In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: March 17, 2022

MARY MALONEY,	*	PUBLISHED
Petitioner,	*	No. 19-1713V
v.	*	Special Master Nora Beth Dorsey
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Ruling on Entitlement; Pneumococcal Conjugate ("Prevnar 13") Vaccine; Guillain-Barré Syndrome ("GBS").
Respondent.	*	

Jeffrey S. Pop, Jeffrey S. Pop & Associates, Beverly Hills, CA, for petitioner.
Colleen Clemons Hartley, U.S. Department of Justice, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

On November 4, 2019, Mary Maloney ("petitioner"), filed a petition for compensation under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42 U.S.C. § 300aa-10 et seq. (2012),[2] alleging that she suffered Guillain-Barré Syndrome ("GBS") as the result of a pneumococcal conjugate ("Prevnar 13") vaccination she received on July 7, 2017. Petition at Preamble (ECF No. 1). Respondent argued against compensation, stating "this case [was] not appropriate for compensation under the terms of the Act." Respondent's Report ("Resp. Rept.") at 2 (ECF No. 30).

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

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

After carefully analyzing and weighing the evidence presented in this case in accordance with the applicable legal standards, the undersigned finds that petitioner has provided preponderant evidence that her proper diagnosis was GBS, and that the Prevnar 13 vaccine she received caused her GBS, satisfying her burden of proof under Althen v. Secretary of Health & Human Services, 418 F.3d 1274, 1280 (Fed. Cir. 2005). Accordingly, petitioner is entitled to compensation.

I. ISSUES TO BE DECIDED

Diagnosis is at issue. Petitioner's experts, Dr. Steven Sykes and Dr. Lawrence Steinman, opined that petitioner's correct diagnosis is GBS, whereas respondent's expert, Dr. Vinay Chaudhry disagreed. Petitioner's Exhibit ("Pet. Ex.") 65 at 3; Pet. Ex. 36 at 4; Resp. Ex. A at 13-15. Dr. Chaudhry opined that petitioner's clinical presentation and diagnostic studies were not consistent with GBS. Resp. Ex. A at 13-15; Resp. Ex. C at 14.

The parties also dispute causation. Petitioner does not allege a Table injury, and thus, she must prove causation-in-fact by preponderant evidence. Petitioner contended that she has provided preponderant evidence of the Althen criteria, and respondent disagreed. Pet. Motion for a Ruling on the Record and Brief in Support Thereof ("Pet. Mot."), filed Dec. 24, 2020, at 13-24 (ECF No. 41); Resp. Response to Pet. Mot. ("Resp. Response"), filed May 10, 2021, at 17-22 (ECF No. 52). Respondent argued that even if petitioner had GBS, she failed to (1) provide a reliable scientific or medical theory establishing that the Prevnar 13 vaccine can cause GBS, (2) provide evidence of a logical sequence of cause and effect between petitioner's Prevnar 13 vaccine and her alleged GBS, and (3) establish a medically appropriate temporal relationship between petitioner's Prevnar 13 vaccine and her alleged GBS. Resp. Response at 15-22.

II. BACKGROUND

A. Procedural History

In November 2019, petitioner filed her petition, medical records, and a declaration. Petition; Pet. Exs. 1-13. This case was reassigned to the undersigned on November 19, 2019. Notice of Reassignment dated Nov. 19, 2019 (ECF No. 12). Petitioner filed additional declarations on March 16, 2020. Pet. Exs. 14-19.

Petitioner filed an expert report from Dr. Steven Sykes on March 24, 2020. Pet. Ex. 20. On August 11, 2020, respondent filed an expert report from Dr. Vinay Chaudhry. Resp. Ex. A. On August 25, 2020, respondent filed his Rule 4(c) Report, stating "this case [was] not appropriate for compensation under the terms of the Act." Resp. Rept. at 2.

Thereafter, the undersigned held a Rule 5 conference on November 10, 2020. Rule 5 Order dated Nov. 16, 2020 (ECF No. 34). The undersigned agreed with the treating physicians' diagnosis of GBS, and preliminarily found petitioner would likely be able to satisfy all Althen prongs. Id. at 3-5. Given petitioner's age, and in order to expediate a ruling, the undersigned and parties agreed to resolve entitlement through a ruling on the record. Id, at 5.

In December 2020, petitioner filed a supplemental expert report from Dr. Sykes, an expert report from Dr. Lawrence Steinman, and a motion for a ruling on the record. Pet. Exs. 30, 36; Pet. Mot. On April 9, 2021, respondent filed a supplemental expert report from Dr. Chaudhry along with an expert report from Dr. J. Lindsay Whitton. Resp. Exs. C-D. Respondent filed a response to petitioner's motion for a ruling on the record on May 10, 2021. Resp. Response. On June 9, 2021, petitioner filed a reply to respondent's response, along with supplemental expert reports from Drs. Steinman and Sykes. Pet. Reply Brief ("Pet. Reply"), filed June 9, 2021 (ECF No. 55); Pet. Exs. 56, 65.

A status conference was held on June 29, 2021, upon request from respondent. Order dated June 29, 2021 (ECF No. 56). The undersigned set deadlines for supplemental expert reports and sur-reply briefs from both parties. Id. at 1-2.

Respondent filed supplemental expert reports from Drs. Chaudhry and Whitton in August 2021, and petitioner filed a supplemental expert report from Dr. Steinman in October 2021. Resp. Exs. G-H; Pet. Ex. 66. Thereafter, both parties filed sur-reply briefs. Resp. Sur Reply Brief ("Resp. Sur-Reply"), filed Nov. 29, 2021 (ECF No. 61); Pet. Second Reply Brief ("Pet. Sur-Reply"), filed Nov. 29, 2021 (ECF No. 62).

This matter is now ripe for adjudication.

B. Medical Terminology

GBS "is an acquired disease of the peripheral nerves that is characterized by rapidly progressing (with peak of [less than] 4 weeks) ascending paralysis with paresthesias." Resp. Ex. A at 12 (citing Resp. Ex. A, Tab 1 at 1;[3] Resp. Ex. A, Tab 2 at 2-3).[4] The condition is "relatively rare, with a reported incidence of 0.89-1.89 cases per 100,000 person-years in Western countries," affecting all ages, with an increased risk in older adults. Pet. Ex. 20 at 2-3 (citing Pet. Ex. 22 at 1).[5] Weakness is the prominent manifestation. Id. at 3. Other symptoms may include "sensory disturbances, cranial nerve palsies, and dysautonomia."[6] Id.; see also Resp. Ex. A at 12. Generally, weakness is progressive "over a period of 12 hours to 28 days before reaching a plateau." Pet. Ex. 20 at 3. Deep tendon reflexes are usually decreased or absent. Id.

[3] Hugh J. Willison et al., Guillain-Barré Syndrome, 388 Lancet 717 (2016).

[4] Francine J. Vriesendorp, Guillain-Barré Syndrome in Adults: Clinical Features and Diagnosis, UpToDate, https://www.uptodate.com/contents/guillain-barre-syndrome-in-adults-pathogenesis-clinical-features-and-diagnosis (last updated Dec. 4, 2018).

[5] Nobuhiro Yuki & Hans-Peter Hartung, Guillain-Barré Syndrome, 366 New Eng. J. Med. 2294 (2012).

[6] Dysautonomia is "malfunction of the autonomic nervous system." Dysautonomia, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=15146 (last visited Feb. 7, 2022).

In GBS, "[t]he myelin portion of the peripheral nerve is affected by inflammation . . . resulting in [] motor and/or sensory dysfunction." Pet. Ex. 20 at 3. Diagnosis is based on clinical history, physical examination, especially the neurological examination, and results of diagnostic tests, including electromyography/nerve conduction velocity ("EMG/NCV") testing[7] and lumbar puncture with analysis of cerebrospinal fluid ("CSF"). Id. Lumbar puncture usually reveals albuminocytological dissociation, or CSF with elevated protein and otherwise normal cell counts. Id.; Resp. Ex. A at 12; Resp. Ex. A, Tab 1 at 6. GBS is treated with intravenous immune globulin ("IVIG") or plasma exchange. Pet. Ex. 20 at 3; Resp. Ex. A at 12.

The causes of GBS are not known, however, it "is thought to be an autoimmune process that is triggered by antigenic stimulation, resulting in demyelination and destruction of peripheral nerves." Resp. Ex A, Tab 9 at 1.[8] GBS is thought to be "triggered by infections or immunizations." Pet. Ex. 20 at 3. "[A]proximately two-thirds of all cases are preceded by a gastrointestinal or respiratory infection within the prior 3 months." Resp. Ex. A, Tab 9 at 1. GBS has also been reported after several different vaccinations, including influenza, hepatitis B, Menactra, measles-mumps-rubella, polio, and varicella. Pet. Ex. 20 at 3. It usually occurs within six weeks after vaccination, with the highest incidence reported one to three weeks post-vaccination. Id.

"Molecular mimicry has been proposed to be a pathogenic mechanism . . . based on epidemiological, clinical, and experimental evidence of the association of infectious agents with autoimmune diseases and an observed cross-reactivity of antibodies raised by microbial components with host 'self' antigens." Resp. Ex. C, Tab 13 at 1.[9] The underlying etiology of GBS, although not known, "is considered to be an immune-mediated disorder resulting from generation of autoimmune antibodies and/or inflammatory cells which cross-react with epitopes on peripheral nerves and roots, leading to demyelination or axonal damage or both." Resp. Ex. A, Tab 13 at 2.[10] In an article filed by respondent, the way infection and vaccines may cause GBS is described below:

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[7] An EMG is "an electrodiagnostic technique for recording the extracellular activity (action potentials and evoked potentials) of skeletal muscles at rest, during voluntary contractions, and during electrical stimulation." Electromyography, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=15854 (last visited Feb. 7, 2022). NCV tests "the speed, in meters per second, at which an impulse moves along the largest fibers of a peripheral nerve." Nerve Conduction Velocity, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=117402 (last visited Feb. 7, 2022).

[8] Roger Baxter et al., Lack of Association of Guillain-Barré Syndrome with Vaccinations, 57 Clinical Infectious Diseases 197 (2013).

[9] Nobuhiro Yuki, Ganglioside Mimicry and Peripheral Nerve Disease, 35 Muscle & Nerve 691 (2007).

[10] James J. Sejvar, Guillain-Barré Syndrome and Fisher Syndrome: Case Definitions and Guidelines for Collection, Analysis, and Presentation of Immunization Safety Data, 29 Vaccine 599 (2011).

> Antigenic challenge by an antecedent infection or immunization leads to antigen-specific humoral and/or cellular immunity, and as such, this immune stimulation could theoretically result in GBS through a number of possible mechanisms. The concept of "molecular mimicry" involves a situation in which epitopes of a pathogen or vaccine protein could initiate development of antibodies and/or T-cells that could cross-react with epitopes on peripheral nerve myelin or axonal glycoproteins or ganglioside moieties. Activated macrophages could potentially be targeted to antigens on the myelin sheath and subsequently invade the basement membrane resulting in demyelination or, alternatively, invade at the nodes of Ranvier to result in axonal damage.

Id. at 3.[11] Furthermore, "GBS has been associated temporally with numerous vaccines; however, such temporal association must be differentiated from causality. In general, specific biological markers indicative of a cause-and-effect associated with a particular pathogen or vaccine are absent in GBS."[12] Id.

C. Summary of Medical Records[13]

1. Pre-Vaccination History

Petitioner was born on October 13, 1927, and was 89 years of age at the time of the vaccination at issue. Pet. Ex. 3 at 3. Her past medical history was significant for hypothyroidism, hypertension, possible stroke in April 2016 when she had an episode of dizziness, slurred speech, and mild facial asymmetry, and left-sided facial paralysis in January 2017. Id. at 3, 12; Pet. Ex. 5 at 1115. At the time of the vaccination at issue, she was living independently, able to drive, and able to care for herself. Pet. Ex. 3 at 3; Pet. Ex. 1 at ¶ 4. Petitioner had regular visits to her primary care physician, Dr. Yubelkis Tinoco, to monitor her blood pressure and for preventative care, including vaccinations.

2. Vaccination on July 7, 2017

On July 7, 2017, petitioner presented to Dr. Tinoco for a routine follow up visit. Pet. Ex. 3 at 3. At that visit, Dr. Tinoco documented that petitioner was driving and independent, and had no current health concerns. Id. Her hypertension was well controlled on medication. Id. She had no current complaints. Id. Review of symptoms was negative for any neurological problems, including weakness. Id. at 5. Dr. Tinoco performed a neurological examination and documented that petitioner was "alert and oriented to person, place and time," "ha[d] normal

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[11] Additional possible mechanisms are described in the article, but they do not involve molecular mimicry, or the theories proposed here. See Resp. Ex. A, Tab 13.

[12] There is evidence to support cause and effect in the instance of GBS following *Campylobacter jejuni* ("*C. jejuni*") infection. See, e.g., Resp. Ex. A, Tab 1 at 1-2; Resp. Ex. A, Tab 2 at 1-2.

[13] For a thorough medical chronology, see Resp. Ex. A at 2-12.

strength," and had no sensory deficit. Id. at 5-6. She also had "[g]ood mobility and balance." Id. at 6. Petitioner received a Prevnar 13 vaccine at that visit. Id. at 6-7.

3. Post-Vaccination Care

On July 18, 2017, petitioner was transported by ambulance to Martin Health System Emergency Department ("ED"). Pet. Ex. 5 at 81. ED triage note was documented by Registered Nurse ("RN") Stephen Baldwin, who noted "[chief complaint] of slurred speech since 7am, [patient] [states] some weakness also, weakness started yesterday but was worse this am." Id. at 80. She was seen by emergency room ("ER") physician Dr. Karl Weller, who also noted petitioner's chief complaint of aphasia[14] and complaint of left lower extremity weakness. Id. at 73. His NIH stroke scale examination of petitioner revealed "[n]o aphasia" and "[m]ild-to moderate dysarthria."[15] Id. at 76-77. Thereafter, a neurology consult was done by Dr. Lara Fix to evaluate petitioner for transient ischemic attack ("TIA").[16] Id. at 81-82, 148. Dr. Fix's history, taken at approximately 10:30 AM, stated that petitioner presented with

> slurred speech and left>right leg weakness for 2.5 hours prior to arrival. She did note some weakness of the bilateral lower extremities yesterday and had difficulty walking. Upon awakening this morning[,] she had even more difficulty ambulating and utilized a cane. In the ED, she reports the leg weakness has improved and while the slurred speech has improved she does not feel it has returned to baseline.

Id. at 148. Dr. Fix's note continued, stating that "[s]he reports that she was diagnosed with

[14] Aphasia is "a large group of language disorders involving defect or loss of the power of expression by speech, writing, or signs, or of comprehending spoken or written language, due to injury or disease of the brain or to psychogenic causes." Aphasia, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=3694 (last visited Feb. 7, 2022).

[15] Dysarthria is "a speech disorder consisting of imperfect articulation due to loss of muscular control after damage to the central or peripheral nervous system." Dysarthria, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=15144 (last visited Feb. 7, 2022).

[16] TIA is "a brief attack (from a few minutes to an hour) of cerebral dysfunction of vascular origin, with no persistent neurologic deficit." Transient Ischemic Attack, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=59631 (last visited Feb. 7, 2022).

pneumonia last week and has not fully recovered her strength and energy."[17] Id. at 149. In review of systems petitioner reported no fever, chills, nausea, or vomiting. Id. at 150. She had no nasal discharge, hemoptysis,[18] or pleurisy.[19] Id. Physical examination revealed that petitioner's lungs were clear bilaterally. Id. Mentally, petitioner was awake, alert, and oriented to person, place, and time. Id. Dr. Fix noted that petitioner had "[v]ery subtle dysarthria which may even be attributed to malaise and sleep-deprivation." Id. Dr. Fix's assessment was TIA. Id. at 151. Petitioner's "stroke-like symptoms" had "nearly resolved." Id. Petitioner was not a candidate for tissue plasminogen activator ("TPA") treatment[20] due to her improvement and resolution of her symptoms. Id. at 79. CT scan showed no intracranial abnormality. Id.

