In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 17-1915V
Filed: September 20, 2024

ANGELA APUZZO,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

Special Master Horner

Ronald Craig Homer, Conway, Homer, P.C., Boston, MA, for petitioner.
Debra A. Filteau Begley, U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

On December 8, 2017, petitioner filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10, *et seq.* (2012),[2] alleging that she suffered chronic inflammatory demyelinating polyneuropathy ("CIDP") as a result of an influenza ("flu") vaccine administered on September 17, 2015. (ECF No. 1.) For the reasons set forth below, I conclude that petitioner is *not* entitled to an award of compensation.

I. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations, including showing that an individual received a vaccination covered by the statute;

[1] Because this document contains a reasoned explanation for the action taken in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the document will be available to anyone with access to the internet.** In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, I agree that the identified material fits within this definition, I will redact such material from public access.

[2] All references to "§ 300aa" below refer to the relevant section of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury.

In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table. If so, the Table Injury is presumed to have been caused by the vaccination unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B). In many cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table. In such instances, an alternative means exists to demonstrate entitlement to a Program award. That is, the petitioner may gain an award by showing that the recipient's injury was "caused-in-fact" by the vaccination in question. § 300aa-13(a)(1)(B); § 300aa-11(c)(1)(C)(ii). In such a situation, of course, the presumptions available under the Vaccine Injury Table are inoperative. The burden is on the petitioner to introduce evidence demonstrating that the vaccination actually caused the injury in question. *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines ex rel. Sevier v. Sec'y of Health & Human Servs.*, 940 F.2d 1518, 1525 (Fed. Cir. 1991).

The showing of "causation-in-fact" must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); *see also Althen*, 418 F.3d at 1279; *Hines*, 940 F.2d at 1525. Under that standard, the petitioner must show that it is "more probable than not" that the vaccination was the cause of the injury. *Althen*, 418 F.3d at 1279. The petitioner need not show that the vaccination was the sole cause but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition, and was a "but for" cause. *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). Thus, the petitioner must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury[,]" with the logical sequence being supported by "reputable medical or scientific explanation, *i.e.*, evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F.3d at 1278; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). Ultimately, petitioner must satisfy what has come to be known as the *Althen* test, which requires: (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 proximate temporal relationship between vaccination and injury. *Id*.

A petitioner may not receive a Vaccine Program award based solely on his or her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1). Medical records are generally viewed as particularly trustworthy evidence, because they are created

contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. § 300aa-13(b)(1). A petitioner may also rely upon circumstantial evidence. *Althen*, 418 F.3d at 1280. The *Althen* court noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279-80. While scientific certainty is not required, that expert's opinion must be based on "sound and reliable" medical or scientific explanation. *Boatmon v. Sec'y of Health & Human Servs*., 941 F.3d 1351, 1359 (Fed. Cir. 2019).

Cases in the Vaccine Program are assigned to special masters who are responsible for "conducting all proceedings, including taking such evidence as may be appropriate, making the requisite findings of fact and conclusions of law, preparing a decision, and determining the amount of compensation, if any, to be awarded." Vaccine Rule 3. Special masters must ensure each party has had a "full and fair opportunity" to develop the record but are empowered to determine the format for taking evidence based on the circumstances of each case, including having the discretion to decide cases without an evidentiary hearing. Vaccine Rule 3(b)(2); Vaccine Rule 8(a); Vaccine Rule (d). Special masters are not bound by common law or statutory rules of evidence but must consider all relevant and reliable evidence in keeping with fundamental fairness to both parties. Vaccine Rule 8(b)(1). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." § 300aa-13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Human Servs*., 3 F.3d 413, 417 (Fed. Cir. 1993).

In this case, petitioner has alleged that the flu vaccine caused CIDP. CIDP is not listed on the Vaccine Injury Table relative to the flu vaccine. Therefore, petitioner must satisfy the above-described *Althen* test for establishing causation-in-fact.

II. Procedural History

This case was initially assigned to another special master. (ECF No. 4.) It was reassigned to the undersigned on August 29, 2019. (ECF No. 69.)

Petitioner filed her medical records between January of 2017 and January of 2018. (ECF Nos. 11-12, 17, 21, 31, 37, 39, 44, 48; Exs. 1-16, 18-27, 30-41.) She also filed three affidavits. (ECF Nos. 13, 23; Exs. 17, 28-29.) Initially the parties attempted informal resolution; however, settlement discussions were halted when respondent concluded that later filed medical records reflected a change in petitioner's diagnosis. (ECF Nos. 33, 43.) Respondent filed his Rule 4 report in February of 2019,

recommending against compensation. (ECF No. 50.) Respondent argued that petitioner's medical records alone were inadequate to meet petitioner's burden of proof with respect to any vaccine-caused CIDP, but also contended that petitioner's more recent medical records indicated her physicians had begun to conclude her condition was actually explained by systemic lupus erythematosus ("SLE") and Sjögren's syndrome, rather than CIDP. (*Id*. at 11-12.)

In the summer of 2019, petitioner filed an expert report by neurologist Nizar Souayah, M.D., along with supporting materials. (ECF Nos. 58-65; Exs. 42-100.) Dr. Souayah opined that petitioner most likely suffered CIDP and that her condition was vaccine-caused. (Ex. 42, p. 28.) In December of 2019, petitioner filed additional medical records marked as Exhibit 101. (ECF No. 71.) Respondent filed responsive reports by neurologist Brian Callaghan, M.D., and rheumatologist Robert Lightfoot, Jr., M.D., in February of 2020. (ECF Nos. 74-75; Exs. A-D.) Dr. Callaghan opined that petitioner did not have CIDP. (Ex. A, p. 4.) Dr. Lightfoot opined that petitioner's presentation is consistent with an incomplete form of Sjögren's syndrome, but that he could not "unequivocally" state that she does have it. (Ex. C, pp. 5-6.) Thereafter, petitioner filed additional medical records (Exhibits 102-03) and a report by rheumatologist Samar Gupta, M.D., as well as a supplemental report by Dr. Souayah, with supporting materials (Exhibits 104-49). (ECF Nos. 76, 78, 84, 86-89.) Dr. Gupta opined that petitioner likely had an incomplete form of Sjögren's syndrome and that her neuropathy, whether CIDP or small fiber neuropathy, was likely related. (Ex. 104, p. 4.) In his supplemental report, Dr. Souayah responded to Dr. Callaghan and, although he maintained that petitioner suffered CIDP, he also observed that she had small fiber neuropathy. (ECF No. 84; Ex. 111.)

In November of 2020, I held a Rule 5 conference. (ECF No. 91.) I expressed concern that the expert reports to date had effectively been siloed by discipline and, given that petitioner had not alleged vaccine-caused Sjögren's syndrome, that the parties' rheumatology opinions appeared to be mismatched to their respective positions. I directed the parties to have their experts clarify their opinions, by explaining the case "holistically and with an interdisciplinary approach," and directed petitioner to clarify whether she is alleging vaccine-caused CIDP to the exclusion of Sjögren's syndrome; vaccine-caused CIDP in the presence of unrelated Sjögren's syndrome; Sjögren's syndrome with associated, but vaccine-caused, neuropathy; or vaccine-caused Sjögren's syndrome. (*Id.*)

In April of 2021, petitioner filed supplemental expert reports responsive to my Rule 5 order. (ECF No. 95; Exs. 150-51.) Dr. Gupta deferred to Dr. Souayah regarding the nature of petitioner's neuropathy, but maintained that petitioner also had incomplete Sjögren's syndrome and that the "mosaic of autoimmunity" therefore best describes her overall condition. (Ex. 151.) Dr. Souayah maintained that petitioner initially had CIDP, but indicated that it may have evolved into small fiber neuropathy. He deferred to Dr. Gupta regarding the presence of Sjögren's syndrome. He indicated that his opinion regarding vaccine-caused CIDP and small fiber neuropathy is compatible with Dr. Gupta's invocation of the mosaic of autoimmunity. (Ex. 150.) Respondent filed a

responsive expert report by Dr. Callaghan in December of 2021. (ECF No. 111; Ex. E.) Dr. Callaghan maintained that petitioner did not suffer CIDP and further opined that petitioner did not have small fiber neuropathy. (Ex. E.)

Petitioner then filed updated medical records (Exhibits 152-56) between May and October of 2022, as well as additional affidavits (Exhibits 157-58). (ECF Nos. 117, 124, 126, 134-35.) Respondent requested an opportunity to have Dr. Callaghan submit an opinion reviewing the updated medical records and also requested the opportunity to substitute an opinion by rheumatologist Mehrdad Matloubian, M.D., Ph.D., in place of Dr. Lightfoot. (ECF No. 132.) Although petitioner objected to the substitution of experts (ECF No. 133), I allowed respondent to complete the requested filings after confirming that Dr. Lightfoot had become unavailable to respondent as a result of winding down his practice and participation in the program (ECF No. 137). Respondent filed reports by Drs. Callaghan and Matloubian in October and November of 2022. (ECF Nos. 139-40; Exs. F-H.) Dr. Callaghan maintained his view, based on his review of the updated medical records. (Ex. F.) Dr. Matloubian opined that petitioner had Sjögren's syndrome unrelated to vaccination and that any neuropathy was attributable to that condition. (Ex. G, pp. 8-9.) Petitioner then filed further updated medical records (Exhibits 159-60) and a further report by Dr. Gupta responding to Dr. Matloubian's report (Exhibit 161). (ECF Nos. 143, 146.) Dr. Gupta maintained his previously stated opinion. (Ex. 161.)

An entitlement hearing had been set for November of 2023 (ECF No. 131); however, in June of 2023, the parties filed a joint status report expressing a preference for proceeding with a ruling on the written record in lieu of any hearing and confirming that the expert presentations were complete (ECF No. 149). Accordingly, the hearing was cancelled. (ECF No. 150.) Petitioner filed her motion for a ruling on the record on September 5, 2023. (ECF No. 152.) Respondent filed his response on October 13, 2023, and petitioner filed a reply on October 30, 2023. (ECF Nos. 154-55.)

This matter is now ripe for resolution as to entitlement. I have concluded that the parties have had a full and fair opportunity to develop the record and that it is appropriate to resolve this case without an entitlement hearing. S*ee Kreizenbeck ex rel. C.J.K. v. Sec'y of Health & Human Servs*., 945 F.3d 1362, 1366 (Fed. Cir. 2020) (citing *Simanski v. Sec'y of Health & Human Servs*., 671 F.3d 1368, 1385 (Fed. Cir. 2012)); *see also* Vaccine Rule 8(d); Vaccine Rule 3(b)(2).

III. Factual History

a. As reflected in the medical records

Petitioner received the flu vaccine at issue on September 17, 2015. (Ex. 1, pp. 1-2.) On October 5, 2015, she was seen in the emergency department with complaints of numbness and tingling in her hands, feet, and the right side of her face. (Ex. 2, pp. 4-5.) She indicated that she had experienced a "short viral-like illness" following her flu vaccination and that her numbness began about four days prior to her emergency department encounter, around the time she had a blood draw. (*Id*. at 5.) Upon physical

exam, she had normal reflexes, muscle tone, strength, and gait. (*Id*. at 6-7.) Neurologic exam further confirmed full strength and normal reflexes in the extremities, as well as normal gait. (*Id*. at 12-13.) However, she had slightly decreased sensation at the fifth cranial nerve in a V2 distribution and some sensation changes her hands and feet. (*Id*.) Petitioner was felt to have mild peripheral neuropathy. (*Id*. at 16.) Hypothyroidism was suspected as a cause; however, an outpatient neurology follow up was recommended to further investigate the cause of petitioner's neuropathy. (*Id*.)

Petitioner followed up first with her primary care provider (Ex. 11, p. 60) and then with a neurologist, Dr. Bronfin, on October 28, 2015 (Ex. 6, p. 4). Dr. Bronfin reviewed petitioner's history prior to her emergency department encounter and then explained:

> Patent presents with complain[t] of weakness in her hands. Patient has difficulties [using] her thumbs. Patient noticed diminished dexterity. Patient reports having pain in her shoulder blades. Patient continues having numbness in her feet. She recently developed balance difficulties. Patient denies weakness. Patient does not feel heat. Patient has difficulties [walking] and uses a c[ane]. Patient reports slow gait.

(*Id*.) On physical exam, petitioner's reflexes were absent at the ankle, normal at the knee, and reduced in the upper extremities. (*Id*. at 6.) Her plantar reflexes (Babinski sign) were normal. (*Id*.) Her gait was ataxic. (*Id*.) Petitioner underwent NCS/EMG, which showed "neurophysiologic evidence for acute moderate predominantly motor demyelinating peripheral polyneuropathy." (*Id*. at 1.) Dr. Bronfin diagnosed Guillain-Barré Syndrome ("GBS") and peripheral demyelinating neuropathy. (*Id*. at 6-7.)

Petitioner returned to the emergency department for treatment of her GBS the same day. (Ex. 2, p. 91.) Petitioner was transferred to inpatient neurology for observation. (*Id*. at 99-100.) At the hospital, petitioner's EMG was characterized as "nonspecific" and so additional work up was pursued. (*Id*. at 91.) A lumbar puncture was attempted to confirm GBS, but was unsuccessful. During the hospitalization, petitioner's blood results were significant for positive antinuclear antibodies ("ANA") and elevated anti-Sjögren's syndrome-related antigen A antibodies ("SSA") (also called anti-"Ro" antibodies). (*Id.* at 92.) Therefore, petitioner had a consult to address "[p]ossible [Sjögren's] syndrome in the setting of neuropathy." (*Id.* at 132.) Petitioner reported a history of arthritis in her PIPs[3] and MCPs,[4] as well as morning stiffness and intermittent swelling of these joints. Petitioner reported relief with prednisone, which she was taking

[3] Proximal interphalangeal ("PIP") joints are the interphalangeal joints located proximally on any digit. *Proximal interphalangeal joint*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=83592 (last visited Sept. 4, 2024).

