In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: July 8, 2025

NOAH E. MUSICK,	*	
	*	No. 18-451V
Petitioner,	*	
v.	*	Special Master Gowen
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
	*	
Respondent.	*	

Lisa A. Roquemore, Law Office of Lisa A. Roquemore, Rancho Santa Margarita, CA, for petitioner.
Lauren Kells, U.S. Department of Justice, Washington, D.C., for respondent.

RULING ON ENTITLEMENT[1]

On March 27, 2018, Noah E. Musick ("petitioner") filed his claim in the National Vaccine Injury Compensation Program.[2] Petition (ECF No. 1). Petitioner alleged that as a result of receiving the Prevnar-13 vaccine on March 31, 2017, he suffered from Guillain-Barré Syndrome ("GBS"). *Id.* at Preamble. After reviewing the evidence, including the reports and testimony of medical experts at an entitlement hearing, medical literature, and petitioner's medical records, the undersigned finds that petitioner is entitled to compensation.

I. Procedural History

Petitioner filed his claim for compensation on March 27, 2018. Petition. He filed accompanying medical records. Petitioner ("Pet'r) Exhibits ("Exs.") 1-8 (ECF No. 2-13). On

[1] Pursuant to the E-Government Act of 2002, *see* 44 U.S.C. § 3501 note (2012), because this decision contains a reasoned explanation for the action in this case, I am required to post it on the website of the United States Court of Federal Claims. The court's website is at http://www.uscfc.uscourts.gov/aggregator/sources/7. **This means the decision will be available to anyone with access to the Internet.** Before the decision is posted on the court's website, each party has 14 days to file a motion requesting redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). "An objecting party must provide the court with a proposed redacted version of the decision." *Id.* **If neither party files a motion for redaction within 14 days, the decision will be posted on the court's website without any changes.** *Id.*

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 to 34 (2012) (hereinafter "Vaccine Act" or "the Act"). Hereinafter, individual section references will be to 42 U.S.C. § 300aa of the Act.

September 9, 2019, respondent filed the Rule 4(c) Report, recommending against compensation. Respondent ("Resp't") Report ("Rept.") (ECF No. 38). The case was re-assigned to my docket on September 10, 2019.

The undersigned held a status conference on March 3, 2020, after which I ordered the parties to file expert reports. Scheduling Order (ECF No. 41). On August 31, 2020, petitioner filed an expert report from Lawrence Steinman, M.D.[3] and supporting medical literature. Pet'r Exs. 17-53 (ECF No. 45-48). Respondent filed an expert report from Vinay Chaudry, M.D and Stephen McGeady, M.D.[4] Resp't Exs. A-C (ECF Nos. 53, 56). Petitioner filed a responsive expert report from Dr. Steinman on May 3, 2021. Pet'r Ex. 55.

The undersigned held a status conference on July 22, 2021, when I explained that the medical records filed by petitioner appear to support a diagnosis of GBS. Dr. Steinman's theory of vaccine causation was considerably similar to theories he offered in other Prevnar-13-GBS cases and in this case, he had appeared to offer additional support for his theory. Rule 5 Order (ECF No. 62). I recommended that the parties attempt to resolve this case informally. *Id.* Respondent's counsel indicated that an entitlement hearing should be scheduled, given respondent's ongoing position to defend Prevnar-13-GBS cases.

Respondent filed a supplemental expert report from Peter Donofrio, M.D.[5] on May 16, 2022. Resp't. Ex. D (ECF No. 77). The undersigned held a second status conference on

[3] Dr. Lawrence Steinman is a board-certified neurologist and has practiced at Stanford University for over 40 years. Pet'r Ex. 99. He received his B.A. from Dartmouth College in 1968 and M.D. from Harvard University in 1973. *Id.* Thereafter, he completed an internship in surgery, residency in pediatrics, and residency in pediatric and adult neurology from Stanford University Hospital, as well as three fellowships. *Id.* Dr. Steinman is currently a professor at Stanford University and treats patients with GBS and CIDP. Pet'r Ex. 17 at 1. He has authored and co-authored over 500 publicans. *Id.* at 1; Pet'r Ex. 99; Tr. 58. His research has focused on the immune system attacking the nervous system. He has received the Charcot Prize and the John Dystel Prize for research in Multiple Sclerosis and the Cerami Prize for translational research. He is an elected member of the National Academy of Sciences and the National Academy of Medicine. Additionally, Dr. Steinman has experience testifying before the Vaccine Court. Based on his qualifications, Dr. Steinman was accepted as an expert in neurology and immunology. Tr. 69.

[4] Dr. Stephen McGeady is currently a Professor of Pediatrics at Jefferson Medical College in Philadelphia, PA. Resp't Ex. B at 1. He received his undergraduate degree from Fordham University in 1963 and his medical degree from Creighton University in 1967. *Id.* Dr. McGeady completed his internship at St. Vincent's Hospital and his residency in Pediatrics at St. Christopher's Hospital in Philadelphia. *Id.* He also had a fellowship in psychiatry and allergy at Duke University. *Id.* Dr. McGeady is board certified in pediatrics, allergy and immunology and laboratory immunology. *Id.* He began teaching at Jefferson Medical College in 1974 and became a Professor of Pediatrics at Jefferson Medical College in 2005. *Id.* Dr. McGeady is licensed to practice medicine in New Jersey, Pennsylvania, and Delaware. *Id.* Dr. McGeady has authored or co-authored approximately 70 peer reviewed medical articles in the field of allergy and immunology. Resp't Ex. C at 1. Based on his qualifications, Dr. McGeady was accepted as an expert in the field of immunology. Tr. 273.

[5] Dr. Peter Donofrio is currently a Professor Emeritus of Neurology at Vanderbilt University Medical Center. Resp't Ex. E at 1. Dr. Donofrio received his undergraduate degree from University of Notre Dame in 1972 and his medical degree from Ohio State University School of Medicine in 1975. Resp't Ex. E at 1. He completed an internal medicine residency in 1978 at Good Samaritan Hospital in Cincinnati, Ohio and his neurology residency at the University of Michigan Medical Center in 1981. *Id.* He is licensed to practice medicine in Ohio, Michigan, North Carolina, and Tennessee. *Id.* at 2. Additionally, Dr. Donofrio is board certified in internal medicine, psychiatry and neurology, electrodiagnostic medicine, and neuromuscular medicine. *Id.* at 1-2. Dr. Donofrio has treated patients with GBS, CIDP, and Miller-Fisher Syndrome. Additionally, Dr. Donofrio has published numerous

November 3, 2022, when respondent's counsel reported that Dr. Donofrio will replace Dr. Chaudry and stated that Dr. Donofrio had raised additional issues with petitioner's diagnosis that should be addressed by petitioner's neurologist. Scheduling Order (ECF No. 85). Petitioner was ordered to file a supplemental report and the parties were ordered to find a date for an entitlement hearing in July 2023.

Petitioner filed a supplemental expert report from Dr. Steinman and additional medical literature on December 29, 2022. Respondent filed a supplemental responsive expert report from Dr. Donofrio on March 14, 2023. An entitlement hearing was held on July 18-19, 2023, when petitioner, Dr. Steinman, Dr. Donofrio, and Dr. McGeady testified. Transcript ("Tr.") Volumes I-II.

Both parties filed post-hearing briefs. *See* Resp't Post-Hearing Brief ("Br.") (ECF No. 121); Pet'r Post-Hearing Br. (ECF No. 122). This matter is now ripe for adjudication.

II. Factual History

a. Summary of petitioner's medical records[6]

On March 31, 2017, petitioner went to his primary healthcare provider for a well adult exam and for his initial Medicare annual wellness exam. Pet'r. Ex. 2 at 7. Petitioner's review of systems indicated that he was positive for eczema at that appointment. *Id.* Petitioner's active diagnoses included stable coronary artery disease and hypertension. *Id.* He received the Prevnar-13 vaccine at this appointment. *Id.* at 11.

Twelve days later, on April 11, 2017, petitioner presented to the emergency department of CHS Union, complaining of a headache for 36 hours and generalized weakness. Pet'r Ex. 4 at 9. Petitioner reported that he was also experiencing nausea and vomited once. *Id.* Petitioner reported that his "hands and feet get cold, especially in the bottom of his feet and toes, [and] can't get them warm." *Id.* The patient was found to have balance difficulties in the emergency department. *Id.* Petitioner was evaluated by Dr. Thanh Truong who wrote that petitioner had a "completely normal neurological exam" and that petitioner's symptoms were "unlikely related to CVA or SAH."[7] *Id.* at 17. His assessment was that petitioner had "severe migraine with dehydration." *Id.* Petitioner was also examined by neurologist, Dr. Harsha Nagaraja. *Id.* at 30. Petitioner reported to Dr. Nagaraja that he had "noticed some numbness and tingling in his bilateral hands and feet." *Id.* Petitioner explained that "it comes and goes and when it comes on its sharp stabbing type sensations just in the palms and plantar aspects bilaterally." *Id.* Petitioner's physical exam revealed that he had 1+ reflexes through his upper extremities and 0 in his bilateral lower extremities. *Id.* at 33. Dr. Nagaraja wrote that petitioner's "neurologic

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medical articles and authored the textbook, "The Textbook of Peripheral Neuropathy," published in 2012. Resp't Ex. E at 1. Dr. Donofrio has testified before the Vaccine Court. Based on his credential, Dr. Donofrio was admitted as an expert in neurology. Tr. 181.

[6] I have identified the records that are most relevant to petitioner's vaccine injury claim and those are summarized below.

[7] CVS=Cerebrovascular accident, SAH-Subarachnoid hemorrhage

examination is otherwise non-focal *except for absent reflexes in the bilateral lower extremities*." *Id.* (emphasis added). Dr. Nagaraja also wrote, "If any symptoms of ataxia and paresthesias in his hands and feet come back, suggest spinal tap to rule out GBS given his examination is also significant for reduced reflexes in the bilateral lower extremities, which could also be from severe peripheral vascular disease versus lumbosacral spine disease." *Id.* Petitioner was discharged from the emergency room.

Petitioner returned to the emergency department on April 14, 2017 complaining of back pain. Pet'r Ex. 4 at 247. Petitioner reported that he was having numbness in the bottom of his feet bilaterally that preceded the back pain. *Id.* He was discharged home. Three days later, on April 16, 2017, petitioner returned to the emergency department, this time with lower back pain and numbness of the lower extremities, along with muscular weakness. *Id.* at 336. An MRI of his lumbar spine showed a "disc extrusion at L4-L5 results in moderate central canal stenosis and probably displaces the descending left L5 nerve root." Id. at 338. Petitioner was again discharged, this time with a diagnosis of possible disc herniation. *Id.*

Petitioner returned to the emergency department of CHS on April 19, 2017 with the inability to walk and extreme pain in his lower back. Pet'r Ex. 4 at 456. Petitioner reported that he has been unable to control his lower extremities. *Id.* The neurological examination indicated that petitioner had ataxia and that he had "no patellar reflexes or Achilles reflexes." *Id.* Further, petitioner had decreased sensation to vibration with no appreciable sensation to vibration in his bilateral feet with decrease to his right tibial prominence. *Id.* Dr. Andrew Wyman assessed petitioner with "weakness" and "acute kidney injury," and wrote, "Given his continued weakness, inability to transfer, and concern for other possible underlying etiology such as GBS or AIDP, I spoke with the hospitalist who accepted the patient for admission and continued evaluation." *Id.* at 457.

