MOG and all four HPV antigens in the vaccine[,]" which could cause TM. No. 15-1521V, 2019 WL 7563239, at *24 (Fed. Cl. Spec. Mstr. Dec. 19, 2019). In that case, Dr. Steinman directed his searches to specific proteins that are "known to be targets of the immune response in [TM]," which, the special master found provided "a sound foundation for the theory of molecular mimicry." *Id.*; *see also Giannetta v. Sec'y of Health & Hum. Servs.*, No. 13-215V, 2017 WL 4249946, at *23 (Fed. Cl. Sept. 1, 2017) (crediting Dr. Steinman's molecular mimicry theory and finding "based on literature, testimony, and affidavits, [that] Dr. Steinman presented a biologically plausible theory to explain how the Menactra vaccine can act as a trigger of MS through molecular mimicry and antigen memory[,]" without presenting additional evidence of findings revealed by conducting BLAST searches.). Petitioner's case is more akin to *White* than *Forrest* in that Dr. Steinman's molecular mimicry theory and identified sequence homologies have been sufficiently developed and largely unrebutted as to *Althen* prong one. *See White,* 2019 WL 7563239, at *24; *Forrest,* 2019 WL 925495, at *1.

In addition, Dr. Steinman's theory regarding the notion of recall response with respect to *Althen* prong one has also been accepted in the Program. In *Quackenbush v. Sec'y of Health & Hum. Servs*., the special master found that Petitioner's receipt of flu vaccines in 2009 and 2011 made it more likely than not that Petitioner had a recall response to the 2013 flu vaccine, which contained several of the same components. No. 14-1000V, 2018 WL 1704523, at *23 (Fed. Cl. Mar. 14, 2018); *but see Rowan v. Sec'y of Health & Hum. Servs.*, No. 17-760V, 2020 WL 2954954, at *17 (Fed. Cl. Apr. 28, 2020) (finding that Dr. Steinman's recall response theory was insufficient to show that a recall to a previously-encountered antigen could occur as fast as 24 hours because "it is unlikely the pathologic period of the autoimmune response would progress enough to produce clinical symptoms immediately thereafter."). While prior decisions of special masters are not binding on my analysis, it is persuasive that Dr. Steinman's theories have been accepted as reputable, medical, or scientific mechanisms in similar Program cases. Therefore, I am not persuaded by Respondent's criticisms.

Dr. Steinman's purported theory accounts for how the flu vaccine can cause small vessel vasculitis. As I have already noted, Dr. Steinman suggested that small vessel vasculitis may be a preliminary condition to small fiber neuropathy following a cross-reactive immune response. However, he provided no medical literature to explain why immune cells and antibodies would *de facto* cause vasculitis. He also provided insufficient evidence to show that small vessel vasculitis is a common comorbidity to small fiber neuropathy. Petitioner remains unable to show by preponderant evidence that she suffers from small vessel vasculitis, and a discussion regarding this condition in the context of vaccine-caused injury is unnecessary.

Petitioner has provided a scientific or medical theory describing the flu vaccine's role in the development of small fiber neuropathy via molecular mimicry and the notion of recall response. As a result, Petitioner has met her burden by a preponderance of the evidence that the flu vaccine can cause small fiber neuropathy. Accordingly, I find Petitioner has satisfied prong one of *Althen.*

C. *Althen* Prong Two

Under the second prong of *Althen*, a petitioner must prove that the vaccine actually did cause the alleged injury in a particular case. *See Pafford*, 2004 WL 1717359, at *4; *Althen*, 418 F.3d at 1279. The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1380; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner does not meet this obligation by showing only a temporal association between the vaccination and the injury; instead, the petitioner "must explain *how* and *why* the injury occurred." *Pafford*, 2004 WL 1717359, at *4 (emphasis in original). The special master in *Pafford* noted petitioners "must prove [] both that her vaccinations were a substantial factor in causing the illness . . . and that the harm would not have occurred in the absence of the vaccination." 2004 WL 1717359, at *4 (citing *Shyface*, 165 F.3d at 1352). A reputable medical or scientific explanation must support this logical sequence of cause and effect. *Hodges v. Sec'y of Health & Hum. Servs.,* 9 F.3d 958, 961 (Fed Cir. 1993) (citation omitted). Nevertheless, "[r]equiring epidemiologic studies . . . or general acceptance in the scientific or medical communities . . . impermissibly raises a claimant's burden under the Vaccine Act and hinders the system created by Congress . . . ." *Capizzano*, 440 F.3d at 1325–26. "[C]lose calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F.3d at 1280.