[4] Metacarpophalangeal ("MCP") joints, or "the knuckles," are the articulations between the metacarpus and the phalanges. *Metacarpophalangeal (MCP)*, STEDMAN'S MEDICAL DICTIONARY (28th ed., 2006).

for asthma. (*Id*.) Given her history of arthritis[5] and positive SSA, as well as the fact that GBS was not definitively diagnosed, rheumatology considered Sjögren's syndrome as a possible explanation for petitioner's peripheral neuropathy and recommended continuing to treat for GBS while monitoring for Sjögren's syndrome. (*Id*. at 135.) During hospitalization, petitioner was treated with four rounds of plasmapheresis, which petitioner reported had made her feel better, though she complained of side effects. (*Id*. at 91, 94, 163-64.) However, rheumatology noted that improvement with plasmapheresis does not necessarily support the GBS diagnosis. (*Id*. at 136.) Thus, it was felt that petitioner should be further evaluated by Dr. Bronfin regarding her correct diagnosis because she "never lost reflexes as is more typical in GBS." (*Id*. at 94.) Outpatient rheumatology follow up to evaluate for Sjögren's syndrome was also recommended. (*Id*. at 136.) Petitioner was discharged on November 3, 2015, with diagnoses of GBS and peripheral demyelinating neuropathy. (*Id*. at 91.)

Petitioner returned to Dr. Bronfin on November 17, 2015. (Ex. 6, p. 10.) Petitioner reported that she felt stronger and with improved balance, but continued to complain of numbness, tingling, and tremor. She reported being unable to walk for long distances, requiring the use of a wheelchair at times. (*Id*. at 11.) Dr. Bronfin maintained his diagnoses of GBS and peripheral demyelinating neuropathy, but also added Sjögren's syndrome to his assessment. (*Id.* at 14.) Dr. Bronfin recommended IVIG infusion (Gammunex 200 gm), which petitioner underwent beginning December 1, 2015. (*Id.*; Ex. 20, pp. 47-58.) Petitioner returned to Dr. Bronfin on December 14, 2015, and January 5, 2016, and reported continued improvement with physical therapy and IVIG treatment, though she had some side effects from the IVIG. (Ex. 6, pp. 16, 21; *see also* Ex. 12, pp. 27-44 (physical therapy records).) By January 5, 2016, she reported being able to ambulate without assistance. (Ex. 6, p. 21.)

On January 19, 2016, petitioner had an initial evaluation with a rheumatologist, Dr. Lee. (Ex. 15, p. 1.) In addition to her positive ANA and SSA and suspected GBS, petitioner's history included osteoarthritis affecting her knees and hips and a prior left-side carpal tunnel release. (*Id*.) However, it was noted that petitioner did not have any symptoms of systemic lupus erythematosus ("SLE"). (*Id*.) Petitioner was assessed as "ANA positive" and it was further noted that she was "Ro+." (*Id*. at 5.) Dr. Lee noted that Sjögren syndrome can present with peripheral neuropathy in the absence of the more classic sicca symptoms[6] of Sjögren's syndrome; however, given petitioner's response to treatment for GBS, he recommended deferring any further, more invasive,

[5] Pertinent to the expert discussion that follows, petitioner argues, however, that bloodwork of January 31, 2012, confirmed that she was negative for antinuclear antibodies and smooth muscle antibodies prior to the vaccination at issue. (ECF No. 152, p. 6 (citing Ex. 21, p. 21).)

[6] Sicca syndrome is characterized as keratoconjunctivitis (*i.e*. dryness and inflammation of eye) and xerostomia (*i.e*. dryness of the mouth) without connective tissue disease. *Sicca syndrome*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=111399 (last visited Sept. 4, 2024); *Keratoconjunctivitis*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=26840 (last visited Sept. 4, 2024); *Xerostomia*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=53881 (last visited Sept. 4, 2024).

workup, which would include lip/muscle/nerve biopsy. (*Id*.) Petitioner was to follow up for a biopsy if she experienced any recrudescence or flare of her condition. (*Id*.)

Petitioner then returned to Dr. Bronfin on February 1, 2016. (Ex. 6, p. 26.) She felt her weakness was increasing and she was experiencing acute shortness of breath. (*Id*.) Dr. Bronfin felt her neurologic exam was stable, but that an emergency department evaluation for her shortness of breath was necessary. (*Id.*) He also recommended that petitioner resume IVIG for her acute demyelinating neuropathy. (*Id*.) Petitioner was then admitted for an overnight stay at the hospital. The history explains that, following her IVIG treatment the prior December, petitioner had only residual numbness in her hands and feet. (Ex. 3, p. 89.) She returned to care due to fatigue, shortness of breath, and low endurance. She also complained of chest tightness radiating to her neck. (*Id*.) However, her neurologic exam confirmed that she had intact reflexes and was not weak in her extremities. (*Id*.) It was noted that "[h]er neuro exam is currently normal in terms of not being Guillain-Barre," given that she had residual neuropathy but no acute muscle weakness with reflexes present. (*Id*. at 90.) Petitioner was felt to be clinically stable neurologically, and her shortness of breath and fatigue were believed to be unlikely related to her neurologic condition. A cardiology and pulmonary consultation was recommended, as well as a second EMG, to assess for CIDP. (*Id*.) Petitioner returned to Dr. Bronfin on March 8, 2016, complaining of extremity weakness, poor balance, and shortness of breath, noting that her condition "is not improving." (Ex. 6, p. 31.) Dr. Bronfin recommended further IVIG and his diagnostic impression, including Sjogren's syndrome, GBS, and peripheral demyelinating neuropathy, did not change. (*Id*. at 31, 34.) Petitioner subsequently had IVIG treatment on March 12 and 15, 2025. (Ex. 20, pp. 94, 102.)

Petitioner sought evaluation by a neuromuscular specialist, Dr. Busono, on March 21, 2016. (Ex. 7, p. 5.) It was noted that her treating neurologists now disagreed as to whether she had GBS or CIDP. (*Id*.) As with prior exams, petitioner had decreased sensation in her feet, though her upper limbs were normal. (*Id*. at 7.) She had normal strength in all extremities and her reflexes were normal. (*Id*.) Dr. Busono assessed CIDP and suggested that autonomic dysfunction, as can be seen in CIDP, might explain petitioner's shortness of breath. (*Id*.) He recommended a repeat EMG and NCS. (*Id*.) Petitioner returned to Dr. Busono on April 12, 2016, for electrodiagnostic testing to evaluate for CIDP. (*Id*. at 9-10.) The EMG and NCS results were normal, and the study showed no evidence of a generalized polyneuropathy. (*Id*. at 10.) Petitioner reported that her energy and endurance improved with IVIG, but her balance remained poor and she was having memory and concentration issues. (*Id*. at 3.) Despite the negative electrodiagnostic test, Dr. Busono maintained his CIDP diagnosis and recommended continued IVIG treatment, as well as neuropsychological testing. (*Id*. at 4.) Petitioner followed up again with Dr. Busono in early June of 2016. (*Id*. at 1-2.) She reported that she was not improving with IVIG and had additionally developed allodynia. (*Id*. at 1.) Accordingly, Dr. Busono noted that he was "beginning to doubt the diagnosis of CIDP" and referred petitioner for a second opinion by neuromuscular specialist, Dr. Brannagan. (*Id*. at 2.) IVIG was discontinued. (*Id*.)

Petitioner then began consulting neurologist, Dr. Kapur, in August of 2016. (Ex. 8, pp. 8-13.) Dr. Kapur felt petitioner's symptoms and examination were consistent with CIDP. (*Id*. at 13.) He recommended continuing IVIG and physical therapy, prescribed gabapentin, and ordered bloodwork. (*Id.*) Petitioner was to follow up after he obtained her EMG records.[7] (*Id.*) Petitioner returned to Dr. Kapur on October 4, 2016. (*Id.* at 1.) Comparing petitioner's first and second EMG/NCS studies, Dr. Kapur was concerned the second study could have resulted from a technical error; however, he also noted that petitioner's September 12, 2016 bloodwork also continued to show positive Anti-SSA. He concluded that petitioner's symptoms and neurologic exam could be consistent with either CIDP or small fiber neuropathy related to Sjögren's syndrome. (*Id.* at 6.) He recommended continuing petitioner's treatment plan and following up in a month to consider whether to repeat the EMG/NCS. (*Id.* at 6-7.) He added Sjögren's-related small fiber neuropathy to petitioner's problem list. (*Id.* at 7.)

On February 3, 2017, petitioner had an evaluation with another neurologist, Dr. Vukic. (Ex. 5, pp. 9-12.) Petitioner presented (in a wheelchair) with a chief complaint of CIDP and described having persistent waxing and waning weakness and numbness accompanied by overriding fatigue and exertion-related shortness of breath. (*Id*.) Petitioner also reported short-term memory problems. (*Id*.) Physical exam showed unsteady gait, near normal strength, and absent Achilles reflexes. (*Id*. at 11.) Dr. Vukic felt petitioner's presentation was consistent with CIDP, but ordered further work up including additional lab work, an MRI of the brain and EEG, and possibly a lumbar puncture. (*Id*. at 12.) Petitioner underwent MRI of the brain on February 4, 2017. (*Id*. at 14-15.) There was no acute abnormality, but petitioner had patchy foci of T2 prolongation, potentially consistent with either minimal chronic microangiopathic changes or chronic demyelination. (*Id*. at 15.) Two days later, an EEG was normal. (*Id*. at 16.) Petitioner also underwent a third EMG/NCS study on February 13, 2017. (*Id*. at 19.) EMG showed "mild right median mononeuropathy at the wrist consistent with a clinical diagnosis of carpal tunnel syndrome with a superimposed evidence of absent F response minimal latencies in the left peroneal nerve." (*Id*. at 1, 19.) Petitioner then had a lumbar puncture on February 28, 2017. (*Id*. at 17-18.) The results were normal. (Ex. 4, p. 143.) Dr. Vukic felt the lumbar puncture results were "limited" and may need to be repeated. He felt the unremarkable EMG was likely attributed to petitioner's response to treatment. (Ex. 5, p. 4.) The diagnosis of CIDP was maintained. (*Id*.)

On August 22, 2017, petitioner saw another neurologist, Dr. Ma. (Ex. 16, pp. 254-58.) After reviewing petitioner's history, Dr. Ma felt that petitioner was experiencing gait dysfunction due to sensory ataxia and dysesthesias from neuropathic pain, both of which would be related to CIDP. However, "it is also quite likely that patient has a superimposed predominantly sensory metabolic axonal polyneuropathy, possibly in

[7] Of note, the history documented by Dr. Kapur indicates that petitioner did not bring her recent NCS/EMG results with her, but she reported that they were consistent with CIDP. (Ex. 8, p. 8.) However, although Dr. Busono maintained the CIDP diagnosis following the electrodiagnostic testing, he interpreted the study results as normal. (Ex. 7, p. 10.)

association with Sjogren's syndrome and/or hypothyroidism, which is likely also contributing to her neuropathy-related issues." (*Id*. at 258.)

About a month later, petitioner was admitted to the hospital from September 22 to 25, 2017, for worsening weakness, fatigue, and shortness of breath. (Ex. 16, p. 26.) She was admitted again from October 2 to 8, 2017. (Ex. 4, p. 196.) The neurology impression included both CIDP exacerbation and Sjögren's syndrome.[8] (*Id*. at 210.) In a follow up, petitioner returned to Dr. Vukic, who felt petitioner had improved after treatment with plasmapheresis during her hospitalization. Petitioner was to resume IVIG and follow up in six weeks. (Ex. 30, pp. 5-8.) A month later, petitioner reported to Dr. Vukic that her leg numbness and facial dysesthesias was worsening despite her ongoing IVIG, though her overall strength was improving. (*Id.* at 9.) She wanted to stop treatment and consider alternatives, such as Imuran or CellCept. (*Id*.) Dr. Vukic stopped petitioner's IVIG, but required a repeat EMG and lumbar puncture before considering whether to start Imuran. (*Id*. at 12.) As of January 8, 2018, petitioner reported worsening lower extremity pain and profound fatigue. (*Id*. at 16.) She requested an additional course of in-patient plasmapheresis and proposed having a lumbar puncture at that time. She noted that she intended to see Dr. Brannagan (as previously recommended by Dr. Busono) in April 2018 for a second opinion as to diagnosis and future treatment. (*Id.*) Dr. Vukic agreed with that plan and noted that he had concerns regarding petitioner's differential diagnosis. (*Id*. at 19.) Petitioner was then admitted for treatment from January 9 to 16, 2018. (Ex. 37, p. 24.) Petitioner felt her pain and strength improved after plasmapheresis and petitioner ultimately declined to complete the lumbar puncture. (*Id*.) It was recommended that petitioner seek an outpatient rheumatology evaluation for her Sjögren's syndrome. (*Id*. at 165.) Dr. Vukic agreed to continue plasmapheresis treatments pending petitioner's second opinion from Dr. Brannagan. (Ex. 30, p. 24.)

Petitioner presented to Dr. Brannagan on February 14, 2018, for an EMG/NCS study. (Ex. 24, pp. 10-11.) Dr. Brannagan noted petitioner had been treated with IVIG for six months with minimal improvement, but that she had dramatic improvement with plasmapheresis. (*Id*. at 10.) Upon presentation, she had some imbalance and numbness on the right side, but full strength in all extremities and normal reflexes with the exception of reduced Achilles reflex. She had decreased vibration in her toes and decreased sensation to light touch on the right side of her body. (*Id*.) Dr. Brannagan's NCS/EMG study found evidence of mild right median mononeuropathy consistent with carpal tunnel syndrome and borderline findings suggestive of a left phrenic neuropathy.[9] However, there was no evidence of large fiber polyneuropathy, demyelination, or cervical or lumbosacral radiculopathy. (*Id*. at 11.) Dr. Brannagan concluded during an

[8] During this hospitalization, petitioner underwent brain and spinal MRIs. (Ex. 4, pp. 345-47.) The spinal MRI showed some degenerative changes of the cervical spine without compression, but no indication of demyelination. The brain MRI showed no significant change since her prior MRI.

[9] The phrenic nerve is a motor nerve of the diaphragm, but it also sends sensory fibers to the mediastinal parietal pleura, the pericardium, the diaphragmatic pleura and peritoneum, and branches that communicate with branches from the celiac plexus. *Phrenic nerve*, STEDMAN'S MEDICAL DICTIONARY (28th ed., 2006).