Upon admission, petitioner had a neurology consultation with Dr. Sarise Freiman. Pet'r Ex. 478. Petitioner reported to Dr. Freiman that he was unable to walk since he was discharged on April 17th and he has not had a bowel movement for a week. *Id.* At this time, petitioner was reporting numbness in both hands and slight weakness in his arms and hands, but that the weakness in his legs "are so severe that he can barely move them." *Id.* at 479. Dr. Freiman noted that petitioner was unable to walk. *Id. a*t 480. Petitioner was unable to resist gravity at hip flexion, he was numb below both knees and legs, vibration sensation was diminished in his toes and bilateral knees, and he was numb on the dorsal aspects of both hands. *Id.* at 481. Additionally, petitioner had absent knee and ankle reflexes bilaterally, absent triceps reflexes bilaterally, and his reflexes in his biceps supinator were "trace" bilaterally. *Id.* Dr. Freiman observed that petitioner's comprehensive metabolic panel from April 11, 2017 "was completely normal, including rental function. Then his free T4 and TSH were normal." *Id.* She also reviewed his multiple MRIs and wrote, "Although patient has moderate lumbar stenosis at L4-L5 and nerve root compression left L5 and right S1, and degenerative diseases in his right hip, *I do not believe his findings are all explained by the above."* *Id.* at 482 (emphasis added). "Guillain-Barre syndrome better known as acute inflammatory demyelinating polyneuropathy would best explain his clinical course." *Id.* Steroids were discontinued and a spinal tap was ordered. *Id.* at 483. However, after two unsuccessful spinal taps, petitioner was transferred to Carolinas Medical Center on April 21, 2017. Pet'r Ex. 5 at 4.

When petitioner was admitted to Carolinas Medical Center, he was evaluated by neurologist Dr. Thomas Stout on April 22, 2017. Pet'r Ex. 5 at 34. Dr. Stout wrote that petitioner was still complaining of numbness and tingling throughout his entire body, on the left side more than the right, and continued to have lower-extremity weakness. *Id.* Dr. Stout performed a neurological exam and wrote that petitioner had "absent deep tendon reflexes throughout," and "decreased sensation to light touch and pinprick throughout his extremities on the left greater than the right." *Id.* at 36. Dr. Stout's impression was, "suspect GBS," and recommended a repeat lumbar puncture and IVIG. *Id.* at 39. However, Dr. Stout wrote an addendum indicating that an attempt at another lumbar puncture was not necessary and to begin plasmapheresis instead of IVIG. *Id.* at 34.

Petitioner was also seen by nephrologist, Dr. John Dashiell while admitted to the hospital. Pet'r. Ex. 5 at 118. With Dr. Dashiell, petitioner reported that he "developed new distal leg weakness about one month after receiving Pneumovax vaccine. His weakness has progressively worsened and is now distal." *Id.* Petitioner's ALT and AST levels were reported as high, but were decreasing. *Id.* at 119.

Petitioner received five days of plasmapheresis and was discharged on April 28, 2017 to the Carolinas Healthcare System Rehabilitation Pineville Facility. Pet'r. Ex. 5 at 5; *see generally* Pet'r Ex. 6. Petitioner had multiple discharge diagnoses, but the primary one was "Guillain-Barre syndrome, status post-5 days of plasmapheresis." Pet'r. Ex. 5 at 5. The hospital discharge summary also indicated that petitioner was treated by pain management with bilateral steroid injections to control petitioner's pain associated with his L4-5 disc extrusion finding and multilevel lumbar spondylosis. *Id.* at 4. Petitioner had "steady improvement in this profound weakness and numbness," with the plasmapheresis. *Id.* at 5.

Upon admission at Pineville Rehabilitation, petitioner reported that he continued to have numbness in his bilateral arms, legs, and trunk. Pet'r Ex. 6 at 11. The numbness in his face had improved but he was having mild swallowing difficulty, which petitioner attributed to his "permacath." *Id.* His neurological examination on admission noted that he had decreased sensation to light touch and pinprick on all extremities and on his trunk. *Id.* at 13. Petitioner had absent deep tendon reflexes bilaterally in his biceps, triceps, patellar, and Achilles. *Id.* His strength exam showed decreased strength but equivalent on both sides. *Id.* The assessment stated, "Due to the patient's numbness and weakness, he has decreased ability to ambulate, perform mobility tasks, perform ADLs ("Activities of Daily Living") as compared to his baseline." *Id.* Petitioner was to received physical, speech, and occupational therapy for at least 3 hours a day, five days a week for approximately two weeks. *Id.* at 14.

On May 17, 2017, petitioner was re-evaluated by Dr. George Thomas. Pet'r Ex. 6 at 52. There was a note from the physical therapist at 8:00 AM that noted, "pain well controlled today reporting no pain during therapy. Pt functioning at a mod-i-supervision/SBA[8] level for ADL's and transfers overall with occasional modified techniques and assistive devices." *Id.* at 56. Petitioner was seen by a physical therapist again at 12:30 pm and wrote, "Pt has made excellent gains over course of therapy program. Pt has progressed from required [moderate assistance] for

[8] SBA-Standby Assist.

mobility to [contact guard assistance] with [rolling walker]. Patient has progressed strength, balance, ataxia, and safety. Patient has been ordered a [rolling walker] as a primary mode of mobility at [discharge]. Patient will benefit from skilled physical therapy to progress to [previous level of functioning] of independence and improve continued balance and strength deficits." *Id.* Dr. Thomas wrote that patient should continue a comprehensive rehabilitation program but could be cared for in a less intensive environment and that petitioner could be discharged the following day. *Id.* at 57. Petitioner was discharged from the rehabilitation facility on May 18, 2017, with his primary diagnoses being "low back pain" and "Guillain-Barré syndrome." *Id.* at 4. Petitioner was given a home health plan of care from May 19, 2017 to July 17, 2017. Pet'r. Ex. 7 at 2.

Petitioner had an appointment with Dr. Lester on May 26, 2017 for a follow-up from his hospitalization and rehabilitation admissions. Pet'r Ex. 2 at 2. Petitioner reported severe pain in his lower back and weakness in his lower legs. *Id.* He was also using a walker but had numbness in his legs. *Id.* Petitioner had weakness in his left-hand grip and his strength in his lower extremities was 4 out of 5. *Id.* at 5. His diagnoses were low back pain and Guillain-Barre syndrome. *Id.* at 6.

On June 26, 2017, petitioner had a follow-up with neurologist Dr. Nagaraja. Pet'r Ex. 11 at 3. The physical exam revealed that petitioner had 1+ reflexes in his upper extremities bilaterally and still absent in his bilateral lower extremities. *Id.* at 6. He had patchy sensation response to light touch and pinprick in his feet bilaterally. *Id.* Dr. Nagaraja ordered an EMG. *Id.* Additionally, Dr. Nagaraja wrote, "No objective evidence of GBS. He should have gotten better by now has been almost two months since onset of symptoms. Typically, this comes and goes within 4-6 weeks, particularly with him getting plasmapheresis which typically hastens recovery. I feel like his bilateral lower extremity pain is probably multifactorial potentially from neuropathy, however, also addition to severe lumbosacral spine disease from an extruded L4-5, as well as vascular disease." *Id.* On July 3, 2017, petitioner had an EMG/NCS. *Id.* at 23.

The EMG/NCS results were "an abnormal study," and found:

> [E]lectrophysiologic evidence of bilateral moderate median neuropathies at the wrist (i.e.carpal tunnel syndrome), bilateral on localized ulnar neuropathies, as well as a mixed mild demyelinating more than axonal mixed sensorimotor large-fiber length-dependent peripheral neuropathy on this examination. No obvious signs of a right lumbosacral radiculopathy were found.

Pet'r. Ex. 11 at 26.

On October 5, 2017, petitioner had an appointment at the Sanger Heart and Vascular Institute with Dr. Philip Iuliano. Pet'r. Ex. 11 at 35; *see also* Pet'r. Ex. 10 at 3. Dr. Iuliano wrote that petitioner had Guillain-Barre syndrome and that he was treated with plasmapheresis, went to rehab but had "very slow convalescence." Pet'r. Ex. 11 at 35. Petitioner reported that he still had some residual weakness and has "diffuse paresthesia." *Id.* Petitioner's diagnoses from this appointment included "coronary artery disease," that was classified as "stable and can be followed conservatively," and that petitioner was to remain on antiplatelet therapy. *Id.* at 39.

Petitioner's hypertension was stable and his "peripheral arterial occlusive disease status post-lower extremity stenting in April 2009" was "clinically stable without significant or limiting claudication." *Id.* Dr. Iuliano recommended increasing exercise and to continue on a statin. *Id.* at 40.

On September 13, 2017, petitioner presented to Southeast Pain & Spine Care for "pain: mid-back, both hands and feet." Pet'r. Ex. 10 at 20. Petitioner reported that he was "experiencing the same neuropathic pain in his upper and lower extremities unchanged from Guillain-Barre syndrome." *Id.* The medication change from Nucynta to an extended release version had improved pain relief in the extremities and the gabapentin was also reducing his pain moderately. *Id.* It was recommended that he continue the Nucynta ER for his neuropathic pain and his gabapentin for the neuropathic pain as well. *Id.* at 26.

Petitioner returned to Southeast Pain & Spine Care on November 15, 2017 for "generalized joint pain." Pet'r. Ex. 13 at 14. Petitioner reported using Gabapentin 800 mg three times a day. *Id.* Petitioner still had pain "into his lower extremities with numbness and tingling." *Id.* Additionally, the Nucynta ER was working well, but it was costing him a lot of money. *Id.* Petitioner was prescribed MS Contin 30 mg every 8 hours and to continue gabapentin three times a day. *Id.*

Petitioner had an appointment with Dr. Lester on May 23, 2018 for an annual Medicare exam. Pet'r. Ex. 10 at 2. Dr. Lester noted that petitioner was seeing Southeast Pain & Spine Care for "chronic neuropathic pain secondary to his GBS." *Id.* Petitioner reported that his pain was controlled with his current medication but still had "good days and bad [days]." *Id.* Petitioner's coronary artery disease was "stable without symptoms," and the note under the diagnosis of Guillain-Barré syndrome was "has follow-up with pain management." *Id.*

Petitioner went back to pain management on December 14, 2018 and then again on February 15, 2019. Pet'r. Ex. 16 at 28-31. At the February 15, 2019 appointment petitioner explained that the change to Lyrica for neuropathic pain was better at providing relief. *Id.* He reported having stiffness in his hands. *Id.* His Lyrica medication was refilled, along with Contin. *Id.* at 31.

At petitioner's Medicare annual exam with Dr. Lester on June 5, 2019, Dr. Lester noted that petitioner was still going to the pain clinic for neuropathic pain "related to his Guillain-Barre," and that petitioner was "now ambulating better without assistance." Pet'r. Ex. 16 at 42. Under comments, Dr. Lester wrote, "We discussed his Guillain-Barré and it appears that he received only a Prevnar vaccine prior to his Guillain-Barré starting. There is no evidence of receiving an influenza vaccine." *Id.* at 46.

On July 26, 2021, petitioner went to Atrium Health Union Pain Management for "chronic pain affecting his mid-back as well as pain into the lower extremities/feet secondary to neuropathy." Pet'r. Ex. 64 at 1. Petitioner described his pain as "aching, burning that can be throbbing or stabbing in nature with numbness and tingling that is usually increased with activity." *Id.* His assessment was degenerative disc disease (lumbar), lumbar spondylosis, and

thoracic spondylosis without myelopathy, and neuropathic pain. *Id.* at 2-3. He had his MS Contin refilled and prescribed Lyrica. *Id.*

Petitioner's wife contacted Dr. Lester on May 6, 2022, reporting that petitioner has been "vomiting a lot lately" and that "it seems like everything he eats makes him sick." Pet'r Ex. 68 at 104. Petitioner's wife reported that he had stopped eating late in the evening and he still vomits around 2 and 5 am. *Id.* Petitioner's wife requested that he be seen by neurologist, Dr. Nagaraja because the frequence of episodes of confusion during the middle of night, lasting 2-4 hours, and occurring about twice a week. *Id.* at 115. Petitioner was becoming disoriented, unable to walk, and was having increased arm/leg pain during episodes. *Id.* Petitioner's wife reported that these symptoms have "occurred since his diagnosis of Guillain-Barre syndrome about 5 years ago." *Id.*

Petitioner had an appointment with neurologist Dr. Shoba Jayaram on July 20, 2022. Pet'r Ex. 68 at 66. Dr. Jayaram wrote that after petitioner underwent PLEX treatments his symptoms improved and he had a "good prognosis except for the past one year." *Id.* Petitioner showed Dr. Jayaram videos where he would "freeze" and moan and mumble in pain. *Id.* He explained that he would begin to have pain all over his body, then cold chills, then freeze. He stated that he was unaware of his surroundings during these episodes and cannot walk or move during the episodes. *Id.* Dr. Jayaram wrote that petitioner is being treated by spine surgery and pain management services and uses Morphine as necessary and Lyrica TID. *Id.* Petitioner's strength was equal in his upper and lower extremities, his sensation to light touch, pinprick and vibrations were intact, and his reflexes were 2 out of 4 in his upper extremities and 3 out of 4 in his lower extremities. *Id.* at 67. Dr. Jayaram's impression was that petitioner's neuropathy could be due "to combination of GBS in 2017 as well as spondylosis which leads to radiculopathy. Patient has undergone MRI L-spine in the past. He has multilevel spondylosis and has seen spine surgeon in the past. He has brisk reflexes in the bilateral lower extremities which could be due to spondylosis." *Id.* at 68. Another EMG and lumbar puncture were ordered. *Id.*

Petitioner's EMG/NCS on August 10, 2022, showed carpal tunnel syndrome of the petitioner's right wrist and there was evidence of right ulnar neuropathy, primarily demyelinating type with axonal loss, localized electro-diagnostically across the elbow segment due to focal slowing. Pet'r Ex. 68 at 180. The EMG/NCS of petitioner's right lower extremity was normal and there was "no evidence of peripheral neuropathy or lumbosacral motor radiculopathy," and there was "no definite evidence of demyelinating peripheral neuropathy." *Id.* Petitioner's lumbar puncture showed that he had an elevated CSF protein. Pet'r Ex. 69 at 3.