While in the ED on July 18, at 1:45 PM, RN Dawn M. Maynard also took a history from petitioner. Pet. Ex. 5 at 80. Ms. Maynard wrote, "[patient] reports a progressive, generalized weakness over 1 week after receiving pneumonia vaccine." Id. She added that petitioner noted slurred speech and severe left lower extremity weakness that was new that morning. Id. At 3:51 PM, Ms. Maynard conducted a physical assessment, finding that petitioner had weakness in all four extremities during the musculoskeletal exam. Id. at 105.

On July 18, petitioner was also evaluated by Occupational Therapist ("OT") Marisa Mueller, who wrote "patient states her weakness started after receiving a [pneumonia] shot several days ago." Pet. Ex. 5 at 96. Ms. Mueller assessed petitioner with "generalized weakness and decreased ability to perform mobility tasks independently." Id. at 97. Petitioner was also seen by Physical Therapist ("PT") Michaela Bundy, who observed that petitioner had an unsteady gait, decreased functional mobility, decreased balance and strength, and required a rolling walker for ambulation. Id. at 100-01.

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[17] On July 23, Dr. Fix wrote "[i]t is now learned that apparently [petitioner] received a pneumonia vaccine 1 week prior to admission after which she began to have progressive, generalized weakness with an acute change the day of admission including dysarthria and [lower leg extremity] weakness which prompted presentation to the hospital." Pet. Ex. 5 at 303. Dr. Fix added that petitioner "exhibited only subtle dysarthria, no lower extremity weakness" when arriving to the ED. Id.

[18] Hemoptysis is "expectoration of blood or of blood-stained sputum." Hemoptysis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=22096 (last visited Feb. 7, 2022).

[19] Pleurisy is "inflammation of the pleura," or lining of the lungs. Pleurisy, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=39590 (last visited Feb. 7, 2022). "Symptoms include localized chest pain and dry cough . . . ." Id.

[20] Tissue plasminogen activator, or TPA, is "a serine endopeptidase synthesized by endothelial cells, the major physiologic activator of plasminogen; when bound to fibrin clots it catalyzes the conversion of plasminogen to plasmin by hydrolysis of a specific arginine-valine bond." Tissue Plasminogen Activator, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=54759 (last visited Feb. 7, 2022).

Petitioner was admitted for observation for possible TIA versus cerebrovascular accident ("CVA").[21] Pet. Ex. 5 at 108. Admitting history and physical examination was completed by Physician Assistant ("PA") Peter Vo on July 18. Id. at 113. He wrote, "[p]atient reported since she received her pneumo[nia] vaccine a week ago on Monday, July 10, 2017,[22] she started not feeling very well. Last night on July 17, 2017, she felt acute weakness lower extremity more right than left with questionable slurred speech earlier this morning around 7 AM . . . ." Id. at 108. Mr. Vo noted that petitioner's speech was normal during his examination. Id. at 110. Chest X-ray was performed, and no acute abnormalities were reported. Id. at 112. Admitting assessment was "? TIA (transient ischemic attack) vs reaction to pneumovax[23] given on Monday 7/10/2017." Id.

On July 21, 2017, a neurosurgery consult was performed by Dr. Oszkar Szentirmal and Brian Foster, PA. Pet. Ex. 5 at 142. Chief complaint was bilateral lower extremity weakness. Id. Dr. Szentirmal noted that petitioner had an "acute onset of bilateral lower extremity weakness after aerobics class." Id. MRI showed severe lumbar stenosis but no myelopathy. Id. History documented by Mr. Foster, stated that petitioner's "legs started to feel weak and heavy and walking became very difficult" this week. Id. at 143. He added, "during this admission[,] her symptoms have steadily worsened to the point that she does not feel she can stand or walk at all." Id. Mr. Foster's physical examination documented 4- to 4/5 strength throughout, sensory perception was decreased to pinprick slightly in a stocking pattern bilaterally, and reflexes were trace to 1+ and symmetrical. Id. at 146. Petitioner's lungs were clear bilaterally and she had no labored breathing or shortness of breath. Id. His assessment was bilateral lower extremity weakness. Id. at 147. Due to petitioner's "global weakness," he recommended further workup, including EMG testing and neurology work up. Id.

On July 23, petitioner was noted to have acute diarrhea. Pet. Ex. 5 at 302. But, by the following day, July 24, her medical records noted her diarrhea improved. Id. at 296.

Dr. Jason P. Stabley conducted an EMG/NCV on July 24, 2017. Pet. Ex. 5 at 297. He noted that petitioner had "onset of progressive bilateral lower extremity and upper extremity weakness, sensory loss and legs[24] beginning within several days of receiving pneumococcal

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[21] CVA, or stroke, is "a condition with sudden onset caused by acute vascular lesions of the brain, such as infarction from hemorrhage, embolism, or thrombosis, or rupturing aneurysm. It may be marked by any of a variety of symptoms . . . including hemiparesis, vertigo, numbness, aphasia, and dysarthria." Stroke Syndrome, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=111462 (last visited Feb. 7, 2022).

[22] Petitioner's correct date of vaccination was July 7, not July 10, 2017. Even though Mr. Vo referenced the incorrect vaccination date, the undersigned finds Mr. Vo's note supports a finding that petitioner's weakness began several days after vaccination and prior to her hospital admission on July 18.

[23] Petitioner received the Prevnar 13 vaccine, not the Pneumovax vaccine.

[24] Dr. Stabley may have meant to write "sensory loss in legs."

vaccine." Id. His clinical examination "reveal[ed] significant neck flexor weakness, bilateral upper and lower extremity proximal and distal weakness, areflexia[,][25] and stocking distribution sensory loss to pinprick to the level of the mid calves." Id. CSF revealed cytoalbuminologic dissociation, with an elevated protein of 112 mg/dL (normal 15-40) and elevated glucose of 88 mg/dL (normal 40-70). Id. at 297, 393-95. Petitioner's clinical diagnosis was GBS. Id. at 297. Dr. Stabley interpreted the EMG as "consistent with acute inflammatory demyelinating polyneuropathy" ("AIDP"), also known as GBS. Id. Petitioner was treated for GBS with a five-day course of IVIG. Id. at 115.

Dr. Devang Patel performed a pulmonary consult on July 24, 2017. Pet. Ex. 5 at 136. He wrote petitioner had progressive weakness bilaterally in lower and upper extremities, and had sensory loss that began with the legs. Id. at 138. Dr. Patel's diagnoses were weakness of both lower extremities and GBS. Id. at 140-41. Review of systems was also significant for shortness of breath. Id. Physical examination found petitioner's lung sounds were diminished and she had "[s]cattered rhonchi."[26] Id. at 139. Dr. Patel assessed petitioner with "respiratory insufficiency" and "bibasilar atelectasis."[27] Id. at 141. His diagnosis was "lower respiratory infection" and he ordered ceftriaxone and repeat chest X-ray. Id. On July 26, petitioner's chest X-rays showed "low lung volumes with basilar scarring or subsegmental atelectasis." Id. at 158.

On July 25, Dr. Paul Gaeta examined petitioner. Pet. Ex. 5 at 280. Under history of present illness, he noted petitioner "received a pneumonia vaccine [] prior to admission," and "[a]bout a week later," she developed weakness in her lower extremities and then developed slurred speech on the day of admission. Id. Petitioner "also noticed that she developed some weakness of the hands." Id. At the time of his examination, GBS was suspected, and petitioner was receiving IVIG. Id. One of petitioner's daughters stated petitioner "usually has irritable bowel syndrome" but she did not remember petitioner complaining of "loose or worse bowel movements prior to coming into the hospital." Id. Dr. Gaeta's physical examination revealed decreased sensation in lower extremities. Id. at 281. Assessment was "[w]eakness of both lower extremities suspected [GBS] at this time on 2 IgG." Id. at 282.

On July 30, Dr. Jean Vickers performed a renal consult and observed that petitioner's urinary retention "seem[ed] to be a long-standing problem." Pet. Ex. 5 at 202. Later that day, Dr. Gaeta examined petitioner again and his diagnosis remained "[w]eakness of both lower extremities secondary to [GBS]." Id. at 193. On July 31, a progress note authored by a medical

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[25] Areflexia is the absence of reflexes. Areflexia, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=4035 (last visited Feb. 7, 2022).

[26] Rhonchus is "a whistling or snoring sound heard on auscultation of the chest when the air channels are partly obstructed." Rhonchus, Merriam-Webster Dictionary, https://www.merriam-webster.com/dictionary/rhonchus (last visited Feb. 7, 2022).

[27] Atelectasis is the "incomplete expansion of a lung or a portion of a lung; it may be a primary (congenital), secondary, or otherwise acquired condition." Atelectasis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=4646 (last visited Feb. 7, 2022).

student and co-signed by Dr. Gaeta stated that petitioner's "symptoms started a week prior to admission with fatigue and malaise. [T]he precipitating cause was believed to [be the] pneumonia vaccination." Pet. Ex. 6 at 79.

Physical therapy notes on July 31, showed that petitioner had left and right lower extremity buckling and an ataxic gait, consistent with GBS. Pet. Ex. 5 at 189. After petitioner's diagnostic work up, her medical records contain multiple references to her diagnosis of GBS. See, e.g., Pet. Ex. 5 at 51, 114-15, 173, 177, 181, 185, 194, 197, 201, 211, 215, 220, 227, 242, 275, 293.

Studies on petitioner's CSF were conducted to determine the etiology of her GBS. Gram stain and cultures were negative, and varicella zoster and herpes simplex viruses were not detected. Pet. Ex. 5 at 439, 441. Acid-Fast Bacillus ("AFB") stain, fungal culture, cytomegalovirus, enterovirus, venereal disease research laboratory ("VDRL"), and antinuclear antibodies ("ANA") studies were also negative. Id. at 390, 395, 411-12, 432-37.

Petitioner was discharged to a rehabilitation facility on August 2, 2017. Pet. Ex. 6 at 153. Petitioner's diagnosis on admission to the rehabilitation facility was "[GBS] d/t[28] Pneumonia Vaccine." Id. With rehabilitation, petitioner's strength improved but her physical limitations prevented her from returning home. Pet. Ex. 9 at 92-112. Since her hospital discharge in 2017, petitioner has resided at several assisted living facilities, and her records reveal that she moved to Bethel Park Senior Living facility in 2018. Pet. Ex. 1 at ¶¶ 10-15.

D. Declarations

1. Petitioner

Before petitioner received the Prevnar 13 vaccine on July 7, 2017, she "did not have any difficulty walking or weakness in [her] arms or legs," and she "was very active." Pet. Ex. 1 at ¶ 4. She would walk regularly with her neighbors, attend aerobic classes, play bridge, and "was independent in all areas of [her] life and was able to drive and care for [herself] and [her] home." Id.; see also Pet. Ex. 14 at ¶ 2.

A few days after vaccination, petitioner became fatigued, "but was back to [her] normal energy level and routine within a few days." Pet. Ex. 14 at ¶ 3; see also Pet. Ex. 1 at ¶ 6. Between July 7, the date of vaccination, and July 18, 2017, petitioner initially felt some fatigue, but otherwise felt healthy. Pet. Ex. 14 at ¶ 4. She did not have a cough, runny nose, fever, or pneumonia. Id. Petitioner also remained active during this time. Id.

On July 17, 2017, petitioner had no health concerns. Pet. Ex. 14 at ¶ 7. On July 18, 2017, when she woke up around 7 AM, she was unable to move her legs, unable to walk, could not feel her feet, and had pain in her legs. Id.; Pet. Ex. 1 at ¶¶ 7-8. She was hospitalized from July 18 to August 2, 2017. Pet. Ex. 1 at ¶ 9. She underwent a lumbar puncture and EMG/NCV,

[28] The abbreviation d/t means "due to."

which confirmed GBS diagnosis. Id. She received five days of IVIG infusions, as well as physical therapy and occupational therapy. Id.

Thereafter, she was discharged to an acute rehabilitation facility, Solaris HealthCare. Pet. Ex. 1 at ¶¶ 9-10. Petitioner "was bedbound and unable to turn or feed [herself]. [She] was able to get out of bed only with the assistance of a mechanical lift and the assistance of two attendants." Id. at ¶ 10. Petitioner also needed a catheter and was frequently incontinent. Id. After one week at Solaris, petitioner was transferred to Water's Edge Extended Care on August 8, 2017 for daily rehabilitation. Id. at ¶¶ 10-11. On admission, she was still unable to get out of bed on her own, was unable to turn herself, and needed continue care to assist with bowel movements. Id. at ¶ 11. "[She] had daily physical therapy, occupational therapy, and speech therapy." Id. A few days before her discharge on September 22, 2017, her catheter was removed. Id. She was sent to Grand Oaks of Jensen Beach assisted living facility. Id. at ¶¶ 11-12.

Petitioner lived at various assisted living facilities until November 2018, when she moved to a retirement home. Pet. Ex. 1 at ¶¶ 12-15. As of the date of her first declaration, October 31, 2019, petitioner continued to have intermittent numbness and tingling in her hands and feet, and fatigued easily. Id. at ¶ 20. She was no longer able to drive or live independently. Id.

2. Sharon Newton

Sharon Newton is the daughter of petitioner. Pet. Ex. 15 at ¶ 4. She has worked as a RN since 1974. Id. at ¶ 3. Ms. Newton noted petitioner was "remarkably active for a person of her age," and petitioner "was well enough to care for her home on her own and to travel independently." Id. at ¶ 6.

In July 2017, Ms. Newton lived in a different state than petitioner, but they would speak on the phone at least twice per week. Pet. Ex. 15 at ¶ 5. Because of petitioner's planned travel later that month, Ms. Newton was in close contact with petitioner. Id. at ¶ 9. Petitioner told Ms. Newton that after her vaccination, she was exhausted, but was otherwise feeling back to normal the following day. Id. Ms. Newton stated petitioner was in her usual state of good health. Id. at ¶ 11. In the week before her hospitalization on July 18, 2017, petitioner told Ms. Newton that she was going to aerobics class, playing bridge, and getting her hair done. Id. at ¶ 10.

On July 18, 2017, Ms. Newton received a call from petitioner and her cousin informing her that petitioner "lost the ability to walk due to weakness and numbness in both[] of her feet." Pet. Ex. 15 at ¶ 12. Ms. Newton arrived in Florida on July 23, 2017, and stayed for five weeks. Id. at ¶ 13.

Ms. Newton stated petitioner "gradually regained her ability to walk and to care for her own personal hygiene needs[,] but it was a long and difficult process. [Petitioner] never regained her energy to live without extensive assistance." Pet. Ex. 15 at ¶ 15. As of March 8, 2020, the date in which Ms. Newton executed her declaration, petitioner intermittently suffer[ed] from the feeling of pins and needles, require[d] a cane or walker for balance when she got tired, and "continue[d] to be an extreme fall risk." Id. at ¶ 16.

3. Erin Fortunato

Petitioner is the mother of Erin Fortunato. Pet. Ex. 17 at ¶ 4. Ms. Fortunato lives in Pennsylvania. Id. at ¶ 1. She speaks with petitioner on the phone about two to three times per week. Id. at ¶ 4. Prior to petitioner's GBS diagnosis, Ms. Fortunato remembers petitioner going on a daily neighborhood walk and driving to various activities including hair appointments, bridge games, aerobics classes, church, school events for petitioner's grandniece and grandnephew, the bank, and grocery shopping. Id. at ¶ 5.

Ms. Fortunato recalls petitioner feeling tired shortly after her Prevnar 13 vaccine, "but that she felt back to normal a few days later." Pet. Ex. 17 at ¶ 6. She spoke to petitioner on the phone on the evening of July 17, 2017, and petitioner told Ms. Fortunato that she went on a walk and to her aerobics class that day. Id. at ¶ 8. Petitioner "was healthy and did not have any cold symptoms at this time." Id.

Ms. Fortunato received a call from petitioner at about 7:30 AM on July 18, 2017. Pet. Ex. 17 at ¶ 9. Ms. Fortunato stated petitioner was screaming that she could not stand or walk, and Ms. Fortunato called the police to have an ambulance dispatched. Id. On Wednesday, July 19, 2017, Ms. Fortunato received a call from petitioner, where petitioner stated she was not doing well, and her symptoms were worsening. Id. at ¶ 11. Petitioner also told her she was not sure she would live through the night and requested Ms. Fortunato to come to Florida. Id. Ms. Fortunato and her daughter arrived in Florida at 9:10 AM on July 20, 2017, and went straight to the hospital to visit petitioner. Id. at ¶¶ 12-13.