In Program cases, contemporaneous medical records and the opinions of treating physicians are favored. *Capizzano*, 440 F.3d at 1326 (citing *Althen*, 418 F.3d at 1280). This is because "treating physicians are likely to be in the best position to determine whether 'a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" *Id.* In addition, "[m]edical records, in general, warrant consideration as trustworthy evidence. The records contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium. These records are also generally contemporaneous to the medical events." *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). While a special master must consider these opinions and records, they are not "binding on the special master or court." 42 U.S.C. § 300aa-13(b)(1). Rather, when "evaluating the weight to be afforded to any such . . . [evidence], the special master . . . shall consider the entire record . . . ." *Id.* The record often includes "evidence of possible sources of injury" that can show alternate causes for the alleged vaccine-related injury. *See Stone v. Sec'y of Health & Hum. Servs.,* 676 F.3d 1373, 1379 (Fed. Cir. 2012).

Petitioner's medical theory describes how "the immune response to alpha 3 nicotinic acetylcholine receptor triggered by molecular mimicry [to the components of the flu vaccine] would block a major suppressive pathway in the blood vessel wall, and predispose the Petitioner to vasculitic inflammation, and then subsequently to small-fiber neuropathy." Pet'r's Ex. 40 at 17. However, I have already concluded that Petitioner failed to show by preponderant evidence that she suffers from small vessel vasculitis. Therefore, I must determine whether Petitioner can satisfy *Althen* prong two in relation to her small fiber neuropathy diagnosis without providing preponderant evidence that she first suffered from small vessel vasculitis.

Dr. Steinman testified that "the traditional use of the word vasculitis . . . isn't critical for the theory." Tr. 149:8–9. But the way he used "vasculitis" in Petitioner's case is to refer to inflammation generally as an umbrella term, which is "necessary for molecular mimicry to work in her particular case[.]" Tr. 149:10–14. As I have already noted, there is no evidence in Petitioner's medical records or biopsy results that any traditional subcategory or version of small vessel vasculitis was present given Petitioner's clinical presentation. Petitioner's biopsy results did not show necrotizing small vessel vasculitis and her medical records failed to demonstrate that she experienced any other common manifestations of small vessel vasculitis such as fever, arthralgias, myalgias, and malaise. Instead, Petitioner's clinical presentation consisting of dysesthesias in the face, hands, and feet, was consistent with small fiber neuropathy alone. Therefore, Dr. Steinman's use of the word "vasculitis" to refer to inflammation generally, makes sense. Based on Dr. Steinman's theory, which, through the literature,[102] has been shown can result in neuroinflammation via molecular mimicry of the alpha3 AChRs that are associated with small fiber neuropathy specifically, it is more likely than not that Petitioner could have developed small fiber neuropathy without first developing small vessel vasculitis. Petitioner has presented preponderant evidence showing that the flu vaccine caused her small fiber neuropathy, separate and apart from small vessel vasculitis. Indeed, Petitioner's treaters attributed causation of her small fiber neuropathy to the flu vaccine without first diagnosing her with small vessel vasculitis, as discussed in more detail below. Petitioner's treating physicians based their opinions on her symptom presentation which showed evidence of inflammation and small fiber neuropathy, without evidence of small vessel vasculitis. Therefore, based on her medical record, I find that Petitioner's inability to show that she suffers from small vessel vasculitis does not preclude her ability to satisfy *Althen* prong two.

Petitioner's medical records and notations from treating physicians provide direct evidence of causation that is not based on a temporal association alone. *See Capizzano*, 440 F.3d at 1326 (citing *Althen*, 418 F.3d at 1280); *see also Pafford*, 2004 WL 1717359, at *4. A majority of Petitioner's treating physicians opined that her small fiber neuropathy was caused by her August 23, 2011 flu vaccine. For example, Dr. Purath noted on numerous occasions, including during her testimony, that she believed that Petitioner's small fiber neuropathy was caused by the flu vaccine she received on August 23, 2011. Pet'r's Ex. 10 ¶ 26; Pet'r's Ex. 2 at 29, 34, 37; Tr. 21:21–25. Dr. Marquez de Leon noted that "[t]he possibility of a reaction to her vaccination appears to be the most likely etiology[]" for Petitioner's small fiber neuropathy. Pet'r's Ex. 4 at 542. Dr. Barboi noted that Petitioner suffers from "[a]utonomic neuropathy, worse after flu vaccination or caused by it[.]" Pet'r's Ex. 9 at 227. However, it is true that Dr. Remler noted "[i]t is uncertain whether there is a causal relationship with a flu vaccination[,]" but still noted a temporal association, nonetheless. Pet'r's Ex. 6 at 10.