Petitioner was hospitalized for pneumonia from August 29, 2022 to September 3, 2022. Pet'r Ex. 69 at 21. He completed antibiotics and had improvement in his symptoms. *Id.* Petitioner was diagnosed with hypertension, a vitamin B12 deficiency, a vitamin D deficiency, and a vitamin B6 deficiency. *Id.* at 27. Petitioner also continued to be treated by pain management for chronic low back pain, lumbar spondylosis, and a "history of GBS." *Id.* at 36-56; *see also* Pet'r Ex. 116 at 252. At a December 27, 2022 appointment with Dr. Lester, petitioner reported having "GBS-flare-ups that lasts three days before returning to normal." Pet'r Ex. 116 at 224. He also had a follow-up for his kidney function. *Id.* Dr. Lester wrote that he had

discussed with petitioner that "while his GBS has resolved, it may have caused these permanent issues. Discussed that we do not use chronic Guillain-Barre or Guillain-Barre flareups terminology. Nonetheless he is quite disabled from this." *Id.* Petitioner was diagnosed with "prediabetes," a vitamin B12 deficiency, dyslipidemia, stage 2 chronic kidney disease, and primary hypertension. *Id.* at 225.

That same day petitioner had an appointment with neurologist Dr. Jayaram. *Id.* at 211. After reviewing petitioner's EMG/NCS, Dr. Jayaram assessed petitioner with "History of Guillain-Barré syndrome," and wrote that petitioner has "flares of vomiting, shaking, excruciating pain, constipation, episodes last for almost 18 hours. He calls them a GBS flare….Discussed with him about IVIG and side effects. He wants to talk to his wife and let me know." *Id.* at 215. After speaking to his wife, petitioner's wife messaged Dr. Jayaram and indicated that petitioner would like to move forward with the IVIG infusions. *Id.* at 150. Dr. Jayaram ordered petitioner to receive IVIG infusions every four weeks. *Id.* at 99.

At an appointment with pain management on April 20, 2023, petitioner reported that he was receiving IVIG infusions every six weeks, and it was helping with his neuropathic pain. *Id.* at 7. On November 21, 2023, petitioner had a follow-up appointment with neurologist Dr. Jayaram. *Id.* at 295. At this appointment, Dr. Jayaram noted that petitioner had finished the IVIG infusions, he had been hospitalized in June for pneumonia, and his blood pressure was slightly elevated. *Id.* IVIG was stopped because his renal function was not at baseline. *Id.* at 296. Dr. Jayaram wrote that petitioner had gotten better with the IVIG treatments. He had no change in his reflexes in his upper and lower extremities since 2022 examinations. *Id.* at 298. Dr. Jayaram assessed petitioner with "history of GBS" and "acquired polyneuropathy," and noted that petitioner was "not having much of the neuropathy issues," and that IVIG was going to be on hold. *Id.* at 299. On August 11, 2023, Dr. Jayaram discontinued the IVIG infusions and wrote that infusion therapy was complete. Pet'r. Ex. 121 at 477.

b. Testimony of Mrs. Patricia Musick

Mrs. Patricia Musick, wife of petitioner testified during the hearing. Tr. 6-54. She and the petitioner have been married 28 years. Tr. 6. Ms. Musick testified that prior to the Prevnar-13 vaccine petitioner received in March 2017, he was active working in the garden and yard, and participating in horseshoe tournaments, along with fishing and walking. *Id.* at 7. He had small pains prior to the vaccination and the stents placed in his legs in 2009 for cardiac artery disease. *Id.* Mrs. Musick testified that after the stents were placed in his legs, his doctor recommended that he stop working as a drywall installer because the stilts that were buckled to his leg would cut off the circulation and it would cause a disruption in blood flow. *Id.* at 9.

After petitioner received the Prevnar vaccine on March 31, 2017, they had house guests who were present when he began to experience symptoms of his GBS. *Id.* at 11. Mrs. Musick stated that "a few days later, petitioner started complaining about having some tingling and numbness in his feet and his legs and fingers," but they did not do anything about it. *Id.* Mrs. Musick called petitioner's primary care physician after he had collapsed on the floor and "he didn't have any feelings in his legs, no movement, no feelings in his hands and arms, no movement." *Id.* at 12. She put him on an office chair and wheeled him to the Florida room

while she was on the phone with primary care physician's office. *Id.* Mrs. Musick testified that on April 10, 2017, she was getting ready to go to work and petitioner came to kiss her goodbye and then he just collapsed. *Id.* at 13.

The following day, on April 11, Mrs. Musick stated that petitioner was in a lot of pain and couldn't move his legs. *Id.* She stated that petitioner could not move his arms and he had no feelings in any of his extremities. *Id.* Mrs. Musick's friend assisted her in lifting petitioner into an office chair, wheeled him out to her SUV, and helped lift him into the car. *Id.* at 14. Petitioner was complaining about pain the lower part of his legs, his arms, and about back pain. *Id.* She testified that they ran a lot of tests and eventually sent petitioner home. *Id.* at 15. However, petitioner was unable to walk, and he was transported by wheelchair to the car. *Id.* They returned to the hospital three days later, on April 14th. *Id.* at 16. Petitioner was still unable to walk, and she and her friend used the same office chair to wheel him to the car. *Id.* Petitioner was held at the hospital for a few days and given a "cocktail of pain medication." *Id.* at 17.

During cross-examination, Mrs. Musick testified that when she first took petitioner to the emergency department on April 11th, he had a headache, generalized weakness and fatigue, and he also was complaining of a cold sensation in his hands and feet. *Id.* at 38. The second time Mrs. Musick took him to the emergency room, on April 14th, he had back pain, and pain in his legs and arms. *Id.* at 40-41. Mrs. Musick confirmed that the complaint of occasional numbness in the soles of his feet was accurate when he went back to the emergency room. *Id.* The third time petitioner was taken to the hospital by Mrs. Musick, on April 16th, she recalls petitioner still having numbness in his legs and arms, being unable to stand up on his legs, and some back pain. *Id.* at 42.

On the fourth time petitioner went to the emergency department, on April 19, 2017, petitioner was admitted to the hospital and then transferred to a hospital in Charlotte. *Id.* at 20. When he was transferred, Mrs. Musick stated that petitioner's symptoms were "numbness and tingling in his legs and feet," and that "they were paralyzed." *Id.* at 18. Petitioner was stuttering his speech and had some slight back pain. *Id.* Mrs. Musick testified that neurologist, Dr. Freiman indicated that "the symptoms all led to Guillain-Barre," and that he never had any other alternative diagnosis. *Id.* at 18, 21. She stated that, "Dr. Freiman is the one that said it looked like [petitioner] had an allergic reaction to this vaccine." *Id.* at 23.

After petitioner received plasmapheresis, he was transferred to Pineville Rehabilitation. He was there for two weeks. *Id.* at 23. Mrs. Musick characterized petitioner's rehabilitation as "extensive" and that he was doing thirty to forty minutes of physical therapy, then occupational therapy, and speech therapy. *Id.* at 24. When petitioner was transferred to Pineville, he was unable to use his arms and having problems swallowing. *Id.* at 23. She explained that they would get him to walk with a gait belt and go up and down stairs, and they showed him how to lay on the floor and get up off the floor. *Id.*

Mrs. Musick testified that at discharge, petitioner was able to walk, but "stumbling walking," and that his "gait was off." *Id.* at 25. Petitioner had to wear a gait belt at home and he continued to complain about tingling in his fingertips and arms. *Id.* at 25. He used a special fork

to feed himself given by the speech therapist. *Id.* Petitioner had in-home physical therapy because he was unable to walk without assistance. *Id.* at 26. Mrs. Musick described petitioner's gait as unsteady and weak. *Id.* With the in-home physical therapy petitioner progressed and was able to walk with a walker. *Id.*

After the in-home physical therapy was completed, petitioner's gait was "off and slow," according to Mrs. Musick. *Id.* at 27. He was still using a walker but could not walk long distances. *Id.* By July 2017, petitioner was able to walk with a cane but used the walker on occasion. *Id.* By September 2017, petitioner would use the cane occasionally while walking because he was still "stumbly." *Id.* at 28. On their anniversary on September 23, Mrs. Musick and petitioner went to a scenic overlook and walked about 500 feet from the car to the overlook, but after the short walk he was tired. *Id.* at 29. Mrs. Musick explained that petitioner would take smaller, careful steps. *Id.*

At the time of the hearing, Mrs. Musick testified that petitioner was still experiencing numbness and tingling in his legs and because of that he was unable to walk long distances. *Id.* at 31. Petitioner also had pain in his legs. *Id.* Mrs. Musick stated that petitioner had constant tingling in his finger and arms, along with pain, but does not have any issues using them. *Id.* However, he is unable to play his guitar because of his fingers going numb, which he used to do. *Id.*

III. Expert Opinions

1. Petitioner's Expert, Dr. Lawrence Steinman

a. Diagnosis

Petitioner's expert, Dr. Steinman opined that petitioner was correctly diagnosed with Guillain-Barré syndrome by the treating neurologists, Dr. Freiman and Dr. Nagaraja. Pet'r Ex. 98 at 2-3; Tr. 86. Dr. Steinman testified that GBS is "an inflammatory disease of the peripheral nerves." Tr. 70. The National Institute of Neurologic Disease and Stroke ("NINDS") Fact Sheet describes GBS as follows:

> The first symptoms of the disorder include varying degrees of weakness or tingling sensations in the legs. In many instances, the symmetrical weakness and abnormal sensations spread to the arms and upper body.

Pet'r Ex. 77 at 1; *see* Tr. 71. Additionally, the NIND fact sheet also states, "After the first clinical manifestations of the disease, the symptoms can progress over the course of hours, days, or weeks. Most people reach the stage of greatest weakness within the first 2 weeks after symptoms appear, and by the third week of the illness 90 percent of all patients are at their weakest." Pet'r Ex. 77 at 1.

In addition to the numbness and tingling and weakness, pain can also be a symptom of GBS. Tr. 71. The paper by Ropper and Shahani described how pain preceded weakness in some

patients with GBS and why the pain occurs in patients with GBS. Pet'r. Ex. 107.[9] Ropper and Shahani evaluated 29 patients presenting with symptoms of GBS, 16 of whom described the pain early in the illness as similar to muscle discomfort or discomfort one would experience after exercising vigorously or lifting heavy objects. *Id.* at 2. Low back pain at onset was also common. *Id.* Ropper found that, "Pain usually occurred in the most profoundly weak muscles in any individual patient…All but three patients with early pain went on to have severe generalized paralysis and were bedridden within one week." *Id.* at 3. Additionally, Ropper wrote, "Most of our patients experienced discomfort in large proximal muscles, including the lower part of the back, buttocks, quadriceps, and hamstrings." *Id.* at 3.

