In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: January 17, 2024

BETTE M. ANDERSON, as personal representative of the estate DONALD D. MEYER, deceased,	*	PUBLISHED
Petitioner,	*	No. 18-484V
v.	*	Special Master Nora Beth Dorsey
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Ruling on Entitlement; Pneumococcal Conjugate ("Prevnar 13") Vaccine; Guillain-Barré Syndrome ("GBS"); Death.
Respondent.	*	

Kathleen Margaret Loucks, Lommen Abdo Law Firm, Minneapolis, MN, for Petitioner.
Emilie Williams, U.S. Department of Justice, Washington, DC, for Respondent.

RULING ON ENTITLEMENT[1]

On April 3, 2018, Bette M. Anderson[2] ("Petitioner"), as personal representative of the estate of Donald D. Meyer ("Mr. Meyer"), deceased, filed a petition for compensation under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42 U.S.C. §

[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 and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the 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] Petitioner's last name changed from Meyer to Anderson during litigation. Order dated May 10, 2023 (ECF No. 133).

300aa-10 et seq. (2018),[3] alleging that as a result of a pneumococcal conjugate ("Prevnar 13") vaccine administered on July 26, 2017, Mr. Meyer developed Guillain-Barré Syndrome ("GBS") and subsequently died on August 26, 2017. Petition at ¶¶ 1, 6 (ECF No. 1). Respondent argued against compensation, stating "[P]etitioner is not entitled to compensation under the Act and that the petition should be dismissed." Respondent's Amended Report ("Resp. Am. Rept.") at 2 (ECF No. 35).

After carefully analyzing and weighing the evidence presented in accordance with the applicable legal standards, the undersigned finds Petitioner has provided preponderant evidence that the Prevnar 13 vaccine Mr. Meyer received caused his GBS and death, satisfying Petitioner's 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 not in dispute. Joint Submission of Stipulated Facts ("Joint Submission"), filed Mar. 21, 2023, at 2 (ECF No. 117). Further, the parties do not dispute that GBS was the immediate cause of Mr. Meyer's death, as evidenced by his death certificate. Id.

The parties dispute (1) whether Petitioner presented preponderant evidence of a reliable medical theory that the Prevnar 13 vaccine can cause GBS (Althen prong one), (2) whether Petitioner presented preponderant evidence of a logical sequence of cause and effect that the Prevnar 13 vaccine did cause Mr. Meyer's GBS and death (Althen prong two), and (3) whether Petitioner presented preponderant evidence that the onset of symptoms fits the medically-accepted time frame and is therefore medically-appropriate (Althen prong three). Joint Submission at 2.

II. BACKGROUND

A. Procedural History

Petitioner filed her petition on April 3, 2018, along with an affidavit and medical records. Petition; Petitioner's Exhibits ("Pet. Exs.") 1-6. Petitioner filed additional medical records in May and September 2018. Pet. Exs. 7-13. Respondent filed a Rule 4(c) Report on December 14, 2018; however, Respondent was unable to provide an evaluation from the Division of Injury Compensation Programs ("DICP") at that time. Resp. Rept. at 2 (ECF No. 20). Petitioner filed additional medical records in February 2019. Pet. Ex. 14.

Petitioner filed expert reports from Dr. Praful Kelkar and Dr. M. Eric Gershwin on April 12, 2019. Pet. Exs. 15, 23. On September 17, 2019, Respondent filed an amended Rule 4(c) Report, arguing against compensation, along with expert reports from Dr. J. Lindsay Whitton

[3] 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 (2018) ("Vaccine Act" or "the Act"). All citations in this Ruling to individual sections of the Vaccine Act are to 42 U.S.C.A. § 300aa.

and Dr. Peter D. Donofrio. Resp. Am. Rept.; Resp. Exs. A, C. Thereafter, this case was reassigned to the undersigned. Notice of Reassignment dated Oct. 10, 2019 (ECF No. 39).

The undersigned held a Rule 5 conference on October 31, 2019. Rule 5 Order dated Nov. 5, 2019 (ECF No. 40). The undersigned agreed that Mr. Meyer suffered from GBS and that his onset was August 5, 2017, consistent with the medical records. Id. at 1. The undersigned preliminarily found Petitioner would be able to provide preponderant evidence of all three Althen prongs. Id. at 1-2. Petitioner indicated that she would like to file responsive expert reports and provide a demand to Respondent. Id. at 2.

Petitioner filed supplemental expert reports from Dr. Gershwin and Dr. Kelkar on December 24, 2019. Pet. Exs. 129, 136. Petitioner transmitted a demand to Respondent in December 2019, but by March 2020, Respondent decided to proceed with litigation. Pet. Status Rept., filed Jan. 6, 2020 (ECF No. 43); Resp. Status Rept., filed Mar. 27, 2020 (ECF No. 49). Respondent filed a supplemental expert report from Dr. Whitton on May 26, 2020 and a supplemental expert report from Dr. Donofrio on July 27, 2020. Resp. Exs. E-F.

On September 29, 2020, the undersigned held a status conference to discuss next steps. Order dated Sept. 29, 2020 (ECF No. 58). Thereafter, the parties began informal resolution discussions again until February 2021, when Respondent indicated he would like to proceed with litigation. Joint Status Rept., filed Oct. 29, 2020 (ECF No. 59); Resp. Status Rept., filed Feb. 4, 2021 (ECF No. 65). A status conference was held on February 11, 2021, after which the parties agreed to set this case for an entitlement hearing in May 2022. Order dated Feb. 11, 2021 (ECF No. 66); Joint Status Rept., filed Mar. 16, 2021 (ECF No. 67). Thereafter, Petitioner filed a supplemental expert report from Dr. Gershwin on April 12, 2021. Pet. Ex. 143.

On February 7, 2022, "Petitioner request[ed] a status conference with the Court to discuss the impact of the Pierson [] decision and whether Petitioner [was] entitled to either substitute experts or file a supplemental expert report from Dr. Gershwin on the Glycerophospholipid theory and the BLAST research conducted by Dr. [Lawrence] Steinman." Joint Status Rept., filed Feb. 7, 2022 (ECF No. 85); see Pierson v. Sec'y of Health & Hum. Servs., No. 17-1136V, 2022 WL 322836 (Fed. Cl. Spec. Mstr. Jan. 19, 2022). A status conference was held with the parties on February 17, 2022. Order dated Feb. 17, 2022 (ECF No. 86). The undersigned granted Petitioner's request to retain Dr. Steinman and file an expert report from him on the basis that Petitioner should be afforded a full and fair opportunity to present her case. Id. at 1. The May 2022 hearing was continued and set to be rescheduled once the parties had the opportunity to file expert reports. Id.

Petitioner filed an expert report from Dr. Steinman on April 28, 2022. Pet. Ex. 156. Respondent filed a responsive expert report from Dr. Whitton on August 5, 2022. Resp. Ex. G. On October 24, 2022, Petitioner filed a responsive expert report from Dr. Steinman. Pet. Ex. 189. Thereafter, the entitlement hearing was rescheduled for April 2023. Prehearing Order dated Dec. 7, 2022 (ECF No. 107).

An entitlement hearing was held from April 25 to April 27, 2023. Order dated Apr. 27, 2023 (ECF No. 129). Petitioner, Dr. Steinman, Dr. Kelkar, Dr. Donofrio, and Dr. Whitton

testified at the hearing. Transcript ("Tr.") 6, 31, 189. On May 10, 2023, the parties confirmed that they did not wish to file post-hearing briefs. Joint Status Rept., filed May 10, 2023 (ECF No. 131).

This matter is now ripe for adjudication.

B. Medical Terminology

GBS is an illness that causes "acute flaccid paralysis, characterized by symmetrical weakness of the limbs, and hyporeflexia or areflexia, which reaches a maximum severity within [four] weeks []. Sensory symptoms, such as [] numbness, usually start distally and have a symmetrical pattern." Resp. Ex. A, Tab 7 at 1.[4] The most common subtype of GBS is acute inflammatory demyelinating polyneuropathy ("AIDP"). Id. Other subtypes of GBS relevant to this case include acute motor axonal neuropathy ("AMAN") and acute motor and sensory neuropathy ("AMSAN"). 42 C.F.R. § 100.3(c)(15)(ii). AMAN is "predominated by axonal damage that primarily affects motor nerves," while AMSAN "also affects the sensory nerves and roots." Id. Miller Fisher Syndrome ("MFS") is another "subtype of GBS characterized by ataxia,[5] areflexia, and ophthalmoplegia."[6] 42 C.F.R. § 100.3(c)(15)(iii).

GBS 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. 29 at 1.[7] Most patients have symptoms that progress for one to three weeks after initial symptoms begin. Id. at 3. The majority are "unable to walk independently when maximum weakness is reached." Id. Respiratory difficulty and other complications may occur. Id. Weakness is the prominent manifestation. Id. Other symptoms may include sensory disturbances, cranial nerve

[4] Bianca van den Berg, Guillain-Barré Syndrome: Pathogenesis, Diagnosis, Treatment and Prognosis, 10 Nature Revs. Neurology 469 (2014).

[5] Ataxia is "failure of muscular coordination" or "irregularity of muscular action." Ataxia, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=4630 (last visited Dec. 4, 2023).

[6] Ophthalmoplegia is the "paralysis of the eye muscles." Ophthalmoplegia, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=35269 (last visited Dec. 4, 2023).

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

palsies, and dysautonomia.[8] Id. at 9. "[U]p to 20% of patients remain severely disabled and approximately 5% die" after GBS, even after treatment. Id. at 1.

GBS is thought to be an autoimmune disease. Pet. Ex. 193 at 1.[9] "[T]he immune system starts to destroy the myelin sheath that surrounds the axons of [] peripheral nerves." Id. The axons of nerves may also be affected. Id. Once the myelin sheath or axons of the peripheral nerves are injured, the nerves are unable to send signals in the usual fashion. Id. "[M]uscle weakness and tingling sensations" occur in the "hands and feet and progress upwards." Id. GBS may be triggered by infections or immunizations. Id.; see also Resp. Ex. G, Tab 6 at 1 ("[A]proximately two-thirds of all cases are preceded by a gastrointestinal or respiratory infection within the prior [three] months.").[10]

In summary, the underlying etiology of GBS "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." Pet. Ex. 74 at 2.[11]

C. Stipulated Facts

The parties agreed to the following stipulated facts as set forth in their Joint Prehearing Submission. See Joint Submission at 1-2.

Mr. Meyer's health history was significant for cardiomegaly, carotid artery blockage, tonsillar cancer, depression, lumbar disc disease, and hypothyroidism. Joint Submission at 1. He was seen by his primary care provider on July 26, 2017, and at that visit, he had no concerns other than elbow pain. Id. Physical examination was normal. Id. Mr. Meyer received a Prevnar 13 vaccination the same date, July 26, 2017. Id.

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[8] Dysautonomia is a "malfunction of the autonomic nervous system." Dysautonomia, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=15146 (last visited Dec. 4, 2023). The autonomic nervous system is "the portion of the nervous system concerned with regulation of the activity of cardiac muscle, smooth muscle, and glandular epithelium; usually restricted to the two visceral efferent peripheral components, the sympathetic nervous system, and the parasympathetic nervous system." Autonomic Nervous System, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=111779 (last visited Dec. 4, 2023).

[9] Nat'l Inst. Neurological Disorders & Stroke, Guillain-Barré Syndrome Fact Sheet, https://www.ninds.nih.gov/guillain-barre-syndrome-fact-sheet (last modified Mar. 16, 2020).

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

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

Symptom onset likely began on August 5, 2017. Joint Submission at 1. Subsequently, Mr. Meyer was diagnosed with an axonal form of GBS with oculomotor manifestations as the initial presentation. Id.

Testing for methicillin-resistant *Staphylococcus aureus* ("MRSA"), Enterovirus, *Campylobacter*, *Escherichia* ("*E.*") *coli*, *Shigella*, and *Salmonella* infections was negative. Joint Submission at 1. A spinal fluid culture was negative, but neuron specific enolase[12] and spinal fluid protein were both elevated. Id. Specifically, cerebrospinal fluid ("CSF") results were protein 210, cell count 0, and glucose 69. Id. Bacterial cultures, Lyme antibodies, and Herpes Simplex virus testing were negative. Id. A paraneoplastic was performed and a "P/Q-Type Calcium Channel" antibody was detected at 0.02 (reference panel range nmol/L ≤ 0.02). Id. at 1-2. The paraneoplastic panel was interpreted as negative or within normal limits. Id. at 2.

Mr. Meyer died on August 26, 2017. Joint Submission at 2. Mr. Meyer's death certificate lists "Guillain-Barr Syndrome" as the immediate cause of death. Id.

D. Summary of Additional Medical Records[13]

In addition to the facts stipulated to by the parties, the following summary of facts provides additional relevant information.

Prior to the vaccination at issue, Mr. Meyer's medical history was significant for cardiomegaly, carotid artery blockage, tonsillar cancer, depression, lumbar disc disease, and hypothyroidism. Pet. Ex. 3 at 2; Pet. Ex. 7 at 8-9; Joint Submission at 1.

On July 26, 2017, Mr. Meyer saw his primary care provider for an annual physical examination. Pet. Ex. 3 at 1. Mr. Meyer noted no concerns other than elbow pain that he developed after lifting a heavy object. Id. Physical examination was normal. Id. at 3. Mr. Meyer, at the age of 62, was given a Prevnar 13 vaccination. Id. at 1, 4-6; Pet. Ex. 1 at 1-2.

On August 2, 2017, Mr. Meyer presented to the emergency room ("ER") for sudden onset of pain in his right upper abdominal quadrant that radiated to both flanks and began that morning. Pet. Ex. 7 at 11, 16. He reported no history of a fever, nausea or vomiting, or urinary symptoms. Id. at 16. An examination was essentially normal, and a computed tomography

[12] Neuron-specific enolase is "an isozyme of enolase that is found in normal neurons and in all the cells of the diffuse neuroendocrine system; it serves as a marker for neuroendocrine differentiation in tumors." Neuron-Specific Enolase, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=73264 (last visited Dec. 4, 2023).

[13] This summary of medical records is taken from Petitioner's Brief and Respondent's Brief, as the undersigned finds the parties provided an accurate representation of the records. See Pet. Pre-Hearing Brief, filed Feb. 28, 2023, at 1-7 (ECF No. 109); Resp. Prehearing Brief, filed Mar. 21, 2023, at 1-6 (ECF No. 116).

("CT") scan of his abdomen and pelvis was unrevealing. Id. at 16, 20-21. He improved with pain medication and was discharged that night. Id. at 16.