On arrival, Ms. Fortunato explained petitioner's situation was a mess. Pet. Ex. 17 at ¶ 13. Ms. Fortunato's sister, Ms. Newton, asked Ms. Fortunato to have the doctors test petitioner for GBS. Id. at ¶ 14. Three days later, petitioner tested positive for GBS. Id. at ¶¶ 14-15. Ms. Fortunato explained that petitioner, after six days in the hospital without a proper diagnosis, was hallucinating and having difficulty breathing. Id. at ¶ 17. After petitioner's first treatment, Ms. Fortunato saw petitioner's treatment was helping. Id. at ¶ 18.

Ms. Fortunato stated petitioner has not fully recovered and has been unable to fully return to the active life she had prior to her GBS diagnosis. Pet. Ex. 17 at ¶ 19. As of March 9, 2020, the date in which Ms. Fortunato executed her declaration, petitioner remained less active than she was pre-GBS, and continued to suffer from instability with walking and standing. Id. at ¶ 20.

4. Joan Lohrer

Joan Lohrer was petitioner's neighbor in Florida. Pet. Ex. 18 at ¶ 5. She would go on daily walks with her dogs and petitioner. Id. at ¶ 6. Ms. Lohrer does not recall petitioner being sick before her hospitalization. Id. at ¶ 8. Ms. Lohrer "thought [petitioner] was in pretty good shape." Id. She visited petitioner once in the hospital. Id.

5. Kathleen Maloney

Kathleen Maloney is petitioner's niece. Pet. Ex. 19 at ¶ 4. She lived ten minutes from petitioner's home in Florida. Id. at ¶ 5. She would see petitioner several times per month, and would talk to her regularly on the phone. Id. Ms. Maloney stated that before petitioner's hospitalization on July 18, 2017, petitioner was "very active," always doing daily activities. Id. at ¶ 7. Petitioner would also come to Ms. Maloney's house for dinner and attend Ms. Maloney's children's school functions. Id. Ms. Maloney spoke to petitioner one to two weeks prior to her hospitalization, and saw her a few weeks earlier. Id. at ¶ 8. To her knowledge, petitioner was healthy before her hospitalization. Id. at ¶ 11.

On the morning of July 18, 2017, Ms. Maloney was at church when she received a call from petitioner stating that she could not move her legs. Pet. Ex. 19 at ¶ 12. Ms. Maloney arrived at petitioner's home before the paramedics. Id. at ¶ 13. After petitioner was hospitalized, she visited her regularly, and continued to visit petitioner at her assisted living facilities before petitioner moved to Pennsylvania. Id. at ¶ 14.

E. Expert Reports[29]

1. Petitioner's Expert, Dr. Steven Sykes

a. Background and Qualifications

Dr. Sykes is board certified in clinical neurophysiology and neurology. Pet. Ex. 21 at 1. After receiving his B.S. in neuroscience from the University of California, Los Angeles, he attended University of Michigan School of Medicine where he received his M.D. Id. He completed an internship in internal medicine, a residency in neurology, and a fellowship in clinical neurophysiology. Id. Dr. Sykes currently works as an Attending Neurologist at Cedars-Sinai Medical Group, where he practices general neurology and clinical neurophysiology, and an Assistant Clinical Professor at Cedars-Sinai Medical Center. Id. He is also the Neurology Panel Leader in the Cedars-Sinai Medical Care Foundation. Id.; Pet. Ex. 20 at 1. "The majority (over 85%) of [his] practice is dedicated to clinical practice and includes the diagnosis and management of peripheral nervous system disorders (such as [GBS])." Pet. Ex. 20 at 1.

b. Opinion

i. Diagnosis

Dr. Sykes opined that, to a reasonable degree of medical certainty, the "vaccine administered to [petitioner] on July 7, 2017 caused an abnormal activation of her immune system" leading to the development of GBS. Pet. Ex. 20 at 4; see also Pet. Ex. 30 at 4. The majority of Dr. Sykes' opinion focused on the debated issue of petitioner's diagnosis of GBS,

[29] This Ruling does not include every detail of each expert's opinions. Instead, the undersigned focuses on the material opinions, as they relate to the two relevant issues, diagnosis and causation.

and he generally deferred to Dr. Steinman's immunology expertise regarding any detailed discussion of the applicable biological mechanism. Pet. Ex. 65 at 1.

Regarding diagnosis, Dr. Sykes opined that petitioner's clinical presentation, diagnostic testing, and opinions of her treating physicians support the diagnosis of GBS. Pet. Ex. 65 at 3. While Dr. Sykes agreed that petitioner's initial presentation on July 18, 2017 included left lower extremity weakness and slurred speech (dysarthria), which warranted a workup for stroke, "the evolution of [petitioner's] generalized weakness, findings reported on her neurological exam (including hyporeflexia), elevated CSF protein, and findings on EMG/[NCV] [were] all consistent with a GBS diagnosis." Id.

In contrast, respondent's expert, Dr. Chaudhry, opined that petitioner's presentation was not consistent with GBS for several reasons, including documentation of aphasia, the acute onset of her symptoms, the references to the diagnosis of stroke, the timing of her elevated CSF protein, EMG results, presence of urinary retention, and other potential causes that could explain her weakness. Resp. Ex. A at 13-15. Each of these factors were addressed by Dr. Sykes.

When the petitioner arrived at the ED, a diagnosis of stroke/TIA was considered due to petitioner's prior history of stroke and the asymmetry of her weakness. Pet. Ex. 30 at 2. However, Dr. Sykes emphasized that petitioner's primary symptom was generalized weakness, characteristic for GBS, and her diagnostic workup for stroke was negative. Id. Moreover, petitioner's weakness was not "markedly or persistently asymmetric and [] therefore not atypical for [GBS]." Id. While Dr. Sykes agreed that petitioner initially had some asymmetric weakness in her lower extremities, her condition evolved to the point that she had severe weakness in both legs, specifically described by Dr. Fix as symmetrical. Id. (citing Pet. Ex. 5 at 278, 292, 318, 329). Further, the fact that the NIH stroke scale was used to evaluate petitioner for a stroke, an issue raised by Dr. Chaudhry, does not mean that petitioner had a stroke. Pet. Ex. 65 at 2.

In his supplemental expert report, Dr. Chaudhry opined that petitioner had resolution of her stroke-like symptoms, characteristic of a TIA, and thus, he opined that her initial presentation was not due to GBS but to TIA or stroke. Resp. Ex. C at 2-4. Dr. Sykes emphasized the point that while early on petitioner may have had symptoms of a TIA or stroke, these diagnoses would not explain the "evolution of generalized weakness in a manner quite typical for GBS." Pet. Ex. 65 at 2 (citing Pet. Ex. 5 at 240-42, 329-30).

Next, Dr. Chaudhry opined that petitioner had aphasia, which is inconsistent with GBS. Resp. Ex. A at 13. When petitioner presented on July 18, 2017, the ED records describe her chief complaint as "aphasia." Pet. Ex. 5 at 73. However, Dr. Sykes explained that what petitioner had was "dysarthria," a symptom that is commonly seen in GBS. Pet. Ex. 30 at 1-2. Dr. Sykes defined "aphasia" as "the loss of the ability to produce or understand language." Id. at 1. In contrast, dysarthria is slurred speech, caused by "weakness of muscles involved in producing speech, including muscles of the tongue, mouth, and/or palate." Id. Dr. Sykes referenced a number of citations from the medical records supporting his opinion on this point. See id. (citing Pet. Ex. 5 at 73, 75, 83, 95, 138, 148, 207).

Further, Dr. Sykes pointed to Dr. Weller's physical examination, where he specifically stated that petitioner had "[n]o aphasia," but that she had "[m]ild-to-moderate dysarthria." Pet. Ex. 30 at 1 (quoting Pet. Ex. 5 at 77). Dr. Sykes also referenced a nursing assessment on July 18, 2017, documenting that petitioner had no "expressive or receptive aphasia," but that she had "dysarthria." Id. (citing Pet. Ex. 5 at 104). Dr. Fix's neurological exam noted "[n]aming, comprehension[,] and repetition [were] intact," which Dr. Sykes explained means aphasia was absent, and petitioner had "dysarthria." Id. (quoting Pet. Ex. 5 at 150).[30] After reviewing petitioner's medical records, Dr. Sykes found no physical examination that described aphasia, "whereas dysarthria/slurred speech is documented repeatedly in the records." Id. at 2.

Another reason that Dr. Chaudhry argued that petitioner did not have GBS is based on the "acute" onset of her symptoms. Resp. Ex. A at 13. In response, Dr. Sykes explained that GBS is an "acute inflammatory demyelinating neuropathy," or AIDP, which by its nature is an acute illness. Pet. Ex. 30 at 2. Dr. Sykes also opined that the evolution of petitioner's course, including the progression of her weakness over a period of several days, is consistent with GBS. Id.

Dr. Chaudhry also suggested that the fact that petitioner had elevated protein in her CSF "within the first week of symptoms," weighed against a diagnosis of GBS, and cited to Willison et al. in support. Resp. Ex. A at 14 (citing Resp. Ex. A, Tab 1). Dr. Sykes disagreed and opined that an elevated protein in CSF is common, even early in the course of the illness. Pet. Ex. 30 at 2. Dr. Sykes stated that the Willison et al. article referenced by Dr. Chaudhry does not state that CSF is generally normal in the first week of symptoms, but instead states that a normal CSF protein level during the first week of symptoms does not make the diagnosis of GBS unlikely. Id. at 3 (citing Resp. Ex. A, Tab 1 at 6 ("[N]ormal protein level (especially when determined in the first week after onset of disease) does not make the diagnosis unlikely or even exclude [GBS].")).

Dr. Sykes cited to a New England Journal of Medicine article authored by Yuki & Hartung, another article referenced by Dr. Chaudhry, in which the authors stated that "albuminocytologic dissociation is present in no more than 50% of patients with [GBS] during the first week of illness." Pet. Ex. 30 at 3 (quoting Pet. Ex. 22 at 3). Thus, Dr. Sykes observed that the takeaway from these articles is that an absence of elevated protein does not exclude a diagnosis of GBS, although the finding of protein elevation in CSF is common in the first week of symptoms. Id.

Regarding the EMG/NCV test, Dr. Chaudhry questioned the findings of AIDP because "no data [was] provided to support the interpretation." Resp. Ex. A at 14. In response, Dr.

[30] Dr. Sykes explained that the reason that the word "aphasia" appeared so often in the medical records is a result of the "'copy forward' function clinicians routinely use when documenting in the electronic medical record . . . , which often perpetuates misinformation (or outdated information) in the medical record." Pet. Ex. 30 at 1.

Sykes found "no reason to doubt the interpretation of the test by a board-certified neurologist[31] when the clinical features of progressive generalized weakness (regardless of asymmetry early in the course), generalized hyporeflexia, and elevated CSF protein are present." Pet. Ex. 65 at 3 (citing Pet. Ex. 5 at 297, 303-04).

Next, Dr. Chaudhry opined that petitioner's urinary retention is not characteristic of GBS. Resp. Ex. A at 14. Dr. Sykes acknowledged that Willison et al. noted "bladder dysfunction at onset or severe and persistent bladder dysfunction . . . would suggest an alternate diagnosis." Pet. Ex. 30 at 3 (citing Resp. Ex. A, Tab 1 at 5). However, he countered by explaining that dysautonomia is seen in GBS, and it can lead to urinary retention. Id. Moreover, petitioner had pre-existing urinary retention, prior to the onset of her GBS. Id. Thus, Dr. Sykes opined that it was a chronic issue for her. Id. (citing Pet. Ex. 5 at 202).

Lastly, Dr. Chaudhry suggested alternate reasons for petitioner's weakness, including diarrhea, urinary tract infection, and abnormal potassium and phosphate levels. Resp. Ex. A at 14-15. Dr. Sykes agreed that while these factors may have contributed to petitioner's weakness, they would be unlikely to cause the "protracted course of weakness" that petitioner experienced. Pet. Ex. 30 at 3; Pet. Ex. 65 at 2.

ii. Causation

With regard to Althen Prong One, Dr. Sykes generally deferred to Dr. Steinman, due to his specialized expertise. Pet. Ex. 65 at 1. However, he opined that molecular mimicry is the "mechanism underlying the autoimmune and inflammatory responses affecting the peripheral nervous system that can occur following vaccination." Pet. Ex. 20 at 4. Dr. Sykes explained that the "antigens of a vaccine can resemble 'host' antigens" and that "activation of an[] immune response by the vaccine can result in an attack against those host antigens. If those antigens reside on cells of the peripheral nervous system, an autoimmune response occurs, with inflammation occurring in and around the peripheral nerves." Id. at 3-4.

In support of his opinion that petitioner's Prevnar 13 vaccine caused her GBS, Dr. Sykes noted that GBS has been reported after pneumococcal infections. Pet. Ex. 30 at 3. He cited the El Khatib et al.[32] case report, where "antigens associated with the pneumococcal bacteria . . . 'triggered an immune response and cross-reacted with peripheral nervous system surface components due to molecular mimicry.'" Id. at 4 (quoting Pet. Ex. 32 at 2).

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[31] The EMG/NCV was performed by Dr. Jason Stabley, who, according to the Cleveland Clinic Martin Health website, is a neurologist who completed his Residency in Neurology at Pennsylvania State University College of Medicine and his Fellowship in Neurology at Milton S. Hershey Medical Center-Penn State University. Jason Stabley, DO, Cleveland Clinic Martin Health, https://www.martinhealth.org/jason-stabley-do (last visited Feb. 22, 2022). He is board certified in Neurology by the American Osteopathic Board of Neurology and Psychiatry. Id.

[32] Hassan El Khatib et al., Case Report: Guillain-Barre Syndrome with Pneumococcus – A New Association in Pediatrics, 11 IDCases 26 (2018).

Dr. Sykes also noted that GBS was reported after the Prevnar 13 vaccine in a case report authored by Ravishankar.[33] Pet. Ex. 30 at 4 (citing Pet. Ex. 35). In Ravishankar, a 66-year old female received a Prevnar 13 vaccine in January 2015 and a 23-valent pneumococcal polysaccharide vaccine[34] in August 2015. Pet. Ex. 35 at 1. In September 2015, she was unable to move her legs, and by November 2015, her symptoms worsened. Id. A lumbar puncture showed albuminocytologic dissociation, and an EMG/NCV "showed evidence of mixed axonal and demyelinating sensorimotor polyradiculopathy." Id. at 2. Thereafter, she was diagnosed with GBS. Id.

Dr. Sykes opined that the onset of petitioner's development of neurological symptoms of weakness approximately ten days after vaccination "is consistent with the range observed in other cases of vaccination preceding the development of [GBS]." Pet. Ex. 20 at 4.

2. Petitioner's Expert, Dr. Lawrence Steinman

a. Background and Qualifications

Dr. Steinman is board certified in neurology and has practiced neurology at Stanford University for over 40 years. Pet. Ex. 36 at 1; Pet. Ex. 39 at 2. He received his B.A. from Dartmouth College in 1968 and his M.D. from Harvard University in 1973. Pet. Ex. 39 at 1. Thereafter, he completed an internship in surgery, residency in pediatrics, and residency in pediatric and adult neurology from Stanford University Hospital, as well as three fellowships. Id. He currently works as a Professor at Stanford University. Id. Dr. Steinman is also "actively involved in patient care" and has cared for hundreds of adults and children with various inflammatory neuropathies, including GBS, transverse myelitis, acute disseminated encephalomyelitis, neuromyelitis optica, and multiple sclerosis ("MS"). Pet. Ex. 36 at 1. He has authored or co-authored over 500 publications. Pet. Ex. 39 at 5-47.

b. Opinion

i. Diagnosis

Dr. Steinman opined that petitioner was diagnosed with GBS, as confirmed by EMG testing, lumbar puncture, use of IVIG for treatment, and supported by her treating physicians and Dr. Sykes. Pet. Ex. 36 at 4; Pet. Ex. 56 at 2; Pet. Ex. 66 at 32-33. The lumbar puncture and CSF analysis revealed "albumin-cytologic dissociation characteristic of GBS with elevated protein . . . and normal cell counts and glucose." Pet. Ex. 56 at 2.