Petitioner's expert provided a medical theory showing that the components of prior flu vaccines Petitioner received in 2005, 2008, 2009, and 2010, mimicked the alpha3 AChR associated with small fiber neuropathy and induced a recall response to those same components following the 2011 Fluarix vaccine. He reasoned that this response likely triggered the immune cross-reaction to alpha3 AChR, resulting in Petitioner's small fiber neuropathy. I accept Dr. Steinman's theory regarding how the flu vaccine could have triggered Petitioner's small fiber neuropathy, and I find that his theory fits the facts of this case. Petitioner's symptom presentation was consistent with

[102] *See* Gautam, et al., *supra* note 54.

small fiber neuropathy as described in the Lacomis[103] article. Pet'r's Ex. 19 at 2. Indeed, her symptomology matched the clinical features of small fiber neuropathy described by Lacomis including tingling, burning, prickling, shooting pain, or aching. *Id.* For example, two days after her August 23, 2011 flu vaccine, she experienced tingling in her face, which moved into her arms, followed by numbness, weakness, and eventual radiating pain shooting into her buttocks. Pet'r's Ex. 2 at 37, 43. Petitioner was later diagnosed with small fiber neuropathy by Dr. Marquez de Leon in November 2011, having had several episodic symptoms following her flu vaccine. Pet'r's Ex. 4 at 542. Therefore, it is reasonable to conclude that Petitioner's August 23, 2011 flu vaccine provided the necessary trigger for the onset of her small fiber neuropathy.

Dr. Donofrio argued Dr. Steinman could not show the homologies he identified resulted in the production of autoantibodies against acetylcholine receptors resulting Petitioner's small fiber neuropathy. He stated that Dr. Steinman's "analysis makes logical sense as a theory and hypothesis, but its application to [P]etitioner . . . is speculative[,]" because her testing for antibodies did not detect those against acetylcholine receptors. Resp't's Ex. L at 2; Pet'r's Ex. 4 at 522, 725. Dr. Steinman agreed that this is a fair assessment and admitted that identifying the homologies was just the first step in the analysis. *See* Tr. 101:16–17, 128:15–17. Dr. Steinman repeatedly stated that he "would be really close to certainty about linking the molecular mimicry with the alpha 3 acetylcholine receptor, had they been positive[]" in Petitioner. Tr. 250:4–6. Dr. Donofrio found this fact to be conclusive evidence that Petitioner does not suffer from small fiber neuropathy as a result of the flu vaccine. I do not agree. In fact, it is difficult to consider Dr. Donofrio's argument regarding causation because of his appreciable reversal of his original conclusion that Petitioner did not suffer from small fiber neuropathy at all. Dr. Donofrio's significant concession undercuts any assertion previously made regarding his beliefs about why Petitioner's August 23, 2011 flu vaccine did not cause her small fiber neuropathy. Indeed, while the presence of these antibodies when tested would have been direct evidence that Petitioner's small fiber neuropathy was caused by the flu vaccine, Dr. Steinman has provided literature and documentation that demonstrates that Petitioner's use of Decadron, an immunosuppressive corticosteroid,[104] could have blocked or suppressed the test's ability to detect the relevant antibodies.

Dr. Steinman relied on pharmacokinetic and pharmacodynamic principles to explain that Petitioner's rather lengthy, 22-day, course of Decadron suppressed her antibodies for months after the treatment. First, Dr. Steinman explained that pharmacokinetics refers to "how long it takes for [the drug] to be out of your system[,]" Tr. 249:7, while "[p]harmacodynamics is how long the effects of the drug are lasting." Pet'r's Ex. 84 at 1. Next, Dr. Steinman established that Petitioner was indeed on Decadron for twenty-two days, not one week as Dr. Donofrio originally contended.[105] Petitioner's medical records show that on August 26, 2011, Dr. Purath placed her on 2mg Decadron, three times a day for seven days. Pet'r's Ex. 2 at 43. Dr. Purath noted that

[103] *See* Lacomis, *supra* note 44, at 173–88.