April 13, 2018 follow up that neither petitioner's nerve conduction study nor her neurological examination were consistent with CIDP or any large fiber neuropathy. (Ex. 41, pp. 3-4.) However, he noted that her Sjögren's syndrome could cause small fiber neuropathy and recommended a skin biopsy and a follow up with rheumatology. Dr. Brannagan indicated that there are reports in the literature of plasmapheresis being used to treat Sjögren's syndrome. (*Id.*) Dr. Vukic then noted that Dr. Brannagan does not believe petitioner has CIDP and therefore concluded that "[t]he cause of her symptoms remains elusive." (Ex. 30, pp. 35, 39.) He withheld further recommendation pending her formal rheumatologic evaluation. (*Id*. at 39.) Dr. Vukic agreed that petitioner's response to plasmapheresis could point to a rheumatologic process. (*Id.* at 45.)

Petitioner had a skin biopsy on April 30, 2018. (Ex. 30, p. 40.) Samples were taken from the lateral thigh and distal leg, both on the left side, and were sent to Therapath for analysis. (*Id*.) Both samples showed significantly reduced nerve fiber density consistent with small fiber neuropathy. (Ex. 154, p. 63.) She was then evaluated by rheumatologist, Dr. Kepecs, on August 2, 2018. (Ex. 36, pp. 2-4.) Dr. Kepecs felt there is "fair evidence" for SLE and/or Sjögren's syndrome, given petitioner's positive SSA and peripheral neuropathy without a metabolic explanation. (*Id*. at 3.) It was noted that petitioner had a family history of SLE (her mother). (*Id*. at 2.) Her history was not suggestive of Churg-Strauss syndrome.[10] He felt that "[w]hatever the name for the syndrome it is certainly autoimmune." Accordingly, he felt it may respond to immunosuppressive treatment such as CellCept or Imuran, though he did not believe steroids were justified. (*Id*. at 3.) Dr. Kepecs ordered a trial of CellCept and directed petitioner to follow up in 5-6 weeks, noting that he may repeat petitioner's serology and possibly include a myositis panel. (*Id*. at 3-4.) Petitioner returned about a month later and reported that she was tolerating CellCept. (*Id*. at 5-6.) Petitioner reported feeling somewhat better, but Dr. Kepecs felt it was too soon for real effect. (*Id.*) Dr. Kepecs now felt that a SLE/Sjögren's syndrome overlap with peripheral neuropathy was "probable." (*Id*. at 6.) He continued CellCept and ordered bloodwork. (*Id*.)

On October 15, 2018, petitioner was again admitted for treatment when she presented to the hospital with a "few week history" of progressive generalized weakness, difficulty swallowing, dyspenea on exertion, and constipation. (Ex. 39, p. 12.) Neurology reviewed petitioner's history, including her prior presentation for suspected CIDP (noting diagnosis is "not categorically" made) and subsequent diagnosis of confirmed small fiber neuropathy and an autoimmune disease ("uncertain if it's purely Sjogren's or Lupus"). (*Id.* at 28-29.) Petitioner was treated as having a "CIDP exacerbation" and was treated with five days of plasmapheresis. (*Id*. at 32.) It was questioned whether petitioner's recent decline was related to her CellCept or coincidental. (*Id*.) In follow up, Dr. Vukic maintained that petitioner's condition is "elusive" but likely a rheumatologic condition. (Ex. 154, p. 52.) He indicated he would

[10] Churg-Strauss syndrome is a type of small vessel vasculitis with prominent lung involvement. *Churg-Strauss syndrome*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=110417 (last visited Sept. 13, 2024).

discuss the case further with Dr. Kepecs. (*Id.*) Petitioner subsequently switched from CellCept to Plaquenil, which she felt was helping. (*Id*. at 42.) As of December 11, 2018, Dr. Vukic noted that petitioner's symptoms continued to flare. (*Id*. at 42, 46.) He concluded that her condition appears to be a mixture of neurologic and rheumatologic conditions and remarked that "I suspect they are direct result of her prior immunization." (*Id.* at 46.)

After relocating to Florida, petitioner presented to the emergency department with another flare of her condition on June 30, 2019. (Ex. 101, pp. 12-17.) Petitioner's chief complaint was increasing pain and weakness in her left lower extremity. (*Id*. at 26.) The pain also spread to include her hands and she also had one week of dysphagia, urinary retention, and constipation. She reported that she had previously been receiving plasmapheresis every six months, but that she had not had a treatment since October of 2018 because she was doing well. She reported chronic weakness as well as pain from small fiber neuropathy. She was scheduled to see a new neurologist in Florida beginning in October. (*Id*.) Upon neurologic exam, Dr. Sonbol indicated that petitioner's exam was "not necessarily consistent with CIDP and there are some non-physiologic exam findings." (*Id*. at 29.) Petitioner was admitted for workup, which was to include MRIs that were ultimately unremarkable. (*Id*. at 19, 29.) Petitioner was discharged on July 2, 2019. (*Id.* at 18.) Although her admission diagnosis was CIDP, her discharge diagnosis was neuropathy. During hospitalization petitioner was started on Vimpat,[11] which reportedly helped. (*Id*.) Whereas petitioner reported being wheelchair bound when initially examined, she was able to stand and walk unassisted at her discharge exam. (*Id*. at 19, 28.)

Petitioner had a follow up with neurologist, Dr. Suresh, on July 31, 2019. (Ex. 102, p. 7.) At that time, she reported having "severe" loss of function and pain, along with bowel and bladder issues and episodes of flushing and sweating in connection with pain flares. (*Id*.) On exam, petitioner had full strength and intact reflexes, though her ankle reflexes were reduced. (*Id*. at 12.) Dr. Suresh assessed petitioner as having small fiber neuropathy, suspected to be autoimmune and confirmed by biopsy, with an autonomic component. (*Id*.) He further opined that there was "no clear and convincing evidence of CIDP given lack of response, electrodiagnostic findings at Columbia, marginally elevated CSF protein to 60, and reflexes that are preserved in the legs." (*Id*.) He felt that petitioner had good prior responses to both plasmapheresis and IVIG and recommended a trial of IVIG.[12] Given that petitioner was having a flare of uncontrolled pain, he referred petitioner for pain management. (*Id*.) She was later evaluated by a pain management specialist in New Jersey. (Ex. 154, pp. 27-31.)

[11] Vimpat is an orally or intravenously administered anticonvulsant used as an adjunct in the treatment of partial seizures. *Vimpat*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=53152 (last visited Sept. 4, 2024); *Lacosamide*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=27378 (last visited Sept. 4, 2024).

[12] Petitioner subsequently presented to the emergency department on September 4, 2019, reporting an adverse reaction (nausea and vomiting) to her IVIG treatment. (Ex. 101, pp. 168-69.)

Petitioner sought another opinion from neurologists, Drs. Lee (resident) and Hurst (assistant professor), on January 21, 2020. (Ex. 103, p. 15.) Petitioner was reportedly concerned with her lack of response to typical treatments for CIDP. (*Id*. at 20.) Dr. Lee cautioned that sequela of GBS can be persistent, but given the lack of response she recommended discontinuing IVIG and plasmapheresis. She also recommended new electrodiagnostic testing, given that prior study was not indicative of a demyelinating polyneuropathy. She felt petitioner's pain and hyperesthesia were more likely due to her small fiber neuropathy. Dr. Lee recommended that petitioner follow up with a rheumatologist. (*Id*.) Petitioner questioned whether she could get into a clinical trial and also raised this issue when she followed up with Dr. Suresh a month later. (*Id*. at 9, 22.) When petitioner saw Dr. Suresh in February of 2020, he noted that her symptoms have been essentially unchanged for about 3-4 years, except for episodes of chest pressure with hyperventilation. (*Id*. at 9.) Dr. Suresh maintained his diagnosis of small fiber neuropathy, but offered to repeat petitioner's EMG/NCS testing. (*Id*. at 14.) However, petitioner declined. He noted that petitioner does not qualify for plasmapheresis or IVIG, due to her lack of demyelinating features, and indicated that "we are out of options for her in terms of treatment for [small fiber neuropathy]." Petitioner was directed to follow up in one year. (*Id*.)

Petitioner then returned to Dr. Vukic on October 22, 2020. (Ex. 154, p. 2.) Petitioner reported that her symptoms had worsened while she was in Florida, describing generalized weakness in the arms and legs, as well as generalized numbness, including the tongue. (*Id*.) Dr. Vukic now assessed small fiber neuropathy, indicating "[t]he etiology of her symptoms is not entirely clear but I am suspicious this is a manifestation of her underlying rheumatologic condition with a superimposed component of small fiber polyneuropathy." (*Id*. at 6.) He recommended a repeat EMG to evaluate for large fiber polyneuropathy. (*Id*.) Her electrodiagnostic study "demonstrate[d] carpal tunnel syndrome but no other explanation for her numbness which is different from her typical small fiber neuropathy numbness." (*Id*. at 1.) Brain and cervical spine MRIs were recommended. (*Id*.) However, Dr. Vukic did not find the MRIs remarkable and ordered a further study with contrast to evaluate the cranial nerves, given petitioner's reported facial numbness. (Ex. 155, pp. 15, 20.) As of January 5, 2021, Dr. Vukic again opined that petitioner's symptomatology and prior response to IVIG were consistent with CIDP, and he recommended resuming IVIG. (*Id*. at 20.) As of May 4, 2021, petitioner reported that her strength was improving, but her facial symptoms persisted. (*Id*. at 9.) Her MRI showed microvascular changes. (*Id*.) Dr. Vukic felt the facial symptoms were manifestations of CIDP, but also recommended testing for Lyme titer. (*Id*. at 14.) As of July 6, 2021, petitioner reported increased confusion and forgetfulness, difficulty controlling her temperature, and altered feeling in her face radiating over the top of her head. (*Id*. at 2-3.) Dr. Vukic felt the etiology for petitioner's memory symptoms was not clear and ordered further workup, including a repeat MRI and EEG. (*Id.* at 7.)

On August 23, 2021, petitioner established care with a new neurologist, Dr. Dover. (Ex. 153, p. 9.) Dr. Dover remarked that petitioner had a "complicated" history.

(*Id*. at 12.) Dr. Dover recommended continuing IVIG while Dr. Vukic's records were obtained, along with petitioner's prior autoantibody testing and skin biopsy results. (*Id*.) Petitioner saw Dr. Dover again in December of 2021 and February of 2022 with no change in plan. (*Id*. at 5-8.) Dr. Dover did not confirm whether she reviewed petitioner's prior records, but characterized petitioner as having "a known history of CIDP." (*Id.*) As of May of 2022, petitioner reported that her condition continued to worsen despite resuming IVIG, noting fatigue in particular. (*Id.* at 2.) Petitioner wanted to be assessed for use of rituximab.[13] (*Id*.) Dr. Dover characterized petitioner's CIDP as an "established diagnosis, stable." (*Id*. at 3.) She explained that "I see no evidence of objective worsening of [petitioner's] polyneuropathy. In fact, her symptoms appear to be well controlled." (*Id*.) Dr. Morris would not recommend rituximab because it benefits only a specific type of polyneuropathy and she did not feel comfortable switching petitioner from IVIG absent objective signs of decline. She recommended petitioner see a neuro-immunologist. (*Id*.) During this period, petitioner was also referred to a neuro-ophthalmologist due to diplopia. (Ex. 159.) It was concluded that the diplopia was non-specific, having no finding to suggest myasthenia gravis. (*Id*. at 7.)

On November 9, 2022, petitioner saw neurologist and multiple sclerosis specialist, Dr. Sylvester. (Ex. 160, p. 93.) Dr. Sylvester took a history from petitioner, reviewed petitioner's prior medical records and results, and conducted a neurologic exam. (*Id.* at 93-95.) He characterized petitioner's diagnosis as being in need of confirmation, but was willing to prescribe rituximab or another immune suppressive if ongoing treatment was warranted. (*Id*. at 95.) As of January 27, 2023, Dr. Sylvester planned to obtain a new EMG of petitioner's upper and lower extremities and intended to discuss the case further with Dr. Dover. (*Id*. at 22-23.) He was willing to consider initiating treatment with rituximab. (*Id.*)

No further records were filed.

b. As reflected in affidavits

Petitioner has filed four affidavits in this case. (Exs. 17, 28, 29, 157.) Her son, Matthew Bogholtz, also provided an affidavit. (Ex. 158.) These affidavits go into detail regarding the effect that petitioner's injury, and the process of pursuing a claim in this program, have had. Petitioner expresses that her illness "has stripped my life away and left me with a shell of my former existence." (Ex. 28, p. 15.) I have reviewed these affidavits carefully. However, because it is the significance of the medical facts, rather than the facts themselves, that are at issue, it is not necessary to describe petitioner's

[13] Rituximab is an intravenously administered chimeric murine/human monoclonal antibody that binds the CD 20 antigen and is used as an antineoplastic in the treatment of CD20-positive, B-cell non-Hodgkin lymphoma. *Rituximab*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=43977 (last visited Sept. 4, 2024). However, it has also been used to treat CIDP. (Emily K. Mathey et al., *Chronic Inflammatory Demyelinating Polyradiculopathy: From Pathology to Phenotype*, 86 J. NEUROLOGY NEUROSURGERY & PSYCHIATRY 973 (2015) (Ex. 74); C.A. Vedeler et al., *Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)*, 127 ACTA NEUROLOGICA SCANDINAVICA SUPPLEMENTUM 48 (2013) (Ex. 98).)

affidavits in detail. With respect to the issues discussed in this decision, these affidavits primarily have the effect of stressing from petitioner's own perspective that her condition arose post-vaccination. Petitioner asserts that she suffers CIDP, Sjögren's syndrome, tinnitus, and dysphagia. (Ex. 17, p. 4.)