Mr. Meyer's pain continued and he returned to the ER during the early morning hours of August 3, 2017. Pet. Ex. 7 at 44. In addition to his prior symptoms, he now complained of generalized joint pain that was not controlled by pain medication. Id. at 45. Mr. Meyer denied any known sick contacts, but "[h]e did state he got a pneumonia shot a week ago, but thinks that is unrelated." Id. at 47. Physical examination revealed mild left flank tenderness, but was otherwise normal. Id. at 47-48. ER personnel were "not really sure the cause of his pain" and thought "[i]t could represent a viral syndrome, especially with the joint pain being more of his complaint now." Id. at 48. Mr. Meyer was again treated with pain medication and discharged around 4:40 a.m. on August 3, 2017. Id.

Later that day, on August 3, 2017, Mr. Meyer saw his primary care physician for persisting symptoms. Pet. Ex. 3 at 40. He further explained that he sought treatment in the ER that morning because he developed severe and progressive pain in his arms and legs. Id. Physical examination revealed tenderness throughout his muscles, but he had normal reflexes and strength. Id. The primary care physician was unsure of the reason for Mr. Meyer's pain. Id. at 43. He prescribed additional pain medication. Id. His primary care physician noted Mr. Meyer "did have his pneumonia shot last week, however [Mr. Meyer's] symptoms [were] not consistent with [GBS]." Id. His primary care physician considered "[a]n acute flareup of polymyalgia rheumatica" or "a viral illness that is just causing terrible muscle pains." Id.

That afternoon, on August 3, 2017, Mr. Meyer called his primary care physician and explained that he was seeking additional treatment at the hospital because his symptoms were increasing. Pet. Ex. 3 at 44. Mr. Meyer presented to North Memorial Health ER and was admitted for observation. Pet. Ex. 8 at 199, 205. Following a history and physical examination, the differential diagnoses included "viral syndrome vs possible rheumatological illness," and further testing was ordered. Id. at 214. Mr. Meyer's C-reactive protein ("CRP") and white blood cell ("WBC") count were both mildly elevated. Id. at 205.

On August 4, 2017, a registered nurse noted that Mr. Meyer reported feeling nauseated, so he was given Zofran, an anti-nausea medication. Pet. Ex. 8 at 218. He was also given Miralax and Senna because he had no bowel movements for two days. Id. Mr. Meyer then "had a medium amount of emesis [vomiting] containing food" right after taking medication. Id. Mr. Meyer was monitored for further vomiting and nausea. Id. at 219.

Mr. Meyer was seen by gastroenterologist, Dr. Thomas B. Koenig, on August 5, 2017, for an "evaluation of abdominal pain, nausea[,] and vomiting." Pet. Ex. 8 at 221-22. Dr. Koenig observed Mr. Meyer's changing labs, including an elevated WBC and lipase. Id. at 222, 225-26. Mr. Meyer "state[d] the pain [was] improved now but he [was] nauseated and unable to eat without vomiting." Id. at 222. Mr. Meyer had not had a bowel movement in four days. Id. Mr. Meyer also saw internist, Dr. Qamar Iqbal, on August 5, 2017 and noted his "concern[] about throwing up, he had nausea early on." Id. at 228. His abdominal pain had reportedly improved and he denied joint pain and swelling. Id. Dr. Iqbal noted the etiology for Mr. Meyer's generalized pain was "not fully known but likely vi[r]al." Id. at 230. In an addendum to his

note, Dr. Iqbal wrote Mr. Meyer was "[f]eeling more weak and tired now" and was "now having mild hand [t]ingling." Id. Dr. Iqbal noted Mr. Meyer had intact sensation and motor strength. Id. He ordered neurology to see Mr. Meyer the following morning. Id.

On August 6, 2017, Mr. Meyer was evaluated by neurologist, Dr. Ivan Brodsky. Pet. Ex. 8 at 232. During this examination, Mr. Meyer reported new onset of double vision, lack of coordination, tingling in his hands and feet, and difficulty handling objects. Id. Dr. Brodsky noted that Mr. Meyer had "definite ataxia" upon testing, but he had intact sensation and normal reflexes. Id. at 237. He also noted Mr. Meyer's "abdominal pain seem[ed] to have resolved as ha[d] the joint pain," but Mr. Meyer now had new symptoms of double vision and definite ataxia. Id. at 238. Dr. Brodsky was "somewhat puzzled with this presentation." Id. He noted "[t]here [were] many possibilities," including myasthenia gravis and the MFS variant of GBS, "but none of them fit well" because neither condition was associated with pain. Id. Dr. Brodsky ordered further testing, however, to further investigate these diagnoses. Id. Dr. Iqbal was also unsure of the "exact etiology" of Mr. Meyer's new onset symptoms, and agreed with Dr. Brodsky. Id. at 245.

Later that same day, August 6, 2017, Mr. Meyer choked on food (meat) while eating and became unresponsive, so he was intubated and transferred to the intensive care unit ("ICU"). Pet. Ex. 8 at 242-43, 246-47. During the intubation procedure, it was noted that he might have a pharyngeal mass, but a later examination ruled out that consideration. Id. at 246, 423-26, 467. After intubation, Mr. Meyer was able to nod in response to questions and appeared to understand his surroundings, but he remained ventilator dependent. Id. at 263.

On August 7, 2017, Dr. Brodsky noted that Mr. Meyer was not very responsive, his eye movement was limited, and his pupils were unequal and unresponsive; however, he was also receiving significant pain medication that could influence testing. Pet. Ex. 8 at 265, 268. Dr. Brodsky noted a subjective assessment of "[p]rogressive brain stem deterioration." Id. at 265. Updated labs showed that Mr. Meyer's WBC count was elevated at 13.5 (reference range 4.3-10.8). Id. at 266. He found Mr. Meyer "remain[ed] a puzzle" with "no obvious etiology to date." Id. at 268. Dr. Brodsky "[r]eviewed literature and discussed with [c]olleagues" and noted Mr. Meyer's "[p]resentation could fit with [MFS], a variant of GB[S]." Id. Mr. Meyer was started on intravenous immunoglobulin ("IVIG"). Id. at 268, 275.

Dr. Brodsky ordered a lumbar puncture and electromyography ("EMG") on August 8, 2017. Pet. Ex. 8 at 291. CSF on lumbar puncture revealed elevated protein of 210 (reference range 15-45), cell count of 0, and glucose of 69 (reference range 40-70), and Dr. Brodsky found these results showed albuminocytological disassociation and fit with the diagnosis of an axonal variant of GBS. Id. at 311, 317. He also found Mr. Meyer's EMG "consistent with axonal variant of GB[S]" that "[began] with a [MFS] [p]resentation." Id. at 317; see also Pet. Ex. 9 at 1 ("EMG is consistent with an axonal polyneuropathy. . . . [T]his study could fit with [] [GBS]."). Dr. Brodsky recorded that Mr. Meyer "[d]id have [p]neumococcal [v]accine [one] w[ee]k prior to onset. ? If playing a role." Pet. Ex. 8 at 317. Dr. Brodsky's subjective assessment was an axonal variant of GBS. Id. at 315. He noted Mr. Meyer was "[s]till flaccid, areflexic quadriplegia with limited eye [movements]." Id. By August 10, 2017, Dr. Brodsky noted "[n]ot much change neurologically;" Mr. Meyer was on his fourth round of IVIG and there was "not

much if any response." Id. at 327. Once IVIG was completed, he ordered treatment with plasmapheresis. Id.

Testing for *Helicobacter pylori*, MRSA, Enterovirus, *Campylobacter*, *E. coli*, and Salmonella infections was negative. Pet. Ex. 8 at 323, 511-12, 518-19. A spinal fluid culture was negative, but neuron specific enolase and spinal fluid protein were both elevated. Id. at 513, 592, 597. Bacterial cultures, Lyme antibodies, and Herpes Simplex virus testing were negative. Id. at 516, 592-94. A paraneoplastic panel was performed, and a P/Q Type Calcium Channel antibody was detected at 0.02 (reference range ≤ 0.02). Id. at 617-20. The paraneoplastic panel report stated that "[n]o informative autoantibodies were detected." Id. at 617. Testing for ganglioside antibodies, including GQ1b, was also normal. Id. at 598-600.

Treating neurologist Dr. Brodsky wrote a letter dated August 11, 2017. Pet. Ex. 4 at 1. In this letter, he stated,

> Mr. [] Meyer is a 62-year-old male who is under my care. He ha[d] a pneumococcal vaccination and within a week developed [GBS]. I have done extensive testing and there is not a more likely alternative diagnosis for the weakness. He is currently quadriplegic, apneic, ventilator dependent with complete ophthalmoplegia. Within reasonable medical certainty, his [GBS] is causally related to the preceding pneumococcal vaccination.

Id.

On August 12, 2017, neurologist Dr. Kelkar saw Mr. Meyer and reported that he "ha[d] movements in eyebrows with which he communicates," but had "[n]o other movements." Pet. Ex. 8 at 383. He "respond[ed] to questions appropriately with [y]es no with eyebrows" and "[was] aware of [diagnosis] of GBS and paralysis." Id. Dr. Kelkar noted Mr. Meyer's "[history] of pneumococcal vaccine prior to onset of GBS." Id. Dr. Kelkar noted Mr. Meyer had "[n]o response to IVIG" and was now on plasmapheresis (PLEX) treatment, which started the day prior. Id. at 383-84. His assessment was "severe axonal GBS with prior pneumococcal vaccine" and negative *Campylobacter*. Id. at 384.

Mr. Meyer received his third round of plasmapheresis on August 14, 2017, and it was noted that he "[did] not seem to be making progress." Pet. Ex. 8 at 437. A progress note dated August 17 noted "there ha[d] not been improvement with PLEX." Id. at 447.

Dr. Brodsky evaluated Mr. Meyer again on August 18, 2017. Pet. Ex. 8 at 459. Dr. Brodsky noted Mr. Meyer "[w]ill twitch eyebrows to command but less vigorously than previously," Mr. Meyer's "[p]upils [were] still fixed and unreactive with complete [ophthalmoplegia]," and Mr. Meyer could now move his jaw to command. Id. at 460. Ganglioside GQ1b testing was negative. Id. at 461. Mr. Meyer remained ventilator dependent. Id. Diagnosis remained axonal variant of GBS. Id. at 460.

Later that day, Mr. Meyer was discharged into inpatient rehabilitation. Pet. Ex. 8 at 461-62, 471-74. Discharge diagnoses included "[a]xonal [GBS] with [MFS] presentation" and

"[a]cute respiratory failure secondary to severe axonal [GBS]." Id. at 472. Mr. Meyer's hospital course summarized that Mr. Meyer, following intubation on August 6, 2017, continued to have "worsening generalized weakness" and "significant abnormalities of cranial nerves." Id. at 473. A lumbar puncture and EMG confirmed diagnosis of "axonal [GBS] with a [MFS] presentation." Id. Despite IVIG and plasmapheresis treatments, it was noted that "there ha[d] not been a lot of improvement in his neurologic condition." Id. Mr. Meyer remained intubated throughout his hospital course. Id.

On August 23, 2017, Mr. Meyer became unresponsive while in inpatient rehabilitation. Pet. Ex. 8 at 1843. While he had been communicating by raising his eyebrows and blinking, he appeared to lose that ability a few hours earlier. Id. Mr. Meyer was transferred to North Memorial for further evaluation that same day. Id. Pneumonia was suspected and Mr. Meyer was treated with antibiotics. Id. at 1846-47.

A brain magnetic resonance imaging ("MRI") conducted August 23, 2017 revealed chronic sinusitis, but there were no findings that would explain Mr. Meyer's unresponsiveness. Pet. Ex. 8 at 1859. An electroencephalogram ("EEG") conducted on August 24, 2023 documented "[a]typical spread of theta rhythms into the central and frontal areas," but there was no evidence of epileptiform activity. Id. at 1909. Despite treatment with antibiotics, he "continue[d] to deteriorate." Id. at 1879.

Dr. Brodsky, on August 25, 2017, noted Mr. Meyer was "[n]ow [] unresponsive to pain, corneal[] with absent gag reflex." Pet. Ex. 8 at 1911. His "[p]upils [were] midposition and fixed." Id. He was flaccid and areflexic. Id. Dr. Brodsky had a long discussion with Mr. Meyer's family, noting "[Mr. Meyer] ha[d] a very severe form of GB[S] and [was] not responding to any therapies[] [a]nd [had] rapid deterioration despite our best efforts." Id. at 1913. After a long discussion, life support was discontinued and Mr. Meyer passed away on August 26, 2017, at 1:46 p.m. Id. at 1913, 1919-22. Cause of death was listed as GBS. Id. at 1921. The family declined an autopsy. Id. at 1923.

Mr. Meyer's death certificate lists GBS as the cause of death. Pet. Ex. 6 at 1.

E. Petitioner's Hearing Testimony and Affidavit[14]

Petitioner was married to Mr. Meyer at the time of his vaccination and death. Tr. 7; Pet. Ex. 205 at ¶ 1. Prior to his Prevnar 13 vaccination on July 26, 2017, Mr. Meyer was in good health, with a prior medical history of high blood pressure controlled by medication, throat cancer in 2010, blocked right artery in 2015, lumbar disc disease with a discectomy, and depression controlled by medication. Tr. 8-9; Pet. Ex. 205 at ¶ 2.

Mr. Meyer had not been sick prior to his Prevnar 13 vaccination. Tr. 9. He did not have diarrhea, vomiting, sore throat, fever, chills, runny nose, or fatigue. Id. From July 26, 2017 to August 1, 2017, Mr. Meyer had no symptoms or complaints of any illness. Tr. 10. He did not

[14] Petitioner also provided notes she took during Mr. Meyer's hospital course. See Pet. Ex. 206; see also Tr. 17, 26-27.

have a fever, chills, vomiting, abdominal pain, fatigue, diarrhea, sweating, or running nose. Tr. 10-11.

Petitioner recalled that on August 2, 2017, Mr. Meyer asked her to bring him to the ER because "[h]e was in severe pain[,] [] he was sweating profusely, and he complained of abdominal pain." Tr. 11; see also Pet. Ex. 205 at ¶ 4. At the ER, Mr. Meyer underwent a CT scan and bloodwork. Tr. 12. Petitioner was told everything looked normal, except Mr. Meyer's appendix was in the wrong quadrant. Id.; Pet. Ex. 205 at ¶ 4. Mr. Meyer received pain medication and was discharged. Tr. 12. He was not given a diagnosis at that time. Id. Nor was it indicated that Mr. Meyer had any type of infection at that time. Tr. 13.

Petitioner drove Mr. Meyer back to the ER around 2:00 a.m. on August 3, 2017. Tr. 13. Mr. Meyer had "severe abdominal pain" that was worsening and profuse sweating. Id. Mr. Meyer was given additional pain medication. Id.; Pet. Ex. 205 at ¶ 4. ER providers did not indicate Mr. Meyer had an infection at this visit. Tr. 13-14.