Dr. Steinman observed that when petitioner presented to the emergency department on April 11, 2017, he was complaining of many symptoms that are consistent with GBS. Tr. 72; Pet'r Ex. 98 at 2. Dr. Steinman stated that petitioner's symptoms of bilateral numbness and tingling in his hands and feet is "rather significant because GBS begins distally…in [the] toes and fingers, and it's known as an ascending paralysis." Tr. 73. Additionally, these symptoms were symmetric and bilateral with a widespread distribution, which would "rule out something like a lumbosacral disc, because that shouldn't affect the hands." *Id.* Further, the symmetry of the symptoms "makes it very much unlikely that it would be due to a structural impingement of nerve roots or peripheral nerve." *Id.* Dr. Steinman also stated that petitioner's diminished reflexes in his upper extremities and absent reflexes in his lower extremities bilaterally was also consistent with GBS. *Id.* at 75-6; *see also* Pet'r Ex. 4 at 33. He testified that "the strongest piece of objective evidence" to support a diagnosis of GBS was petitioner's absent reflexes bilaterally in the lower extremities. Tr. 76. Dr. Steinman observed that petitioner had also presented with balance difficulties which he opined is "contributable to Guillain-Barré." Tr. 79.

In his third expert report, Dr. Steinman explained when petitioner returned to the hospital for the fourth time on April 19, 2017, he had "now paralysis in the lower extremities," and had absent reflexes in his lower extremities. Pet'r Ex. 98 at 2; Pet'r Ex. 4 at 448. He testified that the motor examination given to petitioner by neurologist Dr. Sarise Freiman on April 20, 2017 was also consistent with GBS. Tr. 84. Specifically, petitioner's inability to resist gravity, only has a slight ability to put his legs together or spread them apart, he has numbness below the knees bilaterally, vibration sensation is diminished, and was hypersensitive to pinprick on his feet. *Id.* Dr. Steinman testified that the petitioner's absent deep tendon reflexes in his triceps, knees, and ankles and trace reflexes in his biceps and supraspinatus are consistent with GBS. *Id.* He stated, "…. between his deep tendon reflexes and his sensory exam and his distal motor weakness in his hands, it's very consistent with an inflammatory neuropathy as is seen in GBS." *Id.*

During the hearing, Dr. Steinman reviewed the Asbury and Willison papers, which provide diagnostic criteria for GBS. Tr. 141. Both Asbury and Willison explain that "Features needed for diagnosis of GBS in clinical practice," include, "1) progressive weakness in legs and arms; and 2) areflexia (or decreased tendon reflexes)." Resp't Ex. G-2 at 5[10]; Resp't Ex. G-1 at

[9] Ropper, A. & Shahani, B., *Pain in Guillain-Barre syndrome,* 41 Arch. Neurol. 511-14 (1984). [Pet'r. Ex. 107].
[10] Willison, H. et al., *Guillain-Barre Syndrome,* 388 The Lancet, http://dx.doi.org/10.1016/S0140-6736(16)00339-1 (2016). [Resp't. Ex. G-2].

1.[11] Asbury explains that weakness can range from "minimal weakness of the legs, with or without mild ataxia, to total paralysis of the muscles of all four extremities," and areflexia can include "distal areflexia with definite hyporeflexia of the biceps and knee jerks will suffice if other features are consistent." Resp't Ex. G-1 at 1. Further, both papers suggest that bladder or bowel disfunction at onset can "cast doubt on the diagnosis" of GBS. *Id.* at 2; Resp't Ex. G-2 at 5. Dr. Steinman noted that the Asbury articles explains that "transient bladder paralysis may occur during the evolution of symptoms," but that the sphincter is typically not affected. Tr. 142; *see also* Resp't Ex. G-1 at 2. Dr. Steinman testified that at least Asbury, suggests that urinary retention can occur and that it does not rule out a diagnosis of GBS. Tr. 141.

Comparing petitioner's symptoms to the criteria provided in the Asbury and Willison papers, Dr. Steinman testified that petitioner had progressive motor weakness of more than one limb and the weakness was symmetric. Tr. 144. Additionally, petitioner had areflexia in the lower extremities. *Id.* Petitioner's symptoms were symmetric, and he had mild sensory symptoms. *Id.* Further, the progression of petitioner's symptoms was also consistent with the progression of GBS described in the Asbury paper. *Id.*

Dr. Steinman agreed with Dr. Freiman's assessment that any lumbar spinal issues would not have explained all of petitioner's symptoms. Tr. 82-83; Pet'r Ex. 98 at 3. In his supplemental report, Dr. Steinman observed that Dr. Freiman acknowledged petitioner's lumbar stenosis and nerve root compression at the L4-L5 level, but wrote, "I do not believe these findings are all explained by the above. Guillain-Barre Syndrome better known as acute inflammatory demyelinating polyneuropathy would best explain his clinical course." Pet'r Ex. 98 at 3 (referencing Pet'r Ex. 4 at 490). Further evidence that petitioner's diagnosis was GBS, important to Dr. Steinman was that he was treated with plasmapheresis, which is one of two treatments available for GBS, the second being IVIG. Tr. 88.

Dr. Steinman testified that even without a confirming lumbar puncture, the diagnosis of GBS was made by petitioner's treating physicians. Tr. 94. He stated that petitioner had three unsuccessful lumbar punctures, and the treating physicians decided nevertheless to do a five-day course of plasmapheresis. Tr. 94. He stated, "The treating doctors, as well, as I, think that the diagnosis of GBS is correct." *Id.* at 95.

He also considered petitioner's EMG/NCS that was conducted on July 3, 2017, which was abnormal and found "a mixed mild demyelinating more than axonal mixed sensory motor large fiber length dependent peripheral neuropathy." Tr. 88; *see also* Pet'r Ex. 11 at 26. Dr. Steinman testified that these results are consistent with GBS. Tr. 88. He further explained that the specific findings of "latencies in the peroneal extensor digitorum brevis borderline peak latency slowing of the conduction velocities," "tibial edge has borderline low amplitude," and "common peroneal tibialis anterior had borderline low amplitude," suggest that there were abnormalities in petitioner's legs and arms. *Id.* at 89. Additionally, the EMG study did not show any evidence of lumbosacral radiculopathy because there was no slowing of the velocity of the F waves coming off the nerves in the lumbar spine. *Id.* at 90.

[11] Asbury, A. & Cornblath, D., *Assessment of Current Diagnostic Criteria for Guillain-Barre Syndrome*, 27 Ann. Neurol. S21-S24 (1990). [Resp't. Ex. G-1].

Dr. Steinman testified that even after treatment of GBS with plasmapheresis, patients can continue to have deficits. *Id.* at 92. He reviewed Dr. Nagaraja's comments that petitioner should have "gotten better by now," and stated that, "people who get GBS often have very good recoveries, but not uncommonly, they don't, and there's some residual which continues to bother them the rest of their life." *Id.* He disagreed with Dr. Nagaraja's opinion that petitioner should have "gotten better by now." *Id.*

Dr. Steinman contended that petitioner's elevated CPK level does not rule out GBS, as respondent's expert, Dr. Donofrio asserted. Tr. 95; Pet'r Ex. 98 at 6-8. Dr. Donofrio had opined that petitioner did not have GBS, but developed rhabdomyolysis with a CPK level "as high as 4260. Resp. Ex. E at 2. Dr. Steinman, again referencing the Ropper article, stated that elevated creatine kinase levels were found in 13 out of 16 GBS patients, who also experienced pain prior to the onset of weakness. Pet'r Ex. 98 at 5; Pet'r Ex. 107 at 2-3. Ropper observed that "serum [CPK] concentrations were elevated between 50%-700% above normal levels," in GBS patients that were experiencing pain before the onset of weakness. Pet'r Ex. 107 at 2. Further, Ropper noted that "earlier determinations tended to be higher in those with sequential testing, but in a few patients, CK levels remained elevated for six to 11 days after the onset of weakness." Ropper explained the connection of pain and elevated CPK levels, stating:

> The finding of elevated CK levels in most [GBS] patients with pain, but very few without pain, and the absence of consistent involvement of any particular portion or system of the peripheral nerves suggest that changes in muscle of neurogenic origin cause pain in GBS.

Id. at 4.

Dr. Steinman testified that the Ropper paper, along with a paper by Scott et al. suggests that elevated CPK levels and rhabdomyolysis is a manifestation of GBS, and not a separate disease entity that would explain petitioner's illness. Tr. 149-50; Pet'r. Ex. 98 at 9. Scott described a case report of a 25-year-old male with GBS who also presented with a markedly elevated CPK who was also found to have acute rhabdomyolysis. Pet'r. Ex. 108 at 1.[12] The article describes the patient's neurological examination:

> In the arms, there was profound weakness of intrinsic hand muscles and finger flexion, with mild weakness of wrist flexion and finger extension. There was flaccid weakness of the legs, complete on the right but for a flicker of hip flexion, with moderate proximal and mild distal weakness on the left. Tendon reflexes were normal in the arms, but absent in the legs. The left plantar was flexor and the right was mute. There was a sensory level to pinprick at T2 with impairment of vibration and light touch appreciation below the right knee.

Id. The patient in Scott had "markedly elevated" CK serum upon admission, but his EMG/NCS showed "severe demyelinating neuropathy affecting both proximal and distal segments of motor sensory nerves in all four limbs." *Id.* Even with treatment, the Scott patient had little initial

[12] Scott, A.J., *Acute rhabdomyolysis associated with Atypical Guillain-Barre Syndrome*, 67 Postgrad. Med. J., 73-74 (1991). [Pet'r. Ex. 108].

improvement and had residual symptoms for ten months, which included muscle weakness in both legs and arms. *Id.* at 2. Scott acknowledged that the cause of elevated CPK levels in early GBS and the mechanism "remains open to speculation," but that "modestly raised levels of CK (up to seven times the upper limit of normal) have been documented in the early stages of GBS, correlating with the occurrence of pain, which was a presenting symptom in this patient." *Id.* at 2. Scott concluded that, "raised levels of CPK can be a feature of the early course of GBS and may cause diagnostic confusion with other conditions." *Id.*

Dr. Steinman also referenced a case report by Statoh et al. which described a case report of a GBS patient with elevated CPK levels and rhabdomyolysis. Pet'r. Ex. 98 at 9; *see also* Pet'r. Ex. 110 at 1.[13] The GBS patient developed progressive generalized muscle weakness following a one-week episode of diarrhea. *Id.* The patient complained of a deep aching pain in his lower back and both legs, and he was unable to move his legs and arms. *Id.* Upon admission the patient's CPK level was normal, but then progressively increased. *Id.* This corresponded with the patients' complaints of intense cramping pain in the bilateral quadriceps, hamstrings, and upper arms. *Id.* The authors hypothesized that the cause of the elevated CPK values and the cramps was "rapid extensive denervation due to severe axonal degeneration of motor nerve terminals occurring most frequently in GBS with a preceding *c.jejuni* infection might cause hyperexcitability in regional muscles, leading to recurrent muscle cramps and the persistent release of muscular CK." *Id.* at 3.

Dr. Steinman also addressed Dr. Donofrio's assertion that petitioner may have developed statin induced rhabdomyolysis. Tr. 95. He testified, "I don't think the treating doctors would have put [petitioner] back on statins if he had statin rhabdomyolysis. There are other things they could have put him on to keep his cholesterol down besides Atorvastatin." *Id.*; Tr. 148.

b. Vaccine causation

i. *Althen* prong one

With respect to vaccine causation, Dr. Steinman opined that the Prevnar-13 vaccine petitioner received on March 31, 2017 caused him to develop GBS. Pet'r Exs. 17, 44, 98; Tr. 100. He proposed a theory of molecular mimicry as the mechanism to explain how the Prevnar-13 vaccine could cause GBS. Pet'r Ex. 17 at 24. In his first report, referencing the Prevnar-13 package insert, Dr. Steinman wrote, "Prevnar-13, Pneumococcal 13-valent Conjugate Vaccine…is a sterile suspension of saccharides of the capsular antigens of *streptococcus pneumonia serotypes* 1,3,4,5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F, individually linked to non-toxic diphtheria CRM197 protein." Pet'r Ex. 17 at 5. He opined that "there are two molecular mimics that are relevant to GBS in the composition of Prevnar-13, one from the phosphoglycerol link to the pneumococcal polysaccharide antigen, and the second from the CRM protein conjugate." *Id.* at 6.