IV. Summary of Expert Opinions

a. Diagnosis

i. Petitioner's neurology expert, Nizar Souayah, M.D.[14]

Dr. Souayah explains that CIDP represents a group of acquired polyneuropathies characterized by symmetric weakness involving the proximal and distal muscles that progresses over at least two months. (Ex. 42, p. 17.) It has a variable clinical course, which can be either progressing or relapsing, but is characterized by longstanding multifocal demyelination affecting the spinal roots, major plexus, and proximal nerve trunks. (*Id.* (citing James H. Austin, *Recurrent Polyneuropathies and Their Corticosteroid Treatment: With Five-Year Observations of a Placebo-Controlled Case Treated with Corticotrophin, Cortisone, and Prednisone*, 81 BRAIN 157 (1958) (Ex. 46); Peter James Dyck et al., *Chronic Inflammatory Polyradiculoneuropathy*, 50 MAYO CLINIC PROC. 621 (1975) (Ex. 57); J.W. Prineas & J.G. *McLeod*, *Chronic Relapsing Polyneuritis*, 27 J. NEUROLOGICAL SCIS. 427 (1976) (Ex. 81); Gérard Said, *Chronic Inflammatory Demyelinating Polyneuropathy*, 16 NEUROMUSCULAR DISORDERS 293 (2006) (Ex. 91); P.K. Thomas et al., *Chronic Demyelinating Peripheral Neuropathy Associated with Multifocal Central Nervous System Demyelination*, 110 BRAIN 53 (1987) (Ex. 97)).) The most common or "classic" form of CIDP involves both motor and sensory deficits. (*Id*. at 18.) However, there are sensory-predominant forms of CIDP that are characterized by paresthesia and gait dysfunction. (*Id.* (citing Xavier Ayrignac et al., *Sensory Chronic Inflammatory Demyelinating Polyneuropathy: An Under-Recognized Entity?*, MUSCLE & NERVE, November 2013, at 727 (Ex. 47); Emily K. Mathey et al., *Chronic Inflammatory Demyelinating Polyradiculopathy: From Pathology to Phenotype*, 86 J. NEUROLOGY NEUROSURGERY & PSYCHIATRY 973 (2015) (Ex. 74); Francisco T. Rotta et al., *The Spectrum of Chronic Inflammatory Demyelinating*

[14] Dr. Souayah received his medical degree from Medical School of Tunis, Tunisia, in 1990, before going on to complete several internships and residencies in internal medicine and neurology. (Ex. 43, p. 1.) He also completed clinical and research fellowships in electromyography/neuromuscular diseases and neuroscience, with a specific focus in neuroinflammation in neurodegenerative disorders. (*Id.*) Dr. Souayah has been board certified in neurology, with a subspecialty in electrodiagnostic medicine and neuromuscular medicine, and he maintains an active medical license in New Jersey. (*Id.* at 1-2; Ex. 42, p. 1.) He currently works as a professor of pharmacology and neurology at Rutgers-New Jersey Medical School and maintains a clinical practice as director of the MDA Clinic, as well as director of the electromyography laboratory and peripheral neuropathy center, at Rutgers-New Jersey Medical School. (Ex. 43, p. 2; Ex. 42, p. 1.) In his clinical practice, Dr. Souayah regularly diagnoses and treats patients with CIDP. (Ex. 42, pp. 1, 4.) In his research capacity, Dr. Souayah has investigated the causal relationship between vaccines and adverse events, particularly the incidence of neurological adverse reactions related to vaccines. (*Id.* at 1.) He has authored several peer-reviewed journal articles that he contends inform the issues of this case. (*Id.* at 1-4; *see also* Ex. 43, pp. 12-24.)

Polyneuropathy, 173 J. NEUROLOGICAL SCIS. 129 (2000) (Ex. 89); C.A. Vedeler et al., *Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)*, 127 ACTA NEUROLOGICA SCANDINAVICA SUPPLEMENTUM 48 (2013) (Ex. 98)).) Despite the sensory predominance, this form of CIDP can demonstrate distal weakness and motor nerve conduction abnormalities on electrodiagnostic testing. (*Id*. (citing Mathey et al., *supra*, at Ex. 74; Shin J. Oh et al., *"Chronic Sensory Demyelinating Neuropathy": Chronic Inflammatory Demyelinating Polyneuropathy Presenting as a Pure Sensory Neuropathy*, 55 J. NEUROLOGY NEUROSURGERY & PSYCHIATRY 677 (1992) (Ex. 80); Vedeler et al., *supra*, at Ex. 98).)

In petitioner's case, Dr. Souayah finds the following features indicative of CIDP:

- numbness starting in the hands and progressing to her feet three days later;
- subsequent unsteady gait and reduced dexterity;
- reduced deep tendon reflexes upon neurologic examination in both upper extremities and absent in the ankles bilaterally;
- abnormal vibration sensation;
- positive Romberg sign;
- a relapsing course of neuropathy;
- electrodiagnostic evidence of acute moderate predominantly motor demyelination; and
- partial improvement with IVIG treatment.

(*Id.* at 19-20.)

Dr. Souayah agrees with Dr. Callaghan that petitioner does not meet the European Federation of Neurological Societies/Peripheral Nerve Society ("EFNS/PNS") CIDP diagnostic criteria.[15] (Ex. 111, p. 2.) However, he indicates that these diagnostic criteria reflect the typical forms of CIDP and are not very sensitive, especially for sensory forms of CIDP. (*Id*.) He is critical of Dr. Callaghan for relying on medical records from more than two years after the initial onset of her condition to doubt her diagnosis and for failing to offer any other plausible diagnosis. (*Id.* at 2-3.) Nonetheless, he acknowledges that over time petitioner's neurophysiological evaluation changed such that she no longer fits the typical manifestations of CIDP or inflammatory neuropathy. (*Id*. at 3.) However, contrary to Dr. Callaghan's interpretation of the records, Dr. Souyah stresses that he believes petitioner's condition did respond to IVIG treatment. (*Id*.)

Dr. Souayah acknowledges that, as of April 13, 2018, Dr. Brannagan found no clinical or neurophysiological evidence of large fiber neuropathy and that petitioner subsequently had a skin biopsy that was positive for small fiber neuropathy, consistent

[15] Although both parties' experts reference the ECFNS/PNS CIDP diagnostic criteria, neither has actually filed the published criteria. However, because both parties' experts agree petitioner does not meet these criteria, this is not a critical omission.

with autonomic neuropathy. (Ex. 150, p. 1.) Thus, to the extent Dr. Callaghan cited symptoms beyond the scope of CIDP (namely, shortness of breath, chest tightness, dizziness, lightheadedness, vertigo, constipation, difficulty urinating, and dysphagia), Dr. Souayah opined that these are likely symptoms of small fiber neuropathy, though he also observed that autonomic dysfunction is reported in many cases of CIDP. (Ex. 111, p. 3.) However, Dr. Souayah concedes that petitioner's diagnosis changed from CIDP to small fiber neuropathy. (Ex. 150, p. 2.)

ii. Respondent's neurology expert, Brian Callaghan, M.D.[16]

Dr. Callaghan acknowledges that petitioner presented with numbness in the hands and toes that was initially diagnosed as GBS and then CIDP; however, he does not agree that petitioner suffered CIDP. (Ex. A, p. 3.) Dr. Callaghan indicates that CIDP is frequently misdiagnosed – with 47% of patients referred for evaluation of CIDP having a different condition. (*Id.* (citing Jeffrey A. Allen & Richard A. Lewis, *CIDP Diagnostic Pitfalls and Perception of Treatment Benefit*, 85 NEUROLOGY 498 (2015) (Ex. E, Tab 1)).) He cites the EFNS/PNS CIDP criteria as instructive. (*Id*.) Those diagnostic criteria require progressive, symmetric proximal weakness, as well as supportive findings on EMG/NCS, which he asserts petitioner does not have. (*Id*.) Dr. Callaghan cites several factors that inform his diagnostic opinion, specifically:

- Although petitioner's initial EMG/NCS revealed demyelinating neuropathy, she had four subsequent EMG/NCS studies that revealed no demyelinating features;
- Although she has had sensory signs, her physical exams have consistently shown normal or near normal strength over seven years;
- Her reportedly disabling symptoms (such as not being able to get out of bed) have a "clear disconnect" from her near normal neurologic examinations;
- She has numerous symptoms not associated with CIDP, including shortness of breath, chest tightness, dizziness, lightheadedness, headache, vertigo, fatigue, memory issues, constipation, difficulty urinating, dysphagia, rectal pain, tinnitus, loss of smell, shaking, depression, hopelessness, and weight gain;

[16] Dr. Callaghan received his medical degree from the University of Pennsylvania Medical Center in 2004, before going on to complete a residency in neurology at the University of Pennsylvania Medical Center in 2008, a neuromuscular fellowship at the University of Michigan Health System in 2009, and a Center for Healthcare Research and Transformation Policy Fellowship at the University of Michigan in 2016. (Ex. B, p. 1.) In the interim, Dr. Callaghan received a master's degree in clinical research design and statistical analysis from the University of Michigan in 2011. (*Id.*) He is board certified in psychiatry, neurology, and electrodiagnostic medicine, and he maintains a medical license in Michigan. (*Id.*) He currently works as an associate professor of neurology and the director of the ALS Clinic at the University of Michigan Health System, as well as a staff physician in the Department of Neurology at VA Ann Arbor Health System. (*Id.* at 1-2; Ex. A, p. 1.) Dr. Callaghan is a neuromuscular specialist with a primary interest in patients with neuropathy, such as CIDP. (Ex. A, p. 1.) In his clinical practice, he treats approximately 30-50 GBS and CIDP patients per year. (*Id.*) In his research capacity, Dr. Callaghan has authored numerous peer-reviewed articles, book chapters, and abstracts concerning neuropathy. (Ex. B, pp. 10-17.)

- She did not have a consistent response to IVIG and plasmapheresis, which are highly effective therapies for CIDP; and
- Her treating neurologists doubted the CIDP diagnosis. In particular, it was noted as of July 31, 2019, that there is no clear or convincing evidence of CIDP, given a lack of response to treatment, lack of supportive EMG/NCS findings, only marginally elevated CSF protein; and preserved reflexes upon neurologic exam.

(*Id*. at 3; Ex. F, pp. 3-4.)

Dr. Callaghan acknowledges that he has no alternative diagnosis, but urges that this does not mean that CIDP must therefore be the diagnosis. (Ex. E, p. 2.) He asserts that it is not unusual for patients with a multitude of symptoms to lack a clear explanation. (*Id.*) Dr. Callaghan disputes Dr. Souayah's suggestion that petitioner has a sensory-predominant form of CIDP because she had difficulty getting out of bed and eventually became wheelchair bound secondary to weakness (*Id.* at 1), even though he otherwise questioned whether that symptom could be explained by her neurologic findings (Ex. A, p. 3; Ex. F, p. 3).

Dr. Callaghan also disagrees that petitioner has small fiber neuropathy. (Ex. E, p. 2.) He cites the following exclusion criteria for the condition: (i) any sign of large fiber impairment (light touch and/or vibratory and/or proprioceptive sensory loss and/or absent deep tendon reflexes); (ii) any sign of motor fiber impairment (muscle waste and/or weakness); (iii) any abnormality on sensorimotor NCS. (*Id*. (citing Grazia Devigili et al., *Diagnostic Criteria for Small Fiber Neuropathy in Clinical Practice and Research*, 142 BRAIN 3728 (2019) (Ex. F, Tab 1)).) In petitioner's case, she did have features of large fiber involvement (decreased vibration sensation at the ankles, and decreased ankle jerks), as well as motor fiber impairment (4+ left hip flexion strength). (*Id.*) Dr. Callaghan also disagrees that petitioner meets the inclusion criteria for small fiber neuropathy, because she did not have a QST[17] performed. (Ex. F, p. 4 (citing Devigili et al., *supra*, at Ex. F, Tab 1).) Dr. Callaghan acknowledges petitioner had a skin biopsy that showed reduced nerve fiber; however, he indicates that, in his experience, the specific test used for petitioner's biopsy (Therapath skin biopsy) has a high rate of false positives. (*Id*.) And, again, he cites petitioner as having numerous other symptoms that are not consistent with small fiber neuropathy, ultimately opining that "[n]o known neurologic disease can account for the multitude of symptoms that the petitioner experienced." (Ex. E, p. 2.)

In sum, Dr. Callaghan opines that petitioner's clinical presentation is irreconcilable. Her reported symptoms would require "severe" large fiber nerve involvement; however, she had four normal EMG/NCS studies, which are the "gold

[17] Quantitative sensory testing involves applying various tactile stimuli, such as light touch, heat, cold, and vibrations, and monitoring the patient's response as compared to either the patient's response when stimuli are applied to the other side of the body or a control subject's response. *Quantitative sensory testing*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=113107 (last visited Sept. 13, 2024).

standard" for evaluating large fiber nerves. (Ex. F, p. 5.) Conversely, a diagnosis of small fiber neuropathy requires the absence of large nerve involvement; this therefore means that a small fiber neuropathy diagnosis is incompatible with petitioner's disabling symptoms. (*Id*.)

iii. Petitioner's rheumatology expert, Samar Gupta, M.D. [18]

Although petitioner had an initial presentation suspicious for either GBS or CIDP, Dr. Gupta observes that she was also found to have high levels of ANA and SSA (or anti-RO) antibodies, which are specific for Sjögren's syndrome. (Ex. 104, p. 2.) In contrast to Dr. Matloubian, who opined petitioner's pre-vaccination ANA test may have been a false negative (Ex. G, p. 10), Dr. Gupta stresses his view that these antibodies first arose post-vaccination (Ex. 161, pp. 2-3; Ex. 151, p. 1). Dr. Lightfoot, conversely, suggested petitioner's post-vaccination anti-SSA result may have been a false positive. (Ex. C, p. 5.) Dr. Gupta did not directly respond to that point, but stressed petitioner had two positive SSA tests post-vaccination. (Ex. 161, p. 2.)

Sjögren's syndrome is usually suspected in individuals with persistent dry eye and/or dry mouth (also known as sicca symptoms), parotid gland enlargement, and anti-SSA serology. (Ex. 104, p. 2.) However, though not diagnostic criteria, the 2016 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification system for primary Sjogren's syndrome places significant weight on serology. (*Id*. (citing Caroline H. Shiboski et al., *2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for Primary Sjögren's Syndrome: A Consensus and Data-Driven Methodology Involving Three International Patient Cohorts*, 76 ANNALS RHEUMATIC DISEASE 9 (2016) (Ex. 106)).) Although Dr. Lightfoot suggested an anti-centromere pattern of ANA titer is indicative of a limited scleroderma only, Dr. Gupta opines that the pattern of ANA is usually non-specific. (*Id*. at 5.)

Dr. Gupta agrees with Dr. Lightfoot that positive anti-SSA is not alone diagnostic, but stresses that he finds other features of Sjögren's syndrome in petitioner's case. (Ex.