[33] Nidhi Ravishankar, Guillain-Barre Syndrome Following PCV Vaccine, 2 Clinics Surgery 1413 (2017).

[34] The undersigned acknowledges that petitioner did not receive this vaccine. However, as described in further detail below, the Prevnar 13 and 23-valent pneumococcal polysaccharide vaccines contain some of the same components. Additionally, the package insert for Pneumovax 23, a 23-valent pneumococcal vaccine, reported GBS as an adverse event during post-approval use. Pet. Ex. 70 at 6-7.

Dr. Steinman cited the EMG/NCV report by Dr. Stabley that was abnormal, "consistent with [AIDP] ([GBS])." Pet. Ex. 56 at 2 (quoting Pet. Ex. 5 at 297). The report states as follows:

> Clinical history: 89-year-old female with onset of progressive bilateral lower extremity weakness and upper extremity weakness, sensory loss and legs beginning within several days of receiving pneumococcal vaccine. Clinical exam reveals significant neck flexor weakness, bilateral upper and lower extremity proximal and distal weakness, areflexia and stocking distribution sensory loss to pinprick to the level of the mid calves. CSF revealed cytoalbuminologic dissociation.
>
> Clinical diagnosis GBS[.]
>
> Nerve conductions and electromyography performed of right upper and lower extremities.
>
> Electrodiagnostic impression:
> Study consistent with acute inflammatory demyelinating polyneuropathy [GBS.]

Pet. Ex. 5 at 297 (emphasis omitted).

Further evidence that petitioner's diagnosis was GBS, important to Dr. Steinman, was the fact that she was prescribed and underwent treatment for five days with IVIG, which is an "FDA approved therapy for GBS." Pet. Ex. 56 at 2; Pet. Ex. 66 at 33. Moreover, Dr. Steinman agreed with the treating physicians' diagnosis of GBS. Pet. Ex. 66 at 33.

ii. Causation: Althen Prong One

The focus of Dr. Steinman's expert reports is how the Prevnar 13 vaccine can trigger GBS via molecular mimicry, a mechanism whereby shared structures "in a vaccine can trigger a cross-reactive response to self." Pet. Ex. 36 at 4. He proposed two mechanisms whereby molecular mimicry can trigger GBS following Prevnar 13 vaccination. The first involved homology between "[p]hosphoglycerol[35] [] present in serotypes 18C and 23F in the Prevnar 13 vaccine," and phospholipids[36] in the human myelin sheath. Pet. Ex. 36 at 5-6; Pet. Ex. 56 at 13;

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[35] Phospho- is a "prefix[] indicating the presence of phosphorus in a compound." Stedman's Medical Dictionary 1486 (28th ed. 2006). Glycerol is "[a] sweet viscous fluid obtained by the saponification of fats and fixed oils; used as a solvent, as a skin emollient, . . . and as a vehicle and sweetening agent." Stedman's at 820.

[36] Phospholipid is defined as "any lipid that contains phosphorus, including those with a glycerol backbone (phosphoglycerides and plasmalogens) . . . . Phospholipids are the major form of lipid in all cell membranes." Phospholipid, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=38759 (last visited Feb. 22, 2022).

Pet. Ex. 66 at 12. The second involved homology between CRM_{197}[37] in the vaccine and Contactin-1,[38] a protein found in humans. Pet. Ex. 66 at 25-32.

1. Phosphoglycerol in Serotypes 18C and 23F

"Prevnar 13 has 13 complex sugars, chemically modified into saccharides from [*Streptococcus pneumoniae* ("*S. pneumoniae*")] then linked chemically to CRM_{197} . . . ." Pet. Ex. 66 at 1. That is, the vaccine contains "saccharides of the capsular antigens of (13 different serotypes of) [*S.*] *pneumonia*[*e*] . . . linked to non-toxic diphtheria CRM_{197} protein [carrier]." Pet. Ex. 36 at 5. Two of the 13 serotypes (18C and 23F) contain phosphoglycerol. Pet. Ex. 66 at 1.

Based upon information obtained from the vaccine patent,[39] Dr. Steinman explained that the glycerol phosphate side chains in the vaccine are necessary for its immunogenicity.[40] Pet. Ex. 66 at 5 (citing Pet. Ex. 55). Both vaccine components 18C and 23F have a phosphoglycerol moiety.[41] Id. at 5-6 (citing Pet. Ex. 67 at 1).[42] "Phosphoglycerol is linked to the saccharide moieties and the whole complex is linked to CRM_{197} by reductive amination." Id. at 19. Dr. Steinman stressed the fact that the phosphoglycerol components are retained during the process

[37] Protein carrier "CRM_{197} is a nontoxic variant of diphtheria toxin isolated from cultures of *Corynebacterium diphtheriae* strain C7 (β197) grown in a casamino acids and yeast extract-based medium or in a chemically-defined medium." Pet. Ex. 48 at 25 (Prevnar 13 package insert).

[38] Contactin-1, or CNTN1, "is a key axonal adhesion molecule, which interacts with CNTNAP1 (previously known as Caspr1) on the axon and neurofascin-155 on the glial side, and is essential for the formation of the paranodal septate-like junction." Pet. Ex. 73 at 2 (Yumako Miura et al., Contactin I IgG4 Associates to Chronic Inflammatory Demyelinating Polyneuropathy with Sensory Ataxia, 138 Brain 1484 (2015)).

[39] The patent is filed as petitioner's exhibit 55. The description of the glycerol phosphate side chain in 18C can be found at page 34, and a diagram of the chemical structure is at page 6.

[40] Immunogenicity is defined as "the property that endows a substance with the capacity to provoke an immune response, or the degree to which a substance possesses this property." Immunogenicity, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=24893 (last visited Feb. 22, 2022).

[41] Moiety is defined as "any part or portion." Moiety, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=31829 (last visited Feb. 22, 2022).

[42] Kang Yu et al., Synthesis of the Biological Repeating Unit of *Streptococcus pneumoniae* Serotype 23F Capsular Polysaccharide, 14 Organic & Biomolecular Chemistry 11462 (2016).

of conjugating the vaccine[43] because they are necessary for the vaccine to be immunogenic.[44] Id. at 12, 19-21.

Dr. Steinman cited a paper by Chang et al.[45] to support his opinion that the phosphoglycerol component is preserved during the process of making the vaccine. Chang et al. wrote "it is shown that glycerol-phosphate must be preserved for conserving adequate antigenicity of the 18C capsular polysaccharide." Pet. Ex. 51 at 1.

In addition to the evidence regarding component 18C in Chang et al., Dr. Steinman stated there is evidence "that humans make antibodies targeting the phosphoglycerol regions" in the 23F serotype. Pet. Ex. 66 at 11-12. He cited an article by Bryson et al.,[46] which showed X-rays of antibodies targeting the 23F component of *S. pneumoniae*. Id. at 12 (citing Pet. Ex. 63). Dr. Steinman explained that Bryson et al. "show[ed] that a human antibody response to 23F, contained in the Prevnar 13 vaccine, is mounted." Id. While the Bryson et al. study involved only the Pneumovax 23 vaccine, both Pneumovax 23 and Prevnar 13 contain 23F, and therefore, Dr. Steinman stated that the Bryson et al. findings also apply to Prevnar 13. Id. at 12-16. "[T]he 23F target is the same serotype regardless of whether the vaccine is Prevnar 13 or Pneumovax 23." Id. at 12. Dr. Steinman asserted that "[Bryson et al.] show[ed] that phosphoglycerol is directly targeted by the core of the two human antibodies targeting 23F." Id. at 13.

Summarizing the information from the patent, Yu et al., and Bryson et al., Steinman found "compelling support . . . that the immune response to serotypes 18C and 23F in Prevnar 13 targets the phosphoglycerol moiety in those serotypes."[47] Pet. Ex. 66 at 16. He concluded by asserting the Bryson et al. study "demonstrate[d] unequivocally that the immune response to the serotype 23F component of Pneumovax 23 targets the phosphoglycerol in serotype 23F." Id. (emphasis omitted).

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[43] A conjugate vaccine is "a vaccine composed of an immunogenic polysaccharide conjugated with a protein carrier." Conjugate Vaccine, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=116508 (last visited Feb. 22, 2022).

[44] For a detailed explanation of the evidence cited by Dr. Steinman to support his position that the phosphoglycerol components are necessary for immunogenicity of the vaccine, see Pet. Ex. 36 at 7-10; Pet. Ex. 66 at 20-21.

[45] Janoi Chang et al., Relevance of O-acetyl and Phosphoglycerol Groups for the Antigenicity of the *Streptococcus pneumoniae* Serotype 18C Capsular Polysaccharide, 30 Vaccine 7090 (2012).

[46] Steve Bryson et al., Structures of Preferred Human IgV Genes–Based Protective Antibodies Identify How Conserved Residues Contact Diverse Antigens and Assign Source of Specificity to CDR3 Loop Variation, 196 J. Immunology 4723 (2016).

[47] Dr. Steinman referenced the X-ray images from Bryson et al. and opined that they "demonstrate[d] that the immune response to the phosphoglycerol in the polysaccharide capsule of serotype 23F is critical to the human immune response to serotype 23F." Pet. Ex. 66 at 15 (citing Pet. Ex. 63).

Dr. Steinman explained how the data from the vaccine patent and the studies described above relate to the pathogenesis of GBS. He opined that phospholipids are the targets of antibodies in GBS. Pet. Ex. 36 at 5. He asserted that antibodies to phosphoglycerol structures interact with myelin components triggering GBS. Id. at 9. Based on his own research, Dr. Steinman explained that "phospholipids are components of the myelin sheath in humans, and they are targeted by antibodies" leading to neuroinflammation and GBS. Id. at 6.

In support of this part of his opinion, Dr. Steinman relied on several articles. The first was authored by Ho et al.,[48] and Dr. Steinman is also a named author. See Pet. Ex. 45. The authors showed that in the demyelinating disease MS, autoantibodies "target a phosphate group," with the primary target a phosphoglycerol component of myelin. Pet. Ex. 36 at 6. The "findings indicate[d] that myelin phospholipids are targeted by autoimmune responses in MS." Pet. Ex. 45 at 9.

In Gilburd et al.,[49] the authors "studied the reactivity of GBS sera with various phospholipids which are known to be important constituents of myelin, and serve as autoantigens in other autoimmune conditions." Pet. Ex. 49 at 1. Six of the 16 patients with GBS had autoantibodies to various phospholipids. Id. at 1, 5. However, the authors suggested this was "probably [] a result of [] myelin damage rather than [the] cause of demyelination." Id. at 1, 6.

In another study by Nakos et al.,[50] all nine GBS patients in the study had anti-phospholipid antibodies and no such antibodies were detected in the nine control subjects. Pet. Ex. 50 at 1. The authors "detected a wide range of anti-phospholipid antibodies in patients with idiopathic GBS," and "[a]ll nine GBS patients developed anti-phospholipid antibodies directed against at least one lipid during the course of the disease." Id. at 5. They wrote "[t]he association of GBS and certain autoimmune diseases, including systemic lupus erythematosus, is well recognized," and they noted "[h]igh levels of anti-phospholipid antibodies were expressed in a patient with lupuslike syndrome who developed secondary GBS." Id. at 6. The authors explained that "[i]t is thought that whenever polyneuropathy occurs in the context of autoimmune diseases, mainly in systemic lupus erythematosus, where anti-phospholipid activity already exists, these antibodies can cross-react with phospholipids and mediate damage in neural structures containing the particular phospholipids." Id. Of note, the GBS patients in the Nakos et al. study had primary GBS, not the secondary form like that which occurs in patients with lupus. Id. The authors also observed anti-ganglioside antibodies, but only in 44% of the patients. Id. They concluded that,

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[48] Peggy P. Ho et al., Identification of Naturally Occurring Fatty Acids of the Myelin Sheath That Resolve Neuroinflammation, 4 Sci. Translational Med. 1 (2012).

[49] B. Gilburd et al., Autoantibodies to Phospholipids and Brain Extract in Patients with the Guillain-Barre Syndrome: Cross-Reactive or Pathogenic?, 16 Autoimmunity 23 (1993).

[50] G. Nakos et al., Anti-Phospholipid Antibodies in Serum from Patients with Guillain-Barré Syndrome, 31 Intensive Care Med. 1401 (2005).

> It is not well understood whether these anti-phospholipid antibodies play a role in the pathogenesis of the polyneuropathy or represent a part of a more extensive immunoreaction that takes place in the GBS. However, immunopathology in autopsies suggests that antibody mediated injury is a predominant disorder in the demyelinating form of GBS. The immune attack is directed against components of Schwann cell membrane and is accompanied by the characteristic feature of vesicular demyelination. Therefore, it is crucial to investigate how anti-phospholipid antibodies are related to specific antigens in Schwann cell membrane.
>
> . . . .
>
> Our findings suggest that in GBS there is a more extensive immune reaction, beyond the well known antiganglioside production, which has been related to the demyelination of the peripheral nerves.

Id. at 6-7.

In summary, Dr. Steinman's theory is based on molecular mimicry, and he posited that antibodies to the phosphoglycerol structures present in the components of Prevnar 13 interact with phospholipids in the myelin components of peripheral nerves, triggering GBS. Pet. Ex. 36 at 9, 11.

2. CRM_{197} and Contactin-1

The second homology posited by Dr. Steinman is between the protein carrier in the vaccine, CRM_{197}, and Contactin-1, a protein found in humans. Pet. Ex. 66 at 25. Prevnar 13 is a conjugate vaccine, in which the individual polysaccharides of the capsular antigens of *S. pneumoniae* are linked to a non-toxic diphtheria CRM_{197} protein. Pet. Ex. 36 at 5. "CRM_{197} is a nontoxic variant of diphtheria toxin," used as a protein carrier which makes the vaccine more immunogenic. Pet. Ex. 66 at 5, 17 (quoting Pet. Ex. 48 at 25). "CRM_{197} differs from diphtheria toxin by only one amino acid," and therefore, it "is not toxic, though like diphtheria toxoid[,] it is quite immunogenic." Id. at 17.

Based on his own research, Dr. Steinman opined that molecular mimicry might occur between CRM_{197} and Contactin-1, a molecule that has been identified in patients with GBS. Pet. Ex. 66 at 25. Dr. Steinman relied on Miura et al., a study done on patients with chronic inflammatory demyelinating polyneuropathy ("CIDP"). Id. at 25-26 (citing Pet. Ex. 73). Prior to the Miura et al. study, another group of researchers reported finding autoantibodies against Contactin-1 in patients with CIDP. Pet. Ex. 73 at 1. The patients had an aggressive onset and did not respond well to treatment with IVIG. Id. Based on the findings reported in that study, Miura et al. set out to replicate the finding of Contactin-1 autoantibodies and determine the relevance of the findings. Id. Miura et al. focused their research on patients with CIDP, but used sera from patients with GBS, MS, and healthy patients as controls. Id. at 2. Anti-Contactin-1 IgG antibodies were found in 16 of the 533 patients with CIDP, with 13 of the 533 CIDP patients

(2.4%) having anti-Contactin-1 IgG4 antibodies. Id. at 3, 5, 6 tbl.2. They also found that five of the 200 patients with GBS had anti-Contactin-1 IgG antibodies. Id. at 3, 6 tbl.2.

The Miura et al. authors did not reach any conclusions about the presence of the anti-Contactin-1 antibodies in the patients with GBS. See Pet. Ex. 73. But they did explain the theory of pathogenesis relevant here to Dr. Steinman's theory, as it relates to Contactin-1. They stated,

> Cell adhesion molecules play a crucial role in the formation of the nodes of Ranvier[51] and in the rapid propagation of the nerve impulses along myelinated axons. In the peripheral nerves, the domain organization of myelinated axons depends on specific axo-glial contacts between the axonal membrane and Schwann cells[52] at nodes, paranodes[,] and juxtaparanodes. Recently, we showed that some of the patients with CIDP present IgG autoantibodies directed against the nodes of Ranvier or the paranodal axo-glial apparatus. Notably, we identified . . . contactin 1 (CNTN1) as [one of] the targets of autoantibodies in some patients with CIDP.

Id. at 2.