Later that morning, August 3, 2017, Mr. Meyer visited his primary care physician. Tr. 14; Pet. Ex. 205 at ¶ 5. Mr. Meyer told Petitioner that testing during this visit was normal. Tr. 14. Mr. Meyer received additional pain medication. Id.

In the evening of August 3, 2017, Petitioner took Mr. Meyer back to the ER. Tr. 14; Pet. Ex. 205 at ¶ 6. Mr. Meyer "was in severe pain and he was sweating profusely." Pet. Ex. 205 at ¶ 6; see also Tr. 15. Mr. Meyer was admitted for observation, given additional pain medication, and underwent additional blood tests that showed an elevated WBC and red blood cell count. Pet. Ex. 205 at ¶ 6; Tr. 15-16. No medical professional in the ER indicated to Petitioner that Mr. Meyer had an infection. Tr. 15-16.

Petitioner explained that on August 4, 2017, Mr. Meyer was hungry but could not eat or drink, he "just wanted to sleep," and he "was still sweating profusely." Pet. Ex. 205 at ¶ 7. Around 8:00 p.m. that night, Mr. Meyer drank water, but was nauseous and vomited. Id.

On August 5, 2017, Petitioner recalled Mr. Meyer required the assistance of two people to carry him to and from the bathroom. Tr. 17; Pet. Ex. 205 at ¶ 8. Mr. Meyer "wasn't talking much" and "his hands were numb at that time." Tr. 17. "Dr. Iqbal[] said that [Mr. Meyer] could have GBS." Id. This was the first time a treating physician mentioned a possible diagnosis of GBS to Petitioner. Id.

The next morning, on August 6, 2017, Mr. Meyer reported to Petitioner he had double vision and "felt like he had to urinate all the time." Tr. 18; see also Pet. Ex. 205 at ¶ 9. Following a CT scan, Mr. Meyer was eating and started to choke on his food and had to be intubated. Tr. 18; Pet. Ex. 205 at ¶ 9. Testing confirmed Mr. Meyer did not have any mass at that time. Tr. 19; Pet. Ex. 205 at ¶ 9.

Petitioner recalled that following the lumbar puncture and EMG, Mr. Meyer was diagnosed with GBS and treated with IVIG. Tr. 20; Pet. Ex. 205 at ¶ 10. Mr. Meyer received numerous tests and all were negative for any infection. Tr. 20. Dr. Brodsky indicated the IVIG

treatment was not working and he was ordering Mr. Meyer to begin plasmapheresis. Pet. Ex. 205 at ¶ 11.

By August 13, 2017, Mr. Meyer was unable to move his hands or legs and could only communicate with his eyebrows. Pet. Ex. 205 at ¶ 13. He contracted *Clostridium* ("*C.*") *difficile* in the hospital, resulting in diarrhea. Id. at ¶ 14; Tr. 22. Prior to this, Mr. Meyer had no diarrhea. Tr. 22-23.

Mr. Meyer was discharged and transferred to inpatient rehabilitation on August 18, 2017. Pet. Ex. 205 at ¶ 15. He remained on a ventilator. Id. at ¶ 13, ¶ 16. He returned to the ER on August 23 after Petitioner noticed he was unresponsive. Id. at ¶ 18; Tr. 23-24. The family chose to remove Mr. Meyer from life support on August 26, 2017 and he passed shortly thereafter. Tr. 24-25; Pet. Ex. 205 at ¶ 18. Petitioner testified that she was told Mr. Meyer's cause of death was GBS. Tr. 25.

Petitioner testified that Dr. Brodsky asked whether Mr. Meyer received any recent vaccinations, and he stated he would report Mr. Meyer's recent Prevnar 13 vaccination. Tr. 20-21; Pet. Ex. 205 at ¶ 10. Petitioner added that Dr. Kelkar or Dr. Brodsky told her about the Vaccine Program, and Dr. Brodsky wrote a letter Petitioner thought would be helpful for this claim in the Vaccine Program and for Mr. Meyer's work. Tr. 21, 28.

F. Dr. Brodsky's Letter

Treating neurologist Dr. Brodsky wrote a letter dated August 11, 2017. Pet. Ex. 4 at 1. In this letter, he stated,

> Mr. [] Meyer is a 62-year-old male who is under my care. He ha[d] a pneumococcal vaccination and within a week developed [GBS]. I have done extensive testing and there is not a more likely alternative diagnosis for the weakness. He is currently quadriplegic, apneic, ventilator dependent with complete ophthalmoplegia. Within reasonable medical certainty, his [GBS] is causally related to the preceding pneumococcal vaccination.

Id.

G. Expert Reports[15]

1. Petitioner's Expert, Dr. M. Eric Gershwin[16]

a. Background and Qualifications

Dr. Gershwin is board certified in internal medicine, rheumatology, and allergy and clinical immunology. Pet. Ex. 142 at 2. He completed his M.D. at Stanford University after which he completed an internship and residency in internal medicine at Tufts New England Medical Center and trained in immunology at the National Institutes of Health ("NIH") in Maryland. Id. at 1-2. He currently works in the Division of Rheumatology, Allergy, and Clinical Immunology at the University of California Davis School of Medicine as Director of the Allergy-Clinical Immunology Program and as a professor. Id. Dr. Gershwin has held various editor and reviewer positions on medical journals, and has authored or co-authored over 1,000 publications during his career. Id. at 3-138.

b. Opinion

Dr. Gershwin opined that, "more likely than not, the etiology of Mr. Meyer's [GBS] was molecular mimicry following [] vaccination." Pet. Ex. 23 at 11. He provided a detailed overview of GBS, including a summary of its history, incidence, subtypes, prevalence in different geographical areas, as well as detailed description of the different causal mechanisms that have been proposed and studied. See id. at 1-5, 8-9. He also discussed the diagnostic criteria, treatment options, and prognosis. See id. at 5-7.

i. Althen Prong One

Specific to Prevnar, Dr. Gershwin explained that it is a heptavalent vaccine that "contains the cell capsule sugars of [seven] different serotypes of [*Streptococcus pneumoniae* ("*S. pneumoniae*")]," [17] including serotypes 18C and 23F, "conjugated with Diphtheria proteins." Pet. Ex. 23 at 9-10. He further stated that it has "the potential via molecular mimicry[] to cross-react with a self-antigen." Id. at 10.

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[15] Although the undersigned has reviewed all the expert reports, for the sake of brevity this Ruling does not include every detail of the experts' opinions. Instead, the undersigned focuses on the experts' material opinions, as they relate to the relevant issue of causation.

[16] Dr. Gershwin provided three expert reports. Pet. Exs. 23, 129, 143. He did not testify at the hearing. The undersigned provides only a brief summary of Dr. Gershwin's opinions, since the parties focused most of their attention on the opinions of Dr. Steinman.

[17] A heptavalent vaccine is "effective against seven different entities." Heptavalent, Dorland's Online Med. Dictionary, https://www.dorlandsonline.com/dorland/definition?id=22301 (last visited Dec. 4, 2023). Prevnar 13 is not a heptavalent vaccine, as it protects against 13 serotypes of *S. pneumoniae*. See Pet. Ex. 166 at 1-2 (Prevnar 13 package insert).

In support of his opinion that molecular mimicry is an accepted mechanism to explain how vaccinations can cause GBS, Dr. Gershwin cited several papers, including one by Schafflick et al.,[18] which summarizes the current knowledge about antigenic targets in GBS and other inflammatory neuropathies. Pet. Ex. 155. The authors explained that in GBS, while the "primary target antigen . . . remains elusive," the hypothesis of molecular mimicry "has been substantiated in the axonal subtypes of [] GBS by several lines of evidence." Id. at 2. For example, "there is strong epidemiological association between GBS and preceding infections with *Campylobacter jejuni* (*C. jejuni*) and other infectious diseases." Id. "Cell wall components of these infectious agents resemble endogenous lipids and may trigger a cross-reactive autoimmune response." Id. Autoantibodies evidencing this type of autoimmune mechanism can be found in GBS cases.[19] See id. And "[a]utoantibodies binding components of the axonal membrane are found in a significant proportion of GBS cases." Id. Samukawa et al.,[20] another paper cited by Dr. Gershwin, discussed antibodies studies in axonal forms of neuropathy. See Pet. Ex. 154.

In further support of his opinions, Dr. Gershwin cited case reports of GBS after pneumococcal vaccinations. The first was a case report by Ravishankar.[21] Pet. Ex. 186. Quoting Ravishakar, Dr. Gershwin summarized the case report:

> [a] 66-year old female with a past medical history of hypertension, hyperlipidemia, gastroesophageal reflux disease presented to her local clinic in January 2015 for an annual exam. She was on the cusp of retirement and was told by her physician to receive all the immunizations. She received the first dose of [Prevnar 13] in January 2015 and then the second dose of [pneumococcal polysaccharide vaccine ("PPSV23")] in August 2015. . . . In September 2015, the patient began to feel weakness in the knees but dismissed it thinking it was mild arthritis. Few days later (approximately 41 days), she was unable to move her legs at all.

Pet. Ex. 143 at 1 (quoting Pet. Ex. 186 at 1).

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[18] David Schafflick et al., Novel Pathomechanisms in Inflammatory Neuropathies, 14 J Neuroinflammation 1 (2017).

[19] For a thorough discussion by Dr. Gershwin about the role of gangliosides and antiganglioside antibodies in GBS, see Pet. Ex. 23 at 3-4.

[20] Makoto Samukawa et al., Electrophysiological Assessment of Guillain-Barré Syndrome with Both Gal-C and Ganglioside Antibodies; Tendency for Demyelinating Type, 301 J. Neuroimmunology 61 (2016).

[21] Nidhi Ravishankar, Guillain-Barre Syndrome Following PCV Vaccine, 2 Clinics Surgery 1413 (2017). Petitioner also filed this article as Petitioner's Exhibit 128.

The second case report, authored by Thaler,[22] described the onset of MFS approximately one week after influenza and Pneumovax vaccinations. Pet. Ex. 144 at 2. The patient's clinical course was characterized by "rapidly progressive ascending limb weakness, accompanied by paresthesias, pain, and cranial nerve dysfunction." Id. at 1. She also had "ataxia, ophthalmoplegia, and decreased reflexes." Id.

In addition to the case reports above, Dr. Gershwin cited three reports of GBS following *S. pneumoniae* infection. The first, White et al.,[23] described a 68-year-old woman who developed complications of *S. pneumoniae* in her blood (bacteremia) and CSF, including "meningitis, pneumonia[,] and endocarditis." Pet. Ex. 132 at 1. She then developed "an atypical variant of [GBS]" diagnosed by EMG as "acute motor-sensory axonal neuropathy." Id. at 1-2. Anti-ganglioside antibodies were negative. Id. at 2.

El Khatib et al.[24] reported on a 13-year-old who complained of progressive lower extremity weakness and episodes of choking. Pet. Ex. 131 at 1. Subsequently he developed respiratory distress and septic shock, and blood cultures revealed *S. pneumoniae.* Id. at 1-2. The "history of inability to bear weight[] that was followed by choking with his clinical deterioration suggested [] the diagnosis of [GBS] in particular especially because of absent deep tendon reflexes." Id. at 2. GBS could not be confirmed by lumber puncture due to his unstable status. Id. The authors suggested the possibility of an antigen triggered immune response due to molecular mimicry. Id.

The third report, by Bianchi and Domenighetti,[25] described a 78-year-old man with a lung infection with *Pneumococcus pneumoniae* ("*P. pneumoniae*") who developed acute symmetrical paralysis. Pet. Ex. 133 at 1. Antiganglioside antibodies anti-GM1 and anti-GD1a were positive. Id. Nerve conduction studies revealed mixed acute motor axonal and demyelinating polyneuropathy. Id. at 2. The patient required a lengthy period of mechanical ventilation. Id. The authors stated that the case "may explain why different infections associated with GBS may contribute to the clinical and immunologic variety of th[e] disease." Id.

ii. Althen Prongs Two and Three

Dr. Gershwin noted that Mr. Meyer did not have "any antecedent evidence of an infection or another stimulus that could have caused GBS." Pet. Ex. 23 at 9. He further opined that Mr.

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[22] Adam Thaler, Miller Fisher Syndrome in a 66-Year-Old Female After Flu and Pneumovax Vaccinations, 4 J. Am. Med. Dirs. Ass'n 283 (2008).

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

[24] Hassan El Khatib et al., Case Report: Guillain-Barre Syndrome with Pneumococcus – A New Association in Pediatrics, 11 IDCases 36 (2018).

[25] Giorgia Bianchi & Guido Domenighetti, Pneumococcus Pneumoniae Infection and Guillain-Barré Syndrome: Fortuitous or Specific Association?, 32 Intensive Care Med. 338 (2006).

Meyer had an "intense local reaction, which would be consistent with a self-response against a cross-reactive antigen and therefore reflective of molecular mimicry." Id.

1. Petitioner's Expert, Dr. Lawrence Steinman[26]

a. Background and Qualifications

Dr. Steinman is board certified in neurology and has practiced neurology at Stanford University for over 40 years. Pet. Ex. 156 at 2; Pet. Ex. 157 at 1-2. He received his B.A. from Dartmouth College in 1968 and his M.D. from Harvard University in 1973. Pet. Ex. 157 at 1. Thereafter, he completed a surgery internship, pediatrics residency, and pediatric and adult neurology residency at Stanford University Hospital, as well as three fellowships, including one in clinical immunology. Id. Dr. Steinman is currently a Professor at Stanford University. Id. Dr. Steinman "is actively involved in patient care" and "ha[s] cared for hundreds of adults and children with various forms of inflammatory neuropathy, [GBS], transverse myelitis, acute disseminated encephalomyelitis[], neuromyelitis optica[,] and multiple sclerosis (MS)." Pet. Ex. 156 at 2. He has authored or co-authored over 600 publications. Pet. Ex. 157 at 5-49. Dr. Steinman has authored papers on molecular mimicry, as demonstrated by his CV. Id.; see also Pet. Ex. 156 at 2. One of Dr. Steinman's specialties is in the area of MS, and he has received a Charcot Prize for Lifetime Achievement due to his research in MS. Pet. Ex. 156 at 3. In 2015, he was elected to the National Academy of Sciences. Id. Dr. Steinman is also a member in the National Academy of Medicine. Id.

b. Opinion

i. Althen Prong One

Dr. Steinman opined that the Prevnar 13 vaccination can cause GBS. Pet. Ex. 156 at 5. The focus of Dr. Steinman's expert reports and opinions was on how the Prevnar 13 vaccine can trigger GBS via molecular mimicry.[27] Id. He reviewed the components of the vaccine and the main targets of the human immune response in GBS and proposed two mechanisms whereby molecular mimicry can trigger GBS following Prevnar 13 vaccination. The first involves homology between the components in the vaccine and phosphoglycerol components in the myelin and axons of peripheral nerves. Id. at 6-14. The second involves homology between CRM_{197} in the vaccine and Contactin-1, a protein found in humans. Id. at 14-24.