[18] Dr. Gupta received his medical degree from Maharshi Dayanand University in Rohtak, India, in 1988, before going on to complete a residency in internal medicine and orthopedic surgery from the same university, followed by an internship in internal medicine at Rush University Medical Center in Chicago, Illinois, in 1996; a residency in internal medicine at Wayne State University in Detroit, Michigan, in 1998; and a rheumatology and immunology fellowship at University of Michigan in 2000. (Ex. 105, p. 1.) He is a member of the American College of Rheumatology, Arthritis Foundation, Scleroderma Foundation, national Psoriasis Foundation, and Group for Research and Assessment of Psoriasis and Psoriatic Arthritis. (Ex. 104, p.1.) He currently works as rheumatology professor at VA Ann Arbor Healthcare System and the University of Michigan - Ann Arbor and as a co-director of the Rheumatology Dermatology collaborative clinic at University of Michigan Veterans Affairs Medical Center. (Ex. 105, p. 1; Ex. 104, p. 1.) His clinical and research interests focus on rheumatic diseases, including Sjögren's syndrome. (Ex. 104, p. 1.) He has treated over 200 patients with Sjögren's syndrome. (*Id.*) In his research capacity, he has authored numerous peer-reviewed articles that have been published in journals, such as New England Journal of Medicine, The Lancet, and Arthritis & Rheumatism. (*Id.*)

104, p. 5.) Dr. Gupta opines that petitioner may have had an early or incomplete presentation of Sjögren's syndrome based on the following features:

- Elevated inflammatory markers;
- Abnormal brain MRI;
- Prednisone responsive inflammatory hand arthritis;[19]
- Peripheral neuropathy by NCS/EMG and skin biopsy;
- Cutaneous rash;
- Parotid enlargement; and
- Sicca symptoms.

(*Id*. at 2-3.) Dr. Gupta acknowledges that petitioner does not meet the ACR/EULAR criteria for Sjögren's syndrome, but stresses that the classification criteria "are intended to eliminate all but those who have incontrovertible disease." (*Id*. at 3.)

Dr. Gupta explains that about 10% of Sjögren's syndrome patients also have some form of peripheral neuropathy. (Ex. 104, p. 3 (citing P. Brito-Zerón et al., *Classification and Characterisation of Peripheral Neuropathies in 102 Patients with Primary Sjögren's Syndrome*, 31 CLINICAL & EXPERIMENTAL RHEUMATOLOGY 103 (2013) (Ex. 107)).) In these cases, neuropathic symptoms can precede diagnosis and can involve either the large or small fibers. (*Id*.) Both small fiber neuropathy and CIDP have been described in patients with Sjögren's syndrome. (*Id*. (citing Keiko Mori et al., *The Wide Spectrum of Clinical Manifestations in Sjögren's Syndrome-Associated Neuropathy*, 128 BRAIN 2518 (2005) (Ex. 108); Julius Birnbaum et al., *Biopsy-Proven Small-Fiber Neuropathy in Primary Sjögren's Syndrome: Neuropathic Pain Characteristics, Autoantibody Findings, and Histopathologic Features*, 71 ARTHRITIS CARE & RES. 936 (2019) (Ex. 109)).) Thus, Dr. Gupta opines that petitioner's peripheral neuropathy is a part of her Sjögren's syndrome presentation. He defers to Dr. Souayah on the exact nature of petitioner's neuropathy (Ex. 151, p. 1); however, given that both small fiber neuropathy and CIDP are associated with Sjögren's syndrome, he opines that petitioner's neuropathy is associated with her Sjögren's syndrome regardless of diagnosis (*Id.*; Ex. 104, p 4).

iv. Respondent's rheumatology expert, Robert Lightfoot, Jr., M.D. [20]

[19] Dr. Gupta further explained: "Dr. Lightfoot also mentions a history of intermittent arthritis in the small joints of the hands, occasional swelling, and 'up to one hour of morning stiffness' noting that when [petitioner] took steroids for her asthma, her finger joints felt relieved. This may indicate inflammatory arthritis. Although osteoarthritis would get better with steroids, . . . osteoarthritis pain generally would not present with joint swelling in hands." (Ex. 104, p. 3.) When Dr. Matloubian entered the case, he suggested that this passage by Dr. Gupta indicated that petitioner's Sjögren's syndrome would have necessarily predated her vaccination based on Dr. Gupta's assessment. (Ex. G, p. 9.) However, Dr. Gupta indicates that this "overstates" his opinion, noting that there are no pre-vaccination medical records addressing petitioner's arthritis and further stressing that the records confirm petitioner was negative for ANA and ESR prior to vaccination. (Ex. 161, pp. 2-3.)

[20] Dr. Lightfoot received his medical degree from Vanderbilt University School of Medicine in 1961, before going on to complete an internship and residency at Columbia Presbyterian Medical Center in 1962 and 1963, respectively; a residency at Vanderbilt University Hospital in 1964; and a rheumatology fellowship

Dr. Lightfoot indicates,

> To me, a crucial aspect of petitioner's illness is that her symptoms were entirely subjective (numbness, tingling, pain, weakness), rather than objective (swelling, warmth, redness, induration, discoloration). Thus, the outcome of any therapeutic attempt is rendered difficult to measure, and the provider must rely on 'patient global' impression of his/her disease status.

(Ex. C, p. 4.) With regard to Sjögren's syndrome, Dr. Lightfoot indicates that petitioner does not meet either the ACR or the ACR/EULAR classification criteria. (*Id*. at 5 (citing Shiboski et al., *supra*, at Ex. 106; S.C. Shiboski et al., *American College of Rheumatology Classification Criteria for Sjögren's Syndrome: A Data-Driven, Expert Consensus Approach in the Sjogren's International Collaborative Clinical Alliance Cohort*, 64 ARTHRITIS CARE & RES. 475 (2012) (not filed)).) However, he acknowledges these are stringent and not diagnostic criteria. (*Id*.) He opines that "[w]hile I cannot say that petitioner unequivocally HAS Sjogren's, I also cannot say that she does not have an incomplete form that has not risen to unequivocality yet." (*Id*.)

Dr. Lightfoot raises some concern with respect to petitioner's serology. First, he notes that petitioner's positive ANA titer was 1:320, which is a level that can be seen in a small number (3%) of normal individuals. (Ex. C, p. 5.) Second, he suggests that petitioner's record, which indicates she had "ANA screen with anti-SSA positive" likely indicate her test was sent to a lab that uses "ANA Direct (screening) assay." (*Id*.) This methodology screens for seven to nine antibodies at once, which Dr. Lightfoot indicates produces a high likelihood of chance findings. (*Id*.) Thus, he opines that "[i]t is not possible to say if the anti-SSA had any pathophysiological role on petitioner's illness." (*Id*.) For this reason, Dr. Lightfoot indicated that "[t]here is no clear evidence that the anti-SSA is causally related to the alleged CIDP." (*Id.* at 6.) However, because his report pre-dated Dr. Gupta's involvement in the case, he did not address Dr. Gupta's discussion of the association between Sjögren's syndrome and peripheral neuropathies.

v. Respondent's rheumatology expert, Mehrdad Matloubian, M.D., Ph.D. [21]

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at Columbia University College of Physicians and Surgeons in 1966. (Ex. D, p. 1.) He is board certified in internal medicine and rheumatology. (*Id.*) At the time his expert report was submitted, Dr. Lightfoot maintained an active medical license in Kentucky, and he worked as a Professor of Medicine Emeritus at the University of Kentucky, a staff physician at Veterans Administration Medical Center, and active medical staff at Albert B. Chandler Medical Center. (*Id.* at 2.) He had also authored several peer-reviewed articles, book chapters, and abstracts concerning rheumatology. (*Id.* at 18-26.)

[21] Dr. Matloubian received his medical degree and Ph.D. in virology from the University of California in 1996, where he remained to complete an internship in 1997, residency in 1998, rheumatology fellowship in 2001, and post-doctoral fellowship in 2004. (Ex. H, p. 1.) He is board certified in internal medicine and rheumatology, and he maintains an active medical license in California. (*Id.* at 1-2.) Dr. Matloubian currently works as a professor of medicine at the University of California, as well as an inpatient rheumatology and molecular medicine consultant. (*Id.* at 2-3.) He is also a member of the American College of Rheumatology, Northern California Chapter of Arthritis Foundation, American Association of

Dr. Matloubian suggests that, based on his review of petitioner's medical history, "it is quite apparent that there was a lack of consensus among her treating neurologists regarding specific diagnoses that would explain her symptomology." (Ex. G, p. 7.) He defers to Dr. Callaghan regarding any specific neurologic diagnosis. (*Id*.) However, he does agree that many patients with rheumatologic diseases do have neurological manifestations. (*Id*.) Consistent with Dr. Gupta's opinion, Dr. Matloubian explained that both CIDP and small fiber neuropathy can be associated with Sjögren's syndrome and that the neurological symptoms can be the first manifestations of Sjögren's syndrome. (*Id.* at 8 (citing Alen N. Baer & Shamik Bhattacharyya, *UpToDate: Neurologic Manifestations of Sjögren's Syndrome* (2022) (Ex. G, Tab 1); Mary Margaretten, *Neurologic Manifestations of Primary Sjögren Syndrome*, 43 RHEUMATIC DISEASES CLINICS N. AM. 519 (2017) (Ex. G, Tab 4)).) Thus, although petitioner did not have sicca symptoms typical of Sjögren's syndrome, this is still compatible with Sjögren's associated neurological disease. (*Id*.) Dr. Matloubian opines that, "[i]f petitioner was diagnosed with CIDP and/or SFN, I think it would be reasonable to attribute them to Sjogren's in light of a positive SSA and history of an intermittent inflammatory arthritis affecting the MCP joints of hands."[22] (*Id*. at 8-9.) Although petitioner's neurologic diagnosis is unsettled, Dr. Matloubian opines that "in the setting of a peripheral neuropathy and history of arthritis she was appropriately labeled as having Sjogren's." (*Id*. at 12.) However, based on his assessment of petitioner's hand arthritis and the possibility of a false negative ANA result in 2012, Dr. Matloubian opines that petitioner's Sjögren's syndrome predated her vaccination. (*Id*. at 9-10, 12.) Dr. Matloubian stresses that petitioner was never tested for SSA prior to vaccination. (*Id*. at 9.)

b. Causation

i. Petitioner's experts (Drs. Souayah and Gupta)

Dr. Souayah grounds petitioner's theory of causation first and foremost in the context of CIDP, suggesting that CIDP patients have often had an infection or vaccination within the six weeks preceding onset of their condition. (Ex. 42, p. 19 (citing Pamela A. McCombe et al., *Studies of HLA Associations in Male and Female Patients*

Immunologists, and American Society for Clinical Investigation. (Id. at 3.) He has authored peer-reviewed articles concerning innate and adaptive immune responses, including those of T and B cells, to acute and chronic viral infections. (Ex. G, p. 1; Ex. H, pp. 10-14.)

[22] Dr. Matloubian indicated that one of petitioner's treating physicians "considered her history of arthritis affecting her MCP and PIP joints with prolonged morning stiffness and intermittent swelling as possible manifestations of Sjogren's (Ex. 2 at 132 and 135)." (Ex. G, p. 8.) He explained that,

> [a]lthough petitioner does have a history of osteoarthritis, this disease mainly affects the PIP and DIP [distal interphalangeal joints] of the hands and spares the MCP joints. MCP joints, which were symptomatic in petitioner are usually involved in inflammatory arthritis, such as rheumatoid arthritis, lupus and Sjogren's and not in osteoarthritis . . . .

(*Id*. (citing James R. O'Dell et al., *Chapter 15. Rheumatoid Arthritis*, *in* CURRENT DIAGNOSIS & TREATMENT: RHEUMATOLOGY (3rd ed., 2013) (Ex. G, Tab 5, fig.15-1)).)

with Guillain-Barré Syndrome (GBS) and Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP), 180 J. NEUROIMMUNOLOGY 172 (2006) (Ex. 76); Said, *supra*, at Ex. 91).) Dr. Souyah indicates that, like GBS, CIDP is a B cell mediated condition of humeral immunity responsive to unknown antigens; however, unlike GBS, CIDP has a more persistent or recurrent course, that is likely explained by T-cell dysfunction. (*Id*. at 19-20 (citing Richard A.C. Hughes et al., *Pathogenesis of Chronic Inflammatory Demyelinating Polyradiculneuropathy*, 11 J. PERIPHERAL NERVOUS SYS. 30 (2006) (Ex. 65); Sandra Bick et al., *Intravenous Immunoglobulin Inhibits BAFF Production in Chronic Inflammatory Demyelinating Polyradiculoneuropathy – A New Mechanism of Action?*, 256 J. NEUROIMMUNOLOGY 84 (2013) (Ex. 49); Simon Rinaldi & David L.H. Bennett, *Pathogenic Mechanisms in Inflammatory and Paraproteinaemic Peripheral Neuropathies*, 27 CURRENT OP. NEUROLOGY 541 (2014) (Ex. 88)).) Dr. Souayah cites a number of case reports for the proposition that CIDP has been identified following several different vaccines, including the flu vaccine. (*Id*. at 21-22 (citing Claude Vital et al., *Postvaccinal Inflammatory Neuropathy: Peripheral Nerve Biopsy in 3 Cases*, 7 J. PERIPHERAL NERVOUS SYS. 163 (2002) (Ex. 100); Karissa L. Gable et al., *Distal Acquired Demyelinating Symmetric Neuropathy After Vaccination*, 14 J. CLINICAL NEUROMUSCULAR DISEASE 117 (2012) (Ex. 60); Krista Kuitwaard et al., *Recurrences, Vaccinations and Long-Term Symptoms in GBS and CIDP*, 14 J. PERIPHERAL NERVOUS SYS. 310 (2009) (Ex. 69); J.M. Brostoff et al., *Post-Influenza Vaccine Chronic Inflammatory Demyelinating Polyneuropathy*, 37 AGE & AGEING 229 (2008) (Ex. 51); Praful Kelkar, *Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) with Rapid Progression After Influenza Vaccination: A Report of Three Cases*, 8 J. CLINICAL NEUROMUSCULAR DISEASE 20 (2006) (Ex. 67); Gauthier Remiche et al., *Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) Associated to Hereditary Neuropathy with Liability to Pressure Palsies (HNPP) and Revealed After Influenza AH1N1 Vaccination*, 113 ACTA NEUROLOGICA BELGICA 519 (2013) (Ex. 85); Shee Ten Tay & Wing P. Chan, *A 9-Year-Old Femail with Bilateral Leg Weakness After Influenza Vaccination*, 43 PEDIATRIC ANNALS 440 (2014) (Ex. 96)).) Dr. Souayah suggests that the same concepts that support vaccine-causation of GBS – molecular mimicry, epitope spreading, bystander activation, and polyclonal activation – can support vaccine causation of CIDP. (*Id*. at 24-26 (citing Nancy Agmon-Levin et al., *Vaccines and Autoimmunity*, 5 NATURE 648 (2009) (Ex. 44); Penina Haber et al., *Vaccines and Guillain-Barré Syndrome*, 32 DRUG SAFETY 309 (2009) (Ex. 62)).) In his second report, Dr. Souyah further defended his application of these concepts to CIDP in response to Dr. Callaghan's criticism that his theory relied primarily on case reports. (Ex. 111, pp. 4-6.) Thus, in his first two reports, Dr. Souayah posited a direct causal relationship between petitioner's vaccination and her proposed CIDP. (*Id.* at 6; Ex. 42, pp. 26-27.)