[104] Dr. Steinman relied on The Advisory Committee on Immunization Practices for the CDC to prove that Decadron is, in fact, an immunosuppressive corticosteroid. Pet'r's Ex. 81 at 3. He indicated that the CDC warns that "severe immunosuppression can be caused by large amounts of corticosteroids." Pet'r's Ex. 78 at 4.

[105] On cross-examination, Dr. Donofrio eventually admitted that Petitioner was on a 22-day course of Decadron. Tr. 216:1–22.

originally, Petitioner was to finish her course of treatment on September 1, 2011. However, on September 16, 2011, Dr. Purath noted that Petitioner "will be off of Decadron tomorrow [September 17, 2011]." *Id.* at 32. Her notes from September 29, 2011, reveal that Petitioner was "off the Decadron completely." *Id.* Therefore, Petitioner has shown by preponderant evidence that she was on Decadron for twenty-two days.

Dr. Steinman then described how this length of treatment with a corticosteroid could influence Petitioner's antibody testing over one month after her cessation of Decadron. Indeed, Dr. Steinman's explanation of pharmacokinetic and pharmacodynamic principles is dispositive. Dr. Steinman noted that Decadron is physically "gone from the system in a matter of days." Tr. 249:10–11. But, "it depletes your T cells and B cells and they come back very slowly. It takes weeks and months for, particularly the B cells[,] that are the antibody lineage[,] to come back." Tr. 249:19–22. Conversely, Dr. Donofrio stated that Decadron's duration of action is 36–54 hours, and that it would be out of one's system in a couple of weeks. Resp't's Ex. N at 1. Dr. Steinman's reliance on the Baris et al.[106] study, which noted that the immune suppressive reaction caused by extended corticosteroid use can last for months, even years, is advantageous to Petitioner's case. Pet'r's Ex. 78 at 2. The authors found that "[t]he change of B cells and B cell subtypes (CD27+ memory) shows prolonged effect of CSs [CS=corticosteroids] on B cells which may alter antibody production even after [three] months of CSs cessation." Pet. Ex. 79 at 2. The patients in the Baris et al. study were on daily corticosteroids for one month, followed by treatment every other day over the next month, which tapered completely by the third month. *Id.* As previously stated, Petitioner was on daily corticosteroids for twenty-two days. Based on this, it is more likely than not that Petitioner's antibody was below the level of detection on November 4, 2011, because her Decadron was likely still in her system one- and one-half months after cessation of treatment with a corticosteroid.

It is also important to note that in general, "even when [this antibody] is detected [in other patients], it's only about 50[%] of the time . . . even detected." Tr. 98:21–23, 213:19–25. Dr. Steinman provided persuasive support for this contention by citing an article by Vernino et al.,[107] which noted that '"[a]ntibodies that specifically bind to the ganglionic AChR are detectable in about 50% of patients[.]"' Pet'r's Ex. 78 at 1 (citing Pet'r's Ex. 69). He therefore opined that "it is not surprising that [Petitioner's test] was negative, from the steroid treatment done already on a background where in general 50% of cases are negative anyway in autoimmune autonomic ganglionopathy[.]" Pet'r's Ex. 78 at 2 (citing Pet'r's Ex. 69 at 3). Therefore, I find that Petitioner's negative antibody results do not undercut her ability to satisfy *Althen* prong two because there are multiple, reasonable explanations for why those results were negative.

Overall, Petitioner has established by a preponderance of the evidence that the flu vaccine administered on August 23, 2011, caused her to develop small fiber neuropathy. *See Capizzano*, 440 F.3d at 1326; *see also Althen*, 418 F.3d at 1280 (finding that "close calls regarding causation are resolved in favor of injured claimants."). Therefore, Petitioner has satisfied prong two of *Althen.*

[106] *See* Baris, et al., *supra* note 59, at 685–93.
[107] *See* Vernino, et al., *supra* note 48, at 63–69.