[26] Dr. Steinman testified at the hearing and provided two expert reports. Tr. 31; Pet. Ex. 156, 189.

[27] While Dr. Gershwin focused on the role of gangliosides and antiganglioside antibodies in GBS, Dr. Steinman examined the immune response to phosphoglycerol in the myelin lipids in the context of GBS, specifically phosphatidyl-ethanolamine, phophatidyl-choline, and phosphatidylserine, based on Ho et al. See Pet. Ex. 156 at 6 (citing Pet. Ex. 163 (Peggy P. Ho et al., Identification of Naturally Occurring Fatty Acids of the Myelin Sheath That Resolve Neuroinflammation, 4 Sci. Translational Med. 1 (2012))).

1. Phosphoglycerol[28] in Serotypes 18C and 23F

The first mechanism described by Dr. Steinman involves homology between phosphoglycerol in the Prevnar 13 vaccine, present in the antigens of *S. pneumoniae* serotypes 18C and 23F, and phospholipids, specifically glycerophosphate and glycerocholine in the human myelin sheath. Pet. Ex. 156 at 5-14; see also Pet. Ex. 166 at 24 (Prevnar 13 package insert); Tr. 53-84.

Based upon information obtained from the vaccine patent,[29] Dr. Steinman explained that the glycerol phosphate side chains in the vaccine are necessary for its immunogenicity.[30] Pet. Ex. 156 at 9; Tr. 58-59. Dr. Steinman cited an article by Chang et al.[31] to support his opinion that the phosphoglycerol component is preserved during the process of making the vaccine. Pet. Ex. 156 at 7-9 (citing Pet. Ex. 169 at 1). Chang et al. wrote "it is shown that glycerol-phosphate must be preserved for conserving adequate antigenicity of the 18C capsular polysaccharide." Pet. Ex. 169 at 1.

Dr. Steinman explained how the data from the vaccine patent and the studies relate to the pathogenesis of GBS. Pet. Ex. 156 at 6-9. He opined that phospholipids[32] are the targets of antibodies in GBS. Id. at 6. He asserted that antibodies to phosphoglycerol structures interact with myelin components triggering GBS. Id. 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 in GBS. Id.

In support of this aspect of his opinion, Dr. Steinman relied on several articles. The first was authored by Ho et al. and Dr. Steinman is also a named author. Pet. Ex. 163. The authors

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[28] 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.

[29] The patent is filed as Petitioner's Exhibit 171. 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.

[30] 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 Dec. 4, 2023).

[31] 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).

[32] 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 Dec. 4, 2023).

showed that in the demyelinating disease MS, autoantibodies primarily target a phosphoglycerol component of myelin. Pet. Ex. 156 at 6 (citing Pet. Ex. 163 at 1). The "findings indicate[d] that myelin phospholipids are targeted by autoimmune responses in MS." Pet. Ex. 163 at 9; see also Tr. 69-72. Moreover, "[l]ipids constitute 70% of the myelin sheath." Pet. Ex. 163 at 1; Tr. 72; see also Tr. 75 (noting Barbar et al. shows "binding of an antibody to a complex structure that contains a phosphate head group") (citing Pet. Ex. 196).[33]

In Gilburd et al.,[34] 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. 167 at 2. Six of the 16 patients with GBS had autoantibodies to various phospholipids. Id. at 2, 5; Tr. 76. However, the authors suggested this was "probably [] a result of [] myelin damage rather than [the] cause of demyelination." Pet. Ex. 167 at 2, 6.

Nakos et al.[35] studied anti-phospholipid antibodies in nine patients with GBS. Pet. Ex. 168 at 1; Tr. 77-79. All nine patients in the study had anti-phospholipid antibodies and no such antibodies were detected in the nine control subjects. Pet. Ex. 168 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 lupus like 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 (relevant here), 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,

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[33] Elisar Barbar et al., Binding of Phenylophosphocholine—Carrier Conjugates to the Combining Site of Antibodies Maintains a Conformation of the Hapten, 35 Biochemistry 2958 (1996).

[34] B. Gilburd et al., Autoantibodies to Phospholipids and Brain Extract in Patients with the Guillain-Barré Syndrome: Cross-Reactive or Pathogenic?, 16 Autoimmunity 57 (1993). The authors of Gilburd et al. discussed myelin damage, and so it does not appear that they discussed other forms of GBS. Tr. 131, 440. However, the study was done before there was a "wide awareness of axonal" GBS, and so it is not known whether the study was done on patients with "axonal or demyelinating" GBS. Tr. 440.

[35] G. Nakos et al., Anti-Phospholipid Antibodies in Serum from Patients with Guillain-Barré Syndrome, 31 Intensive Care Med. 1401 (2005). Nakos et al. studied the demyelinating subtype of GBS. Tr. 126, 439.

> [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. 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[36] 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.

Matà et al.[37] was referenced by Dr. Steinman to further support his opinions. Tr. 79-82 (citing Pet. Ex. 202). In that study, anti-cardiolipin antibodies were increased in some GBS patients as compared to controls. Pet. Ex. 202 at 4. The authors observed that the pathogenesis of GBS is complex, and while autoantibodies to gangliosides constitute the predominant autoantibody response in patients, "antibodies to other lipid antigens can be detected in GBS in a lower but statistically significant proportion of cases." Id. at 5. They found "increased autoantibody titers to cardiolipin [] in 20% of GBS patients." Id.

Lastly, Dr. Steinman cited a study by Bryson et al.[38] of antibodies directed to serotype 23F "from humans who were immunized with a pneumococcal vaccine (Pneumovax 23) that contains 23F."[39] Pet. Ex. 156 at 10-13 (citing Pet. Ex. 172 at 2); see also Tr. 65-67. He

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[36] Schwann cells are "any of the 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=64407 (last visited Dec. 4, 2023).

[37] Sabrina Matà et al., Anti-GM1, Anti-Central Myelin Proteins, and Anti-Cardiolipin Autoantibodies During Plasma-Exchange in Guillain-Barré Syndrome (GBS), 13 J. Clinical Apheresis 155 (1998).

[38] 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).

[39] Serotype 23F is included in both Prevnar 13 and Pneumovax 23. See Pet. Ex. 166 (Prevnar 13 package insert); Pet. Ex. 174 (Pneumovax 23 package insert).

explained Bryson et al. showed X-rays of "human antibody targeting the 23F component of *S. pneumonia*." Pet. Ex. 156 at 10 (citing Pet. Ex. 172 at 2). Dr. Steinman opined the X-rays demonstrate the "human antibody response to 23F after the human received a pneumococcal vaccine intended to elicit antibodies to 23F." Id. at 11. Dr. Steinman concluded that the "data from the Bryson [et al.] article demonstrate unequivocally that the immune response to the serotype 23F component of Pneumovax 23 targets the phosphoglycerol in serotype 23F." Id. at 13 (emphasis omitted).

Respondent's expert, Dr. Whitton discussed Bryson et al. and opined that the antibodies that targeted the 23F serotype recognized phosphoglycerol plus sugar rhamnose. See Tr. 344-46, 367-70. Dr. Steinman agreed. Tr. 440. Dr. Steinman explained that the phosphate head group of phosphoglycerol "has a tremendous attraction for antibodies, regardless of what it is attached to." Tr. 441. But the "antibody [] can and does recognize the phosphate head group of phosphoglycerol." Id. Dr. Steinman compared the phosphate head group to "one of the strongest hooks" on the landing pad of an aircraft carrier, which hooks the fighter aircraft as it lands on the carrier. Id.

In summary, Dr. Steinman's theory is based on molecular mimicry, and he opined that antibodies to the phosphoglycerol structures present in the components of Prevnar 13 (via serotypes 18C and 23F) target an immune response in phospholipids in the myelin components of peripheral nerves, triggering GBS. Pet. Ex. 156 at 6-15; Tr. 84-85.

2. CRM_{197} and Contactin-1

The second homology posited by Dr. Steinman is between the protein carrier in the vaccine, CRM_{197},[40] and Contactin-1,[41] a protein found in humans. Pet. Ex. 57 at 14; Tr. 86-88. 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. 57 at 5-6 (citing Pet. Ex. 166 at 24). "CRM_{197} is a nontoxic variant of diphtheria toxin," used as a protein carrier which makes the vaccine more immunogenic. Id. at 6, 14 (quoting Pet. Ex. 69 at 24). CRM_{197} differs from diphtheria toxin by only one amino acid, the enzymatically active domain of the toxin, and therefore, it is not toxic. Id. at 6, 21; see also Pet. Ex. 184 at 1.[42]

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[40] 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." Pet. Ex. 166 at 24 (Prevnar 13 package insert).

[41] 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. 176 at 2 (Yumako Miura et al., Contactin I IgG4 Associates to Chronic Inflammatory Demyelinating Polyneuropathy with Sensory Ataxia, 138 Brain 1484 (2015)).

[42] Michael Bröker et al., Biochemical and Biological Characteristics of Cross-Reacting Material 197 (CRM_{197}), a Non-Toxic Mutant of Diphtheria Toxin: Use as a Conjugation Protein in Vaccines and Other Potential Clinical Applications, 39 Biologicals 195 (2011).

Again, based on his own research, Dr. Steinman determined that molecular mimicry might occur between CRM_{197} and Contactin-1, a molecule that has been identified in patients with GBS. Pet. Ex. 156 at 14. Dr. Steinman relied on Miura et al., a study done on patients with CIDP. Id. (citing Pet. Ex. 176). Miura et al. focused their research on patients with CIDP, but used sera from patients with GBS, MS, and healthy patients as controls. Pet. Ex. 176 at 2. They found that five of the 200 patients with GBS had anti-Contactin-1 immunoglobulin G ("IgG") antibodies. Id. at 3, 6 tbl.2.

The Miura et al. authors explained the theory of pathogenesis relevant to Dr. Steinman's theory, as it relates to Contactin-1. They stated,

> [c]ell adhesion molecules play a crucial role in the formation of the nodes of Ranvier[43] 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 at nodes, paranodes[,] and juxtaparanodes.

Pet. Ex. 176 at 2.

Miura et al. identified Contactin-1 (CNTN1) as one of the targets of autoantibodies in some patients with GBS. Pet. Ex. 176 at 3. Dr. Steinman also cited several other articles noting that antibodies to paranodal proteins are found in GBS, including Lanz et al.,[44] which Dr. Steinman is a named author. Tr. 87-88 (citing Pet. Ex. 198 at 3 ("Antibodies to paranodal proteins are found in MS and in both [GBS] and chronic inflammatory polyneuropathy.")). The second article is by Fehmi et al.[45] and illustrated the structure of the peripheral nervous system nodes, paranodes, and Contactin (CNTN1 and CNTN2). Tr. 89-90 (citing Pet. Ex. 194 at 3 fig.1). And Devaux et al.[46] showed that nodal proteins are targets in GBS, and that Contactin is an "immune target of autoantibodies" in GBS. Pet. Ex. 197 at 1, 6; see also Tr. 91-93.

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[43] The nodes of Ranvier are "constrictions occurring on myelinated nerve fibers at regular intervals of about [one] 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 Dec. 4, 2023).

[44] Tobias V. Lanz et al., Roadmap for Understanding Mechanisms on How Epstein-Barr Virus Triggers Multiple Sclerosis and for Translating These Discoveries in Clinical Trials, 12 Clinical & Translational Immunology e1438 (2023).

[45] Janev Fehmi et al., Nodes, Paranodes and Neuropathies, 89 J. Neurology Neurosurgery & Psychiatry 61 (2018).

[46] Jérôme J. Devaux et al., Nodal Proteins Are Target Antigens in Guillain-Barré Syndrome, 17 J. Peripheral Nervous Sys. 62 (2012).

Based on this information about the potential importance of Contactin-1, Dr. Steinman conducted a BLAST[47] search to determine whether there was homology between CRM_{197} in the vaccine and Contactin-1.[48] Pet. Ex. 156 at 14. He found a sequence[49] ("WEQ sequence") that "might be capable of inducing a neuroinflammatory disease." Id. at 20. He found it is an epitope in diphtheria toxin, which provides the basis for CRM_{197}. Id. at 21-22.

During rebuttal, Dr. Steinman responded to criticism offered by Dr. Whitton about his BLAST search. Dr. Whitton criticized the expected value ("E-value")[50] of Dr. Steinman's BLAST search, which was 2.7. Tr. 374-80. To respond, Dr. Steinman referenced the landmark

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[47] A BLAST (Basic Local Alignment Search Tool) search "finds regions of similarity between biological sequences. The program compares nucleotide or protein sequences to sequence databases and calculates the statistical significance." BLAST, https://blast.ncbi.nlm.nih.gov/Blast.cgi (last visited Dec. 4, 2023).

[48] 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 conducting his BLAST searches and his research using the Immune Epitope Database ("IEDB"), see Pet. Ex. 156 at 14-24; Tr. 94-105. Based on his IEDB search, Dr. Steinman was referred to a paper by Raju et al. that reported a human immune response to the diphtheria toxin and identified the WEQAKALSVE sequence. Pet. Ex. 156 at 20-24 (citing Pet. Ex. 185 at 2 (Raghavanpillai Raju et al., Epitope for Human CD4+ Cells on Diphtheria Toxin: Structural Features of Sequence Segments Forming Epitopes Recognized by Most Subjects, 25 Euro. J. Immunology 3207 (1995))). Based on this research, Dr. Steinman opined that humans can "mount an immune response" to the "region of diphtheria toxin that . . . [has] five out of 10 amino acids that are identical to Contactin-1." Tr. 106.

[49] The sequence is "WEQAKALSVE," which "has five of ten identical amino acids." Pet. Ex. 156 at 20.

[50] Expected value, or E-value, "in statistics, [is] the value of an estimate that is the mean of its sampling distribution." Expected Value, Dorland Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=116686 (last visited Jan. 4, 2024). Relying on Silvanovich et al., Dr. Whitton opined that in a BLAST search, "the identified homology must have an E-value below a threshold of 3.9×10^{-7}. A homology with E-value larger than that threshold should be discarded." Resp. Ex. G at 30 (citing Resp. Ex. G, Tab 13 (Andre Silvanovich et al., The Value of Short Amino Acid Sequence Matches for Prediction of Protein Allergenicity, 90 Toxicological Scis. 252 (2006))). The other Silvanovich et al. criteria are a sequence of at least 80 amino acids long and at least 28 of the amino acids be aligned. Id. (citing Resp. Ex. G, Tab 13 at 7). Dr. Steinman opined that the Silvanovich et al. criteria are not applicable due to the findings of Fujinami and Oldstone, showing that short sequences (five or eight out of a sequence of 12) of amino acids induce disease. Tr. 431-34 (citing Pet. Ex. 192 (Robert S. Fujinami & Michael B. A. Oldstone, Amino Acid Homology Between the Encephalitogenic Site of Myelin Basic Protein and Virus: Mechanism for Autoimmunity, 230 Science 1043 (1985))); see also Pet. Ex. 189 at 18.

study from Fujinami and Oldstone[51] showing that a short sequence of similar amino acids could induce experimental allergic encephalomyelitis ("EAE") through the mechanism of molecular mimicry. Tr. 433 (citing Pet. Ex. 192). Dr. Steinman repeated the search done by Fujinami and Oldstone, and found that their E-value was 3.8, higher than his search value of 2.7. Id. (citing Pet. Ex. 207 at 2). Dr. Steinman reiterated that the Gautam et al. studies[52] showed that sequences of five or six out of 11 or 12 amino acid sequences could cause paralysis in animal studies. Tr. 434.