[13] Satoh, J., *Cramping Pain and Prolonged Elevation of Serum Creatine Kinase Levels in a Patient with Guillain-Barre Syndrome following Campylobacter jejuni Enteritis*, 7 J. of Neurol., 10-109 (2000). [Pet'r. Ex. 110].

More specifically, Dr. Steinman opined that there is homology between the phosphoglycerol present in serotypes 18C and 23F in the Prevnar-13 vaccine and phospholipids in the human myelin sheath. *Id.* at 10-14. He also proposed that there is homology between CRM197 in the vaccine and contactin-1, a protein found in humans. *Id.* at 15. Additionally, Dr. Steinman opined that the adjuvant alum in the Prevnar-13 vaccine contributes to the development of inflammatory neuropathy. Pet'r Ex. 17 at 24.

A) Molecular Mimicry as a Theory for the Cause of Autoimmune Disease

Dr. Steinman explained that molecular mimicry is a theory to explain how "shared structures on a virus or bacteria or in a vaccine can trigger a cross-reactive response to self," which leads to an autoimmune disease. Pet'r Ex. 17 at 4. He wrote, "The mechanism is the immune cross-reaction due to homologies with antigens that are homologous mimics of the vaccine and that are targeted in these neuroinflammatory conditions." *Id.* at 22. Based on some of his own research, Dr. Steinman stated that "a viral peptide with homology at just 5 amino acids with a self-peptide can induce clinical signs of experimental autoimmune encephalomyelitis ("EAE") in mice," and that the "amino acids need not even be consecutive." *Id.* The Gautam et al.[14] article, on which Dr. Steinman is a named author, found that "very few amino acids need to interact with MHC class II molecules and with [T-cell receptors] to initiate specific responses in vivo resulting in autoimmune disease," and that "only four or five native residues in a peptide were able to induce [experimental autoimmune encephalopathy], it is conceivable that a pathogen with limited homology to self at few amino acid residues may trigger autoimmune disease." Pet'r Ex. 38 at 4.

B) Phosphoglycerol in the Prevnar-13 Vaccine

Dr. Steinman testified that the Prevnar-13 vaccine itself contains "glycerol attached to two of the sugars, 18C and 23F," which are components of the vaccine. Tr. 104. "The polysaccharides in Pneumococcus that are contained in Prevnar are complex and allow for the chemical attachment of polysaccharides via glycerol moieties known as phosphoglycerol and phosphocholine." Pet'r. Ex. 17 at 7.

Dr. Steinman reviewed the patent application for Prevnar-13 which stated that the glycerol phosphate side chains in the vaccine are necessary to for its immunogenicity. Pet'r Ex. 17 at 12; *see also* Pet'r Ex. 24.[15] The Prevnar-13 patent application explained, "An important consideration during conjugation is the development of conditions that permit the retention of potentially sensitive non-saccharide substitute functional groups of the individual components, such as 0-Acyl, phosphate or glycerol phosphate side chains that may form part of the saccharide epitope." Pet'r. Ex. 17 at 10; *see also* Pet'r. Ex. 24 at 34.

[14] Gautam, A. et al., *A Polyalanine Peptide with Only Five Native Myelin Basic Protein Residues Induces Autoimmune Encephalomyelitis,* 176 J. Exp. Med. 605-09 (1992). [Pet'r Ex. 38].

[15] The patent is filed as Petitioner's Exhibit 24. 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.

This statement was verified by the Chang et al. study, which also demonstrated that the glycerol phosphate side chains are important to retain immunogenicity and effectiveness of the Prevnar-13 vaccine. Tr. 108; Pet'r Ex. 30.[16] The authors identified the 18C serotype structure as "a branched pentasaccharide with two apparently labile substituents: glycerol-phosphate and O-acetyl group." Pet'r Ex. 30 at 1. Both the Prevnar-13 patent and Chang confirmed to Dr. Steinman that the "phosphate head group on the glycerophosphate is a central component of the 18C polysaccharide structure," and the immune response is to the phosphoglycerol. Tr. 110.

Additionally, Dr. Steinman referenced the Bryson et al. article which demonstrated the human antibody response to the phosphate group of 23F (polysaccharide). Tr. 113. Bryson studied the antibody response to 23F in the Pneumovax vaccine, which is an antigen contained in the Prevnar-13 vaccine. Pet'r Ex. 60.[17] According to Dr. Steinman, Bryson shows phosphoglycerol is directly targeted by two antibodies targeting the 23F polysaccharide and that the phosphoglycerol in the 23F serotype is critical for the human response to serotype 23F. Pet'r Ex. 55 at 11; Tr. 111. Dr. Steinman agreed that the immune response is not only directed to the phosphate group of 18C or 23F, but also directed to the pentasaccharides or sugar components of the vaccine. Tr. 111. However, he emphasized that if the phosphoglycerol group is removed, there will be no immune response. *Id.* He explained that this multi-faceted immune response gives us the highly specific immunity to all of those different components." *Id.* at 112.

Then Dr. Steinman explained that phospholipids are components in the myelin sheath, which are targeted by antibodies, resulting in GBS. Pet'r Ex. 17 at 9-10; Tr. 103. To support this part of his opinion, Dr. Steinman referenced the article by Ho et al., on which he is a senior author. Pet'r. Ex. 28.[18] The authors found that in multiple sclerosis patients, autoantibodies target the polar head group in phosphoglycerol and phosphocholine found in the central nervous system myelin. Pet'r. Ex. 28 at 1; Tr. 104-05. The article explained that "lipids constitute 70% of the myelin sheath, and autoantibodies may contribute to the demyelination that characterizes MS." *Id.* The authors examined the lipid structures and found that "six of the seven targeted lipids had a phosphate group," and that antibodies in MS patients target the phosphoglycerol moiety of phospholipids, independent of the fatty acid side chains which are bound to the phosphoglycerol. *Id.* at 3. Ho et al. found that "myelin phospholipids are targeted by autoimmune responses in MS." *Id.* at 9. During the hearing, Dr. Steinman explained that while GBS is a disease of the peripheral nervous system and MS is a central nervous system disease, the structure of the phospholipids in the myelin sheath in both the central and peripheral nervous systems are similar. Tr. 106.

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[16] Chang, J. et al., *Relevance of O-acetyl and phosphoglycerol groups for the Antigenicity of Streptococcus Pneumoniae serotype 18C Capsular Polysaccharide*, 30 Vaccine 7090-7096 (2012). [Pet'r Ex. 30].

[17] Bryson, S. 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 Immunol 4723-4730 (2016). [Pet'r Ex. 60].

[18] Ho, P. et al, *Identification of Naturally Occurring Fatty Acids of the Myelin Sheath that Resolve Neuroinflammation*, 4 Sci. Transl. Med. (2012). [Pet'r Ex. 28].

To further elaborate on the role of anti-phospholipid antibodies in demyelinating diseases, Dr. Steinman referenced the Nakos et al. article, which found anti-phospholipid antibodies in GBS patients. Pet'r. Ex. 26.[19] Nakos examined the serum of nine GBS patients and found that all nine "developed anti-phospholipid antibodies directed against at least one lipid during the course of their disease," while no similar antibodies were discovered in the controls. *Id.* at 11. Dr. Steinman testified that the antibodies made to the phospholipids had a higher level, even early in the disease course, than antibodies to ganglioside. Tr. 103. Nakos makes the point that antibodies to gangliosides have been well studied, but that only 15-20% of patients with GBS develop anti-gangliosidic antibodies. Pet'r. Ex. 26 at 1. Dr. Steinman testified that "the fact that the antibodies to the phospholipids were higher than the antibodies to ganglioside," shows that gangliosides are not the only target in GBS. Tr. 103. The Nakos paper concluded, "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." Pet. Ex. 26 at 6.

Dr. McGeady asserted that this part of Dr. Steinman's theory was "unlikely to be valid," because of the prevalence of phosphocholine in the body and that an antibody to phosphocholine would be unlikely to have such a focused target in the peripheral nervous system. Res. Ex. C at 3. Using the example of the Aquaporin-4 ("AQP-4") water channel, which is expressed in both the kidneys and nervous system, Dr. Steinman explained how the targeting of the aquaporin-4 antigen causes neuromyelitis optica but does not affect kidney function. Pet'r. Ex. 55 at 7; Tr. 135. He stated that the AQP-4 is the "main antigen associated with neuromyelitis optica" but kidney function is normal in patients with NMO. *Id.* at 8; Tr. 135. The Nakos paper makes a similar observation, stating that, "anti-phospholipid antibodies were expressed in a patients with lupus like syndrome who developed secondary GBS," and, "It is thought that whenever polyneuropathy occurs in the context of autoimmune disease, mainly in systemic lupus, where anti-phospholipid activity already exists, these antibodies can cross-react with phospholipids and mediate damage in neural structures containing *particular* phospholipids." Pet'r. Ex. 26 at 6 (emphasis added). In the patients that Nakos studied, their primary disease was GBS as none of the patients suffered from any other kind of autoimmune disease, nor did any clinical or laboratory findings indicate anti-phospholipid syndrome. *Id.* at 6. These examples demonstrate that antibodies can target structures that may exist in multiple parts of the biological system which results in different diseases, contradicting Dr. McGeady's assertion that phosphocholine is too widespread to be a specific target of antibodies generated to the phosphoglycerol structures of the Prevnar-13 vaccine.

In summary, this component of Dr. Steinman's theory is based on molecular mimicry, between the phosphoglycerol component in the Prevnar-13 vaccine and the phosphate containing polar head groups in the peripheral nerve myelin. He opined that antibodies developed to the necessary phosphoglycerol components of the Prevnar-13 interact with the phosphoglycerol components in the myelin of the peripheral nerves, triggering GBS. Tr 106; Pet. Ex. 17 at 15.

C) Molecular Mimicry with CRM-197

[19] Nakos, G., *Anti-phospholipid Antibodies in Serum from Patients with Guillain-Barre Syndrome,* 31 Intensive Care Med. 1401-1408 (2005). [Pet'r. Ex. 26].

Dr. Steinman also examined the role of the CRM-197 conjugate in the vaccine as a possible source of cross-reactivity through molecular mimicry with other components of the peripheral nerves, such as Contactin-1, which are known to be attacked in GBS. Pet'r Ex. 17; Tr. 113-14. CRM-197 is the "nontoxic form of diphtheria toxin" to which the polysaccharide antigens are conjugated. Pet'r. Ex. 17 at 15; Tr. 113. According to the Prevnar-13 patent, "The CRM-197 protein is a nontoxic form of diphtheria toxin but is immunologically indistinguishable from the diphtheria toxin….The CRM-197 protein has the same molecular weight as the diphtheria toxin but differs therefrom by a single base change in the structural gene. This single base change…eliminates the toxic properties of diphtheria toxin. The CRM-197 protein is a safe and effective T-cell dependent carrier for saccharides." Pet'r. Ex. 24 at 21. Dr. Steinman opined that the CRM-197 protein contains peptides also found in contactin-1, which is found in the nodal and paranodal area of the peripheral nerves and is among proteins that are known targets of an immune response in both CIDP and GBS. Tr. 114.