D. *Althen* Prong Three

Under the third prong of *Althen*, a petitioner must show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d at 1278. For example, if a petitioner's theory involves a process that takes several days to develop after vaccination, an injury that occurred within a day of vaccination would not be temporally consistent with that theory. Conversely, if the theory is one that anticipates a rapid development of a reaction post-vaccination, the development of the alleged injury weeks or months post-vaccination would not be consistent with that theory. *See de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). Causation-in-fact cannot be inferred from temporal proximity alone. *See Grant,* 956 F.2d at 1148; *Thibaudeau v. Sec'y of Health & Hum. Servs.*, 24 Cl. Ct. 400, 403–04 (1991); *see also Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1983) ("Without more, [a] proximate temporal relationship will not support a finding of causation").

Petitioner has met her burden with respect to *Althen* prong three. Dr. Steinman opined that Petitioner's tingling in her face at 4:00 pm on August 23, 2011, the same day that she received the flu vaccine, was the onset of her small fiber neuropathy. He stated that the "sentinel sign" of Petitioner's symptoms was between four- to- six- hours post-vaccination. Tr. 104:13, 135:2–3, 144:22–24. Dr. Steinman explained that such a rapid reaction, meaning within six hours, occurred in Petitioner's case because of the notion of recall response and her receipt of prior flu vaccines in 2005, 2008, 2009, and 2010. *See* Tr. 102:5–23. Dr. Steinman's reliance on the Lai et al.[108] article is convincing. The authors of the study analyzed memory cells and found that during a recall response reaction, memory cells can react "within six hours [of the vaccine.]" Pet'r's Ex. 77 at 4. The authors noted however, that naïve memory cells take approximately seventy-two hours to manifest a similar reaction. *See id.* Dr. Steinman's theory that Petitioner's prior flu vaccines provided immunological memories to the components of the 2011 Fluarix vaccine she received on August 23, 2011, which lead to a rapid recall response culminating in small fiber neuropathy within four- to- six- hours, is consistent with the filed literature.

Dr. Donofrio disagreed with Dr. Steinman and opined that the onset of Petitioner's symptoms was two weeks prior to her August 23, 2011 flu vaccine. Notably, after repeated questioning, Dr. Donofrio conceded that Petitioner's symptoms did not occur two weeks prior to her flu vaccine as he originally opined, but rather "all started after Tuesday night after she had a flu shot." Tr. 221:5–6, 222:3–10. This is yet another instance where Dr. Donofrio changed his opinion during the hearing. Therefore, I cannot give Dr. Donofrio's opinion regarding onset much, if any, weight.

Nonetheless, Dr. Donofrio indicated that he did not believe that the immune system can produce a response as quickly as Dr. Steinman suggested. Instead, he opined that such a process takes several days or a week to occur. Dr. Donofrio relied on the Langmuir et al.[109] study, which found that reported cases of GBS following a flu vaccination "did not occur until either day three or day four." Tr. 231:22–23; *see also* Resp't's Ex. G at 15, Fig. 1. Dr. Steinman, conversely, relied on the Schonberger et al.[110] study, which "described an increased incidence of [GBS] . . . even

[108] *See* Lai, et al., *supra* note 70, at 133–40.
[109] *See* Langmuir, et al., *supra* note 72, at 841–80.
[110] *See* Schonberger, et al., *supra* note 71, at 105–24.

within 0–1 day" of vaccination. Pet'r's Ex. 40 at 24 (citing Pet'r's Ex. 67 at 8). There was much discussion and contention between the experts regarding these two articles and the apparent discrepancy in the lag time of a manifestation of an autoimmune reaction following vaccination. The experts seemed to talk past each other and did not clarify if the difference of opinion contemplated initial exposure versus recall response. I acknowledge the disagreement between the experts, but I find Dr. Steinman's reliance on recall response controls here. I base my decision, in part, on Dr. Steinman's credentials and expertise in immunology and neuroimmunology specifically, as compared to Dr. Donofrio's focus in neurology. Notably, in relevant part, Dr. Steinman served as the Chairman of the Immunology Program at Stanford for approximately ten years from 2002 to 2011. Pet'r's Ex. 45 at 1. He also completed a post-doctoral fellowship in neuroimmunology. *Id.* His current clinical practice involves treating patients with neuroimmunological diseases. Tr. 80:20; 81:6. Therefore, based on Dr. Steinman's specified knowledge and understanding of immunology, I must afford his account of Petitioner's autoimmune reaction greater weight.