In addition to the WEQ sequence, after additional research, Dr. Steinman identified another sequence[53] that "has known cross-reactivity with epitopes described in humans" on the *Corynebacterium diphtheriae* microbe. Pet. Ex. 156 at 23.

Dr. Steinman opined the two sequences he found were significant due to five identical amino acids in a nervous system protein. Pet. Ex. 156 at 14. He cited a number of papers, including some that he authored or co-authored, to support his opinion that homology of just five amino acids can induce an immune response consistent with his theory here. Id. at 14-17. For example, in his 1993 paper,[54] Dr. Steinman wrote that "[a]n autoimmune response can begin even if the molecular mimicry is not quite exact." Pet. Ex. 165 at 4. He cited the Gautam et al. studies for the proposition that autoimmune encephalomyelitis could be induced with only five amino acids identical to myelin basic protein, out of short sequences of 10 amino acids. Pet. Ex. 156 at 14 (citing Pet. Exs. 177-79); Tr. 98.

In summary, Dr. Steinman averred that "th[is] theory provides actual detailed data for molecular mimics in the CRM in the Prevnar 13 vaccine" and how "these mimics could trigger inflammatory neuropathy culminating in GBS." Pet. Ex. 156 at 24 (emphasis omitted).

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[51] Fujinami and Oldstone, immunologists at Scripps, used computer analysis to identify "six consecutive amino acids" in myelin basic protein which was "sufficient to produce immunologic crossreactivity" via molecular mimicry which was shown to cause histology results similar to EAE. Pet. Ex. 192 at 1-3.

[52] Anand M. Gautam et al., A Polyalanine Peptide with Only Five Native Myelin Basic Protein Residues Induces Autoimmune Encephalomyelitis, 176 J. Experimental Med. 605 (1992); Anand M. Gautam et al., Minimum Structural Requirements for Peptide Presentation by Major Histocompatibility Complex Class II Molecules: Implications in Induction of Autoimmunity, 91 Immunology 767 (1994); Anand M. Gautam et al., A Viral Peptide with Limited Homology to a Self Peptide Can Induce Clinical Signs of Experimental Autoimmune Encephalomyelitis, 161 J. Immunology 60 (1998). Dr. Steinman is a named author in all of these papers.

[53] The second sequence is "EYMAQACAGNRVRR." Pet. Ex. 156 at 23.

[54] Lawrence Steinman, Autoimmune Disease, 269 Sci. Am. 106 (1993).

3. Medical Literature

In addition to setting forth his theories, Dr. Steinman offered medical literature in support of his opinions. He cited the National Institute of Neurological Disorders and Stroke ("NINDS") GBS Fact Sheet, which described GBS, stating that "[i]n rare cases vaccinations may increase the risk of GBS." Pet. Ex. 193 at 1. Dr. Steinman noted that the publication did not limit the causal vaccinations that may increase the risk of GBS to just influenza vaccines. Tr. 46-47 (citing Pet. Ex. 193).

Next, Dr. Steinman cited the same case reports referenced by Dr. Gershwin about GBS after pneumococcal infections. Tr. 47-48 (citing Pet. Exs. 132-33).

He also cited a 2016 Centers for Disease Control and Prevention ("CDC") publication authored by Haber et al.[55] Pet. Ex. 187. There were 11 reports of GBS after the Prevnar 13 vaccination, one in patients aged 19 to 64, and 10 in the age range of 65 and older. Id. at 4-5, 3 tbl.2a, 4 tbl.2b. Median onset was nine days post-vaccination and median patient age was 68 years. Id. at 4. Dr. Steinman stated that the paper "reinforces the likelihood that molecular mimicry following Prevnar 13 vaccination can cause GBS." Pet. Ex. 156 at 25 (citing Pet. Ex. 187).

Another paper referenced by Dr. Steinman studied adverse events following vaccination with Prevnar 13 as compared to PPSV23. See Tr. 51 (citing Resp. Ex. G, Tab 7).[56] Using the Vaccine Safety Datalink data, Tseng et al. reported that out of 313,136 doses of Prevnar 13, four cases of GBS were identified and out of 232,591 doses of PPSV23, eight cases of GBS were reported. Id. at 6 tbl.3. The authors found "no significantly elevated risk" of GBS between the two vaccines. Id. at 7.

Dr. Steinman briefly mentioned the Baxter et al. study, which reviewed GBS cases after vaccinations using Kaiser Permanente data from 1994 through October 2006 and noted that there was no increased risk of GBS observed.[57] Tr. 51-52 (citing Resp. Ex. G, Tab 6 at 1-2). The authors acknowledged the "limited power to fully assess the risk of GBS following vaccination due to the rarity of the outcome." Id. at 7.

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[55] 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).

[56] Hung Fu Tseng et al., Pneumococcal Conjugate Vaccine Safety in Elderly Adults, 5 Open Forum Infectious Diseases 1 (2018).

[57] Prevnar 13 was not included in this study as it was not licensed until 2010. About Pneumococcal Vaccines, Ctrs. for Disease Control & Prevention, https://www.cdc.gov/vaccines/vpd/pneumo/hcp/about-vaccine.html (last reviewed Sept. 21, 2023).

Dr. Steinman concluded that "GBS is a relatively rare illness. Numerous vaccines including Prevnar 13 can in rare instances through the theory of molecular mimicry cause GBS." Pet. Ex. 156 at 25.

ii. Althen Prong Two

Dr. Steinman opined there was "[a] logical sequence of cause and effect showing [] the vaccination was the reason for the injury," since it "has constituents that induce antibodies known to cross-react with myelin and that are found in patients with GBS." Pet. Ex. 156 at 26.

The parties stipulated that Mr. Meyer was diagnosed with an axonal variant of GBS. Joint Submission at 1. During the hearing, Dr. Steinman discussed the relationship between axons and phospholipids, explaining that nerve "axons are surrounded by myelin," and "[i]f the myelin is involved in the pathophysiology of the disease, the axon could take a hit." Tr. 172; see also 438-39. Dr. Steinman also discussed how the phosphoglycerol theory he proposed relates to axonal variants of GBS. Tr. 172-72, 438-39. He stated that "the axonal variants have involvement of molecules that are at the interface between the axon and the myelin. The phosphoglycerol is a component of many of the myelin molecules." Tr. 172. By the process of "bystander damage,[58] there could be damage to the underlying axon and to the conduction at the node of Ranvier." Tr. 172-73. Dr. Steinman noted that the antibodies described in Bryson et al. are not tested for outside of a research context, and therefore, they are not usually ordered in a clinical setting. Tr. 173-74 (citing Pet. Ex. 172). Further, Mr. Meyer was not testified for the antibodies referenced in Bryson et al. Tr. 122 (citing Pet. Ex. 172).

Next, Dr. Steinman explained how the Contactin-1 theory relates to the axonal variants of GBS. Tr. 173. "Contactin is a molecule[] [] at the interface on the axonal side. It's paranodal, . . . near the node of Ranvier, and an immune response to Contactin could certainly cause axonal damage." Id.; see also Tr. 439. He further testified that "an immune response to [C]ontactin is found in both axonal and [] demyelinating forms" of GBS. Tr. 439. Dr. Steinman testified that while anti-Contactin antibodies can be found in both AIDP and AMAN subtype forms of GBS, Mr. Meyer was not tested for them. Tr. 148, 175-76.

After explaining how Petitioner's theory applies to the subtype of GBS at issue here, Dr. Steinman next opined that there was no evidence of an alternative cause for Mr. Meyer's GBS. Tr. 167-69. Dr. Steinman also testified that more likely than not, Mr. Meyer did not have a *C.*

[58] Bystander activation is "B cell stimulation with T cell help provided by a T helper cell responding to an unrelated antigen." Julius M. Cruse & Robert E. Lewis, Illustrated Dictionary of Immunology 119 (3d ed. 2009). Bystander effects are "[i]ndirect, non-antigen-specific phenomena that result . . . [from] cellular interactions that take place without antigen recognition or under conditions in which antigen and receptors for antigen are not involved." Id.

jejuni infection to trigger his GBS.[59] Tr. 45, 169-70. Patients who have GBS caused by *C. jejuni* may have anti-ganglioside antibodies, but Mr. Meyer did not have such antibodies. Tr. 170.

iii. Althen Prong Three

Dr. Steinman opined Mr. Meyer's onset was August 5, 2017, or 10 days post-Prevnar 13 vaccination. Pet. Ex. 156 at 1, 5, 25. He opined this timing was "certainly consistent with the timing known for GBS and the 1976 swine influenza immunization, often used as a surrogate in such cases regarding timing." Id. at 25 (citing Pet. Ex. 188).[60] He also referenced several other articles that supported the onset as appropriate given his theory of molecular mimicry. Tr. 107-09.

Haber et al. identified 11 reports of possible GBS following Prevnar 13 vaccination, with a median onset of nine days (range of two to 34 days). Pet. Ex. 187 at 4; see also Tr. 107-08. Tseng et al. used a risk window of one to 42 days following vaccination with Prevnar 13 and PPSV23. Resp. Ex. G, Tab 7, at 3 tbl.1; see also Tr. 108-09. And a study from Baxter et al. also used a risk interval up to six weeks, or 42 days.[61] Resp. Ex. G, Tab 6 at 1; see also Tr. 109-10. Given these papers, Dr. Steinman noted epidemiologists use the interval of one to 42 days. Tr. 110. Dr. Steinman concluded that the temporal relationship criteria of Althen prong three was fulfilled based on this interval. Pet. Ex. 156 at 26.

[59] Petitioner noted Mr. Meyer contracted *C. difficile* during his hospitalization, resulting in diarrhea. Pet. Ex. 205 at ¶ 14; Tr. 22. Prior to this, Mr. Meyer had no diarrhea. Tr. 22-23. The experts did not opine that the cause of Mr. Meyer's GBS was *C. difficile*. See Tr. 169-70, 238-40, 253, 315-16; Resp. Ex. C at 5. *C. difficile* is "a species that is part of the normal colon flora in infants and some adults" that "produces a toxin that can cause pseudomembranous enterocolitis in patients receiving antibiotic therapy." Clostridium Difficile, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=65630 (last visited Jan. 8, 2024). It appears that Mr. Meyer developed *C. difficile* after receipt of antibiotics during his hospitalization. See Tr. 238. Mr. Meyer did not present to the hospital with a history of diarrhea which would have indicated that he had *C. difficile* before the onset of GBS.

[60] 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).

[61] None of the study patients in Baxter et al. received the Prevnar 13 vaccine prior to GBS onset, although two did receive the PPSV23. Resp. Ex. G, Tab 6 at 4.

2. Petitioner's Expert, Dr. Praful Kelkar[62]

a. Background and Qualifications

Dr. Kelkar received his M.B.B.S. in 1983 and his M.D. in 1987 in India. Pet. Ex. 141 at 1. He then completed a neurology residency and a two-year fellowship in Clinical Neurophysiology and Neuromuscular Diseases at the University of Iowa. Id.; Pet. Ex. 15 at 1. He is board certified in neurology, clinical neurophysiology, EMG, neuromuscular disease, and nerve pathology. Pet. Ex. 15 at 1; Pet. Ex. 141 at 1. Dr. Kelkar has held academic positions in the department of Neurology at the University of Iowa and University of Minnesota. Pet. Ex. 141 at 1. As of the time of the entitlement hearing, he was working at the Minneapolis Clinic of Neurology, where his practice was mostly neuromuscular, and he was the director of the EMG lab at the Minneapolis Clinic of Neurology. Tr. 195. Most of his practice is neuromuscular and in the clinical setting, and includes the treatment of GBS patients. Tr. 195-95. He does hospital rotations about one week every two or three months. Tr. 196. He has authored or co-authored over 50 publications. Pet. Ex. 141 at 2-5. He "ha[s] done research in neuromuscular disorders and neuroimmunology including participation in several trials in MS." Pet. Ex. 15 at 1.

b. Opinion

Dr. Kelkar opined Mr. Meyer "developed rapidly evolving quadriparesis and areflexia leading the respiratory failure within a few days following [Prevnar 13] vaccination." Pet. Ex. 15 at 5. His clinical course, laboratory tests, and electrophysiologic tests confirmed a diagnosis of axonal GBS. Id. at 3-5. Mr. Meyer did not respond to IVIG or plasmapheresis, and succumbed to pulmonary complications. Id. at 5. Mr. Meyer had no other confounding factors such as infections at the onset of GBS. Id. at 4-5. Therefore, he concluded that "more likely than not, to a reasonable degree of medical certainty, that the [Prevnar 13] vaccine served as a trigger for this process." Id. at 5.

Dr. Kelkar did not present opinions as to Althen prong one, and focused his opinions on prongs two and three. He also provided care and treatment to Mr. Meyer on one day of his hospitalization, on August 12, 2017, while covering Dr. Brodsky's patients on hospital rounds. Pet. Ex. 8 at 383-84; Tr. 235.

At the hearing, Dr. Kelkar provided a detailed overview of Mr. Meyer's clinical course to establish that he did not have any antecedent infection or alternative cause of his GBS other than vaccination. See Pet. Ex. 15 at 2-4; Tr. 200-235. Dr. Kelkar noted that on July 26, 2017, Mr. Meyer saw his primary care physician and received the Prevnar 13 vaccine at issue. Tr. 200-01. Dr. Kelkar found nothing of significance was noted on examination or in the record from that visit. Id. Of note, Mr. Meyer was afebrile, and his temperature, blood pressure, and heart rate were normal. Tr. 201. There were no signs of infection. Tr. 201-02.