To determine if there was homology between CRM-197 and protein components in the peripheral nerves such as contactin-1, Dr. Steinman used a BLAST search to identify similar amino acid sequences. Pet'r. Ex. 17 at 15. In his search, he found an amino acid sequence that has "five of ten identical amino acids," which might be capable of inducing neuroinflammatory disease. *Id.* at 20. One sequence he identified, "WEQAKALSVE" was an epitope in the diphtheria toxin, which provided the basis for CRM-197. *Id.* at 21. Dr. Steinman testified that this sequence "had five identical amino acids out of ten, shared between contactin-1 and CRM-197." Tr. 118. The level of homology satisfied the Gautam criteria for inducing neuroinflammation. Pet'r Ex. 17 at 17.

Then Dr. Steinman performed a search of the Immune Epitope Database ("IEDB") to determine if the mimics between CRM-197 and contactin-1 has been described in humans. Pet'r Ex. 17 at 20; Tr. 165. According to his search of the IEDB, "humans do respond" to the sequence WEQAKALSVE, and that part of it is an epitope in diphtheria toxin, which provides the basis for CRM-197. Pet'r Ex. 17 at 21; Tr. 116. The IEDB search led Dr. Steinman to the paper by Raju et al.[20], which examined CD-4 cell response to different sequences of the diphtheria toxin. Dr. Steinman stated that Raju showed that "the second strongest immune response in humans [to the different regions of the diphtheria sequence] was to the region that contained the WEQ et cetera sequence." *Id.* at 116-19.

Dr. Steinman testified that the peripheral nerves are myelinated by Schwann cells and at "every interval there's an area where there's no longer myelin, and the electrical current jumps from one node to the next." Tr. 124. He stated that the nodes of Ranvier, which contain contactin-1, are targeted by auto-antibodies in CIDP and GBS. Pet'r Ex. 55 at 5; Tr. 116. Dr. Steinman referenced an article by Mirua et al. which found anti-contactin-1 antibodies present in 16 patients with chronic inflammatory demyelinating polyneuropathy ("CIDP") and in 5 patients with GBS. Pet'r Ex. 37 at 1-2.[21] In the five GBS patients, the researchers found that IgG1 and

[20] Raju, R. et al., *Epitopes for Human CD4+ Cells on Diphtheria Toxin: Structural Features of Sequence Segments Forming Epitopes Recognized by Most Subjects,* 25 Eur. J. Immunol. 3207-3214 (1995). [Pet'r Ex. 119].

[21] Miura, Y. et al., *Contactin-I IgG4 Associates to Chronic Inflammatory Demyelinating Polyneuropathy with Sensory Ataxia,* 138 Brain 1484-91 (2015). [Pet'r Ex. 37].

IgG2 subclasses were present at significant levels. *Id.* at 5. Miura stated, "we showed that some of the patients with CIDP present IgG autoantibodies directed against the nodes of Ranvier or the paranodal or axo-glial apparatus. Notably, we identified Contactin 1 ("CNTN1") as [one of] the targets of autoantibodies in some patients with CIDP. *Id.* at 2.

Dr. Steinman summarized this part of his theory as a second potential cross-reactivity between the Prevnar vaccine and the peripheral nervous system. Pet'r Ex. 17 at 15-23; Pet'r Ex. 55 at 13; Tr. 125. He stated that the immune reaction to the protein components of the vaccine, CRM-197, which are used to conjugate the pneumococcal polysaccharides, are highly immunogenic and have been shown to cross react with the nodes of Ranvier that are targeted in GBS and CIDP. Based on the criteria established by Gautam, where only five out of twelve identical amino acids were identified as sufficient to trigger an autoinflammatory disease, the sequence identified between contactin-1 and CRM-197, which showed five identical amino acids out of ten, is sufficient to induce GBS. Dr. Steinman stated that this part of the theory may be complementary of the phosphoglycerol theory but also provides a separate basis to explain the development of GBS secondary to the immune response to the Prevnar vaccine. *See* Pet'r Ex. 55 at 7.

D) Alum in Prevnar-13

In Dr. Steinman's two reports which focused on causation, and during the hearing, he explained that the Prevnar-13 vaccine includes alum as an adjuvant, which is included to make a vaccine more immunogenic. Pet'r Ex. 55 at 7; Tr. 125. He testified that the alum "enhances" the cytokine response to the vaccine and is complementary to the other parts of his theory for how the Prevnar-13 can cause GBS. Tr. 126. Dr. Steinman stated that the alum in Prevnar can cause an elevation of IL-18, an inflammatory cytokine, and IL-18 is elevated in GBS patients, which contributes to the pathogenesis of GBS. *Id.*; *see also* Pet'r Ex. 17 at 23.

He referenced the paper by Eisenbarth et al. which explained that the alum activates an intracellular innate immune response system called the Nalp3 inflammasome, which regulates the cleavage and release of the potent pro-inflammatory cytokines IL-1β, IL-18, and IL-33. Pet'r Ex. 43 at 1.[22] Additionally, Eisenbarth explained why alum is an effective adjuvant, the fact that:

> …alum must be encountered simultaneously with [an] antigen *in vivo* for efficient priming suggests that the antigen might provide the first signal either directly, or indirectly by inciting the production of local pro-inflammatory cytokines from resident monocytes or specialized cells recruited by alum. Once the first signal has primed the cell, alum provides the second signal for activation of the Nalp3 inflammasome. These two stimuli must be sensed by the same cell for effective immune activation, thereby increasing the specificity of an immune response and perhaps explaining why alum (which readily adsorbs antigens) is such an effective adjuvant.

[22] Eisenbarth, S. et al., *Crucial Role for the Nalp3 Inflammasome in the Immunostimulatory Properties of Aluminum Adjuvants*, 453 Nature 1122-1127 (2008). [Pet'r Ex. 43].

Id. at 4. Eisenbarth further explained that the Nalp3 inflammasome regulates the cleavage and release of pro-inflammatory cytokines interleukins IL-1β, IL-18 and IL-33. *Id.* at 1.

The Jander paper Dr. Steinman referenced found that the inflammatory cytokine IL-18 is elevated in individuals with GBS. Tr. 127-28; Pet'r Ex. 17 at 22. Jander examined the nerve roots of EAN rats and found IL-18 and caspase-1 levels increased during the stage of active disease progression. Pet'r Ex. 48 at 1[23]; Tr. 128. Jander found a similar result in the CSF of GBS patients, where IL-18 was increased. *Id.* at 5. He added that the Yu et al. paper found that introducing an anti-IL18 antibody can ameliorate experimental autoimmune neuritis and led the researchers to conclude that "…endogenous IL-18 plays a critical role in the pathogenesis of autoimmune demyelinating disease of the peripheral nervous system and that IL-18 antagonists may provide a new therapy for those diseases." Pet'r Ex. 49 at 1.[24] Dr. Steinman opined that "these papers on the role of alum in GBS, based on human and animal studies, constitute a strong scientific foundation for providing a basis for how the alum in the Prevar-13 vaccine containing alum as an adjuvant would lead to an increase in pro-inflammatory cytokines like IL-18, and thus could induce inflammatory polyneuropathy." Pet'r. Ex. 17 at 23. He testified, "It's simple logic. alum in humans increases IL-18. [Petitioner] got a vaccine with alum in it…to increase his response to the components of Prevnar, and alum is known to increase IL-18 when combined with antigens found in vaccines. IL-18 is known to be elevated in GBS. And then in the animal model, you give an antibody to IL-18 and it makes the animals better." Tr. 129.

ii. *Althen* prong two

Dr. Steinman opined that there was a logical sequence of cause and effect between the Prevnar-13 vaccine and GBS to satisfy *Althen* prong two. Based on his two theories of molecular mimicry to show how the Prevnar vaccine could cause GBS, petitioner had no other condition prior to the onset of his GBS that could be the cause of the GBS, and the onset of GBS was 12 days post-vaccination, Dr. Steinman stated that it makes it is "more likely that the vaccine was the cause of the GBS." Pet'r. Ex. 17 at 15, 25.

During the hearing, Dr. Steinman referenced the case report by El Khatib et al. which described a case of a 13-year-old male who developed GBS after having *s. pneumonia,* to demonstrate that GBS can occur after a pneumococcal infection. Pet'r Ex. 70[25]; Tr. 131. The authors of the case report wrote, "GBS is an important cause of acute flaccid paralysis, due to a triggering factor infectious (like mainly campylobacter, CMV, EBV, mycoplasma pneumoniae, influenza-like illness), and non-infectious (like immunization, trauma, surgery, and bone marrow transplant). This triggering factor evokes an immune response that cross-reacts with peripheral

[23] Jander, S, & Stoll, G., *Interleukin-18 Is Induced in Acute Inflammatory Demyelinating Polyneuropathy,* 114 J. of Neuro. Immunol. 253-258 (2001). [Pet'r Ex. 48].

[24] Yu, S. et al., *Neutralizing Antibodies to IL-18 Ameliorate Experimental Autoimmune Neuritis by Counter-Regulation of Autoreactive TH1 Responses to Peripheral Myelin Antigen,* 61 J. of Neuropath. and Exper. Neurol. 614-622 (2002). [Pet'r Ex. 49].

[25] El Khatib, H. et al., *Case Report: Guillain-Barre Syndrome with Pneumococcus-A New Association in Pediatrics,* 11 IDCases 36-28 (2018). [Pet'r. Ex. 70].

nerve components because of the sharing of cross-reactive epitopes (molecular mimicry), this immune response is directed toward the myelin or axon of the peripheral nerve." Pet'r. Ex. 70 at 2. Further, the authors state, "It is possible therefore that pneumococcus has antigens which triggered an immune response and cross-reacted with peripheral nervous system surface components due to molecular mimicry. This is due to natural transformation of *streptococcus pneumoniae's* capsular polysaccharide." *Id.*

Dr. Steinman also referenced a case report by Ravishankar which described a woman developing GBS after receiving a pneumococcal-23 vaccine to demonstrate how GBS can occur after either a wild pneumococcal infection or vaccination for pneumococcus. Tr. 132; Pet'r Ex. 71 at 1.[26] Ravishankar reported that a 66-year-old female received a PCV-13 vaccine in January 2015 and a PPSV-23 vaccine in August 2015, and began to develop GBS symptoms in September 2015. Pet'r. Ex. 71 at 1. The woman developed a mixed axonal and demyelinating sensorimotor polyradiculopathy and eventually suffered respiratory failure. *Id.* Ravishankar wrote, "GBS is commonly linked to different infections, particularly *c.jejuni* enteritis, however, unwanted autoimmunity does not arise in most individuals exposed to *c.jejuni*. The major mechanism resulting in the autoimmunity by adjuvant vaccinations has been proposed to be due to the epitopes of a vaccine that initiates the development of antibodies and/or T cells that could cross-react with epitopes on myelin or axonal glycoproteins." *Id.* at 1-2. Ravishankar differentiated the immune response to the plain polysaccharide vaccines (pneumococcal 23) from the polysaccharide vaccine conjugated to the carrier protein (Prevnar-13). *Id.* at 2. The article states that "the plain polysaccharide vaccines are T-cell independent antigens that cross-link B-cell receptors inducing immediate differentiation to plasma cells then antibodies," while the conjugated vaccine (Prevnar-13):

> … elicits a T-cell dependent response. The polysaccharide conjugated to a carrier protein uses a MHC class II dependent responses to present the carrier protein to carrier specific helper T cells. This leads to enhancement of the B-cell immune response, so that the antibody response is of greater specificity and functionality…Thus, it can be inferred that the conjugated vaccine produces the enhanced B-cell immune response leading to autoimmune reaction to the peripheral nerves.

Id.

Addressing Dr. McGeady's argument that there are numerous molecular mimics between viruses and human tissue is "common place" as described by Kanduc et al.[27], and that if molecular mimicry was an actual cause of autoimmune disease, they would be more prevalent, Dr. Steinman testified that there are "strong counter-regulatory mechanisms that would mitigate that from happening." Tr. 130, 137. He explained that for those who are infected with *c.jejuni*, where molecular mimicry has been successfully demonstrated in humans between glycoproteins and *c.jejuni*, only a small subset of people develop GBS. Tr. 135. Dr. Steinman testified that Kanduc's findings that there is "so much molecular mimicry going on" is not surprising, but that

[26] Ravishankar, N., *Guillain-Barré Syndrome Following PCV Vaccine,* 4 J. Neurol. Neurosurg. http://dx.doi.org/10.19104/jnn.2017.34 (2017). [Pet'r Ex. 71].