However, Dr. Gupta subsequently opined on petitioner's behalf that her neurologic condition, whatever its diagnosis, was an aspect of her separately diagnosed Sjögren's syndrome. (Ex. 104, p. 4.) Dr. Gupta indicated that "[a] mechanism between peripheral neuropathies and [Sjögren's syndrome] is unresolved," but stressed that Sjögren's syndrome, CIDP, and small fiber neuropathy, are all autoimmune conditions. (Ex. 151.) Accordingly, he opined that petitioner's entire presentation is "consistent with

a vaccine induced illness in the mosaic of autoimmunity." (*Id.*) However, Dr. Gupta did not explain any direct causal relationship between vaccination and Sjögren's syndrome. (Exs. 104, 151.) Instead, he deferred to Dr. Souayah with respect to any theory of causation linking petitioner's peripheral neuropathy to her vaccination. (Ex. 161, p. 3.) Thus, Dr. Souayah opined that Dr. Gupta's reference to the mosaic of autoimmunity is consistent with this theory of causation, explaining:

> Importantly, the mechanisms I previously outlined regarding the development of [petitioner's] vaccine-related CIDP/inflammatory neuropathy are best summarized as the loss of immunological tolerance to self-antigens. The mosaic of autoimmunity best describes the interplay of [petitioner's] diagnoses, clinical presentation, electrodiagnostic testing and ANA/SSA serologies.

(Ex. 150, p. 2.) In his final report, Dr. Souayah reiterated that his opinion is premised on the notion that petitioner "most likely developed an inflammatory neuropathy/CIDP variant after vaccination." (*Id.* at 1.) Dr. Souayah did not in any of his reports explain any direct causal relationship between vaccination and small fiber neuropathy. (Exs. 42, 111, 150.) Neither Dr. Souyah nor Dr. Gupta explain exactly what they mean by "mosaic of autoimmunity." This may simply refer to the notion that autoimmunity is believed to be multifactorial, involving both genetic and environmental factors. (Agmon-Levin et al., *supra*, at Ex. 44 (citing reference 27, a publication by Shoenfeld et al., titled "The Mosaic of Autoimmunity: Genetic Factors Involved in Autoimmune Disease").)

Ultimately, Dr. Souayah opines that "[n]one of these conditions were present prior to [petitioner's] vaccination, and all can be attributable to a loss of immunological tolerance to self-antigens." (Ex. 150, p. 2.) Dr. Souayah finds causal significance in the fact that petitioner experienced onset of numbness and tingling in her hands, feet, and face within approximately two weeks of her vaccination and evidence of motor demyelinating peripheral neuropathy upon electrodiagnostic testing as of October 28, 2015. (*Id*.) Dr. Souayah opines this is consistent with the timing of an antibody response to vaccination leading to nerve damage. (Ex. 42, pp. 24, 26.) Dr. Gupta further stresses that petitioner's positive serology likewise first occurred post-vaccination. (Ex. 161, p. 1.)

ii. Respondent's experts (Drs. Callaghan, Lightfoot, and Matloubian)

Dr. Callaghan contends that the link Dr. Souayah proposes between CIDP and vaccination is based merely upon case reports. (Ex. A, p. 4.) However, case reports show only proximate temporal relationship, which does not establish causation. (*Id.*) Moreover, Dr. Callaghan calls into question any parallel between GBS and CIDP, explaining that, in addition to other pathogenic differences, CIDP is rarely preceded by infection, reducing the likelihood that it is explained by the triggering of molecular mimicry. (*Id*. (citing Eroboghene E. Ubogu, *Inflammatory Neuropathies: Pathology, Molecular Markers and Targets for Specific Therapeutic Intervention*, 130 ACTA NEUROPATHOLOGICA 445 (2015) (Ex. A, Tab 1); Marinos C. Dalakas, *Pathogenesis of*

Immune-Mediated Neuropathies, 1852 BIOCHIMICA ET BIOPHYSICA ACTA 658 (2015) (EX. A, Tab 2)).) Dr. Callaghan further cites one study that investigated, but failed to detect, a causal association between CIDP and vaccination. (*Id.* (citing P.E. Doneddu et al., *Risk Factors for Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP): Antecedent Events, Lifestyle and Dietary Habits. Data from the Italian CIDP Database*, 27 EUR. J. NEUROLOGY 136 (2020) (Ex. A, Tab 3)).) Dr. Callaghan agrees that CIDP is "definitely" an autoimmune disease, but stresses that vaccine causation does not necessarily follow from that fact. (Ex. E, p. 3.) He asserts that Dr. Souayah provided no evidence to substantiate that mechanisms such as molecular mimicry or bystander activation explain the flu vaccine as a cause of either CIDP or small fiber neuropathy. (*Id.*)

Although Dr. Lightfoot did not address the causes of Sjögren's syndrome (Ex. C), Dr. Matloubian subsequently opined that the cause of Sjögren's syndrome is unknown (Ex. G, p. 9). However, he stressed that Sjögren's syndrome is not known to follow infection, including influenza infection, which makes it very unlikely that the flu vaccine could cause Sjögren's syndrome via molecular mimicry. (*Id*.) Further, Dr. Matloubian challenges Dr. Souayah's suggestion that loss of immune tolerance is generalizable. (*Id*. at 11.) He indicates that

> This argument is based more on temporal association than on a coherent medical theory. Most autoimmune diseases, such as rheumatoid arthritis, psoriasis, and Sjogren's are not associated with acute infection and therefore, are not considered to be initiated by an acute infection in a matter of weeks . . . . most individuals with clinical diagnosis of Sjogren's are found to have anti-SSA autoantibodies for many years prior to disease presentation. This is also true for rheumatoid arthritis and lupus, indicating that breakdown of immunological tolerance leading to autoimmunity occurs years before the autoimmune disease becomes clinically apparent. An external environmental factor (trigger) for transition from a pre-clinical state to clinically apparent disease for these conditions has not been identified.

(*Id.* (internal footnote omitted).)

V. Analysis

a. Diagnosis

The Vaccine Act requires a petitioner to present a claim for compensation for a "vaccine-related injury or death," as well as preponderant evidence supporting her claim. § 300aa-11(c); § 300aa-13(a)(1)(A); *Stillwell v. Sec'y of Health & Human Servs.*, 118 Fed. Cl. 47, 56 (2014), *aff'd*, 607 F. App'x 997 (Fed. Cir. 2015). Accordingly, a petitioner must specify her "vaccine-related injury and shoulder the burden of proof on causation." *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339, 1346 (Fed. Cir. 2010). Where the identity and nature of the vaccine-related injury is in dispute, the Federal Circuit has concluded that it is "appropriate for the special master

to first determine what injury, if any, [is] supported by the evidence presented in the record before applying the *Althen* test to determine causation." *Lombardi v. Sec'y of Health & Human Servs.*, 656 F.3d 1343, 1352-53 (Fed. Cir. 2011). However, "the function of a special master is not to 'diagnose' vaccine-related injuries." *Andreu ex rel. Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1382 (Fed. Cir. 2009). Instead, the special master must determine, "based on the record evidence as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the [petitioner's] injury." *Id.* (quoting *Knudsen ex rel. Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 549 (Fed. Cir. 1994)).

Petitioner "maintains that she suffered an autoimmune inflammatory neuropathy, described as a CIDP variant, at outset. She subsequently developed small fiber neuropathy. . . ." (ECF No. 152, p. 1 n.2.) Petitioner acknowledges in her brief that she "also had serologic testing consistent with Sjogren's syndrome" (*Id*.), but stresses that she does not fulfill the diagnostic criteria for Sjögren's syndrome (*Id*. at 107). However, petitioner does acknowledge that she developed a rheumatologic condition. (*Id*. at 107-09.) As noted above, petitioner confirms in her affidavit that she considers herself to be suffering Sjögren's syndrome. (Ex. 17, p. 4.) Respondent disputes that petitioner has established that she suffered either CIDP or small fiber neuropathy. (ECF No. 154, pp. 19-24.) Instead, he asserts that petitioner suffers Sjögren's syndrome. (*Id*. at 24.) And, further, any CIDP or small fiber neuropathy, if present, would be attributable to her Sjögren's syndrome. (*Id.*)

i. <u>There is preponderant evidence that petitioner suffers Sjögren's syndrome</u>

First, I confirm that the record evidence preponderates in favor of a finding that petitioner suffers Sjögren's syndrome. As explained above, petitioner tested positive for ANA and SSA antibodies. (Ex. 2, pp. 132, 135.) And, as Dr. Gupta explained, SSA antibodies are specific for Sjögren's syndrome. (Ex. 104, p. 2.) Thus, both parties have presented expert rheumatology opinions (by Drs. Gupta and Matloubian) confirming that petitioner suffered Sjögren's syndrome. (*Id.* at 2-3; Ex. G, pp. 8-9.) Further, although Dr. Lightfoot felt petitioner may have had only an equivocal "incomplete" form of Sjögren's syndrome (Ex. C, p. 5), Dr. Gupta explained that petitioner's presentation was not limited to her serology result, given that she had, *inter alia*, associated peripheral neuropathy (Ex. 104, p. 4). This is consistent with how petitioner's case was viewed by her treating rheumatologists. (Ex. 2, pp. 135-36 (opining Sjögren's syndrome may explain both serology and neurologic symptoms); Ex. 15, p. 5 (noting petitioner's positive SSA and explaining peripheral neuropathies can present without classic signs of sicca); Ex. 36, p. 12 (indicating petitioner has Sjögren's with neurological manifestations).) Respondent's rheumatology expert, Dr. Matloubian, likewise agrees.[23] (Ex. G, p. 8.)

[23] Respondent argues that Dr. Matloubian's opinion should be given greater weight than Dr. Lightfoot's opinion because Dr. Matloubian was able to consider more evidence than Dr. Lightfoot was able to review. (ECF No. 154, p. 29 n.15.) Petitioner disagrees. (ECF No. 155, pp. 2-6.) The potential import of this would be that Dr. Matloubian was more forceful in opining that petitioner suffered Sjögren's syndrome

Accordingly, there is preponderant evidence that petitioner suffers Sjögren's syndrome with neurological manifestations. Whether those neurological manifestations can be further categorized is discussed in the two sections that follow.

ii. There is preponderant evidence that petitioner suffered small fiber neuropathy as a sequela of her Sjögren's syndrome

The diagnostic inclusion criteria for small fiber neuropathy as cited by Dr. Callaghan include: (1) clinical signs of small fiber impairment; (2) abnormal warm or cold thresholds at the foot, assessed by quantitative sensory testing ("QST"); and (3) reduced nerve fiber density at the distal leg. (Devigili et al., *supra*, at Ex. F, Tab 1, p. 2.) Respondent stresses that petitioner never underwent QST, suggesting this precludes a small fiber neuropathy diagnosis. (ECF No. 154, p. 23.) However, the diagnostic criteria requires only that a patient demonstrate two of these three criteria. (Devigili et al., *supra*, at Ex. F, Tab 1, p. 2.) There is no dispute that petitioner has clinical signs of small fiber impairment. (Ex. G, p. 7; Ex. 161, p. 1.) Accordingly, if petitioner's biopsy result is credited, the fact that petitioner never underwent QST is immaterial. Given that the skin biopsy result was accepted by the treating physicians (Ex. 154, p. 42), I do not find Dr. Callaghan's anecdotal experience with false positives (Ex. F, p. 4), standing alone, as sufficient basis for discounting that result. Dr. Callaghan did not identify any specific methodologic deficiency by Therapath nor did he identify any issue with petitioner's own biopsy collection (*see* Ex. 30, p. 40). The actual results showed "significant" reduction in nerve fiber density such that petitioner's results were "abnormal" (as opposed to "low normal") (Ex. 154, p. 63), suggesting it was not an equivocal finding. Thus, petitioner meets the inclusion criteria for small fiber neuropathy.

Ordinarily, under the diagnostic criteria for small fiber neuropathy cited by Dr. Callaghan, patients are excluded from diagnosis if they have: (1) any clinical sign of large fiber involvement; (2) any abnormality on nerve conduction study. (Devigili et al., *supra*, at Ex. F, Tab 1, p. 2.) Dr. Callaghan cites these criteria as a reason for doubting petitioner's small fiber neuropathy diagnosis. (Ex. F, p. 4.) However, petitioner has filed medical literature demonstrating that, in the context of Sjögren's syndrome, 45% of patients will have "mixed," rather than "pure," small fiber neuropathy. (Birnbaum et al., *supra*, at Ex. 109, p. 1.) Patients with "mixed" small fiber neuropathy will have some evidence of large fiber involvement. Specifically, the patients reviewed by Birnbaum et al. demonstrated: "areflexia, positive Romberg test, gait ataxia, and absent sensory nerve action potentials." (*Id.* at 4.) Some patients will even have evidence of motor

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and that Sjögren's syndrome would explain her neuropathy. However, petitioner acknowledges that "the dispute here is between respondent's experts . . . this does not appear to be a disputed matter between opposing parties that requires the Court's adjudication." (ECF No. 152, p. 103 n.28.) Dr. Lightfoot's opinion, though equivocal, was explicit in opining that he could not rule out Sjögren's syndrome (Ex. C, p. 5), and petitioner's own expert, Dr. Gupta, affirmatively opined, in complete agreement with Dr. Matloubian, that petitioner did have Sjögren's syndrome and that her peripheral neuropathy was associated with her Sjogren's syndrome (Ex. 104, p. 4).

involvement on NCS but no detectable weakness on physical examination, suggesting a subclinical motor nerve involvement. (*Id*.) Notably, these same features – areflexia, positive Romberg, and gait ataxia – have been stressed by petitioner as otherwise indicating a sensory variant CIDP. (ECF No. 152, pp. 88-89 (discussing Dr. Souayah's opinion at Ex. 42, p. 19 and Ex. 111, pp. 2-3).)