Based on this information about the potential importance of Contactin-1, Dr. Steinman conducted a BLAST search, to determine whether there was homology between CRM_{197} in the vaccine and Contactin-1.[53] Pet. Ex. 66 at 26. He found a sequence[54] that "might be capable of inducing a neuroinflammatory disease." Id. at 29. He found "it is an epitope in diphtheria toxin, which provides the basis for CRM_{197}." Id. at 30. After additional research, Dr. Steinman

[51] Nodes of Ranvier are "constrictions occurring on myelinated nerve fibers at regular intervals of about 1 mm; at these sites the myelin sheath is absent and the axon is enclosed only by Schwann cell processes." Nodes of Ranvier, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=93095 (last visited Feb. 22, 2022).

[52] Schwann cells are "large nucleated cells whose cell membrane spirally enwraps the axons of myelinated peripheral neurons and is the source of myelin; a single Schwann cell supplies the myelin sheath between two nodes of Ranvier." Schwann Cell, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=66407 (last visited Feb. 22, 2022).

[53] For a complete explanation of Dr. Steinman's investigation, including his discussion on the number of amino acids required for homology relevant to molecular mimicry as well as the procedure he followed in conducted his BLAST searches, see Pet. Ex. 66 at 25-32.

[54] The sequence is "WEQAKALSVE," which "has five of ten identical amino acids." Pet. Ex. 66 at 29.

identified another sequence[55] that "has known cross-reactivity with epitopes described in humans" on the *Corynebacterium diphtheriae* microbe. Id.

As further support, Dr. Steinman found that these two regions of mimicry between Contactin-1 and CRM_{197} in Prevnar 13 vaccine have been studied. Pet. Ex. 66 at 31. Dr. Steinman cited Raju et al.[56] to show that "[h]umans have been shown to mount T cell responses[57] to these regions of the diphtheria molecule, WEQAKALSVE and EYMAQACAGNRVRR." Id. (citing Pet. Ex. 79 at 2 fig.1). Dr. Steinman opined that the two sequences are also present in in the diphtheria toxin, stating "a correlation with detailed studies on the human immune response to diphtheria toxin, differing in only one amino acid from CRM." Id. Thus, he concluded that "[t]he theory provides actual detailed data for molecular mimics in the CRM in the Prevnar 13 vaccine received by [p]etitioner. It shows how these mimics could trigger inflammatory neuropathy culminating in GBS." Id. at 31-32 (emphasis omitted).

iii. Causation: Althen Prongs Two and Three

With regard to Althen Prong Two, a logical sequence of cause and effect, Dr. Steinman stated that "[t]he vaccine has constituents that induce antibodies known to cross-react with myelin and that are found in patients with GBS." Pet. Ex. 36 at 11.

Dr. Steinman agreed that petitioner's onset of GBS symptoms was several days after vaccination, which is "consistent with the timing known for GBS and the 1976 swine [influenza] immunization, often used as a surrogate in such cases." Pet. Ex. 36 at 11. In support of this opinion, he cited Schonberger et al.,[58] who looked at 1,098 patients that developed GBS between October 1, 1976 and January 31, 1977, and found 532 of the patients received a A/New Jersey influenza vaccination prior to onset of GBS. Pet. Ex. 24 at 1-2, 5. Of the 532 patients, 71% developed GBS within four weeks after vaccination, with 52% developing GBS in the second and third weeks after vaccination. Id. at 6. They found the largest percentage of cases (10%) occurred 16 and 17 days post-vaccination. Id. at 6-7, 8 fig.5.

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[55] The second sequence is EYMAQACAGNRVRR. Pet. Ex. 66 at 30.

[56] Raghavanpillai Raju et al., Epitopes for Human $CD4^+$ Cells on Diphtheria Toxin: Structural Features of Sequence Segments Forming Epitopes Recognized by Most Subjects, 25 Eur. J. Immunology 3207 (1995).

[57] T cells, or lymphocytes, are "cells primarily responsible for cell-mediated immunity." T Lymphocytes, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition? id=87562 (last visited Feb. 22, 2022). "When activated by antigen, T lymphocytes proliferate and differentiate into T memory cells and the various types of regulatory and effector T cells." Id.

[58] Lawrence B. Schonberger et al., Guillain-Barré Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976-1977, 110 Am. J. Epidemiology 105 (1979).

Dr. Steinman also cited the Haber et al.[59] article, which reported onset of GBS after Prevnar 13, up to 42 days post-vaccination. Pet. Ex. 34 at 1, 5. Haber et al. found 11 cases of GBS following Prevnar 13 vaccine.[60] Id. at 4-5. "The median onset interval of symptoms was 9 days" with a range of 2 to 34 days. Id. at 4.

3. Respondent's Expert, Dr. Vinay Chaudhry

a. Background and Qualifications

Dr. Chaudhry is board certified in neurology, neuromuscular diseases, electrodiagnostic medicine, and clinical neurophysiology. Resp. Ex. A at 1; Resp. Ex. F at 1. He received his M.B. and B.S. in India, and then completed an internship, residency in neurology, and fellowship in neuromuscular diseases. Resp. Ex. F at 1-2. He is currently a Nominated Clinical Professor at UNC Chapel Hill School of Medicine. Id. at 2. Dr. Chaudhry specializes in the field of neuromuscular diseases. Resp. Ex. A at 1. He has an active clinical practice where he sees over 2,000 patients per year. Id.; Resp. Ex. F at 50. He has authored or co-authored over 200 publications. Resp. Ex. F at 4-22.

b. Opinion

i. Diagnosis

Dr. Chaudhry opined that petitioner's symptoms, testing, and treatment were not consistent with a presentation of GBS based on several different factors. Resp. Ex. A at 13-15. He asserted that "there is no conclusive evidence that [petitioner] had GBS." Resp. Ex. H at 4.

The factors enumerated by Dr. Chaudhry, which he argued weigh against a diagnosis of GBS, are addressed in turn. First, he noted that the medical records document petitioner's chief complaint as "aphasia," which "is not a presenting feature of GBS." Resp. Ex. A at 13. He explained that "[s]udden onset of aphasia . . . or sudden onset of dysarthria . . . are common [in] presentation of stroke or impending stroke ([TIA]) rather than GBS." Resp. Ex. C at 2 (emphasis omitted). In support of his opinion, Dr. Chaudhry cited to information from the National Institute of Neurological Disorders and Stroke, which states "symptoms of a stroke include . . . trouble speaking or understanding speech." Id. (quoting Resp. Ex. C, Tab 1 at 1).[61] Dr.

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[59] Penina Haber et al., Post-Licensure Surveillance of 13-Valent Pneumococcal Conjugate Vaccine (PCV13) in Adults Aged ≥ 19 Years Old in the United States, Vaccine Adverse Event Reporting System (VAERS), June 1, 2012–December 31, 2015, 34 Vaccine 6330 (2016).

[60] One of the 11 cases also received an influenza vaccine prior to onset. Pet. Ex. 34 at 4.

[61] Nat'l Inst. Neurological Disorders & Stroke, Nat'l Inst. Health, Stroke Information Page, https://www.ninds.nih.gov/Disorders/All-Disorders/Stroke-Information-Page (last modified Mar. 27, 2019).

Chaudhry referenced pages in the petitioner's medical records that identified aphasia as the "chief complaint." Resp. Ex. A at 13.

The second factor asserted by Dr. Chaudhry is that petitioner had acute symptoms, starting at 7 AM on July 18, 2017, which is not characteristic of GBS. Resp. Ex. A at 13. He explained that GBS presents with progressive weakness that occurs "over a period of hours to days to weeks." Resp. Ex. C at 2; see also Resp. Ex. A at 12-13. Further, because petitioner had a "sudden onset, her treating physicians considered the possibility of stroke or [TIA]." Resp. Ex. A at 13. Dr. Chaudhry noted that petitioner's treating physicians considered CVA or TIA "as the most likely diagnosis based on [petitioner's] presentation and at least until [July 20, 2017]," and he cited portions of petitioner's medical records for support. Resp. Ex. C at 2, 5. He opined that the treating physicians' records documented symptoms that began at 7 AM, which resolved by approximately 10:30 AM, is not GBS, but "is consistent with CVA/TIA." Resp. Ex. H at 1-2.

In addition to the medical records, Dr. Chaudhry cited portions of petitioner's affidavit, as well as affidavits of family members, that establish petitioner had acute symptoms and was unable to move her legs, stand, or walk when she woke the morning of July 18, 2017. Resp. Ex. C at 4. Dr. Chaudhry emphasized that petitioner and her family members all describe an acute onset of symptoms, which he contended occurs with CVA/TIA, and not GBS. Resp. Ex. H at 1.

Dr. Chaudhry opined that it was not until July 20, 2017, "three days after reversible left sided weakness and aphasia, [that petitioner] complained of generalized bilateral lower extremit[y] [weakness]." Resp. Ex. A at 13. Petitioner was seen by a neurosurgeon, and "[s]ignificant spine disease was confirmed . . . on MRI." Id. Petitioner was treated with steroids. Id. Dr Chaudhry emphasized that these facts are inconsistent with GBS. Id. He further stated that "GBS is a symmetrical disorder," and that petitioner had weakness of one side, which "is typically not seen in GBS." Id.

Next, Dr. Chaudhry opined that petitioner's diagnostic tests were not typical for GBS. Resp. Ex. A at 14. On July 23, 2014, petitioner's CSF revealed an elevated protein level of 112. Id. Dr. Chaudhry explained that in GBS, protein levels are usually normal within the first week after onset of symptoms. Id. He also asserted that an elevated protein level is not specific for GBS. Id.; see also Resp. Ex. C at 14. As for the EMG/NCV findings, Dr. Chaudhry agreed that the study was reported as consistent with AIDP, but because the underlying test data was not provided, he was unable to verify the interpretation. Resp. Ex. A at 14. Additionally, he opined that "[i]n GBS, nerve conduction abnormalities are most pronounced [two] weeks after start of illness," whereas petitioner's test showed abnormalities "within 4-5 days of onset of lower extremity weakness, which is [] not typical for GBS." Id.

Another feature of petitioner's presentation that Dr. Chaudhry opined was inconsistent with GBS was urinary retention. Resp. Ex. A at 14. He opined that urinary retention is not usually associated with GBS, but can been seen with spine disease. Id. Petitioner also had degenerative spine disease, and was seen by neurosurgery specialists, who considered surgery, which Dr. Chaudhry noted weighs against a diagnosis of GBS. Resp. Ex. H at 2-3. Petitioner received steroid treatment for her degenerative spine condition. Id.

Lastly, Dr. Chaudhry noted that petitioner had other confounding features including hypophosphatemia (low phosphate), hypokalemia (low potassium), and diarrhea. Resp. Ex. A at 14; Resp. Ex. C at 14. He asserted that these problems can cause weakness and fatigue. Resp. Ex. A at 14.

In summary, Dr. Chaudhry concluded that the records are inconclusive, although he agreed there was a "possibility" that petitioner "initially had a TIA from which she recovered." Resp. Ex. A at 14. He also opined that petitioner had "lumbar stenosis and cervical radiculopathy, hypokalemia, and hypophosphatemia." Id. However, he conceded that petitioner may have "suffered from 'paraparetic form of GBS,'" which is a "regional form of GBS in which the motor nerves of the legs are most severely affected." Id. at 14-15. He explained that this type of GBS usually has a "faster and more complete recovery" and a "relatively good outcome." Id. at 15.

ii. Causation

Dr. Chaudhry does not dispute that molecular mimicry is a recognized mechanism for how some infectious agents, like *C. jejuni*, can cause GBS. Resp. Ex. A at 20. He agreed that in the context of infection, "[a]n immune response against [an] infectious agent [] will cross-react with the peripheral nerve because of this antigenic sharing." Resp. Ex. C at 8. But he disagreed that vaccination, through the theory of molecular mimicry, can cause GBS. Resp. Ex. A at 20. He opined that "there is no epidemiological or biological evidence to support that [the] pneumococcal vaccine can cause GBS." Resp. Ex. H at 4 (emphasis omitted).

Citing an article from Yuki, Dr. Chaudhry identified four criteria that "must be satisfied to conclude that a disease is triggered by molecular mimicry." Resp. Ex. C at 9 (quoting Resp. Ex. C, Tab 13 at 1). The four criteria are (1) "establishment of an epidemiological association between the infectious agent and the immune-mediated disease;" (2) "identification of T cells or antibodies directed against the patient's target antigens;" (3) "identification of microbial mimics of the target antigen;" and (4) "reproduction of the disease in an animal model." Resp. Ex. C, Tab 13 at 1; Resp. Ex. C at 9.

According to Dr. Chaudhry, these criteria have been met for "only one infections agent, [*C.*] *jejuni*, and only for one [] disease, that of acute motor axonal neuropathy (AMAN) form of GBS." Resp. Ex. C at 9. He opined that here, Dr. Steinman's two proposed molecular mimics are not supported by evidence. Id. at 9-10.

Regarding epidemiological studies, Dr. Chaudhry cited Baxter et al.,[62] who evaluated the relationship between GBS and vaccinations, including the 23-valent pneumococcal polysaccharide vaccine, but not Prevnar 13. Resp. Ex. A, Tab 9 at 1, 4. In Baxter et al., the authors reviewed records of 415 hospitalized patients diagnosed with GBS from 1995 to 2006. Id. at 1. Of these, 25 had received a vaccine within a six-week period prior to onset of their GBS. Id. at 4. The vaccines included influenza (18 patients), 23-valent pneumococcal

[62] Roger Baxter et al., Lack of Association of Guillain-Barré Syndrome with Vaccinations, 57 Clinical Infectious Diseases 197 (2013).

polysaccharide (2 patients), tetanus-diphtheria combination (3 patients), and hepatitis A and B (3 patients). Id. "[U]sing a case-centered method to control for seasonality and other time-varying confounders, [they] found no evidence of an increased risk of GBS following any vaccination." Id. at 5. The authors acknowledged that the study had "limited power to fully assess the risk of GBS following vaccination due to the rarity of the outcome." Id. at 7. They concluded that the results "provide reassurance that the risk of GBS following any vaccine . . . is extremely low." Id.

The second study relied on by Dr. Chaudhry was from Haber et al., who studied vaccine adverse event reports in adults related to the Prevnar 13 vaccine that were reported to the Vaccine Adverse Event Reporting Systems ("VAERS") from June 2012 to December 2015. Pet. Ex. 34 at 2. During that time period, there were 2,976 total reports. Id. Most of the reports related to injection site adverse events (injection site pain, redness, and swelling). Id. at 3 tbl.1. There were eleven cases of GBS reported following Prevnar 13 vaccination, and in ten of those, the Prevnar 13 vaccine was the only vaccine administered. Id. at 4. One patient also received an influenza vaccine. Id. The authors concluded that their "data mining analysis noted no disproportionate reporting for GBS." Id. at 5. Dr. Chaudhry concluded that Haber et al. does not support an association between Prevnar 13 and GBS, since the rate of GBS following vaccination was lower than the background rate for the disease.[63] Resp. Ex. C at 7-8, 11.

About Dr. Steinman's first molecular mimicry theory, based on phosphoglycerol components of the Prevnar 13 vaccine, Dr. Chaudhry raised several objections. First, Dr. Chaudhry disagreed that literature cited by Dr. Steinman supports the theory. Resp. Ex. C at 10. Dr. Steinman cited Nakos et al. as support for the proposition that anti-phospholipids have been found in patients with GBS. Id. (citing Pet. Ex. 50). Dr. Chaudhry took issue with Dr. Steinman's interpretation. He cited Nakos et al. where the authors stated "[i]t is not well understood whether these anti-phospholipid antibodies play a role in the pathogenesis of the polyneuropathy or represent a part of a more extensive immunoreaction that takes place in [] GBS." Pet. Ex. 50 at 6.

Next, Dr. Chaudhry questioned whether the Gilburd et al. paper supports an association between anti-phospholipid antibodies (antibodies to phosphatidyl-ethanolamine, phosphatidyl-choline, or phosphatidylserine) and GBS. Resp. Ex. C at 9. He quoted the authors of Gilburd et al. who stated "no significant association was found between the presence of specific anti[-]phospholipid antibodies . . . and GBS when compared to controls." Id. (quoting Pet. Ex. 49 at 5). Thus, Dr. Chaudhry emphasized that neither Nakos et al. nor Gilburd et al. "conclude that phosphoglycerol is the pathogenic antigen in GBS." Resp. Ex. H at 5.