[27] Kanduc, D. et al., *Massive Peptide Sharing Between Viral and Human Proteomes,* 29 Peptides 1755-1766 (2008). [Resp't Ex. C, Tab 6].

"there's fortunately a lot of mechanisms to suppress unwanted immune response to self." Tr. 137. Dr. Steinman stated that petitioner had no prior condition that could explain the onset of his GBS, which occurred 12 days post-vaccination, the most probable explanation for the development of petitioner's GBS was the immune response to the Prevnar-13 vaccine.

iii) Althen prong three

With respect to *Althen* prong three, Dr. Steinman opined that petitioner developed GBS approximately twelve days after he received the Prevnar-13 vaccine. Pet'r Ex. 17 at 25; Pet'r Ex. 98 at 10. Using the frequently referenced article by Schonberger et al. as a surrogate to demonstrate an appropriate temporal relationship between the Prevnar-13 vaccine and GBS, Dr. Steinman wrote, "the 1976 swine flu studies of the relationship between vaccination and GBS would make this a reasonable temporal interval," between vaccination and the onset of GBS symptoms. Pet'r Ex. 17 at 25; Tr. 138; Pet'r Ex. 52[28]. Dr. Steinman also testified that the Haber et al. article, referenced by respondent's experts, identified 11 cases of GBS within forty-two days of Prevnar-13 vaccination. Tr. 138; Resp't Ex. E, Tab 6.[29] Haber found that the median onset interval of symptoms was 9 days, with the range being 2-34 days. Resp't Ex. E, Tab 6 at 4. Dr. Steinman acknowledged that the paper did not identify a "danger signal," but the paper still identified these cases of GBS in the same timeframe as in the Schonberger paper. Tr. 139. Dr. Steinman testified that the timing of symptom onset in the petitioner post-Prevnar-13 vaccination was "correct" based on Schonberger and Haber. Tr. 139.

2. Respondent's Experts' Opinions Regarding Diagnosis and Vaccine Causation

Respondent presented the opinion of two, Drs. McGeady and Peter D. Donofrio who testified at the entitlement hearing in this matter.[30]

a. Dr. Peter Donofrio's Opinion

i. Dr. Donofrio's Opinion on Petitioner's Diagnosis

Dr. Donofrio opined that petitioner did not have GBS, consistent with Dr. Vinay Chaudhry's opinion. Resp't. Ex. A at 14; Resp't. Ex. E at 7; Resp't. Ex. G at 3; Tr. 182. Dr. Donofrio wrote, "many of the features of this case from the beginning are not commonly observed in GBS." *Id.* at 2. Dr. Chaudhry suggested an array of conditions that would not

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[28] Schonberger, L., et al., *Guillain-Barre Syndrome Following Vaccination in the National Influenza Immunization Program, United States 1976-1977*, 110 Am J. Epidemiology 105 (1979). [Pet'r. Ex. 52].

[29] Haber, P. et al., *Post-Licensure Surveillance of the 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,* 24 Vaccine 6330-334 (2016). [Resp't Ex. E, Tab 6].

[30] Initially, Dr. Vinay Chaudhry had provided his opinion in this matter, but accepted a new position and was unable to testify at the entitlement hearing. Dr. Donofrio endorsed Dr. Chaudhry's opinion. I have considered Dr. Chaudhry's initial expert report and given Dr. Donofrio's acceptance of Dr. Chaudhry's opinion, I will incorporate relevant parts of Dr. Chaudhry's expert report as necessary.

implicate the Prevnar-13 vaccine to explain the petitioner's symptoms, including a migraine condition, rhabdomyolysis, acute renal failure, spinal stenosis, and/or marijuana use. Resp't. Ex. A at 16-17. Dr. Donofrio, mostly agreed with Dr. Chaudhry's many assertions of possible other conditions that could have caused petitioner's symptoms, but mostly focused on the possibility that petitioner may have had acute rhabdomyolysis, which would be associated with muscle weakness. Resp't. Ex. E at 7.

Dr. Donofrio testified that when he diagnoses a patient with GBS, he first goes through the patient's history and does a physical examination. Tr. 186. He stated that GBS often "begins with numbness in the feet and hands. It slowly ascends to the arms and legs and is associated with weakness in four extremities." *Id.* He acknowledged that pain can be present. *Id.* Dr. Donofrio also testified that on examination he would expect "to see weakness in four limbs and most commonly areflexia which is a complete loss of reflexes or at least hyperreflexia in an arm and leg that may disappear over several days." Tr. 187. Dr. Donofrio testified that for someone to be diagnosed with GBS they must meet the criteria established in the Asbury-Cornblath and Willison articles. *Id.* The Asbury-Cornblath GBS diagnostic criteria, to which Dr. Steinman also referred , provides that to make a diagnosis of GBS a patient must have:

> A) progressive motor weakness of more than one limb. The degree ranges from minimal weakness of the legs, with or without ataxia, to total paralysis of the muscles of all four extremities and the trunk, bulbar, and facial paralysis, and external ophthalmoplegia; and B) Areflexia (loss of tendon jerks). Universal areflexia is the rule, though distal areflexia with definite hyporeflexia of the biceps and knee jerks will suffice if other features are consistent.

Resp't Ex. G-1 at 1.

Dr. Donofrio first argued that petitioner did not present with weakness consistent with the Asbury-Cornblath GBS criteria. Tr. 183; Resp't. Ex. E at 2. He asserted that when petitioner initially presented to the emergency department on April 11, 2017, he complained of "headache and generalized weakness," but that the neurological exam the following day, by Dr. Nagaraja, showed that petitioner had "5/5 strength throughout." Tr. 183; Pet'r Ex. 4 at 33. The examination also showed that petitioner had absent reflexes in the lower extremities and recorded as 1+ in the upper extremities and his sensation to light touch, pinprick, and vibration were intact. Pet'r Ex. 4 at 33. Dr. Donofrio testified that a diagnosis of GBS is accompanied by "four-extremity weakness and either areflexia or hyperreflexia in the arms and legs," and that the examination by Dr. Nagaraja showed petitioner had normal strength on April 12th. Tr. 186. He also argued that the examinations from April 14th and 17th also demonstrated that petitioner had normal strength, despite the petitioner's chief complaint to emergency room physicians being that he "can't stand on his legs," and petitioner stating that he has had "bilateral lower extremity weakness, difficulty ambulating *secondary to weakness.*" Tr. 212; *see also* Pet'r Ex. 4 at 339 (emphasis added). Dr. Donofrio acknowledged that the neurological exam on April 19, 2017 where petitioner demonstrated "proximal weakness" in all four limbs would be consistent with the Asbury-Cornblath criteria, however, he stated that distal weakness is usually greater than proximal weakness. Tr. 213.

Dr. Donofrio also argued that petitioner's strength documented on April 29, 2017, was documented as "essentially normal" and that his quick recovery of strength is inconsistent with GBS. Tr. 214. However, Dr. Donofrio acknowledged that in later exams, including when petitioner was in the rehabilitation facility, petitioner had weakness and numbness in his arms, legs, and trunk, and "struggled to explain" why those symptoms would be continuing. Tr. 215. Dr. Donofrio was asked to review petitioner's physical therapy evaluation from May 2, 2017, which included the following strength examination:

MUSCULOSKELETAL: No calf tenderness, full active ROM

Strength Exam

	Right	Left
Shoulder abduction	4	3
Elbow flexion	4	4
Elbow extension	4+	4+
Wrist extension	4	4
Finger abduction	4	4
Hip flexion	3	3
Knee flexion	4	4
Knee extension	4	4
Ankle dorsiflexion	4-	4
EHL	3	3

Pet'r Ex. 6 at 12. After clarifying that the physical therapist was using a five-point scale, Dr. Donofrio was asked if this strength examination, coupled with the note, "Sensation decreased to light touch and pinprick in all extremities and trunk bilaterally. Minimal numbness on face bilaterally. Deep tendon reflexes absent bilateral biceps, brachioradialis, triceps, patellar, and Achilles," would be consistent with GBS, he responded, "…this note, standing by itself, in the areas that you highlighted, could be consistent with GBS." Tr. 260-63.

Dr. Donofrio testified that for petitioner to meet the GBS criteria, he would have needed to show "weakness in four limbs and hyporeflexia or areflexia in four limbs to meet the diagnosis of GBS, and it needs to be consistent from one exam to the next and usually from one day to the next." Tr. 214. On cross-examination, Dr. Donofrio was asked if the Asbury-Cornblath diagnostic criteria for GBS *requires* weakness in all four extremities, and he acknowledged that it does not. Tr. 250. Further, Dr. Donofrio also acknowledged that GBS typically presents as "ascending" weakness and that there is not likely to be involvement of all four extremities right away. *Id.*

Dr. Donofrio also stated that the reports of absent or reduced reflexes in petitioner's medical records could possibly fit a GBS diagnosis "if you accept proximal weakness," as being consistent with GBS, but that the records never show what his baseline reflexes were prior to April 11th, making it difficult to ascertain if absent reflexes were different from petitioner's baseline. Tr. 213. Dr. Donofrio initially testified that petitioner's examinations showed varying reduced or absent reflexes, however, when questioned by the Court, Dr. Donofrio acknowledged that petitioner's lower extremity reflexes were consistently marked as absent or reduced between the April 11th, 17th, and 19th examinations. Tr. 265.

Dr. Donofrio asserted that petitioner's absent reflexes in the lower extremities, along with his numbness and tingling could be "secondary to lumbosacral spine disease, severe peripheral vascular disease or a pre-existing neuropathy." Resp't Ex. G at 3; Tr. 213, 218. Dr. Donofrio reviewed petitioner's MRI spine, which showed:

> …a small disk at L2-L3with mild foraminal stenosis…a disk at L3-L4 with bilateral foramen protrusions, moderate right and mild-to-moderate left foraminal stenosis, disk at L4-L5 with left paracentral disk extrusion with moderate central stenosis may be displacing left L5 route…mild central stenosis at the L5-S1 level. Probably right S1 was compressed as well. Moderate L4-L5 central stenosis, mild right L5-S1 stenosis, left L5 and right S1 compressed.

Tr. 209-10; *see also* Pet'r Ex. 4 at 496. Dr. Donofrio opined that degenerative disk findings in petitioner's MRI would have been the cause of petitioner's lower extremity pain and contributed to petitioner's initial presentation to the hospital on April 11, 2017.

He relied on petitioner's appointment with Dr. Nagaraja three months post-hospitalization to suggest that petitioner's symptoms were more suggestive of degenerative disc disease. On June 26, 2017, Dr. Nagaraja wrote, "I feel like his bilateral lower extremity pain is probably multifactorial, potentially from neuropathy, however also in addition to severe lumbosacral spine disease from an extruded disc [at] L4-5 as well as vascular disease and bilateral lower extremities." Pet'r Ex. 11 at 6. Dr. Donofrio interpreted the note from Dr. Nagaraja as indicating that petitioner's neuropathy was caused by something *other* than GBS. Tr. 218 ("there are potentially three causes of lower extremity numbness, tingling, and pain: a neuropathy, lumbosacral spine disease, as well as peripheral arterial vascular disease."). However, on cross-examination, Dr. Donofrio reviewed petitioner's medical records from his hospitalization and conceded that the treating neurologist, Dr. Freiman, stated that petitioner's spinal disease issues were not the cause of petitioner's absent reflexes or neuropathy. Tr. 260; *see also* Pet'r Ex. 4 at 496-97 ("He has progressive reflex loss in his lower extremities, upper extremities and distal sensory loss in legs and arms, although patient has lumbar stenosis (moderate) and nerve root compression left L5 and right S1….I do not believe his findings are all explained by the above or increased CPK not only a myopathy."). Additionally, Dr. Donofrio conceded that petitioner's discharge summary, which states, "An MRI of the lumbar spine was obtained which demonstrated multi-lumbar spondylosis, left paracentral HNP with moderate stenosis, and right L5-S1 disc osteophyte complex with mild stenosis. *It was deemed that this was the unlikely source of his bilateral lower extremity weakness*," indicated that petitioner's spinal issues were not the source of his lower extremity weakness. Tr. 261.