Finally, to the extent Dr. Callaghan cites various other symptoms as confounding of a small fiber neuropathy diagnosis, this is also not persuasive. At least some of the other symptoms are compatible with her Sjögren's syndrome. (Raphaèle Seror et al., *EULAR Sjögren's Syndrome Disease Activity Index: Development of a Consensus Systemic Disease Activity Index for Primary Sjögren's Syndrome*, 69 ANNALS RHEUMATIC DISEASE 1103 (2010) (Ex. G, Tab 2) (identifying fatigue and mild cognitive dysfunction as potential features of Sjögren's syndrome with neurologic manifestations); Margaretten, *supra*, at Ex. G, Tab 4.) And, as Dr. Lightfoot stressed, petitioner's constellation of other symptoms is largely subjective. (Ex. C, p. 4.) In any event, the fact that the small fiber neuropathy does not explain petitioner's entire constellation of symptoms does not necessary suggest it is not present. Petitioner was diagnosed as having small fiber neuropathy by several treating physicians who were all aware of her overall constellation of symptoms. (Ex. 8, pp. 6-7 (Dr. Kapur); Ex. 41, pp. 3-4 (Dr. Brannagan); Ex. 102, pp. 12 (Dr. Suresh); Ex. 103, p. 20 (Dr. Lee); Ex. 154, p. 6 (Dr. Vukic).) In fact, to the extent some of these symptoms could be the result of autonomic dysfunction, one of petitioner's treating physicians, Dr. Suresh, diagnosed petitioner as having small fiber neuropathy with autonomic involvement. (Ex. 102, p. 12; *see also* Baer & Bhattacharyya, *supra*, at Ex. G, Tab 1, p. 6 (discussing autonomic symptoms as occurring in the context of Sjögren's-related small fiber neuropathy); Margaretten, *supra*, at Ex. G, Tab 4, p. 5 (discussing autonomic neuropathy as a feature of Sjögren's syndrome).) Moreover, the fact that there is otherwise preponderant evidence that petitioner has Sjögren's syndrome with neurologic manifestations further contributes to this conclusion, given that small fiber neuropathy is known to be associated with that condition. There is no debate between Drs. Gupta and Matloubian that small fiber neuropathy, in particular, can be associated with Sjögren's syndrome. (Ex. 104, p. 3; Ex. 161, p. 1; Ex. G, p. 9.) Respondent's other rheumatology expert, Dr. Lightfoot, doubted that petitioner's anti-SSA antibodies would be associated with CIDP, but did not address small fiber neuropathy. (Ex. C.)

Accordingly, there is preponderant evidence that petitioner has small fiber neuropathy as sequela of her Sjögren's syndrome.

iii. <u>There is not preponderant evidence that petitioner suffered CIDP</u>

Throughout the course of her treatment history, petitioner was evaluated on an outpatient basis by ten different neurologists. On the whole, the neurology evaluations reflect an evolution in thinking whereby the initial suspicion of CIDP gave way to small fiber neuropathy related to Sjögren's syndrome as a more likely explanation for petitioner's condition. Dr. Brofin first suspected GBS. (Ex. 6, pp. 30, 34.) However, Dr. Busono subsequently believed petitioner's condition would constitute CIDP, though by

the conclusion of his course of treatment with petitioner he felt that diagnosis was in doubt. (Ex. 7, p. 2.) Thereafter, Dr. Kapur felt the condition was either CIDP or Sjögren's-related small fiber neuropathy (Ex. 8, p. 6), and Dr. Ma then opined petitioner had both conditions (Ex. 16, p. 258). However, Dr. Suresh and Dr. Lee (with Dr. Hurst) then concluded that petitioner had Sjögren's-related small fiber neuropathy without good evidence of CIDP. (Ex. 102, p. 12; Ex. 103, p. 20.) Throughout this course of treatment, Dr. Vukic equivocated. He initially diagnosed CIDP, but then doubted the diagnosis and referred petitioner to a rheumatologist. (Ex. 5, p. 12; Ex. 30, pp. 35-39; Ex. 154, p. 62.) Thereafter, he concluded petitioner had Sjögren's-related small fiber neuropathy. (Ex. 154, pp. 52, 57.) However, he would later revert to believing petitioner's symptomatology was consistent with CIDP. (*Id.* at 46.) Dr. Dover subsequently treated petitioner on the basis that her CIDP diagnosis was previously established and, finally, Dr. Sylvester indicated petitioner's diagnosis was yet to be confirmed. (Exs. 153, p. 3; Ex. 160, p. 95.)

Petitioner's own expert, Dr. Souayah, agrees that petitioner did not meet the diagnostic criteria for CIDP, that her later neurophysiological evaluations did not fit CIDP, and that her diagnosis changed from CIDP to small fiber neuropathy. (Ex. 111, p. 3; Ex. 150, pp. 1-2.) Citing Dr. Souayah's opinion, petitioner argues that the change in diagnosis reflects that petitioner's condition evolved in itself (ECF No. 152, p. 90); however, based on my review of the medical records, the change in diagnosis more likely reflects continued reassessment based on accumulating evidence. I disagree with Dr. Souayah's implicit assertion that the later medical assessments should not be weighed against the earlier treatment records in considering the correct diagnosis. Accordingly, while some of petitioner's treating neurologists did opine that petitioner suffered CIDP, the evidence, considered as a whole, does not preponderate in favor of a diagnosis of CIDP.

Several features of petitioner's clinical history cited by Dr. Souayah as indicative of CIDP do not actually provide a clear-cut distinction, especially when considering that Dr. Souayah readily admits that petitioner does not meet the criteria for a "classic" form of CIDP and instead opines that petitioner suffered a sensory-predominant form of the condition characterized by paresthesia and gait dysfunction. (Ex. 111, p. 2; Ex. 42, pp. 18-19.) Specifically, Dr. Souayah cites numbness starting in petitioner's hands and progressing to her feet three days later as indicative of CIDP. (Ex. 42, pp. 18-19.) What petitioner first reported was tingling and numbness. (Ex. 2, p. 5; Ex. 6, p. 4.) Thus, when petitioner first presented for her condition, her symptoms were felt to be indicative of peripheral neuropathy. (Ex. 2, p. 16.) Regardless of whether numbness can also be seen in CIDP, sensation loss (specifically pin prick and thermal), as well as tingling or pins and needles, are consistent with small fiber neuropathy. (Devigili et al., *supra*, at Ex. F, Tab 1, pp. 2, 5 tbls.1 & 2; Birnbaum et al., *supra*, at Ex. 109, pp. 5-7 tbl.2.) Symptoms beginning in petitioner's hands then progressing to her feet is atypical for either CIDP or small fiber neuropathy; however, the overall pattern of symptoms is consistent with small fiber neuropathy. (Birnbaum et al., *supra*, at Ex. 109, p. 9.) Dr. Souayah also stresses petitioner's unsteady gait and reduced reflexes (absent at the ankles), positive Romberg, and abnormal vibration sensation. (Ex. 42, pp. 18-19.)

Again, however, as discussed in the preceding section, this may be consistent with a "mixed" small fiber neuropathy as specifically seen in Sjögren's syndrome. (Birnbaum et al., *supra*, at Ex. 109, p 4; *see also* Margaretten, *supra*, at Ex. G, Tab 4, p. 2 (noting that small fiber neuropathy in Sjögren's syndrome may have "concomitant large fiber neuropathy").) Thus, for example, one study that Dr. Souayah cites as demonstrating the concept of a sensory-variant of CIDP specifically excluded Sjögren's syndrome patients from its study. (Ayrignac et al., *supra*, at Ex. 47, p. 1.)

Perhaps the most challenging aspect of petitioner's history is her initial electrodiagnostic finding of evidence of demyelination (Ex. 6, p. 1), followed by several subsequent EMG/NCS tests that were entirely negative for demyelination (Ex. 7, pp. 9-10; Ex. 5, p. 19; Ex. 24, pp. 10-11). Dr. Souayah finds significance in the first electrodiagnostic test (Ex. 111, p. 2) and views the later evaluations as indicating of a change in petitioner's condition over time, leading to the subsequent small fiber neuropathy diagnosis (*Id*. at 3). Dr. Callaghan, however, views the electrodiagnostic studies collectively and opines that the later normal studies point away from CIDP or any peripheral nervous system pathology. (Ex. A, p. 3.) He opines that the electrodiagnostic evidence taken as a whole indicates that petitioner never had large fiber involvement. (Ex. F, p. 4.) While petitioner's first electrodiagnostic study does cloud her overall clinical picture, I ultimately find Dr. Callaghan more persuasive in assessing the electrodiagnostic studies holistically. Based on my review of Dr. Souayah's reports, he does not reconcile the change in petitioner's electrodiagnostic findings (from which he seemingly implies resolution of demyelination) with petitioner's subsequent prolonged clinical course.

Another puzzling aspect of petitioner's history is her persistent symptom of weakness that, as Dr. Callaghan stressed, consistently lacked any corresponding finding of significant weakness upon neurologic exam. (Ex. A, p. 3). Dr. Souayah's proposed CIDP diagnosis does not neatly resolve this issue, however, because Dr. Souayah agrees that petitioner's lack of progressive, symmetric, proximal weakness points to a sensory form of CIDP rather than "classic" CIDP. (Ex. 111, pp. 1-2.) In that regard, the literature filed by respondent reflects that primary Sjögren's syndrome can manifest with weakness as a feature of rheumatic disease, rather than as a neurologic manifestation of the condition. (Margaretten, *supra*, at Ex. G, Tab 4, p. 7.)

Finally, the experts disagree regarding the significance, if any, of petitioner's response to IVIG and plasmapheresis, as well as the apparent relapsing nature of petitioner's condition. However, this aspect of petitioner's history does not clearly favor any particular diagnosis. Petitioner's records are inconsistent with respect to whether her condition responded to treatment. Although the records reflect that petitioner responded well to treatment in some instances on a short-term basis, the records otherwise reflect dissatisfaction with petitioner's response to treatment over the longer course. And, although petitioner reported variations in her symptom presentation over time, she appears to have remained continuously symptomatic, and I do not see where her symptoms ever had a relapsing/remitting pattern. This aspect of petitioner's history is difficult to assess because many of her symptoms were subjective and some doubt

was expressed by her treating physicians regarding some of her reported relapses. For example, during her June 2019 hospitalization, Dr. Sonbol felt that, upon neurologic examination, some of petitioner's symptoms may have been non-physiologic. (Ex. 101, p. 29.) In that regard, Dr. Lightfoot's assertion that petitioner may have been susceptible to a placebo effect is not entirely unreasonable. (Ex. C, p. 4.) There was also some suspicion that the acute shortness of breath petitioner experienced may have been panic attacks. (Ex. 101, p. 9.) Later, when petitioner reported to Dr. Dover that she was experiencing worsening of symptoms, Dr. Dover pressed for clarification and elicited that petitioner was suffering only an increase in fatigue, which is fairly non-specific. (Ex. 153, p. 2)

Considering all of the above, there is not preponderant evidence that petitioner suffered CIDP.

b. Medical theory of causation (*Althen* prong one)

Under *Althen* prong one, petitioner must provide a "reputable medical theory," demonstrating that the vaccine received can cause the type of injury alleged. *Pafford v. Sec'y of Health & Human Servs.*, 451 F.3d 1352, 1355-56 (Fed. Cir. 2006) (quoting *Pafford v. Sec'y of Health & Human Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004)). Such a theory must only be "legally probable, not medically or scientifically certain." *Knudsen*, 35 F.3d at 548-49. Petitioner may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *See Andreu*, 569 F.3d at 1378-79 (citing *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1325-26 (Fed. Cir. 2006)). However, "[a] petitioner must provide a 'reputable medical or scientific explanation' for [her] theory. While it does not require medical or scientific certainty, it must still be 'sound and reliable.'" *Boatmon*, 941 F.3d at 1359 (quoting *Moberly ex rel. Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1322 (Fed. Cir. 2010); *Knudsen*, 35 F.3d at 548-49).

As explained above, petitioner's theory of causation is largely predicated on the notion that CIPD can be vaccine-caused in the same manner as GBS. Thus, my finding that petitioner did not suffer CIDP dramatically undercuts petitioner's claim, leaving her with virtually no remaining theory of causation.[24] "Because causation is relative to the injury, a petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case, although the explanation need only be 'legally probable, not medically or scientifically certain.'" *Broekelschen*, 618 F.3d at 1345 (quoting *Knudsen*, 35 F.3d at 548-49). Absent the link Dr. Souayah posited between CIDP and the flu vaccine, petitioner's experts offer nothing more than a vague

[24] Although I do not find it necessary to reach the question of whether the flu vaccine can cause CIDP, it is worth noting that prior cases in which petitioners have alleged that the flu vaccine-caused CIDP have led to mixed results. *See, e.g.*, *Nieves v. Sec'y of Health & Human Servs*., No. 18-1602V, 2023 WL 3580148, at *36 (Fed. Cl. Spec. Mstr. May 22, 2023) (explaining the history of CIDP cases in the program).

reference to the "mosaic of autoimmunity" and a general "loss of immunological tolerance" to support vaccine causation.