Dr. Steinman explained that based on the notion of recall response, memory T cells are primed and ready to cross-react within hours of receipt of a subsequent flu vaccine. Dr. Steinman noted this is possible, in part, because we have the innate immune system "for when our responses are naïve. Once we have memory, fortunately, we . . . get to fight it with adaptive immunity which comes on really fast." Tr. 139:18–21. Dr. Steinman's theory is applicable to Petitioner, as there is evidence in her medical records of an immune response occurring on the same day as her flu vaccine when she experienced tingling in her face around 4:00 pm while putting on makeup. *See, e.g.*, Pet'r's Ex. 2 at 46. I find it is more likely than not that Petitioner experienced a rapid recall reaction within four- to- six- hours of her August 23, 2011 flu vaccine, based on her exposure to prior flu vaccines in 2005, 2008, 2009, and 2010, which contained the same components as the 2011 Fluarix, such as B/Brisbane/60/2008, for example. Petitioner's prior flu vaccines provided the requisite immunological memories to trigger an immune reaction within only a few hours of her subsequent flu vaccine on August 23, 2011.

As further support, Dr. Steinman's theory that a rapid recall response can occur within hours of exposure to a subsequent flu vaccine with similar components, has been previously accepted in the Program with respect to *Althen* prong three. In *Quackenbush*, Petitioner received flu vaccines in 2009, 2011, and the vaccine at issue in 2013. 2018 WL 1704523, at *27–28. The special master found that "[w]hile the rapid onset of [P]etitioner's symptoms [within forty hours of the vaccine] is somewhat unusual, the fact of the likelihood of a recall response to a strain of the flu vaccine which [P]etitioner had received before provides a reasonable and logical explanation." *Id.* at *28; *but see Rowan,* 2020 WL 2954954, at *17 (finding that there was insufficient evidence to support the fact that a recall response to a flu vaccine would occur within 24 hours simply because the petitioner received prior flu vaccines in previous years.). The Petitioner in *Quackenbush* received two flu vaccines in prior years and experienced onset of symptoms within forty hours of a subsequent flu vaccine with similar components. Petitioner's case is not identical to *Quackenbush*, as she received four flu vaccines in prior years and experienced the onset of her symptoms within four- to- six- hours of her subsequent flu vaccine. However, it is similar. Based on Dr. Steinman's theory, it is logical that Petitioner's exposure to flu vaccines in years past provided immunological memory cells, analogous to the Petitioner in *Quackenbush*, which resulted in a manifestation of her recall response to the similar components contained in the 2011 Fluarix on August 23, 2011.

Aside from the concept of "recall response," Respondent's expert admitted that even though he does not believe the onset of Petitioner's small fiber neuropathy occurred within hours of receiving the flu vaccine, such a rapid onset can be explained if her small fiber neuropathy is autoimmune. Specifically, Dr. Donofrio testified that "theoretically," if a small fiber neuropathy is autoimmune, the disease could manifest within hours after the body began to attack itself. Tr. 230:8–19. He clarified under re-direct that he "think[s] it's highly unlikely [this w]ould occur." Tr. 237:18–23. Thus, while I have already determined that Petitioner's small fiber neuropathy is autoimmune in nature, I find it is more likely than not that the onset of Petitioner's small fiber neuropathy occurred within four- to- six- hours of her August 23, 2011 flu vaccine.

Furthermore, the four- to- six- hour time period for onset established by Dr. Steinman is an appropriate and medically acceptable temporal relationship between the flu vaccine and Petitioner's autoimmune reaction. Based on the theory of recall response and Petitioner's receipt of flu vaccines in previous years which contained similar components to the 2011 Fluarix, it is more likely than not that she had ample memory cells to the components of prior flu vaccines, which could have reacted within hours of her receipt of the 2011 Fluarix on August 23, 2011.

I find that Petitioner has presented preponderant evidence to establish that four- to- six-hours is an appropriate timeframe for vaccine-induced small fiber neuropathy to occur following recall response in Petitioner's case. Therefore, she has satisfied her burden under *Althen* prong three.