On the night of August 2, 2017, Mr. Meyer went to the ER and complained of right upper quadrant and right flank pain that began that day. Tr. 202. Mr. Meyer did not have fever,

[62] Dr. Kelkar testified at the hearing and provided two expert reports. Tr. 189; Pet. Exs. 15, 136.

nausea, vomiting, or diarrhea. Tr. 202, 204. Dr. Kelkar noted these records did not indicate a cause for Mr. Meyer's pain following testing and scans. Tr. 202-04. There was nothing significant noted on examination. Tr. 203. Mr. Meyer's blood pressure was elevated. Id. According to Dr. Kelkar, heart rate and blood pressure can increase when someone is in pain. Id. Mr. Meyer's temperature was normal, and his labs revealed normal WBC count. Tr. 203-04. Dr. Kelkar testified that if an infection was present, WBC count would be elevated along with a fever; however, Mr. Meyer had no signs of infection. Tr. 204.

The next visit was in the early morning hours of August 3, 2017. Tr. 204-05. Mr. Meyer returned to the ER and continued to complain of abdominal pain and joint pain in the whole body. Tr. 205. Mr. Meyer denied nausea, vomiting, or fever. Id. His blood pressure was elevated, but his temperature was normal, and examination was unremarkable. Id. Labs revealed normal WBC count. Tr. 206. A CT scan was normal. Id. The assessment noted Mr. Meyer's work-up was negative and no specific diagnosis was made at that time. Id.

Later that morning, Mr. Meyer presented to his primary care physician's office and reiterated his complaints. Tr. 207. Mr. Meyer's pain was progressing and worsening. Tr. 208 (citing Pet. Ex. 3 at 40 ("[O]ver the night and into the early morning[,] he had progressive pain in his arms and legs . . . . His pain [was] worsening.")). Physical examination revealed tenderness throughout the muscles, but no spams, no weakness, normal temperature, and no change in bowel or bladder. Tr. 207-09. X-ray and EKG were normal. Tr. 209. Sedimentation rate and creatine kinase ("CK") were normal, indicating to Dr. Kelkar that Mr. Meyer's muscles were not inflamed. Tr. 210-11. Mr. Meyer still had no nausea, vomiting, fever, or diarrhea, which was significant to Dr. Kelkar because Mr. Meyer would have these symptoms if he had an infection. Tr. 208-09. Mr. Meyer was noted to be sweating; however, Dr. Kelkar testified that would occur when pain is severe enough. Tr. 209. Mr. Meyer's primary care physician was "unsure as to the etiology of the severe pain." Tr. 210 (quoting Pet. Ex. 3 at 43). Mr. Meyer's Prevnar 13 vaccination was noted. Id. However, no specific diagnosis was given at that time. Id. Mr. Meyer was given a steroid injection at that visit, which Dr. Kelkar noted would alter lab testing. Id. Dr. Kelkar testified that there was no sign of infection on August 3, 2017. Tr. 211.

That night, August 3, 2017, Mr. Meyer returned to the ER. Tr. 211. His pain was noted to have "progressed from abdomen to everywhere, but worse in [his] legs." Tr. 212 (internal quotations omitted) (quoting Pet. Ex. 8 at 199). He had difficulty walking due to the pain, reporting that his muscles felt like they were locking up. Tr. 214. He also reported his abdominal pain was improving. Id. He was sweaty without fever. Id. He did not report weakness or numbness. Id. Mr. Meyer had no nausea, vomiting, fever, dysuria, or diarrhea. Tr. 212, 214. His temperature was normal. Tr. 212. Blood pressure was elevated but otherwise, his examination remained unremarkable, including neurologic examination. Id. Mr. Meyer's WBC and glucose levels were elevated. Tr. 213. Dr. Kelkar testified that his WBC count could be elevated due to the steroid injection he received that morning. Id. The treating physician who noted the "mild elevation" in Mr. Meyer's WBC thereafter stated there was no "fever or specific joint swelling that would indicate a possible infection." Tr. 214-15; Pet. Ex. 8 at 205. His CRP, which "is a general marker for any inflammatory condition happening in the body," was borderline elevated. Tr. 213. Mr. Meyer also had no known exposure to ticks, and a tick-borne disease is known to cause similar symptoms. Tr. 214. Lyme testing was pending. Id. Overall,

Dr. Kelkar noted that no treating physician or nurse in the ER noted any sign of infection. Tr. 215.

Mr. Meyer was admitted to the hospital, and on August 5, 2017, he complained of weakness, tingling in his hands, diplopia (double vision), and incoordination. Tr. 216, 221-23. He was seen by neurologist Dr. Brodsky on August 6, who documented that Mr. Meyer had skew deviation,[63] ataxia, but positive reflexes. Tr. 223-34. Dr. Brodsky questioned whether Mr. Meyer had MFS variant of GBS. Tr. 225. Later that day, Mr. Meyer choked on food, and became unresponsive, and a code blue was called. Tr. 227. Mr. Meyer was intubated and placed on a ventilator and moved to the ICU. Id. The next day, Mr. Meyer lost his deep tendon reflexes, he was diagnosed with questionable MFS variant of GBS, and IVIG was started. Tr. 228-29. Antibiotics were begun for aspiration pneumonia. Tr. 229-30. An EMG was consistent with an axonal variant of GBS, and CSF showed elevated protein, also consistent with GBS. Tr. 231-32. Diagnostic studies on the CSF were negative for Enterovirus, Lyme disease, and herpes viruses, and stool cultures were negative for *C. jejuni* or other infections. Tr. 234-35.

Dr. Kelkar saw Mr. Meyer as a patient on August 12, 2017, while covering for Dr. Brodsky's patients. Tr. 235. Dr. Kelkar testified that Mr. Meyer's antiGQ1B[64] was negative, indicating that he did not have the classic form of MFS variant to GBS. Tr. 237. Mr. Meyer was able to communicate by raising his eyebrows to answer questions, and he knew his diagnosis. Id. He was paralyzed in his arms and legs and complained of a headache and back pain. Tr. 237-38. Dr. Kelkar's assessment was "severe axonal GBS with prior pneumococcal vaccine, *Campylobacter* was negative." Tr. 238 (emphasis added) (quoting Pet. Ex. 8 at 384)

Mr. Meyer was discharged from the hospital on August 18, 2017, and transferred to long-term skilled care. Tr. 239-40. His condition declined, and he was taken back to the hospital, where he was diagnosed with anoxic encephalopathy. Tr. 241-42, 256. His condition deteriorated and he passed away on August 26, 2017. Tr. 244-45. Cause of death was GBS. Tr. 245; see also Joint Submission at 2; Pet. Ex. 6 at 1.

In summary, Dr. Kelkar opined that Mr. Meyer's clinical course was consistent with vaccine-induced GBS. Tr. 252. Although axonal GBS, which Mr. Meyer had, is sometimes associated with a *C. jejuni* infection, Dr. Kelkar opined that Mr. Meyer had no evidence of any

[63] Skew deviation is the "downward and inward rotation of the eye on the side of the cerebellar lesion and upward and outward deviation on the opposite side." Skew Deviation, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=69485 (last visited Jan. 8, 2024).

[64] See Pet. Ex. 57 (A. Chiba et al., Serum Anti-GQ1b IgG Antibody Is Associated with Ophthalmoplegia in Miller Fisher Syndrome and Guillain-Barré Syndrome: Clinical and Immunohistochemical Studies, 43 Neurology 1911 (1993)).

infection. Pet. Ex. 15 at 4 (citing Pet. Ex. 20 at 4-5).[65] Dr. Kelkar noted a full work up was done and no infection was found. Pet. Ex. 136 at 1; Tr. 252.

Mr. Meyer's complaints began with abdomen and flank pain, and Dr. Kelkar noted that "pain is often associated with GBS and can be a presenting symptom of [] GBS." Pet. Ex. 136 at 1; see Pet. Ex. 137 at 1 ("Moderate to severe pain is a common and early symptom of GBS and requires aggressive treatment.");[66] Pet. Ex. 138 at 1 ("Pain is a common and often severe symptom in . . . GBS . . . [and] frequently occurs as the first symptom . . . .");[67] Pet. Ex. 139 at 1 (noting "[p]ain was well-characterized in the initial descriptions of GBS by Guillain and coworkers");[68] Pet. Ex. 140 (describing characteristics and incidence of pain during the acute phase of GBS).[69] "The pain is often diffuse, ill-defined and sometimes wrongly diagnosed as some other disease process." Pet. Ex. 136 at 1. Thus, he found "nothing unusual with [Mr. Meyer's presentation of GBS," despite Dr. Donofrio's contentions. Id.

Regarding timing, Dr. Kelkar testified that Mr. Meyer's onset of symptoms began about "[one] week or so" after vaccination, which is consistent with vaccine-induced GBS. Tr. 265.

3. Respondent's Expert, Dr. Peter D. Donofrio[70]

a. Background and Qualifications

Dr. Donofrio is board certified in neurology, internal medicine, electrodiagnostic medicine, and neuromuscular medicine. Resp. Ex. I at 2. After receiving his M.D. from Ohio State University School of Medicine, he completed residencies in internal medicine and neurology and a neuromuscular fellowship. Id. at 1-2. Throughout his career, Dr. Donofrio held various academic appointments at Vanderbilt University School of Medicine, Wake Forest University School of Medicine, and University of Michigan Medical Center. Id. at 2-3. He retired from the practice of neurology in July 2021. Id. at 2; Tr. 267-68. Prior to retirement, Dr. Donofrio was treating around 1,000 to 1,200 patients per year, and around eight to 12 patients with GBS per year. Tr. 269-70. He "has experience [] evaluating a spectrum of neuropathies

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[65] D. Chowdhury & A. Arora, Axonal Guillain-Barré Syndrome: A Critical Review, 103 Acta Neurologica Scandinavica 267 (2001).

[66] D.E. Moulin et al., Pain in Guillain-Barré Syndrome, 48 Neurology 328 (1997).

[67] L. Ruts et al., Pain in Guillain-Barré Syndrome, 75 Neurology 439 (2010).

[68] Kenneth C. Gorson, This Disorder Has Some Nerve: Chronic Pain in Guillain-Barré Syndrome, 75 Neurology 1406 (2010).

[69] Shaoli Yao et al., Pain During the Acute Phase of Guillain-Barré Syndrome, 97 Medicine 1 (2018).

[70] Dr. Donofrio testified at the hearing and provided two expert reports. Tr. 189; Resp. Exs. C, F.

such as [GBS] . . . and the related condition of [MFS]," and he has published on these areas. Resp. Ex. C at 1. Dr. Donofrio also has experience reviewing "literature and data on vaccine-related GBS . . . , MS, and other neurologic conditions." Id. Dr. Donofrio has authored or co-authored over 200 publications. Resp. Ex. I at 13-32.

b. Opinion

Dr. Donofrio opined the Prevnar 13 vaccine did not lead to Mr. Meyer's GBS. Tr. 273.

i. Althen Prong One

In his initial expert report, Dr. Donofrio opined "[i]t [was] difficult . . . to link the development of GBS to the pneumococcal vaccination" due to the lack of supportive literature. Resp. Ex. C at 6. He noted that the 2012 Institute of Medicine ("IOM") Report did not discuss the "relationship of the pneumococcal vaccine to GBS," and given the number of these vaccinations that have been given, if there were a causal association, he would expect a "larger number of reports." Id.

Regarding the case report from Ravishanker that was filed by Petitioner's experts, Dr. Donofrio questioned whether the patient had GBS. Tr. 285 (citing Pet. Ex. 186). He also opined that the reliability of case reports depends on the quality of the report, the journal in which it is published, and the reviewers for the journal. Tr. 285-86.

Next, he addressed the three reports of GBS after pneumococcal infection referenced by Petitioner's experts. Tr. 287-90; Resp. Ex. F at 2; see Pet. Exs. 131-33. He opined that natural infections are known to cause GBS, and based on current available knowledge, he agreed that pneumococcal infections could precipitate GBS. Tr. 287-88. However, Dr. Donofrio disagreed that the report by El Khatib et al., about a 13-year-old who developed GBS after *S. pneumoniae*, was supportive to Petitioner's theory because he questioned the diagnosis of GBS due to lack of sufficient detail in the report. Resp. Ex. F at 2 (citing Pet. Ex. 131); see also Tr. 288-89. Dr. Donofrio also questioned the diagnosis of GBS in the report by White et al., which also described a case of GBS after *S. pneumoniae* infection. Tr. 289-90 (citing Pet. Ex. 132). Dr. Donofrio recognized the Bianchi and Domenighetti case report showed "an association between [GBS] and the natural infection with [*P.*] *pneumonia*[*e*]," but characterized it as a "single case report." Tr. 287 (citing Pet. Ex. 133). He concluded that none of these case reports about GBS after pneumococcal infections relate to the vaccine. Resp. Ex. F at 2.

ii. Althen Prong Two

Dr. Donofrio agreed with the diagnosis of GBS, but he found Mr. Meyer had an atypical presentation because the onset of his GBS was characterized by pain[71] on approximately August

[71] Dr. Donofrio detailed the clinical course of Mr. Meyer's pain and opined that it could explain the "possible delay" in diagnosis and treatment. Resp. Ex. F at 1. Mr. Meyer's clinical course was characterized by pain, however, it did "not alter the diagnosis of GBS" or Dr. Donofrio's opinion that GBS was the correct diagnosis. Id.

2 and 3, 2017. Resp. Ex. C at 5-6. Regarding the subtype of GBS, Dr. Donofrio opined that Mr. Meyer's "EMG [was] consistent with an axonal poly neuropathy, and in this clinical setting, knowing how [Mr. Meyer] presented would be consistent with AMSAN, acute motor sensory axonal neuropathy, because there are abnormalities in both motor and sensory fibers."[72] Tr. 279-80 (citing Pet. Ex. 9 at 1). Dr. Donofrio opined "each subtype [of GBS] has [an] independent immunopathogenesis and has characteristics[] [and] specific clinical features." Tr. 293. But he noted that currently, "there are only two treatments for GBS, IVI[G] and plasma exchange." Tr. 294. Discussing Kubabara and Yuki,[73] Dr. Donofrio noted that in the AMAN subtype there are "pathological changes at the nodal and paranodal axolemma"[74] that occur at the nodes of Ranvier and the paranodal areas beneath the nodal regions instead of segmental demyelination seen in AIDP. Tr. 294-295 (quoting Pet. Ex. 68 at 1). According to Dr. Donofrio, AMAN and AMSAN have similar mechanisms of pathogenesis, and in AMSAN, there would be pathology of the motor nerves with sensory involvement. Tr. 297.

Since Mr. Meyer's EMG did not show demyelination, Dr. Donofrio opined that he did not have the AIDP form of GBS. Tr. 297. For this reason, Dr. Donofrio testified that Nakos et al., which studied patients with AIDP and was relied upon by Dr. Steinman, was not applicable. Tr. 297-98 (citing Pet. Ex. 168). Gilburd et al. found antibodies in six of 16 patients with GBS, but Dr. Donofrio disagreed that this finding was proof of a causal theory. Tr. 300-02 (citing Pet. Ex. 167). Instead, Dr. Donofrio testified that it probably indicated myelin damage. Tr. 300-01 (citing Pet. Ex. 167). He noted that Gilburd et al. did not identify the subtypes of GBS in the patients who were studied. Tr. 302 (citing Pet. Ex. 167).