However, without more, reliance on an unspecified autoimmune process fails on a fundamental level. There are various pathways to autoimmunity and many autoimmune conditions have little to no suspicion of vaccine causation. *E.g.*, *Kelly v. Sec'y of Health & Human Servs.*, No. 16-1548V, 2023 WL 3274159, at *9 (Fed. Cl. Spec. Mstr. May 5, 2023) (explaining that "[t]here is little debate that myasthenia gravis is an autoimmune neuromuscular disorder and there is little debate that molecular mimicry is, in general, a viable theory of autoimmunity that can in at least some contexts implicate vaccination. Importantly, however, these predicates are not enough to meet petitioner's burden of proof."); *Casazza v. Sec'y of Health & Human Servs.*, No. 17-947V, 2023 WL 6214984, at *10 (Fed. Cl. Spec. Mstr. Aug 30, 2023) (explaining "there is no dispute that [rheumatoid arthritis] is an autoimmune condition of uncertain cause" and that [v]ery little on this record apart from Dr. Gershwin's say-so associates any vaccine with [rheumatoid arthritis] whereas much more purports to refute Dr. Gershwin's opinion"). Thus, it is not enough, as Dr. Gupta implies, to simply rely on the fact that Sjögren's syndrome, CIDP, and small fiber neuropathy are all autoimmune conditions. (Ex. 151.) Simply, it is too vague to preponderantly support a theory of causation. *Accord J.F. v. Sec'y of Health & Human Servs.*, No. 13-799V, 2022 WL 5434214, at *32 (Fed. Cl. Spec. Mstr. Sept. 9, 2022) (finding that "petitioner is not persuasive in identifying ASIA as a sound and reliable means of identifying the presence of an autoimmune injury in those who are not suffering a defined autoimmune condition. Given that petitioner did not suffer any recognized autoimmune condition, this is fatal to petitioner's *Althen* prong one showing."); *Kinney v. Sec'y of Health & Human Servs.*, No. 18-1522V, 2024 WL 2831616, at *18 (Fed. Cl. Spec. Mstr. May 8, 2024) (explaining that "[t]he fact that a person may be prone to autoimmunity or experience multiple autoimmune conditions does not automatically lead to the conclusion that the one autoimmune condition is causally related to the other(s)" and rejecting as speculative the expert's premise that "the presence of one autoimmune condition in itself simply raises a suspicion that the same autoimmune process also explains any other condition or symptoms petitioner may have"). For example, prior cases have explained with respect to molecular mimicry, as cited by Dr. Souayah, that it "is a generally accepted scientific principle, [but] mere invocation of the scientific term does not carry a petitioner's burden in a Program case." *Deshler v. Sec'y of Health & Human Servs.*, No. 16-1070V, 2020 WL 4593162, at *20 (Fed. Cl. Spec. Mstr. July 1, 2020) (citing *Forrest v. Sec'y of Health & Human Servs.*, No. 14-1046V, 2019 WL 925495, at *3 (Fed. Cl. Spec. Mstr. Jan. 18, 2019)). Ultimately, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder ex rel. Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl. 706, 743 (2009) (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)); *see also Isaac v. Sec'y of Health & Human Servs.*, No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *aff'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. App'x 999 (Fed. Cir. 2013).

Here, neither Dr. Souayah nor Dr. Gupta provided any explanation or substantiation of a causal theory for Sjögren's syndrome and/or small fiber neuropathy. Moreover, Dr. Matloubian is persuasive in explaining that Dr. Souayah's attempt to rely generically on a loss of immune tolerance is not persuasive in the context of Sjögren's syndrome. (Ex. G, p. 11.) Dr. Matloubian explains that, while autoimmune, the underlying cause of Sjögren's syndrome is unknown and not associated with infectious triggers. (*Id*.) Dr. Callaghan is also persuasive in observing that Dr. Souayah did not substantiate that mechanisms such as molecular mimicry or bystander activation implicate the flu vaccine as a cause of small fiber neuropathy. (Ex. E, p. 3.) Although CIDP, small fiber neuropathy, and GBS are all peripheral neuropathies, they cannot simply be conflated, and the cause of one does not imply a cause of the others, absent some substantiation. *See, e.g. McGill v. Sec'y of Health & Human Servs.*, No. 15-1485V, 2023 WL 3813524, at *26 (Fed. Cl. Spec. Mstr. May 11, 2023) (explaining that "[w]hile Dr. Tornatore is correct that there is some overlap between GBS and [small fiber neuropathy], he is not persuasive in equating the causes of GBS to the causes of [small fiber neuropathy]. In contrast to GBS, [small fiber neuropathy] is generally considered to be caused by underlying systemic conditions, including autoimmune conditions, diabetes, and toxic causes. Only a subset of idiopathic [small fiber neuropathy] cases is suspected to result from tissue-specific dysimmunity in a manner that could potentially be compared to GBS." (internal citation omitted)).

Accordingly, petitioner has not met her burden of proof under *Althen* prong one.

c. Logical sequence of cause and effect (*Althen* prong two)

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326-27; *Grant*, 956 F.2d at 1147-48. Medical records are generally viewed as particularly trustworthy evidence. *Cucuras*, 993 F.2d at 1528. However, medical records and/or statements of a treating physician's views do not *per se* bind the special master. *See* § 300aa-13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder*, 88 Fed. Cl. at 745 n.67 (2009) ("[T]here is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted."). A petitioner may support a cause-in-fact claim through either medical records or expert medical opinion. § 300aa-13(a). The special master is required to consider all the relevant evidence of record, draw plausible inferences, and articulate a rational basis for the decision. *Winkler v. Sec'y of Health & Human Servs.*, 88 F.4th 958, 963 (Fed. Cir. 2023) (citing *Hines*, 940 F.2d at 1528).

There are three issues that warrant attention under *Althen* prong two. First, respondent contends that to the extent the evidence preponderantly establishes that petitioner suffers small fiber neuropathy, then that small fiber neuropathy should be attributed to her Sjögren's syndrome, rather than her vaccination. Second, petitioner's treating physicians did not otherwise support the notion that her Sjögren's syndrome

and small fiber neuropathy were causally related to her vaccination. Third, respondent further contends that petitioner's Sjögren's syndrome predated the vaccination at issue. If petitioner's condition developed prior to vaccination, then logically it could not have been caused by that vaccine. *E.g.*, *L.Z. v. Sec'y of Health & Human Servs.*, No. 14-920V, 2018 WL 5784525, at *18 (Fed. Cl. Spec. Mstr. Aug. 24, 2018) (explaining that "[p]etitioner's direct causation claim cannot succeed, as she cannot demonstrate a vaccine 'caused' an illness predating vaccination").

Both Dr. Matloubian and Dr. Gupta explain that small fiber neuropathy may be a feature of Sjögren's syndrome. (Ex. 104, p. 3 (citing Birnbaum et al., *supra*, at Ex. 109); Ex. G, pp. 7-8.) And, importantly, the medical literature filed in this case supports the proposition that peripheral neuropathies in Sjögren's syndrome, such as small fiber neuropathy (or CIDP[25]), are causally-related manifestations of the Sjögren's syndrome and not merely comorbidities. (Mori et al., *supra*, at Ex. 108; Birnbaum et al., *supra*, at Ex. 109; Margaretten, supra, at Ex. G, Tab 4.) Thus, with respect to petitioner herself, Dr. Gupta opines that "it is more likely than not that the SSA antibodies and Sjogren's Syndrome were associated with the neuropathy in her case." (Ex. 104, p. 4.) And, while Dr. Gupta nonetheless opined that this would remain compatible with a "mosaic of autoimmunity," that opinion is not substantiated for the reasons discussed under *Althen* prong one, above. Neither Dr. Gupta nor Dr. Souayah have presented a theory of causation directly implicating petitioner's vaccination as a cause of Sjögren's syndrome. Accordingly, the fact that petitioner's small fiber neuropathy is a result of her Sjögren's syndrome means there is no logical sequence of cause and effect connecting her vaccination to her small fiber neuropathy. *Winkler*, 88 F.4th at 963 (quoting *Stone v. Sec'y of Health & Human Servs.*, 676 F.3d 1373, 1379 (Fed. Cir. 2012), for the proposition that "evidence of other possible sources of injury can be relevant . . . to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question" (emphasis omitted)); *see also McGill*, 2023 WL 3813524, at *31-33 (finding that petitioner's small fiber neuropathy was more likely related to preexisting rheumatoid arthritis than to the subject vaccinations).

Notably, petitioner's medical records reflect a very long history of evaluation directed at finding a workable diagnosis for petitioner's condition. Throughout that process, petitioner repeatedly presented her post-vaccination onset of symptoms as a pertinent part of her history. However, despite extensive consideration regarding the underlying cause of petitioner's condition, only one of her treating physicians, Dr. Vukic, opined that petitioner's condition was vaccine-caused. (Ex. 154, p. 46.) There are several reasons why Dr. Vukic's opinion is not strong evidence supporting petitioner's claim. As an initial matter, the basis for Dr. Vukic's opinion is not well explained and it appears that it is merely reflective of the fact that petitioner's symptoms arose post-vaccination. However, the Federal Circuit has explained that "[a]lthough probative, neither a mere showing of a proximate temporal relationship between vaccination and

[25] Because both the medical literature and expert opinions support CIDP as among the potential neurologic sequela of Sjögren's syndrome, the presence of Sjogren's syndrome would pose a significant issue with respect to *Althen* prong two, even if I had concluded that petitioner did suffer CIDP and even if I had concluded that CIDP can in some instances be caused by the flu vaccine.

injury, nor a simplistic elimination of other potential causes of the injury suffices, without more, to meet the burden of showing actual causation." *Althen*, 418 F.3d at 1278 (citing *Grant*, 956 F.2d at 1149). Thus, "[a] treating physician's recognition of a temporal relationship does not advance the analysis of causation." *Isaac*, 2012 WL 3609993, at *26. Moreover, to the extent Dr. Vukic's opinion does include anything beyond *post hoc ergo propter hoc* reasoning, his opinion appears to have been predicated on his unwillingness to abandon the prior CIDP diagnosis, even after petitioner's Sjögren's syndrome and small fiber neuropathy were diagnosed. (Ex. 154, p. 46.) However, Dr. Vukic's determination to maintain the CIDP diagnosis does not appear to be reliable, given that he had referred petitioner for rheumatologic evaluation precisely because he had already doubted the CIDP diagnosis. (*Id.* at 62.) Indeed, Dr. Vukic's subsequent records confirm that his diagnostic assessment continued to be equivocal. (*Compare id.* at 6 (indicating symptoms due to small fiber neuropathy related to rheumatologic condition), *with* Ex. 155, p. 20 (indicating symptomatology consistent with CIDP).) And, in any event, petitioner was evaluated by numerous other specialists, neurologists and rheumatologists, who did not express any similar opinion, leaving Dr. Vukic as an outlier among petitioner's treating physicians.

Finally, in opining that petitioner suffered Sjögren's syndrome, Dr. Gupta specifically highlighted that among the potentially diagnostic aspects of her history, petitioner had a history of "prednisone responsive inflammatory hand arthritis." (Ex. 104, p. 4.) This had been reported by petitioner as part of her prior, pre-vaccination history when she first presented for a rheumatologic evaluation and was considered a potential feature of Sjögren's syndrome. (Ex. 2, p. 135.) Given this, Dr. Matloubian opined that petitioner's Sjögren's syndrome pre-dated her vaccination. Specifically, Dr. Matloubian agreed that petitioner's arthritis is consistent with Sjögren's syndrome because inflammatory arthritis (as opposed to osteoarthritis) would present with joint swelling and would be more likely to affect the MCP joints. (Ex. G, p. 9; *see also* Seror et al., *supra*, at Ex. G, Tab 2, p. 4.) Dr. Gupta contended that Dr. Matloubian "overstates" his opinion. He notes that his review of petitioner's clinical history was equivocal in explaining that petitioner "may" have inflammatory arthritis. (Ex. 161, p. 1.) However, while Dr. Gupta may have been more measured in his recitation of petitioner's history, he was unambiguous in his ultimate conclusion that petitioner had inflammatory arthritis as one of "several other features consistent with [Sjögren's syndrome]." (Ex. 104, p. 4.) Accordingly, I agree with Dr. Matloubian's interpretation that Dr. Gupta's assessment effectively places petitioner's Sjögren's syndrome pre-vaccination.

Dr. Matloubian further notes that petitioner was never tested for anti-SSA antibodies prior to vaccination, so it is unknown (and entirely possible) that these antibodies were present prior to vaccination and dating as far back as her arthritis. (Ex. G, p. 9.) Dr. Gupta disagrees, stressing petitioner's prior negative ANA. (Ex. 161, p. 2 (citing Ex. 21, p. 21).) However, the Sjögren's syndrome literature filed by respondent indicates that "ANA should not be used as a screening test for [Sjögren's syndrome] or [Sjögren's syndrome]-related antibodies, since some patients may have anti-Ro/SSA and/or anti-La/SSB antibodies despite a negative immunofluorescence assay for ANA." (Baer & Bhattacharyya, *supra*, at Ex. G, Tab 1, p. 10.) Dr. Gupta asserts that when an

ANA panel undergoes cascade testing, a negative ANA result would usually also indicate a negative SSA result. (Ex. 161, p. 2.) Dr. Matloubian points out, however, that the record of petitioner's 2012 ANA result is inadequate to determine what method of testing was used. (Ex. G, p. 10.) Given all of this, the evidence preponderates in favor of a finding that petitioner's Sjögren's syndrome likely predated her vaccination based on her prior history of inflammatory arthritis, which her own expert opines is consistent with her diagnosed Sjögren's syndrome.

For all these reasons, petitioner has not met her burden of proof under *Althen* prong two.

d. Proximate temporal relationship between vaccination and significant aggravation (*Althen* prong three)

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1278. A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorders etiology, it is medically acceptable to infer causation-in-fact." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.*; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *mot. for recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd*, 503 F. App'x 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877, at *26 (Fed. Cl. Spec. Mstr. May 30, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

Because petitioner's condition predated her vaccination, there is no temporal association between her vaccination and her injury as petitioner asserts. However, even assuming that petitioner satisfied *Althen* prong three based on her preferred timing of onset, that alone would not satisfy petitioner's overall burden of proof. *Veryzer v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 344, 356 (2011) (explaining that a "temporal relationship alone will not demonstrate the requisite causal link and that petitioner must posit a medical theory causally connecting the vaccine and injury"); *Hibbard v. Sec'y of Health & Human Servs.*, 698 F.3d 1355, 1364-65 (Fed. Cir. 2012) (holding the special master did not err in resolving the case pursuant to prong two when respondent conceded that petitioner met prong three).

VI. Conclusion

Petitioner has clearly suffered much over the course of a number of years. She has my sympathy and nothing in this decision is intended to minimize what she has experienced. However, for all the reasons discussed above, I cannot conclude that

there is preponderant evidence causally linking petitioner's vaccination to her condition. Accordingly, this case is dismissed.[26]

IT IS SO ORDERED.

s/Daniel T. Horner
Daniel T. Horner
Special Master

[26] In the absence of a timely-filed motion for review of this Decision, the Clerk of the Court shall enter judgment accordingly.