E. Alternative Causes

If a petitioner presents a prima facie case, the Federal Circuit has held that the burden of proof shifts to the government, and Respondent must prove that the "'injury . . . described in the petition is due to factors unrelated to the . . . vaccine.' 42 U.S.C. § 300aa-13(a)(1)(b)." *Knudsen,* 35 F.3d at 547. Yet, a petitioner's failure to prove any element of his prima facie case mandates that the Court deny entitlement. *See id.* Under such circumstances, the burden of proof does not shift to the respondent to establish an alternate cause for the petitioner's claimed injury. *Althen,* 418 F.3d at 1278; *see also Bradley v. Sec'y of Health & Hum. Servs.,* 991 F.2d 1570, 1575 (Fed. Cir. 1993). However, in considering the reliability of a petitioner's evidence of a prima facie case, the special master may consider alternative causes for a petitioner's condition that are reasonably raised in the record, even if the respondent does not pursue a formal alternative cause argument. *Doe v. Sec'y of Health & Hum. Servs.,* 601 F.3d 1349, 1358 (Fed. Cir. 2010). Thus, in weighing a petitioner's case-in-chief, a special master may consider evidence that the petitioner's alleged injury could have been caused by alternative causes. *Id.*

In this case, Petitioner has established a prima facie case for compensation and has established her burden under *Althen.* Therefore, Respondent has the burden to prove Petitioner's injuries were caused by something other than her August 23, 2011 flu vaccine. *See LaLonde,* 746 F.3d at 1340. However, Respondent has been unable to do so. Respondent's expert, Dr. Donofrio, proffered an extensive list of potential alternative causes for Petitioner's small fiber neuropathy including but not limited to:

diabetes, borderline diabetes, connective tissue disorders such as lupus, HIV

> infection, sarcoidosis, thyroid disease, vitamin B1, B6, and B12 deficiency, paraproteinemias, celiac disease, neurotoxic drug exposure, environmental toxins, paraneoplastic, chronic alcohol abuse, amyloidosis, erythromelalgia, hypertriglyceridemia, Lyme disease, leprosy, restless leg syndrome, Sjogren syndrome, hepatitis C, inherited neuropathies, Fabry's disease[,] and Tangiers disease.

Resp't's Ex. L at 3. Yet, after extensive questioning, he admitted that, out of the many alternative causes of small fiber neuropathy, he could not testify as to which one, if any, caused Petitioner's injury. Tr. 198:19–22. Dr. Donofrio's testimony that the cause of Petitioner's small fiber neuropathy was not vaccine-related but, instead, could have been caused by a seemingly endless list of other conditions is problematic in that he was trying to argue that anything other than the flu vaccine was responsible for causing Petitioner's small fiber neuropathy. Respondent has failed to identify any one condition that could present as small fiber neuropathy or that caused Petitioner's disease. Therefore, Respondent has failed to show by preponderant evidence that Petitioner's small fiber neuropathy was caused by an alternative cause.

VI. Experts

Although special masters have the discretion to rely on past rulings and experiences, case-specific filings and testimony are the most helpful types of evidence, given the fact-specific nature of each decision. *See Doe v. Sec'y of Health & Hum. Servs.*, 76 Fed. Cl. 328, 338–39 (2007). To that end, experts are an essential piece of a petitioner's claim and Respondent's defense. A petitioner's burden is to show causation by a preponderance of the evidence, not absolute certainty. Once that burden is met, Respondent must effectively rebut that evidence in order for a petitioner's claim to fail. *Knudsen,* 35 F.3d at 547. This case ultimately turned not only on Petitioner's medical history, but also the persuasiveness of the written reports, supporting documentation, and expert testimony. Dr. Donofrio is an extremely qualified expert in his field. He has a history of providing useful testimony and persuasive explanations in cases before me, as well as other special masters in the Program. In this case however, his ultimate opinion was delivered with multiple concessions and reversals that significantly undermined his credibility. *See Broekelschen*, 618 F.3d at 1347 (citing *Lampe*, 219 F.3d at 1362) (finding that where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories."). Despite the issues in Petitioner's case, Dr. Steinman's consistency, acknowledgment of the unknown, and expertise in immunology is more persuasive here.

VII. Conclusion

Petitioner has established by preponderant evidence that the flu vaccine she received on August 23, 2011, was the cause-in-fact of her small fiber neuropathy. The evidence in the record supports a finding that, more likely than not, molecular mimicry and antigen memory caused Petitioner's small fiber neuropathy following her 2011 Fluarix vaccine. The record shows by preponderant evidence that Petitioner experienced the onset of her symptoms within four- to- six-hours of the flu vaccine because of the rapid recall response that was established by her receipt of flu vaccines in previous years. Therefore, the evidence Petitioner presented has demonstrated entitlement to compensation. This case shall proceed to damages.

IT IS SO ORDERED.

s/Herbrina D. Sanders
Herbrina D. Sanders
Special Master