According to Dr. Chaudhry, "[t]he specific antibody in [the] AIDP form [of GBS] has not been identified." Resp. Ex. C at 10. He did not agree that either the bacteria *S. pneumoniae* or the Prevnar 13 vaccine share homology with gangliosides (the often-cited theoretical target in

[63] It is not clear whether the authors of Haber et al. used background rates for the incidence of GBS in the population to arrive at their conclusion. They "applied empirical Bayesian data mining methods to identify disproportionality of vaccine-adverse event pairs and stratified by age group, sex, and by year the reports [were] received." Pet. Ex. 34 at 2.

GBS) or otherwise induce injury. Id. Even if they did, Dr. Chaudhry argued that "finding similar conformational structure between an exogenous agent and a self-antigen alone [is] not sufficient to prove that molecular mimicry is the pathogenic mechanism for a disease. Many such homologies exist, and the vast majority of these are not associated with biologically relevant autoimmune phenomena or actual human disease." Id. (citing Resp. Ex. C, Tab 16 at 10).[64]

As for the case report by Ravishankar, cited by both Dr. Sykes and Dr. Steinman, Dr. Chaudhry opined that the patient described in the report had an "evolution of symptoms over five months," which he disagreed supported a diagnosis of GBS. Resp. Ex. C at 10-11 (citing Pet. Ex. 35); see also Resp. Ex. H at 5. Similarly, Dr. Chaudhry disagreed with Dr. Steinman as to the significance of the El Khatib et al. article, disputing that the patient had GBS, and instead Dr. Chaudhry opined that the patient had *S. pneumoniae* which led to septicemia and death. Resp. Ex. C at 11; Resp. Ex. H at 6.

Regarding Althen Prong Two, while Dr. Chaudhry questioned whether petitioner had GBS, he believed that if she did, there were more likely causes other than vaccination. Resp. Ex. A at 15. He pointed to two other causes, a diarrheal illness or upper respiratory tract infection. Id. Dr. Chaudhry stated that petitioner's "records do not pinpoint when she suffered from diarrhea although multiple references are made to this during her admission." Id. He quoted petitioner's treating physician, who noted that "acute diarrhea resolved and unfortunately *Campylobacter* [testing] was never done as patient did not have stool sample." Id. (quoting Pet. Ex. 5 at 264). Dr. Chaudhry opined that "*Campylobacter* is the most well described infection preceding GBS." Id.

In support of his opinion that another likely cause of petitioner's GBS was an upper respiratory tract infection, Dr. Chaudhry cited to an affidavit from a daughter of petitioner and medical records. Resp. Ex. A at 15. Petitioner's daughter, Erin Fortunato, submitted a declaration in which she described her recollection of her mother's condition prior to her illness. See Pet. Ex. 17. Dr. Chaudhry does not specify which specific statements in the declaration support his opinion that petitioner had an upper respiratory illness. See Resp. Ex. A at 15. Presumably, it is the reference that petitioner "started to have labored breathing" on Sunday.[65] Pet. Ex. 17 at ¶ 15. Petitioner's daughter told the doctor about petitioner's "trouble breathing." Id. at ¶ 17. By the next day, the daughter observed that the treatment her mother received for her GBS had "helped to stop the progression of her deterioration." Id. at ¶ 18.

The medical records cited by Dr. Chaudhry include a consultation note by neurologist, Dr. Fix, dated July 18, 2017, in which Dr. Fix wrote, "[petitioner] reports she was diagnosed with pneumonia last week and has not fully recovered her strength and energy." Pet. Ex. 5 at 149. In review of systems, Dr. Fix noted that petitioner did not report fever or chills, and she had

[64] Inst. of Med., Evaluating Biological Mechanisms of Adverse Events, in Adverse Effects of Vaccines: Evidence and Causality 57 (Kathleen Stratton et al. eds., 2012).

[65] Based on the sequence of events described in the declaration, Sunday would have been July 23, 2017, approximately five days after petitioner's admission to the hospital.

no pleurisy. Id. at 150. Physical examination showed that respiratory rate and oxygen saturation was normal. Id. Lungs were "clear to auscultation bilaterally." Id.

Additionally, Dr. Chaudhry cited records of a pulmonary consult and treatment with IV antibiotics. Resp. Ex. A at 15 (citing Pet. Ex. 6 at 121).[66] The pulmonary consult was conducted by Dr. Patel on July 24, 2017. Pet. Ex. 5 at 136-42. He diagnosed petitioner with bibasilar atelectasis and lower respiratory infection. Id. at 140-41.

Dr. Chaudhry also opined that other causes, "such as hypophosphatemia and hypokalemia contributed to [petitioner's] symptoms." Resp. Ex. A at 15. He stated that petitioner had low phosphate blood levels from July 25 to July 29, 2017,[67] and that "[g]eneralized muscle weakness is the most common symptom" of this condition. Id. at 14. Dr. Chaudhry also opined that "dysarthria . . . can be a manifestation of low phosphorus." Id. Petitioner also had low potassium, or hypokalemia, which Dr. Chaudhry opined "is a common cause of weakness." Id. He asserted that petitioner's potassium was low on July 23, when it was 3.1 (normal range 3.5-5.0 mEq/L). Id. Dr. Chaudhry attributed petitioner's low potassium to petitioner's diarrhea, and stated that "ascending weakness has been described with hypokalemia." Id.

4. Respondent's Expert, Dr. Lindsay Whitton

a. Background and Qualifications

Dr. Whitton received his B.Sc. in molecular biology, his M.B., Ch.B. in medicine, and his Ph.D. in herpesvirus transcription from the University of Glasgow in Scotland. Resp. Ex. E at 1. He also completed internships in medicine and surgery, and held various professor positions since 1986. Resp. Ex. A at 1; Resp. Ex. E at 1. He currently works as a Professor in the Department of Immunology and Microbial Science at Scripps Research Institute in California. Resp. Ex. E at 1. Dr. Whitton is a member of various professional societies and editorial boards, and has authored or co-authored almost 200 publications. Id. at 1-15.

b. Opinion

Dr. Whitton did not opine as to petitioner's diagnosis, or take a position on whether the diagnosis of GBS is appropriate. Resp. Ex. D at 3. Instead, he focused on the issue of causation:

[66] The record cited by Dr. Chaudhry does not document a pulmonary consult or antibiotic treatment. However, after a review of the records, the consult appears at Pet. Ex. 5 at 136-42.

[67] Dr. Chaudhry inadvertently wrote the year as 2015.

whether the Prevnar 13 vaccine can cause GBS.[68] See Resp. Exs. D, G. Dr. Whitton opined that "Prevnar 13 has an excellent safety record, and [he] is not aware of any evidence that associates it with GBS." Resp. Ex. D at 18. He raised a litany of objections about Dr. Steinman's opinions. His primary criticisms are addressed below, with responses by Dr. Steinman.

First, Dr. Whitton believed that it is inaccurate for Dr. Steinman to conclude that anti-phospholipid antibodies play a role in disease causation. Resp. Ex. D at 11-12. While Dr. Whitton agreed that that these antibodies "may be the cause of disease," he opined that they may also be "the result of the disease" or "irrelevant to the disease." Id. at 12. Dr. Whitton, like Dr. Chaudhry, quoted Nakos et al., who stated that "[i]t is not well understood whether these anti-phospholipid antibodies play a role in the pathogenesis of the polyneuropathy or represent a part of a more extensive immunoreaction that takes place in [] GBS." Id. (Pet. Ex. 50 at 6).

Instead of phospholipids, Dr. Whitton opined that "gangliosides . . . are the targets of autoimmunity in GBS."[69] Resp. Ex. D at 13; see also Resp. Ex. G at 5. While Dr. Steinman did not disagree with the generally accepted proposition that gangliosides may be targeted in GBS, he did not believe that "gangliosides are the only immune target in GBS." Pet. Ex. 66 at 25; see also Pet. Ex. 56 at 17-18. For support, Dr. Steinman cited Kanter et al.,[70] and his own research, in support of this point. Pet. Ex. 66 at 22-25 (citing Pet. Ex. 44); Pet. Ex. 56 at 16-18 (citing, e.g, Pet. Exs. 44, 49-50). According to Kanter et al., "[l]ipids comprise over 70% of the myelin sheath, and a growing number of reports have shown T-cell and antibody reactivity in [MS]."

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[68] Dr. Whitton's criticisms of Dr. Steinman's expert reports include many issues, some of which are not material to the undersigned's findings and conclusions. For example, Dr. Whitton identified many flaws in the Ravishankar case report cited by Dr. Steinman. See Resp. Ex. D at 15-16; Resp. Ex. G at 6. However, the undersigned does not rely on the Ravishankar article in her analysis, and therefore, does not discuss this aspect of Dr. Whitton's opinions. For the sake of brevity and clarity, the undersigned discusses the material reasons for reaching her findings and conclusions and omits discussion of collateral matters.

[69] Dr. Whitton and Dr. Steinman engaged in a colloquy about a paper written by Kanter et al., where Dr. Steinman is a named author. See Pet. Ex. 56 at 17-18; Pet. Ex. 66 at 22-25; Resp. Ex. D at 12-13; Resp. Ex. G at 5-6; Pet. Ex. 44 at 1. The pertinent statement is, "[a]utoimmune responses directed against phospholipids and gangliosides contribute to the pathogenesis in systemic lupus [] and [GBS], respectively." Pet. Ex. 44 at 1. Dr. Whitton suggested that the statement is an acknowledgement by Dr. Steinman that in GBS, autoimmune responses are directed against gangliosides, not phospholipids. Resp. Ex. D at 13; Resp. Ex. G at 5. After Dr. Steinman explained the basis and origin of the statement in a subsequent report, Dr. Whitton wrote that Dr. Steinman tried to "disown his peer-reviewed statement." Resp. Ex. G at 5 (emphasis omitted). Dr. Whitton further wrote that "Dr. Steinman's attempt to disown [the] statement . . . is risible, and is based on a demonstrable falsehood." Id. at 7. The undersigned finds such rhetoric excessive, and takes no position on the debate, as its resolution is not necessary to determine entitlement in this case.

[70] Jennifer L. Kanter et al., Lipid Microarrays Identify Key Mediators of Autoimmune Brain Inflammation, 12 Nature Med. 138 (2006).

Pet. Ex. 44 at 1. The study by Kanter et al. showed antibody reactivity against myelin lipids in patients with MS. Id. They concluded that the data suggests that lipid-specific responses can "contribute to the pathogenesis of autoimmune demyelinating disease." Id. at 5.

Dr. Whitton also objected to Dr. Steinman's references to articles like the Kanter et al. study, where the disease is MS, because that is not the disease at issue here. Resp. Ex. D at 12; Resp. Ex. G at 5. Dr. Steinman acknowledged that "MS and GBS are different diseases," and that MS is not a model for GBS. Pet. Ex. 66 at 22. He explained, however, that research on immune responses in MS show "that there is vigorous immunity to polar head groups in myelin[,] including immunity to phosphoglycerol and phosphoryl choline chemical structures." Id. (citing Pet. Ex. 45).

As for "Dr. Steinman's reliance on glycerol phosphate," and reference to Chang et al., which illustrates the "phosphate head group," Dr. Whitton had several observations. Resp. Ex. D at 13-14. First, Dr. Whitton suggested that the more likely explanation for the importance of the phosphate group in the vaccine is "related to its role in defining the overall shape of the polysaccharide," which is "distinguishable by the immune system." Id. In turn, Dr. Steinman reiterated his opinion that glycerol phosphate is important for the robust immune response and ability to elicit antibodies to components 18C and 23F of the vaccine. See Pet. Ex. 66 at 12-16.

Secondly, Dr. Whitton stated that the phosphate groups in the vaccine are "very small molecular structures that are ubiquitous in biological materials." Resp. Ex. D at 14. "[W]hile there is no doubt that antibodies can be (and are) directed against large molecules that contain a few phosphate groups," Dr. Whitton "suspect[ed]" that "an antibody response [] focused solely on this small, and ubiquitous, molecule would . . . have extremely widespread effects on the host." Id. (emphasis omitted).

And thirdly, Dr. Whitton's observed that if Dr. Steinman is right, "the glycerophosphate group of one strain [of *S. pneumoniae*] would induce an antibody response that would recognize the glycerophosphate group in a different strain," but there is no such antibody cross reactivity. Resp. Ex. D at 14. Dr. Whitton asserted that "antibodies against *S. pneumoniae* polysaccharides are exquisitely serotype-specific, which means that antibodies against strain 18C do not recognize polysaccharides of other strains. Thus, Dr. Steinman's speculation regarding antibodies that specifically target phosphoglycerol is invalid." Resp. Ex. G at 4. In response, Dr. Steinman agreed that "antibodies to the specific sugar serotypes are highly specific to those sugars," but explained that he was "not referring only to the serotype specific antibodies." Pet. Ex. 66 at 17. Dr. Steinman explained "that immunity to Prevnar 13 is polyclonal and encompasses adaptive immune responses to components including phosphoglycerol, the 13 saccharides including 18C and 23F which are known to contain phosphoglycerol, and CRM_{197}, the protein carrier that includes diphtheria toxin modified by one amino acid." Id.

In his second report, Dr. Whitton raised additional objections to Dr. Steinman's reliance on phosphoglycerol. Dr. Whitton interpreted Dr. Steinman's opinion as suggesting that "the 13 different polysaccharides in Prevnar 13 are attached (conjugated) to CRM_{197} using phosphoglycerol as the link." Resp. Ex. G at 4. Dr. Whitton questioned whether that was possible since most of the polysaccharides do not contain phosphoglycerol. Id. It is not clear

whether Dr. Steinman responded to this point directly; instead, he reiterated the importance of phosphoglycerol as it relates to the immunogenicity of 18C, based on Chang et al. Pet. Ex. 66 at 12-16. Dr. Steinman also emphasized the finding of antibodies targeting 23F, described by Bryson et al. Id. Dr. Steinman believed these studies provide "compelling support . . . that the immune response to serotypes 18C and 23F in Prevnar 13 targets the [phosphoglycerol] moiety in those serotypes." Id. at 16.

Dr. Whitton also criticized Dr. Steinman's use of the phrase "phospholipid linkage," as well as reliance on such a linkage as a tenet of petitioner's theory. Resp. Ex. G at 4. According to Dr. Whitton, the concept of "phospholipid linkage" was created by Dr. Steinman, and not Chang et al. Id. Dr. Whitton argued that "[i]f the phosphoglycerol of 18C were used for conjugation . . . , that chemical reaction would alter the phosphoglycerol, thereby destroying the immunogenicity of the 18C polysaccharide." Id. at 4-5 (emphasis omitted). Dr. Steinman disagreed and stated that "[p]hosphoglycerol is linked to the saccharide moieties and the whole complex is linked to CRM_{197} by reductive amination." Pet. Ex. 66 at 19. Dr. Steinman cited to the patent for the Prevnar 13 vaccine, and stated that "the 13 different saccharides are covalently linked to CRM_{197}." Id. at 20. "Once activated, each capsular polysaccharide is separately conjugated to a carrier protein to form a glycoconjugate." Id. Dr. Steinman contended that the process of reductive amination which links sugars to CRM_{197}, "does not 'destroy' the phosphoglycerol. Instead, it allows successful conjugation to CRM, the vital protein carrier." Id. at 21. According to Dr. Steinman, the importance of the phosphoglycerol to immunogenicity as demonstrated by the patent weighs against any argument that it is destroyed in the process of conjugation. Id.

Next, Dr. Whitton criticized Dr. Steinman's reliance on Haber et al., which discussed case reports of GBS after Prevnar 13 vaccination. Resp. Ex. D at 10-11, 16. Dr. Whitton noted that while Haber et al. identified cases of GBS after vaccination, they did not conclude that there was a causal association. Id. at 10. Instead, they concluded that the data "noted no disproportionate reporting for GBS." Id. at 11 (quoting Pet. Ex. 34 at 5). Dr. Steinman responded that while his theory "does not encompass epidemiology," the case reports described in Haber et al. "provide additional evidence that [the] vaccine could cause GBS." Pet. Ex. 56 at 3-4 (emphasis omitted). Further, Dr. Steinman asserted that the authors' finding that the rate of GBS cases was not disproportionate does not mean that the vaccine could not cause GBS. Pet. Ex. 66 at 36. He noted that the authors were "more cautious about attributing 'absolute safety' or 'safety' regarding the vaccine," and they did not define the phrase "disproportionate reporting." Id. Lastly, Dr. Steinman noted that "[f]or rare diseases, it is difficult to know what is disproportionate." Id. at 36-37.