Antibody testing was also discussed by Dr. Donofrio. Citing to Dimachkie and Barohn,[75] Dr. Donofrio explained that antibody testing is not recommended in GBS, except for patients with MFS variant, because in that type of GBS, polyclonal GQ1B antibodies are highly specific to the disease. Tr. 279-80 (citing Pet. Ex. 19 at 7). Dr. Donofrio testified that no antibody testing was ordered or reported for Mr. Meyer. Tr. 280, 282. But see Pet. Ex. 8 at 461, 598-600 (showing Mr. Meyer's test results for antibody testing, including GQ1b). Dr. Donofrio also noted that Mr. Meyer was not tested for Contactin-1 antibodies. Tr. 304.

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[72] In his first expert report, Dr. Donofrio found Mr. Meyer "suffered from the axonal form of [GBS] with oculomotor manifestations as the initial presentation." Resp. Ex. C at 5. At the hearing, Dr. Donofrio opined Mr. Meyer had sensory involvement. Tr. 279-80, 297.

[73] Satoshi Kuwabara & Nobuhiro Yuki, Axonal Guillain-Barré Syndrome: Concepts and Controversies, 12 Lacet Neurology 1180 (2013).

[74] Axolemma is "the plasma membrane of an axon," also known as sheath. Axolemma, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=5197 (last visited Jan. 8, 2024).

[75] Mazen M. Dimachkie & Richard J. Barohn, Guillain-Barré Syndrome and Variants, 31 Neurologic Clinics 491 (2013).

Dr. Donofrio also opined that the medical literature did not support a causal relationship between Mr. Meyer's Prevnar 13 vaccination and GBS. Resp. Ex. C at 6; Resp. Ex. F at 2; Tr. 306. He discussed Haber et al., who reported 10 cases of GBS in patients 65 and older, and noted Mr. Meyer was 62 years old at the time of vaccination. Tr. 204-06 (citing Pet. Ex. 187 at 4, 4 tbl.2b). Dr. Donofrio noted the results in Haber et al. showed "the incidence of [GBS] after Prevnar 13 was [] lower than the result expected in an age group that had not received any vaccinations" and "that there's no relationship between Prevnar 13" and GBS. Tr. 306 (emphasis omitted). Thus, Dr. Donofrio asserted Haber et al. does not support a causal relationship. Id.

Regarding alternative causes for Mr. Meyer's GBS, Dr. Donofrio's first expert report suggested the inciting event was possibly a viral illness. Resp. Ex. C at 6 ("The [] differential diagnosis raises the possibility of a viral illness of the gastrointestinal tract for several days that may have been a precipitating cause for the GBS."). Thus, his opinion was stated as a possibility. However, later in his first expert report, Dr. Donofrio opined that "more likely than not, GBS in [Mr. Meyer] [was] secondary to another cause most likely viral." Id. at 7. At the hearing, on cross-examination, Dr. Donofrio agreed that Mr. Meyer was never diagnosed with an infection. Tr. 310-18.

In his second expert report, Dr. Donofrio noted that the lack of a finding of any specific triggering agent for Mr. Meyer's GBS is not uncommon. Resp. Ex. F at 2. He discussed the difficulties of screening or testing for "every virus that might incite GBS as there are too many viruses to screen." Id. Further, he stated that "in most cases, what virus may have triggered GBS does not ultimately influence treatment, so comprehensive viral testing is not commonly done." Id. Regardless, Dr. Donofrio disagreed that the vaccine caused Petitioner's GBS. Id.

As described by Dr. Donofrio, Mr. Meyer had GBS that was complicated by the "development of hypoxic encephalopathy after he choked on food . . . and aspirated . . . . This led to a CODE BLUE requiring [Mr. Meyer] to be intubated, placed on a ventilator[,] and moved to the [ICU]." Resp. Ex. C at 5. Dr. Donofrio did not provide any opinions disagreeing with the death certificate which identified GBS as the immediate cause of death. See id. at 5-6.

iii. Althen Prong Three

Mr. Meyer received his Prevnar 13 vaccination on July 26, 2017. Resp. Ex. C at 1. Dr. Donofrio noted in his summary of medical records that on August 5, Mr. Meyer was weak and had tingling in his hands. Id. at 2. Dr. Donofrio opined that the records from August 5 document "[t]he earliest feature of GBS," which is "when he began to complain of weakness and tingling of the hands." Id. at 6.

Dr. Donofrio did not offer opinions rebutting Dr. Kelkar's opinion that there was a temporal association between vaccination on July 26 and the onset of Mr. Meyer's symptoms of GBS on August 5.

4. Respondent's Expert, Dr. J. Lindsay Whitton[76]

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. H at 1. He held various professor positions since 1986. Id. He joined Scripps Research Institute in 1984 and remained for over 35 years before closing his lab in 2020. Tr. 321-22, 325. He remained on the faculty as the chair of the Appointments Promotion Committee at Scripps until April 2023, when he stepped down and retired. Tr. 321, 328. He "studied (and published on) viral pathogenesis, and the immune responses to virus infections and to vaccines," and he has "published on both the adaptive and innate immune responses[] and on molecular mimicry." Resp. Ex. A at 1. Dr. Whitton is a member of various professional societies and editorial boards and has authored or co-authored 200 publications. Resp. Ex. H at 1-13. Dr. Whitton does not hold a medical license, provide patient care, or diagnose or treat patients with GBS. Resp. Ex. A at 2.

While at Scripps Research Institute, he maintained his research lab by NIH grants and did not receive a salary. Tr. 406, 409. The NIH is part of the Department of Health and Human Services, the named Respondent in this case. Tr. 406. In all cases Respondent has contracted with Dr. Whitton to write expert reports in the Vaccine Program, he has opined that the vaccine did not cause the injury. Tr. 403.

b. Opinion[77]

Dr. Whitton did not offer an opinion as to Petitioner's diagnosis or take a position on whether the diagnosis of GBS was appropriate. Resp. Ex. A at 2. His focus was on the question of whether the Prevnar 13 vaccine can cause GBS.[78] See Resp. Exs. A, E, G.

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[76] Dr. Whitton testified at the hearing and provided three expert reports. Tr. 189; Resp. Exs. A, E, G.

[77] For a summary of Dr. Whitton's opinions and conclusions, see Resp. Ex. G at 45-47.

[78] Dr. Whitton's criticisms of Dr. Gershwin's and Dr. Steinman's expert opinions are far ranging. For the sake of brevity and clarity, the undersigned attempts to discuss the material points and omits discussion of criticism that is collateral to the central issues or that is characterized by Dr. Whitton as less important. For example, in his expert report and at the hearing, Dr. Whitton described the difference between the words phosphoglycerol and phosphoglycerate, but he characterized this criticism as "bickering." Tr. 341-42; Resp. Ex. G at 4, 9-10, 14-17. Due to the length of Dr. Whitton's expert reports, some of his points have not been discussed here. However, the undersigned has reviewed Dr. Whitton's reports and the medical literature in its entirety and has taken all of this evidence into consideration in reaching her opinions.

First, Dr. Whitton opined that that "Prevnar 13 has an excellent safety record" and there is no evidence that it is causally associated with GBS. Resp. Ex. A at 8. Dr. Whitton stated that medical literature, such as the Haber et al. study, "showed a small number" of GBS cases temporally associated with the Prevnar 13 vaccination, but they did not report an increased risk of GBS following vaccination. Tr. 335; see also Resp. Ex. A at 6-7; Resp. Ex. G at 5-6.

Second, Dr. Whitton opined that *S. pneumoniae*, which Prevnar 13 protects against, is not generally implicated as a cause of GBS. Tr. 333; Resp. Ex. A at 4-5, 9. He agreed that *C. jejuni* is a known infecting agent in GBS, and that it may evoke molecular mimicry between specific molecules of the bacteria and human gangliosides. Tr. 333-34. He asserted, however, that he is not aware of "any reliable evidence" to suggest that *S. pneumoniae* has been causally associated with GBS. Tr. 334-35. He concluded that since the organism does not trigger GBS, then the vaccine with the same antigens cannot do so. Resp. Ex. A at 5.

For molecular mimicry to occur, Dr. Whitton testified several things must occur. Tr. 337-38; Resp. Ex. G at 6-9. First, the "vaccine has to induce an immune response," and Dr. Whitton agreed that "vaccines are designed to induce immune responses." Tr. 337. But as it relates to Dr. Steinman's theory, he explained the question is whether the vaccine induces a response against phospholipids or Contactin-1. Tr. 337-38. The second step is whether the immune response "can recognize the proposed target molecule on the nerve cell." Tr. 338. And the third step is whether "the cross-reactive antibodies actually cause damage to tissues" so as to induce disease. Id.

Dr. Whitton cited a paper from Rose and Mackay,[79] who wrote that "[t]here are[] [] no clear examples of a human disease caused by molecular mimicry." Resp. Ex. G at 8 (quoting Resp. Ex. G, Tab 8 at 1). He also quoted the IOM,[80] now the National Academy of Sciences, who stated that "[w]hile molecular mimicry is a well-established mechanism in selected animal models, its relevance to human autoimmune disease remains in most cases to be convincingly proven." Id. (quoting Resp. Ex. G, Tab 9 at 15). While Dr. Whitton agreed that molecular mimicry is "real," he believed it "cause[s] disease only rarely." Id. However, he agreed that molecular mimicry has been proposed as the relevant mechanism for GBS. Resp. Ex. A at 3.

After commenting on molecular mimicry generally, Dr. Whitton addressed the specific application of molecular mimicry in the theories offered by Dr. Steinman. According to Dr. Whitton, the target molecules in GBS are "host gangliosides (molecules comprising phospholipids and sugars) . . . present in peripheral nerves" and he acknowledged that it is

[79] N.R. Rose & I.R. Mackay Molecular Mimicry: A Critical Look at Exemplary Instances in Human Diseases, 57 Cellular & Molecular Life Scis. 542 (2000). Dr. Whitton noted Dr. Rose was "an expert in immunology and sometimes referred to as 'the father of autoimmunity.'" Resp. Ex. G at 8.

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

widely accepted that anti-ganglioside antibodies play a "pathological role in GBS." Resp. Ex. A at 3-4. This contrasts with Dr. Steinman's theory regarding phosphoglycerol.[81]

Dr. Whitton did not agree with Dr. Steinman's "interpretation" of Bryson et al. See Tr. 348-53; Pet. Ex. 172. Although Dr. Whitton agreed that the antibodies described by Bryson et al. "touch phosphoglycerol," he asserted this occurs "only at one of the nine contact points." Tr. 352. The antibody "recognizes one tiny point[82] of phosphoglycerol in the context of a much larger contact with the sugars." Id. The "tiny point" was referred to by Dr. Whitton as a "remnant."[83] Tr. 353. He asserted that the Bryson et al. antibodies recognize the sugar and not the phosphoglycerol. Id. Dr. Whitton also argued that Bryson et al. does not discuss molecular mimicry or post-vaccination GBS. Tr. 354.

Regarding Dr. Steinman's reference to Chang et al., Dr. Whitton agreed with Dr. Steinman that Chang et al. showed that phosphoglycerol linkage is necessary for the immunogenicity of the vaccine. Tr. 355. He testified that "if you modify . . . the phosphoglycerol, then the immunogenicity of the polysaccharide is dramatically reduced." Id. However, Dr. Whitton disagreed that Gilburd et al. supported molecular mimicry, and he opined that it did not "show what induced the antibodies" and did not "show that the antibodies [were] pathogenic." Tr. 360; see also Resp. Ex. G at 13-14. Next, he disagreed that Nakos et al. supported the idea that lipid antigens play a role in GBS. Tr. 361. Dr. Whitton also noted that the Nakos et al. paper did not include the word phosphoglycerol and did not conclude that the antibodies were pathogenic. Tr. 361-62; see also Resp. Ex. G at 14. Regarding Ho et al., Dr. Whitton stated that it failed to show that phospholipid autoantibodies initiated GBS. Tr. 363. He agreed that Ho et al. supported the "precept that phospholipids are the target of an autoimmune attack causing [MS]." Tr. 366. And he agreed that Dr. Steinman cited it for the proposition that phospholipids may be the "target in another neuroinflammatory disease, [GBS]." Id. But Dr. Whitton maintained that instead of phospholipids, gangliosides play a role in the pathogenesis of GBS. Tr. 370-72; Resp. Ex. G at 13.

After addressing Dr. Steinman's theory based on phospholipids, Dr. Whitton turned to Petitioner's theory based on CRM_{197} and Contactin-1.[84] He maintained that short homologies are commonplace and do not lead to disease. Resp. Ex. G at 24-27. Dr. Whitton criticized Dr.

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[81] For a more detailed discussion of Dr. Whitton's opinions about this theory, see Resp. Ex. G at 10-24.

[82] Dr. Whitton referred to this as a "remnant" of phosphoglycerol. See Tr. 367-70. Dr. Whitton asserted that "[t]here is no reason to believe" that the antibody could recognize a "chemically altered remnant of phosphoglycerol." Tr. 370.

[83] For a more detailed discussion of this aspect of Dr. Whitton's opinions, see Resp. Ex. G at 11-12, 17-22 (agreeing that the Bryson et al. antibodies "may be a part of a 23F epitope," but believing they recognize a bigger structure that is a "dramatically different chemical structure").

[84] For a detailed discussion of Dr. Whitton's opinions about this second theory, see Resp. Ex. G at 24-41.

Steinman's use of a BLAST search and his proposed amino acid sequence WEQAKALSVE on the basis that the E-value of 2.7 indicated that the sequence was "a chance finding." Tr. 375; see also Resp. Ex. G at 27-34. Dr. Whitton performed the same BLAST search "against the entire human proteome" and "got 5,000 hits, and none of them were [C]ontactin-1." Tr. 376-79. Dr. Whitton explained that when Dr. Steinman did the search, he "identified a longer peptide of which the WEQ [sequence] was a smaller part." Tr. 378-79. However, Dr. Whitton did not perform a "BLAST search of the short peptide against [C]ontactin-1 alone." Tr. 379.

Dr. Whitton opined that Fujinami and Oldstone used a computer algorithm that identified identical amino acids, a process different than the BLAST search. Tr. 385-86. A BLAST search, in contrast, "incorporates amino acid similarity[,] not just identity." Tr. 386. And he opined that a BLAST search returns "peptide sequences aligned one above the other." Id. Dr. Whitton agreed, however, that the use of a different type of search was not a primary criticism of Dr. Steinman's methodology. Tr. 389. Dr. Whitton also criticized the fact that Dr. Steinman used a 70% filter when performing his BLAST search. Tr. 394. For a number of reasons, Dr. Whitton concluded that the BLAST approach used by Dr. Steinman was not reliable. Tr. 398-99; Resp. Ex. G at 31-41.