Dr. Whitton similarly opined that the case reports by El Khatib et al. and White et al.[71] do not support petitioner's experts' opinions. Resp. Ex. D at 16-17. El Khatib et al. described the case of a teenage boy who developed sepsis and "acute respiratory distress syndrome" due to pneumococcal infection, not vaccination. Id. at 16 (citing Pet. Ex. 32 at 1). According to Dr. Chaudhry, to whom Dr. Whitton deferred as to diagnosis, the diagnosis of GBS in the report is

[71] B. White et al., A Novel Pneumococcus with a New Association, 9 Travel Med. & Infectious Disease 84 (2011).

suspect, and Dr. Whitton agreed. Id.; Resp. Ex. C at 11; Resp. Ex. H at 6. White et al. described another case of GBS following *S. pneumoniae* infection, not vaccination, and again, the diagnosis of GBS was questioned by respondent's experts. Resp. Ex. D at 17.

White et al. described a case of systemic *S. pneumoniae* bacteremia which caused meningitis, pneumonia, and endocarditis. Pet. Ex. 33 at 1. The patient also developed an atypical form of GBS (acute motor-sensory axonal neuropathy), not previously reported to be associated with pneumococcal bacteria. Id. at 1-2. The authors concluded that "[t]his new association between invasive pneumococcal disease and an atypical form of [GBS] may help to provide further hypotheses regarding the antigenic triggers of GBS, and whether there is a target on the pneumococcal surface capable of inducing 'molecular mimicry' as is seen in [*Campylobacter*] infections."[72] Id. at 3.

Irrespective of the two case reports by El Khatib et al. and White et al., Dr. Whitton opined that gram positive[73] bacteria like *S. pneumoniae* "[are] not generally considered to be causally associated with GBS." Resp. Ex. D at 8-10, 18. Dr. Whitton cited an article by Jasti et al.,[74] listing 39 infections that may precede GBS. Id. at 8 (citing Resp. Ex. D, Tab 16 at 2). He observed that *S. pneumoniae* was not on the list. Id. at 9.

Dr. Whitton also argued that GBS has no causal association with any other gram positive bacteria because they "lack the [] molecules necessary to trigger GBS." Resp. Ex. D at 8-10. Dr. Steinman disagreed and opined that gram positive bacteria are associated with GBS. Pet. Ex. 56 at 10-13. Dr. Steinman cited a paper by Yuki and Hirata[75] and stated that "though far less common than *C. jejuni*, gram positive bacteria, including *pneumococcus* and *streptococcus*[,] are

[72] The pneumococcal isolates from the patient's blood and CSF were serotype 6A, not one of the serotypes relevant to Dr. Steinman's theory. Pet. Ex. 33 at 2. Of interest in White et al. was the fact that the bacteria had a unique genotype, not seen before. Id. at 2-3. That part of the case report is not discussed here.

[73] Gram-positive bacteria "retain[] the stain . . . in the Gram method of staining, a primary characteristic of bacteria whose cell wall is composed of a thick layer of peptidoglycan with attached teichoic acids." Gram-Positive, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=20907 (last visited Feb. 22, 2022).

[74] Anil K. Jasti et al., Guillain-Barré Syndrome: Causes, Immunopathogenic Mechanisms and Treatment, 12 Expert Rev. Clinical Immunology 1175 (2016). Dr. Whitton referred to this article as Dr. Gershwin's paper; Dr. Gershwin is one of the authors. See Resp. Ex. D at 8; Resp. Ex. D, Tab 16 at 1.

[75] Nobuhiro Yuki & Koichi Hirata, Fisher's Syndrome and Group A Streptococcal Infection, 160 J. Neurological Scis. 64 (1990). For Dr. Whitton's complete response to Dr. Steinman's assertion based on the Yuki & Hirata article regarding whether gram positive bacteria can cause GBS, see Resp. Ex. G at 2.

implicated in GBS and its variants like Fisher Syndrome."[76] Id. at 12 (emphasis omitted and added) (citing Pet. Ex. 58). Dr. Steinman agreed that the Prevnar 13 vaccine and the infection which it protects against, *S. pneumoniae*, are very different. Pet. Ex. 66 at 5. In the context of the issues relevant to the causal theory, however, Dr. Steinman found Dr. Whitton's emphasis on *S. pneumoniae* "misplaced." Id.

Dr. Whitton also disagreed that Dr. Steinman's reference to Conner et al.,[77] a presentation by a medical student at the American College of Chest Physicians, constitutes evidence in support of causation. Resp. Ex. G at 2 (citing Pet. Ex. 57). Conner et al. presented on a 61-year-old male who reported tingling in his feet that progressed to his knees and associated weakness. Pet. Ex. 57 at 2. The patient received the Prevnar 13 vaccine two weeks prior to hospital admission, and he denied upper respiratory infections and diarrhea. Id. Physical examination and testing were consistent with GBS, and the patient was started on IVIG. Id. The authors acknowledged that "[t]he underlying etiology of GBS remains unclear, but the pathophysiology in most cases of GBS is due to stimulation of autoimmunity that produces auto-immune antibodies that attack the myelin sheath of the nerves in the peripheral nervous system." Id. They also noted "[t]here is inconclusive data that the greater immunogenicity of [Prevnar 13] leads to a higher incidence of immune reactions potentially leading to GBS." Id.

Regarding a temporal association between petitioner's Prevnar 13 vaccination and her GBS, Dr. Whitton stated that "the two can be temporally associated . . . but this most certainly is not proof of causation." Resp. Ex. D at 16.

III. DISCUSSION

A. Standards for Adjudication

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

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, petitioner must prove that the

[76] The undersigned acknowledges the disagreement, but does not find it necessary to resolve it, since neither of Dr. Steinman's mechanisms implicate lipo-oligosaccharides ("LOS") or lipopolysaccharides ("LPS") referenced by Dr. Whitton. See Resp. Ex. D at 8-10.

[77] Chad Conner et al., 13-Valent Pneumococcal Conjugate Vaccine-Induced Guillain-Barré Syndrome, 158 Allergy & Airway A59 (2020).

vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Hum. Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). The received vaccine, however, need not be the predominant cause of the injury. Shyface, 165 F.3d at 1351. A petitioner who satisfies this burden is entitled to compensation unless respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B).

B. Factual Issues

A petitioner must prove, by a preponderance of the evidence, the factual circumstances surrounding her claim. § 13(a)(1)(A). To resolve factual issues, the special master must weigh the evidence presented, which may include contemporaneous medical records and testimony. See Burns v. Sec'y of Health & Hum. Servs., 3 F.3d 415, 417 (Fed. Cir. 1993) (explaining that a special master must decide what weight to give evidence including oral testimony and contemporaneous medical records). Contemporaneous medical records are presumed to be accurate. See Cucuras v. Sec'y of Health & Hum. Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). To overcome the presumptive accuracy of medical records, a petitioner may present testimony which is "consistent, clear, cogent, and compelling." Sanchez v. Sec'y of Health & Hum. Servs., No. 11-685V, 2013 WL 1880825, at *3 (Fed. Cl. Spec. Mstr. Apr. 10, 2013) (citing Blutstein v. Sec'y of Health & Hum. Servs., No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)).

There are situations in which compelling testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. Campbell v. Sec'y of Health & Hum. Servs., 69 Fed. Cl. 775, 779 (2006) ("[L]ike any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking."); Lowrie v. Sec'y of Health & Hum. Servs., No. 03-1585V, 2005 WL 6117475, at *19 (Fed. Cl. Spec. Mstr. Dec. 12, 2005) ("[W]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent." (quoting Murphy v. Sec'y of Health & Hum. Servs., 23 Cl. Ct. 726, 733 (1991), aff'd per curiam, 968 F.2d 1226 (Fed. Cir. 1992))). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1379 (Fed. Cir. 2009); Bradley v. Sec'y of Health & Hum. Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

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

C. Causation

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

The causation theory must relate to the injury alleged. The petitioner must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen v. Sec'y of Health & Hum. Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioner cannot establish entitlement to compensation based solely on her assertions; rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether petitioner is entitled to compensation, the special master shall consider all material in the record, including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 13(b)(1)(A). The special master must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in petitioner's favor when the evidence weighs in her favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in petitioner's favor).

IV. ANALYSIS

A. Diagnosis

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

The undersigned finds that there is preponderant evidence that petitioner's diagnosis following vaccination was GBS. This finding is based on the opinions of petitioner's treating physicians, her clinical presentation, diagnostic testing, and the opinions of petitioner's experts. While Dr. Chaudhry is correct in concluding that petitioner's initial presentation suggested a TIA

or stroke, those symptoms resolved within several hours of her arrival to the hospital. Dr. Chaudhry also accurately explains the confounding factors that clouded petitioner's clinical picture and may have made it more difficult to diagnosis GBS. However, after petitioner was hospitalized and her symptoms progressed, her physicians suspected GBS, which was confirmed by diagnostic testing.

According to the literature, weakness is the prominent manifestation of GBS. See, e.g., Pet. Ex. 22 at 2. When she presented to the hospital on July 18, 2017, petitioner reported to Ms. Maynard, RN, that she had experienced "progressive, generalized weakness over 1 week after receiving pneumonia vaccine." Pet. Ex. 5 at 80. Superimposed on that background, petitioner also had new left leg weakness that began that morning. Physical examination by Ms. Maynard revealed that petitioner had weakness in all four of her extremities.

Also on July 18, neurologist Dr. Fix documented that petitioner "report[ed] that she was diagnosed with pneumonia last week." Pet. Ex. 5 at 149. However, there is no evidence in the record to support the statement that petitioner was diagnosed with pneumonia the week prior to her admission. Subsequently, on July 23, 2017, Dr. Fix wrote, "[i]t is now learned that apparently [petitioner] received a pneumonia vaccine 1 week prior to admission after which she began to have progressive, generalized weakness with an acute change the day of admission including dysarthria and [lower leg extremity] weakness which prompted presentation to the hospital." Id. at 303.

In addition, on July 18, Dr. Fix noted petitioner reported bilateral lower extremity weakness the day prior, and that petitioner had an acute change, which began that morning, of more difficulty ambulating. Additionally, Dr. Fix, after physical examination noted petitioner's "stroke-like symptoms" had "nearly resolved." Id. at 151.

Again on July 18, Ms. Bundy, PT, documented that petitioner had an unsteady gait and decreased balance and strength.

On July 21, Mr. Foster, PA, documented that petitioner reported that her legs felt weak and heavy, and that walking had become difficult that week. Mr. Foster's physical examination revealed reduced strength throughout, sensory perception decreased slightly in a stocking pattern bilaterally, and abnormal reflexes noted to be trace to 1+ symmetrically. Due to petitioner's global weakness, he recommended a neurology work up and EMG.

On July 24, Dr. Stabley took a history and performed a physical examination in association with conducting an EMG/NCV. He noted that petitioner had "onset of progressive bilateral lower extremity and upper extremity weakness . . . beginning within several days of receiving pneumococcal vaccine." Pet. Ex. 5 at 297. His clinical examination "reveal[ed] significant neck flexor weakness, bilateral upper and lower extremity proximal and distal weakness, areflexia[,] and stocking distribution sensory loss to pinprick to the level of the mid calves." Id. CSF revealed cytoalbuminologic dissociation, with an elevated protein of 112 mg/dL (normal 15-40). Petitioner's clinical diagnosis was GBS. Dr. Stabley interpreted the EMG as consistent with AIDP/GBS.

The diagnosis of GBS was repeated by Dr. Patel on July 24, and petitioner was treated for GBS with a five-day course of IVIG. On July 30, Dr. Gaeta's diagnosis was GBS. Additionally, on July 31, 2017, physical therapy notes showed petitioner had left and right lower extremity buckling and an ataxic gait, consistent with GBS. After petitioner's diagnostic work up, her medical records contain multiple references to her diagnosis of GBS.

Further, petitioner's diagnostic tests were consistent with her diagnosis of GBS. Dr. Stabley performed an EMG/NCV and interpreted the study to be consistent with AIDP/GBS. There is no reason to suspect that his interpretation of the testing was erroneous.[78] Moreover, CSF testing showed an abnormally elevated protein level in the context of a normal cell count, which is also consistent with GBS.[79]

Based upon the evidence summarized above, the undersigned finds that petitioner has proven by preponderant evidence that she suffered from GBS following her Prevnar 13 vaccination.

B. Causation

1. Althen Prong One

Under Althen Prong One, petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu, 569 F.3d at 1375; Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by a "sound and reliable" medical or scientific explanation. Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1359 (Fed. Cir. 2019); see also Knudsen, 35 F.3d at 548; Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioner relies upon a medical opinion to support her theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen, 618 F.3d at 1347 ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better than the

[78] Dr. Chaudhry observed that the data underlying the petitioner's EMG/NCV was not contained in her medical records. The undersigned notes that based on her experience in reviewing medical records in many similar cases, it is common that the EMG/NCV report interpreting the data be contained in the record, but not the data itself. Presumably, the underlying data could have been obtained pursuant to a specific request or subpoena for it, but neither party requested such discovery.

[79] Dr. Chaudhry also observed that petitioner's urinary retention was not consistent with GBS. However, Dr. Vickers, during a renal consult, observed that petitioner's urinary retention "seem[ed] to be a long-standing problem." Pet. Ex. 5 at 202. This note weighs against Dr. Chaudhry's interpretation that petitioner had acute urinary retention and that it was inconsistent with her diagnosis of GBS.

soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

For the following reasons, the undersigned finds petitioner has provided by preponderant evidence a sound and reliable theory that the Prevnar 13 vaccine can cause GBS, and therefore, petitioner has satisfied the first Althen prong.

Molecular mimicry has long been invoked as the causal mechanism for many different autoimmune diseases, including GBS. Many of the articles filed in this case support the mechanism as the leading hypothesis for the etiology of GBS. See, e.g., Resp. Ex. C, Tab 13 at 1. The theory has been extended from infectious agents to vaccine-associated autoimmune illnesses, including GBS. See, e.g., Pet. Ex. 22; Pet. Ex. 32; Resp. Ex. A, Tab 2.

Molecular mimicry has been accepted as a sound and reliable theory in many demyelinating conditions, including GBS, in the Vaccine Program, forming the basis for petitioners to be entitled to compensation. See, e.g., Conte v. Sec'y of Health & Hum. Servs., No. 17-403V, 2020 WL 5743696, at *23 (Fed. Cl. Spec. Mstr. July 27, 2020) (noting the theory of molecular mimicry in a GBS case is "well-established and well-settled in the Vaccine Program"); Barone v. Sec'y of Health & Hum. Servs., No. 11-707V, 2014 WL 6834557, at *8-9 (Fed. Cl. Spec. Mstr. Nov. 12, 2014) (noting molecular mimicry "has been accepted in other Program cases as a reliable medical explanation for how various autoimmune conditions could develop after the receipt of different kinds of vaccinations"); Koller v. Sec'y of Health & Hum. Servs., No. 16-439V, 2021 WL 5027947, at *18 (Fed. Cl. Spec. Mstr. Oct. 8, 2021); Pierson v. Sec'y of Health & Hum. Servs., No. 17-1136V, 2022 WL 322836, at *31 (Fed. Cl. Spec. Mstr. Jan. 19, 2022); Deshler v. Sec'y of Health & Hum. Servs., No. 16-1070V, 2020 WL 4593162, at *19 (Fed. Cl. Spec. Mstr. July 1, 2020).[80]

Dr. Chaudhry asserts that four criteria that must be met to establish whether a vaccine can cause GBS via molecular mimicry. These criteria include supportive epidemiology, identification of antibodies directed against human antigens, identification of the mimics of the target antigen, and reproduction in an animal model. Given the state of current knowledge, a petitioner cannot satisfy these criteria. Fulfilment of these criteria would require scientific certainty, which is a bar too high. See Knudsen, 35 F.3d at 549 (explaining that "to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program").

Dr. Whitton takes a different tack. He criticizes the fact that petitioner has not invoked a causal mechanism that implicates gangliosides as the targets of autoimmunity. However, the literature filed by the parties does not support the notion that gangliosides are the only player in the game of molecular mimicry.

There is scientific support for Dr. Steinman's theories. To use the language in the criteria cited by Dr. Chaudhry, Dr. Steinman has identified components of a vaccine that could initiate

[80] The undersigned acknowledges that the first two cases in this string cite involve a different vaccine, although the same illness.

development of antibodies that could cross-react with epitopes on peripheral nerve myelin or axonal glycoproteins. He has identified components of the Prevnar 13 vaccine protein that could trigger a human antibody response.

Regarding petitioner's theory based on phosphoglycerol in serotypes 18C and 23F in the vaccine, Dr. Steinman provides evidence in the Bryson et al. paper showing the antibodies that target 23F. There is an immune response that targets the phosphoglycerol moiety in the 23F serotype in the vaccine. Dr. Steinman produced papers to show that in MS, myelin phospholipids are targeted by an immune response. He has also shown that myelin is comprised of phospholipids, and that phospholipids can serve as autoantigens in autoimmune disorders. He has shown that patients with GBS have autoantibodies to phospholipids. In the Gilburd et al. study, the autoantibodies were thought to be due to myelin destruction. However, in the Nakos et al. article, the researchers had a different view. They suggested that anti-phospholipids either "play a role in pathogenesis of the polyneuropathy or represent a part of a more extensive immunoreaction that takes place in GBS." Pet. Ex. 50 at 7. In summary, there is sound support from reputable medical studies for each foundational aspect of the phosphoglycerol theory.

There is also evidence to support Dr. Steinman's second theory based on CRM_{197} and Contactin-1. Dr. Steinman identified sequences of shared homology between the proteins in the vaccine and those in Contactin-1. However, the study by Raju et al. shows that the sequence in CRM_{197} differs, albeit by one amino acid, from the sequence in the diphtheria toxin. Thus, the foundation for this theory is less sound.

Moreover, the causal theory proffered by Dr. Steinman here has previously been accepted as sound and reliable in two recent cases, decided by two different special masters. See Koller, 2021 WL 5027947; Pierson, 2022 WL 322836. While prior decisions are not binding on the undersigned, they can be considered by the undersigned in forming her opinions. See Hanlon v. Sec'y of Health & Hum. Servs., 40 Fed. Cl. 625, 630 (1998), aff'd, 191 F.3d 1344 (Fed. Cir. 1999); Boatmon, 941 F.3d at 1358.

Further, petitioner's evidence here is stronger than that presented in Koller. Here, Dr. Steinman cited the Bryson et al. study, which showed human antibodies targeting serotype 23F, one of the *S. pneumoniae* serotypes included in the Prevnar 13 vaccine.

In a third decision addressing the Prevnar 13 vaccine and GBS, the proffered causal theory was unsupported by evidence, and the Chief Special Master found that petitioner was not entitled to compensation. Deshler, 2020 WL 4593162. There, the petitioner relied on molecular mimicry, and suggested that there was homology between polysaccharide components of the vaccine and the myelin sheath, but evidence was insufficient to establish the scientific soundness of the theory. Id. at *19-21. Due to the lack of supportive evidence, respondent's expert, Dr. Whitton, was effective in establishing that the polysaccharides in the vaccine "do not share structural homology with self-structures of the peripheral nervous system, and therefore do not contribute to the pathogenesis of GBS." Id. at *20. The theory proffered here is far more well-developed and based on supportive foundational evidence from scientific studies.

For all of these reasons, the undersigned finds that petitioner has proven by preponderant evidence a sound and reliable causal theory establishing that the Prevnar 13 vaccine can cause GBS, satisfying Althen Prong One.

2. Althen Prong Two

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

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting Althen, 418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528. While the medical records and opinions of treating physicians must be considered, they are not binding on the special master. The Vaccine Act specifically provides that the "diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court." § 13(b)(1)(B).

The petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

There are three principal reasons why the undersigned finds preponderant evidence of a logical sequence of cause and effect establishing that the Prevnar 13 vaccination administered to petitioner on July 7, 2017, was the cause of her GBS. First, petitioner was appropriately diagnosed with GBS, and petitioner has proffered a sound and reliable mechanism of vaccine causation.

Secondly, petitioner's treating physicians' statements provide circumstantial evidence in support of vaccine causation. On July 23, 2017, Dr. Fix wrote, "[i]t is now learned that apparently [petitioner] received a pneumonia vaccine 1 week prior to admission after which she began to have progressive, generalized weakness with an acute change the day of admission." Pet. Ex. 5 at 303. The next day, July 24, Dr. Stabley stated that petitioner had "onset of progressive bilateral lower extremity and upper extremity weakness . . . beginning within several days of receiving pneumococcal vaccine." Id. at 297. Dr. Fix and Dr. Stabley are neurologists, and as such, they diagnose and treat peripheral neuropathy disorders such as GBS.

In addition to petitioner's neurologists, her other treating physicians also noted an association between her vaccination and GBS. On July 24, 2017, Dr. Patel documented that petitioner received "a pneumonia shot a week prior to this episode. The patient underwent nerve conduction study and was found to [have] [AIDP] . . . ." Pet. Ex. 5 at 136. The next day, July 25, Dr. Gaeta referenced petitioner's "pneumonia vaccine [] prior to admission." Id. at 280. On July 31, a progress note authored by a medical student stated that petitioner's "symptoms started a week prior to admission with fatigue and malaise. [T]he precipitating cause was believed to [be the] pneumonia vaccination." Pet. Ex. 6 at 79. And on August 2, 2017, petitioner's diagnosis on admission to the rehabilitation facility was "[GBS] d/t Pneumonia Vaccine." Id. at 153. Individually and collectively, these statements constitute circumstantial evidence that the petitioner's treating physicians associated her vaccine with the development of her GBS.

Third, the evidence does not support an alternate cause for petitioner's GBS. Dr. Chaudhry raised two potential causes, a diarrheal illness and upper respiratory tract infection. However, a close review of the medical records does not support either of these as potential culprits because the evidence does not show that either occurred prior to the onset of petitioner's GBS.

Here, because petitioner's clinical history presents a logical sequence of cause and effect consistent with vaccine causation, she need not eliminate other potential alternative causes. See Walther v. Sec'y of Health & Hum. Servs., 485 F.3d 1146, 1149-52 (Fed. Cir. 2007) (finding petitioner does not bear the burden of eliminating alternative independent potential causes). While respondent has argued that petitioner's illness was caused by an antecedent diarrheal illness and/or upper respiratory tract infection, he has failed to provide evidence that she had either or that she had either before the onset of petitioner's GBS, and therefore, has failed to prove that petitioner's GBS was caused by something other than her vaccination.

On her admission to the hospital on July 18, petitioner was assessed by physicians and nurses. These assessments have no reference to diarrhea. Likewise, petitioner's history was taken by several health care providers. There is no mention of a diarrheal illness in the histories taken by any of the physicians or other health care providers who saw petitioner the first several days of her hospital stay. On July 23, there is a reference to "[a]cute diarrhea." Pet. Ex. 5 at 302. However, on July 24, the records note that petitioner's diarrhea had improved. Id. at 296.

Most importantly, on July 25, 2017, Dr. Gaeta documented that he questioned one of petitioner's daughter about whether petitioner had diarrhea prior to her admission. Petitioner's daughter reported that her mother had a history of irritable bowel syndrome; however, her mother did not complain of loose stools or worsening bowel movements prior to her hospitalization. So, while Dr. Chaudhry is correct in noting that petitioner had diarrhea in the hospital, Dr. Gaeta specifically asked whether petitioner had any diarrheal illness prior to her hospital admission and the answer was no. Further, there is no indication that any of petitioner's physicians attributed her GBS to the diarrhea petitioner may have had after she was admitted to the hospital.

Moving to the issue of upper respiratory infection, Dr. Chaudhry cites to a declaration from one of petitioner's daughters and petitioner's medical records to support his opinion that an

upper respiratory infection caused petitioner's GBS. Petitioner's daughter, Erin Fortunato, submitted a declaration in which she describes her mother's "labored breathing" and "trouble breathing." Pet. Ex. 17 at ¶¶ 15, 17. The medical records cited by Dr. Chaudhry include a consultation note on July 18, 2017, in which Dr. Fix writes, "[s]he reports she was diagnosed with pneumonia last week and has not fully recovered her strength and energy." Pet. Ex. 5 at 149. However, in that same note, Dr. Fix wrote that petitioner did not report fever or chills, and she had no pleurisy. Petitioner's respiratory rate and oxygen saturation was normal. Her lung sounds were clear. The reference in Dr. Fix's note about petitioner's report of having pneumonia the week before her hospitalization appears to be the only one of its kind. There is no other evidence to corroborate this statement. Instead, all the other records consistently state that petitioner reported that she had a pneumonia vaccine the week before she came to the hospital. And in fact, on July 23, Dr. Fix wrote, "[i]t is now learned that apparently [petitioner] received a pneumonia vaccine 1 week prior to admission." Id. at 303.

Additionally, on July 18, shortly after petitioner arrived at the hospital, Ms. Maynard wrote that the petitioner "report[ed] a progressive, generalized weakness over 1 week after receiving pneumonia vaccine." Pet. Ex. 5 at 80. Petitioner was evaluated by Ms. Mueller, an OT, who noted petitioner's "weakness started after receiving a [pneumonia] shot several days ago." Id. at 96. PA Mr. Vo wrote, "since she received her pneumo[nia] vaccine a week ago . . . , she started not feeling very well." Id. at 108. These records all consistently document that petitioner reported feeling bad following her pneumonia vaccine, not that she had been ill with pneumonia or diagnosed with pneumonia.

Further, there are no records from any health care provider evidencing that petitioner sought treatment for an upper respiratory infection or was diagnosed with any infection or illness prior to her hospitalization.

In support of his opinion, Dr. Chaudhry cites records of a pulmonary consult and treatment with IV Rocephin. Resp. Ex. A at 15 (citing Pet. Ex. 6 at 121). However, the records do not suggest that petitioner had an upper respiratory infection prior to her hospitalization. A chest X-ray done on admission on July 18 showed no acute abnormality. The physical examinations on admission revealed clear lung sounds. However, after petitioner had been hospitalized for approximately six days, a pulmonary consult was done by Dr. Patel on July 24, 2017. He observed decreased breath sounds. He assessed petitioner with respiratory insufficiency and atelectasis and diagnosed her with "lower respiratory infection." Pet. Ex. 5 at 141. There is no evidence that petitioner had an upper respiratory infection prior to or on her admission to the hospital. Instead, all of the evidence points to a lower respiratory illness which petitioner may have developed well after her admission to the hospital. Therefore, there is no evidence of an antecedent infection which could have been the cause of her GBS.

Dr. Chaudhry also opines that other causes, such as hypophosphatemia and hypokalemia, contributed to petitioner's symptoms. While Dr. Chaudhry opines that low levels of phosphate and potassium "contributed" to petitioner's condition, he does not opine that they likely caused her GBS.

During her hospitalization, petitioner underwent diagnostic studies of her CSF to investigate the cause of her GBS. The studies were all negative for any other cause. The only causal association documented in the petitioner's medical record was her Prevnar 13 vaccine.

In conclusion, the undersigned finds that petitioner has proven by preponderant evidence a logical sequence of cause and effect establishing that the Prevnar 13 vaccination caused her GBS and has satisfied the second Althen prong.

3. Althen Prong Three

Althen Prong Three requires petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That phrase has been defined as a "medically acceptable temporal relationship." Id. The petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disease's etiology, it is medically acceptable to infer causation-in-fact." de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen Prong One). Id.; Koehn v. Sec'y of Health & Hum. Servs., 773 F.3d 1239, 1243 (Fed. Cir. 2014); Shapiro v. Sec'y of Health & Hum. Servs., 101 Fed. Cl. 532, 542 (2011), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 503 F. App'x 952 (Fed. Cir. 2013).

The respondent's experts do not disagree that there is a temporal association between petitioner's vaccination and onset of her GBS. Dr. Chaudhry does not offer an opinion on the issue of temporal association. Dr. Whitton states that proof of a temporal association "is not proof of causation." Resp. Ex. D at 16.

On July 18, petitioner was evaluated by numerous medical professionals and reported an onset of weakness after her Prevnar 13 vaccine. Petitioner "report[ed] a progressive, generalized weakness over 1 week after receiving pneumonia vaccine" to Nurse Maynard. Pet. Ex. 5 at 80. During an occupational therapy evaluation, "[petitioner] state[ed] her weakness started after receiving a [pneumonia] shot several days ago." Id. at 96. Additionally, petitioner reported to Mr. Vo that she did not feel well "since she received her pneumo[nia] vaccine a week ago" and that she developed acute weakness the night of July 17. Id. at 108. This history provided by petitioner when she presented to the hospital on July 18 places onset of extremity weakness approximately one week post-vaccination.

On July 21, Mr. Foster notes that petitioner reported her "legs started to feel weak and heavy and walking became difficult" this week. Pet. Ex. 5 at 143. Petitioner reported that "during this admission[,] her symptoms have steadily worsened to the point that she does not feel she can stand or walk at all." Id. Physical exam at that time revealed that petitioner's sensory perception was decreased in a stocking pattern bilaterally, and her reflexes were diminished to trace to 1+ and symmetrical. EMG performed on July 24 confirmed the diagnosis of GBS. Additionally, CSF revealed cytoalbuminologic dissociation, with an elevated protein of 112 mg/dL (normal 15-40).

Based on this timeline, the onset of petitioner's weakness was approximately one week after vaccination, or around July 14, and her weakness and abnormal physician examination on July 21 were characteristic of GBS. Thus, the range for onset is from July 14 to July 21, one to two weeks following vaccination. Although petitioner's initial presentation on July 18 at admission was not clearly GBS, by July 21, CVA and TIA had been ruled out, and petitioner's assessment was bilateral lower extremity weakness. And by July 24, petitioner's GBS diagnosis was confirmed.

This time frame of one to two weeks post-vaccination is appropriate given the theory of molecular mimicry, as demonstrated in the Haber et al. article, which found 11 cases of GBS following Prevnar 13 vaccine, with a median onset interval of 9 days.

This temporal association is also consistent with the onset period of 3 to 42 days as set forth in the Vaccine Injury Table for GBS following influenza vaccination. 42 C.F.R. § 100.3(a)(XIV)(D).

Further, this time frame has been acknowledged as appropriate in other Vaccine Program cases in which molecular mimicry has been proffered as the causal mechanism. See, e.g., Koller, 2021 WL 5027947, at *23 (finding a GBS onset of 12 days after Prevnar 13 vaccination to be "within the medically accepted timeframe consistent with petitioner's theory of molecular mimicry [and] that has been accepted in other Vaccine Program cases."); Barone, 2014 WL 6834557, at *13 ("[S]pecial masters have never gone beyond a two-month (meaning eight week) interval in holding that a vaccination caused a demyelinating illness.").

Therefore, undersigned finds that petitioner has met her burden of proof as to Althen Prong Three.

V. ALTERNATIVE CAUSATION

Because the undersigned concludes that petitioner has established a prima facie case, petitioner is entitled to compensation unless respondent can put forth preponderant evidence "that [petitioner's] injury was in fact caused by factors unrelated to the vaccine." Whitecotton v. Sec'y of Health & Hum. Servs., 17 F.3d 374, 376 (Fed. Cir. 1994), rev'd on other grounds sub nom., Shalala v. Whitecotton, 514 U.S. 268 (1995); see also Walther, 485 F.3d at 1151. As discussed above in the analysis related to Althen Prong Two, the undersigned found respondent failed to establish evidence to show that petitioner's GBS was caused by a source other than vaccination. Thus, respondent did not prove by a preponderance of evidence that petitioner's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B).

VI. CONCLUSION

Based on the record as a whole, and for the reasons discussed above, the undersigned finds there is preponderant evidence to satisfy all three Althen prongs and to establish that petitioner's Prevnar 13 vaccination caused her GBS. Thus, the undersigned finds that petitioner is entitled to compensation. A separate damages order will issue.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master