On cross-examination, Dr. Whitton testified that the pathogenesis of GBS has not been the primary area of his research and he is not familiar with peer reviewed literature that addresses what target antigens are being studied with respect to GBS associated with Covid, Zika virus, mycoplasma, or cytomegalovirus. Tr. 417-18. He agreed that GBS cases caused by *C. jejuni* are autoimmune in nature, but he did not know whether other subtypes of GBS, including AMAN and AMSAN, have been "shown to be autoimmune." Tr. 413. Further, Dr. Whitton testified that he did not know whether molecular mimicry is the proposed mechanism for all subtypes of GBS. See Tr. 413; see also Resp. Ex. A at 3-4; Resp. Ex. G at 8-9, 42. Lastly, he did agree that there are other target antigens in GBS other than gangliosides. Tr. 416.

Dr. Whitton criticized Petitioner's reliance on the Ravishankar case report for many reasons, including that it was written by a medical student, that it was not published in a respected journal, that the case report was very poor, that the patient received Pneumovax 23 and not Prevnar 13, and due to the time frame of onset. Resp. Ex. A at 5-6; Resp. Ex. E at 1-6, 8. The undersigned acknowledges that there are problems with the case report, and this Ruling does not rely on this one case report. Therefore, Dr. Whitton's opinions about the article are not discussed in detail.

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). 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 v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006). Instead, Petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

In particular, a petitioner must prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Hum. Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). 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). However, if a petitioner fails to establish a prima facie case, the burden does not shift. Bradley v. Sec'y of Health & Hum. Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

"Regardless of whether the burden ever shifts to the [R]espondent, the special master may consider the evidence presented by the [R]espondent in determining whether the [P]etitioner has established a prima facie case." Flores v. Sec'y of Health & Hum. Servs., 115 Fed. Cl. 157, 162-63 (2014); see also Stone v. Sec'y of Health & Hum. Servs., 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."); de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the [P]etitioner's evidence on a requisite element of the [P]etitioner's case-in-chief."); Pafford, 451 F.3d at 1358-59 ("[T]he presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the vaccination. . . . [T]he Special Master properly introduced the presence of the other unrelated contemporaneous events as just as likely to have been the triggering event as the vaccinations.").

B. Causation

To receive compensation through the Program, Petitioner must prove either (1) that Mr. Meyer suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that he received, or (2) that Mr. Meyer suffered an injury that was actually caused by a vaccination. See §§ 11(c)(1), 13(a)(1)(A); Capizzano, 440 F.3d at 1319-20. Petitioner must show that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface, 165 F.3d at 1352-53).

Because Petitioner does not allege Mr. Meyer suffered a Table Injury, she must prove a vaccine Mr. Meyer received actually caused his 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. 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).

Testimony that merely expresses the possibility—not the probability—is insufficient, by itself, to substantiate a claim that such an injury occurred. See Waterman v. Sec'y of Health & Hum. Servs., 123 Fed. Cl. 564, 573-74 (2015) (denying Petitioner's motion for review and noting that a possible causal link was not sufficient to meet the preponderance standard). The Federal Circuit has made clear that the mere possibility of a link between a vaccination and a petitioner's injury is not sufficient to satisfy the preponderance standard. Moberly, 592 F.3d at 1322 (emphasizing that "proof of a 'plausible' or 'possible' causal link between the vaccine and the injury" does not equate to proof of causation by a preponderance of the evidence); Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019). While certainty is by no means required, a possible mechanism does not rise to the level of preponderance. Moberly, 592 F.3d at 1322; see also de Bazan, 539 F.3d at 1351.

IV. ANALYSIS

A. 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 v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1375 (Fed. Cir. 2009); Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by a "sound

and reliable" medical or scientific explanation. Boatmon, 941 F.3d at 1359; see also Knudsen, 35 F.3d at 548; Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 257 (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 v. Sec'y of Health & Hum. Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better than the soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

For the following reasons, the undersigned finds Petitioner has provided, by preponderant evidence, a sound and reliable theory by which 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 a leading hypothesis for the etiology of GBS. The theory has been extended from infectious agents to vaccine-associated autoimmune illnesses, including GBS.

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 *57 (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, 2022 WL 322836, at *31; Maloney v. Sec'y of Health & Hum. Servs., No. 19-1713V, 2022 WL 1074087 (Fed. Cl. Spec. Mstr. Mar. 17, 2022); Gross v. Sec'y of Health & Hum. Servs., No. 17-1075V, 2022 WL 9669651 (Fed. Cl. Spec. Mstr. Sept. 22, 2022); Sprenger v. Sec'y of Health & Hum. Servs., No. 18-279V, 2023 WL 8543435, at *18-20 (Fed. Cl. Spec. Mstr. Nov. 14, 2023); Parker v. Sec'y of Health & Hum. Servs., No. 20-411V, 2023 WL 9261248, at *21-22 (Fed. Cl. Spec. Mstr. Dec. 20, 2023).[85]

Although Dr. Whitton offers wide ranging criticism of Dr. Steinman's theories, many of his concerns relate to either collateral issues or identify issues that are not material. This approach undermines the reliability and persuasiveness of his opinions. Moreover, Dr. Steinman has expertise in the causes of MS, and much of this expertise is transferable to GBS, as is shown

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

in his expert reports. Moreover, he maintains an active clinical practice and cares for patients with GBS.

The IOM has proposed the following criteria to establish whether a vaccine can cause GBS via molecular mimicry. The criteria include (1) "a susceptible host" (genetically and via host immune responses), (2) "exposure to an exogenous agent which expresses antigens that are immunologically similar to self-antigen(s), and (3) a host immune response" that causes disease. Resp. Ex. G, Tab 9 at 14. Further, there must be evidence of an "in vivo pathogenic autoimmune attack" and demonstration of the pathogenic mechanisms "in a biologically relevant tissue site." Id. Given the state of current scientific knowledge, it would not be possible for a petitioner to satisfy these criteria. Further, 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. Steinman has identified components of the vaccine that could initiate 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 that could trigger a human antibody response.

Regarding Petitioner's theory based on phosphoglycerol in serotypes 18C and 23F in the vaccine, Dr. Steinman produced papers to show that in MS, myelin phospholipids are targeted by an immune response. He also showed that myelin is comprised of phospholipids, and that phospholipids can serve as autoantigens in autoimmune disorders. He showed 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 Nakos et al., 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. 168 at 6. Dr. Steinman also explained how his phosphoglycerol theory related to the axonal form of GBS. In summary, there is sound support from reputable medical studies for each foundational aspect of Dr. Steinman's 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. He also explained how an immune response to Contactin-1 could cause an axonal form of GBS.

Additionally, the causal theory proffered by Dr. Steinman here has previously been accepted as sound and reliable in other Prevnar 13 cases, decided by different special masters, including the undersigned. See, e.g., Sprenger, 2023 WL 8543435; Gross, 2022 WL 9669651; Maloney, 2022 WL 1074087; Pierson, 2022 WL 322836; Koller, 2021 WL 5027947. 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. The undersigned agrees with the reasoning offered by her colleagues in these other cases, and for many of the

same reasons finds the Petitioner's theory here sound and reliable and proven by preponderant evidence.

The undersigned recognizes that there is not uniformity between the special masters in decisions addressing the Prevnar 13 vaccine and GBS. See, e.g., Deshler v. Sec'y of Health & Hum. Servs., No. 16-1070V, 2020 WL 4593162, at *19 (Fed. Cl. Spec. Mstr. July 1, 2020); Trollinger v. Sec'y of Health & Hum. Servs., No. 16-473V, 2023 WL 2521912, at *26 (Fed. Cl. Spec. Mstr. Feb. 17, 2023), mot. for review denied, 167 Fed. Cl. 127; Bielak v. Sec'y of Health & Hum. Servs., No. 18-761V, 2023 WL 35509, at *31-32 (Fed. Cl. Spec. Mstr. Jan. 3, 2023); Gamboa-Avila v. Sec'y of Health & Hum. Servs., No. 18-925V, 2023 WL 6536207, at *25 (Fed. Cl. Spec. Mstr. Sept. 11, 2023); McConnell v. Sec'y of Health & Hum. Servs., No. 18-1051V, 2022 WL 4008238, at *9 (Fed. Cl. Spec. Mstr. Aug. 19, 2022). The undersigned acknowledges these cases but also notes that the decisions of other special masters or Court of Federal Claims' judges are not binding on special masters. Boatmon, 941 F.3d at 1358; Hanlon, 40 Fed. Cl. at 630.

For 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 v. Sec'y of Health & Hum. Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). While the medical records and opinions of treating physicians must be considered, they are not binding on the special master. § 13(b)(1)(B) (specifically stating that the "diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court").

A 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 reasons why the undersigned finds preponderant evidence of a logical sequence of cause and effect establishing that the Prevnar 13 vaccination administered to Mr. Meyer on July 26, 2017 was the cause of his GBS and subsequent death. First, Petitioner was appropriately diagnosed with GBS, and Petitioner has proffered a sound and reliable mechanism of vaccine causation.

Second, no alternative cause was found for Mr. Meyer's GBS. The records show and the parties stipulated that testing was done for many possible causes, MRSA, Enterovirus, *Campylobacter*, *E. coli*, *Shigella*, and *Salmonella* infections. A spinal fluid culture was negative, and bacterial cultures, Lyme antibodies, and Herpes Simplex virus testing were all negative. A paraneoplastic panel was interpreted as negative.

At the hearing, Dr. Kelkar described Mr. Meyer's clinical course in detail and established that he did not have fever, or any signs or symptoms of an infection prior to onset of GBS. Dr. Kelkar noted that a complete work up was done and no infection was found. Respondent's expert, Dr. Donofrio noted the lack of evidence of any infectious trigger for Mr. Meyer's GBS. He suggested that because Mr. Meyer's clinical presentation was atypical, there was the "possibility of a viral illness." Resp. Ex. C at 6. However, testimony that merely expresses the possibility—not the probability—is insufficient. See, e.g., Waterman, 123 Fed. Cl. at 573; Moberly, 592 F.3d at 1322; Boatmon, 941 F.3d at 1359-60. Later in the same expert report, Dr. Donofrio stated that his opinion that the cause of Mr. Meyer's GBS was a viral infection was held to the standard of "more likely than not." Id. at 7. However, the fact that Dr. Donofrio initially referenced his opinion as a mere "possibility" raises questions about the internal validity of his expert report with regard to this opinion. And at the hearing on cross-examination, Dr. Donofrio agreed that Mr. Meyer was never diagnosed with an infection.

In summary, Petitioner's medical records, physician notes, and diagnostic workup did not identify an infectious or alternate cause of Petitioner's GBS. The only reference to an antecedent event was related to Petitioner's vaccination.

The third reason for finding that Petitioner has proven prong two is based on the statements and opinions by Mr. Meyer's treating neurologist, Dr. Brodsky. Mr. Meyer was admitted to North Memorial Health on August 3, 2017, and on August 6, he was evaluated by Dr. Brodsky, who considered the diagnosis of MFS variant of GBS. Per Dr. Brodsky's orders, EMG and CSF testing were done on August 8. After reviewing the results, Dr. Brodsky diagnosed Mr. Meyer with GBS. He wrote that Mr. Meyer had a "[p]neumococcal [v]accine [one] w[ee]k prior to onset. ? If playing a role." Pet. Ex. 8 at 317.

Several days later, on August 11, 2017, Dr. Brodsky wrote a letter stating,

> Mr. [] Meyer is a 62-year-old male who is under my care. He had a pneumococcal vaccination and within a week developed [GBS]. I have done extensive testing and there is not a more likely alternative diagnosis for the weakness. He is currently quadriplegic, apneic, ventilator dependent with complete ophthalmoplegia. Within reasonable medical certainty, his [GBS] is causally related to the preceding pneumococcal vaccination.

Pet. Ex. 4 at 1.

The opinions of treating physicians are generally more reliable because they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528. Although this opinion was written in the form of a letter, it is contemporaneous with the treatment Dr. Brodsky was providing to Mr. Meyer. Further, the opinions are not inconsistent with his entry three days before, where he questioned vaccine causation once he made the diagnosis of GBS.

Lastly, the undersigned finds Mr. Meyer's GBS led to his death. The parties did not dispute that GBS was the immediate cause of Mr. Meyer's death. See Joint Submission at 1. Mr. Meyer's death certificate indicated GBS was the "immediate cause" of Mr. Meyer's death. Pet. Ex. 6 at 1. Additionally, the experts did not dispute GBS was the cause of Mr. Meyer's death.

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 Mr. Meyer to develop GBS, which led to his death. Thus, Petitioner 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. A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352. The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen prong one). Id.; Koehn v. Sec'y of Health & Hum. Servs., 773 F.3d 1579, 1243 (Fed. Cir. 2014); Shapiro v. Sec'y of Health & Hum. Servs., 101 Fed. Cl. 532, 542 (2011), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 503 F. App'x 952 (Fed. Cir. 2013).

The parties stipulate that Petitioner received his Prevnar 13 vaccination on July 26, 2017, and they also agree that his onset of symptoms was August 5, 2017. Joint Submission at 1. Therefore, onset occurred approximately 10 days after vaccination. Respondent's experts do not rebut the onset time frame agreed on by the parties in the joint stipulation or otherwise disagree that there was a temporal association between the vaccination and onset of GBS consistent with the theory of molecular mimicry.

This time frame from vaccination to the initial manifestation of symptoms is appropriate given the theory of molecular mimicry, as demonstrated in Haber et al., which reported 11 cases of GBS following a Prevnar 13 vaccine, with a median onset interval of nine days. This temporal association is also consistent with the onset period of three 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., Parker, 2023 WL 9261248, at *25 (finding a GBS onset of nine days after Prevnar 13 vaccination to be appropriate); Sprenger, 2023 WL 8543435, at *22 (finding a GBS onset of approximately two weeks after Prevnar 13 vaccination to be appropriate); Gross, 2022 WL 9669651, at *38-39 (finding a GBS onset of 13 days after Prevnar 13 vaccination to be appropriate); Maloney, 2022 WL 1074087, at *36 (finding a GBS onset of seven days after Prevnar 13 vaccination to be appropriate); Koller, 2021 WL 5027947, at *57 (finding a GBS onset of 12 days after Prevnar 13 vaccination to be "within the medically accepted timeframe consistent with [P]etitioner'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. CONCLUSION

Based on the record, and for the reasons discussed above, the undersigned finds there is preponderant evidence to satisfy all three Althen prongs and to establish that Mr. Meyer's Prevnar 13 vaccination caused his GBS and death. 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