Dr. Donofrio also opined that petitioner's EMG/NCS performed on July 7, 2017 was inconsistent with GBS. Tr. 190. Dr. Donofrio testified that petitioner's EMG was "not helpful" because it was not done "at the time of the patient's…greatest weakness and greatest symptoms." Tr. 190. In his initial report, Dr. Donofrio acknowledged that the results of the EMG were "abnormal" and demonstrated "bilateral ulnar neuropathies, and mixed mild demyelinating more than axonal, sensory, and motor large fiber length dependent polyneuropathy," but that the interpreting neurologist, Dr. Nagaraja did not use the term "GBS" in the interpretation, and therefore, petitioner did not have GBS. Resp't Ex. E at 4. Further, Dr. Donofrio opined that the

term, "mild demyelination" on the EMG/NCS is inconsistent with GBS because "the demyelination is usually prominent or severe," and there was no identification of a conduction block or temporal dispersion which was usually present in GBS patients. Tr. 193. His other criticism of the EMG/NCS was that the EMG/NCS report does not indicate the temperature of the patient, which is important so it does not skew results. Tr. 193-94. He testified that without knowing the temperature of the patient, specifically if the petitioner was "cold" when the EMG/NCS was performed could result in "skewed" results showing "the swelling of nerve conduction velocities." Tr. 193. He stated, "I don't know if the swelling of the nerve conduction velocities relates to the underlying illness or to the fact that the patient was cold, and nobody measured the temperature." *Id.*

Instead of GBS, Dr. Donofrio opined that petitioner may have suffered from a myopathy, specifically, rhabdomyolysis, which is where muscle tissue breaks down and the components of the muscle fibers enter the circulatory system, resulting in kidney damage. Resp't Ex. A at 14; Resp't Ex. E at 2; Tr. 195. He testified that a patient is typically diagnosed with rhabdomyolysis when they demonstrate weakness in the arms and legs, muscle pain and has a high CPK or CK level in the bloodstream. Tr. 195. According to the Khan article referenced by Dr. Donofrio, "an elevated plasma creatine kinase (CK) level is the most sensitive laboratory finding pertaining to muscle injury," and the management of rhabdomyolysis is "aggressive fluid resuscitation, elimination of the causative agents, and treatment and prevention of any complications that may ensue." Resp't Ex. E, Tab 5.[31] Khan describes that the most common symptoms in patients with rhabdomyolysis may include muscle tenderness, swelling, stiffness and cramping, accompanied by weakness and loss of function in the involved muscle groups. *Id.* at 5. Additionally, "tea-colored urine is a classical manifestation of rhabdomyolysis." *Id.* Serum CK concentration begins to rise approximately 2 to 12 hours after the onset of muscle injury and peaks within 24 to 72 hours, then declines at a constant rate. *Id.* at 5.

Dr. Donofrio observed that petitioner's CPK levels and aldolase levels were elevated, which are muscle enzymes that are both released when there is an injury to muscles, which would support a diagnosis of rhabdomyolysis, instead of GBS. Tr. 198-99. He also stated that petitioner's presentation of weakness, being more proximal than distal was also consistent with rhabdomyolysis. Tr. 196. In his supplemental report, Dr. Donofrio wrote that some of petitioner's treating physicians also suspected a statin-associated myopathy, and the use of statins was discontinued at the same time petitioner was administered plasmapheresis, making it difficult to discern if petitioner's improvement was associated with the plasma exchange or "natural history of rhabdomyolysis to improve on its own after discontinuation of the offending medication." Resp't Ex. G at 2. However, during the hearing Dr. Donofrio conceded that the medical records from the rehabilitation facility, in early May 2017, continue to document objective weakness, but he argued that the residual weakness was from the rhabdomyolysis. Tr. 215. On cross-examination he was asked if plasmapheresis was an accepted treatment for rhabdomyolysis, he stated that it was not, and he acknowledged that petitioner's discharge summary did not include rhabdomyolysis as a discharge diagnosis. *Id.* at 247, 260.

ii. Dr. Donofrio's Opinion on Vaccine Causation

[31] Khan, F.Y., *Rhabdomyolysis: A Review of the Literature,* 67 The Netherlands J Medicine 272-283 (2009). [Resp't Ex. E, Tab 5].

While most of Dr. Donofrio's opinion focused on petitioner's diagnosis, he also opined that the Prevnar-13 vaccine was not the cause of petitioner's condition. Resp't Ex. E at 7. He testified that there is no medical literature or studies that demonstrate a causal connection between Prevnar-13 and GBS. Tr. 225. He argued that the Haber, Tseng, Baxter, and Bonten studies all show that there is no causal connection between Prevnar-13 and GBS. *Id.*; Resp't Ex. E, Tab 6[32] (Haber et al.); Resp't Ex. A, Tab 13[33]; Pet'r Ex. 41 (Tseng et al.); and Resp't Ex. E, Tab 11[34] (Bonten et al.).

Dr. Donofrio stated that the Haber article, which reviewed VAERS data, only identified 11 reported GBS cases after the Prevnar-13 vaccine was given, but only 8 of those cases met the Brighton criteria for GBS. Tr. 226; Resp't Ex. E at 6. He opined that the "eight cases very likely occurred by chance," and that the Haber article does not support an association between Prevnar-13 and GBS. *Id.* at 227; Resp't Ex. E at 6. Dr. Donofrio emphasized that the article only found a reporting rate of 0.7 cases per million doses of the Prevnar-13 vaccine and asserted that this amount is "markedly less than even the lowest estimation for what would have happened in a population of patients with GBS." Tr. 227. However, the article also explained that they did not find any "disproportionate reporting for GBS," after the Prevnar-13 vaccine compared to GBS case reports after the seasonal influenza vaccine. Resp't Ex. E, Tab 6 at 5. Dr. Donofrio acknowledged that underreporting to VAERS is a problem but argued that "it would have to be the most dramatic underreporting that [he's] ever seen in a VAERS study." Tr. 228.

He also argued that the Tseng article, filed by petitioner, which examined adverse events following the administration of the Prevnar-13 compared to the pneumococcal 23 vaccine, and found that the relative risk of adverse events between the two vaccines was the same. Tr. 229. Dr. Donofrio stated that "the data did not support an increased rate of adverse events following PCV-13 or PPSV23 for GBS and nine other medical conditions." Resp't Ex. E at 6. He testified that following the administration of both vaccines, the occurrence of GBS was equal. Tr. 229.

Then Dr. Donofrio refenced Baxter et al. and concluded that the study found no evidence of an increased risk of GBS following any type of vaccination, which included PPSV23, not the Prevnar-13 vaccine. Tr. 230; *see also* Resp't Ex. A, Tab 13 at 1. Baxter reviewed Kaiser Permanente of Northern California's health data from 1994 through October 2006 to identify GBS cases and if those individuals had received any type of vaccine in the year prior to GBS onset. Resp't Ex. A, Tab 13 at 2. The authors identified 415 eligible cases of GBS (after ruling out others for various reasons) and found that 25 patients had received any vaccine in the six weeks prior to GBS onset. *Id.* at 4. While the authors concluded that there was "no evidence of an increased risk of GBS following any vaccination," they also noted that they were "unable to

[32] Haber, P. 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 6330-6334 (2016). [Resp't Ex. E, Tab 6].

[33] Baxter, R. et al., *Lack of Association of Guillain-Barré Syndrome with Vaccinations*, 57 Clinical Infectious Diseases 197-204 (2013). [Resp't Ex. A, Tab 13].

[34] Bonten, M. et al., *Polysaccharide Conjugate Vaccine Against Pneumococcal Pneumonia in Adults*, 372 N. Engl J Med 1114-1125 (2015). [Resp't Ex. E, Tab 11].

exclude any possible association between vaccines and GBS," and that they had "limited power to fully assess the risk of GBS following vaccination due to the rarity of the outcome [and] the low number of GBS cases that were temporally associated with vaccination." *Id.* at 7. The authors ultimately concluded that the "risk of GBS following any vaccination, including influenza vaccines, is extremely low." *Id.*

The last article Dr. Donofrio referenced to support his opinion was Bonten et al., which examined the efficacy of the PCV13 vaccines in older adults. Resp't Ex. E, Tab 11. Participants in the study either received the influenza vaccine and a placebo or the influenza vaccine and PCV13. *Id.* at 2. Dr. Donofrio asserted that the study found that "the number of serious adverse events was similar in the two groups when measured over 28 days after vaccination," although GBS was not specifically mentioned. Resp't Ex. E at 6-7. The study found that there were 327 serious adverse events within 1 month in the group that received the PCV13 compared to 314 serious adverse events following the receipt of just the influenza vaccine and placebo. Resp't Ex. E, Tab 11 at 16. Dr. Donofrio testified that the Bonten study "did not have any cases of GBS," however, the study did not identify any specific diagnoses under the "serious adverse events" category, but classified events by "system organ class." Tr. 230; *see* Resp't Ex. E, Tab 11 at 16.

Dr. Donofrio stated that he believed that GBS can be a "complication of the 1976 swine flu vaccine," and that a six-week onset of symptoms between the vaccination and GBS would be medically appropriate. Tr. 235. Later, Dr. Donofrio testified that onset of weakness, pain, and tingling that started eight or nine days after vaccination would fit "for a vaccine onset." Tr. 240. Dr. Donofrio was also asked if he agreed with Dr. McGeady's opinion that onset in petitioner's case was "too soon," and he stated, "I have read that onset is seven to 11 to 12 days after exposure to an agent that can cause GBS," and that based on his "reading of molecular mimicry," onset of GBS after a vaccine is appropriate. Tr. 242.

On cross-examination, he was asked if there were any cases of GBS "in which you would agree that even after the 1976 swine flu vaccine, that the flu vaccine could cause GBS," and Dr. Donofrio replied, "I'm not aware that I would ever say that there's a relationship after the '76 [swine flu vaccine] to the flu vaccine." Tr. 236. He was also unaware that GBS following administration of the trivalent and quadrivalent vaccines were added to the Vaccine Table. *Id.* Dr. Donofrio acknowledged that there was no evidence of a preceding infection in petitioner and no evidence of a preceding gastrointestinal infection prior to the onset of symptoms. Tr. 243.

b. Dr. Stephen J. McGeady's Opinion on Vaccine Causation

Dr. McGeady did not opine about petitioner's diagnosis and deferred to Dr. Donofrio. Instead, he focused on whether the Prevnar-13 vaccine can cause GBS. Resp't Ex. C. He opined that the Prevnar-13 vaccine did not cause petitioner's GBS and wrote, "After reviewing Dr. Steinman's report and the supporting references and considering the safety profile of Prevnar-13, I do not think that the proposed immune mechanisms are likely to have occurred, and I do not concur that the vaccine is likely to be responsible for the GBS-like illness which may have developed in [petitioner]." *Id.* at 2; Tr. 270.

Dr. McGeady testified that molecular mimicry is a generally accepted theory of disease for a "very limited small number of diseases." Tr. 274-75. He stated that a form of hemolytic anemia is associated with rheumatic fever and *c.jejuni* infections have been associated with GBS. Both can be caused by molecular mimicry. Tr. 275. He also testified that Dr. Steinman's recent work regarding the Epstein Barre virus ("EBV") and multiple sclerosis is another example of molecular mimicry. *Id.* However, Dr. McGeady opined that molecular mimicry as a viable causative mechanism for autoimmune diseases is circumspect and referred to Albert[35], Oldstone[36], and Rose[37] articles to support his opinion. Tr. 276; Resp't Ex. C at 2. Dr. McGeady stated that the Albert article, which is a review paper, "concluded that there was not any convincing evidence that molecular mimicry could be shown to be a cause of any human disease." Tr. 276; Resp't Ex. C at 2; Resp't Ex. C, Tab 1. The Albert paper describes the immunologic basis for molecular mimicry and describes how both T cells and B cells can contribute to the development of autoimmune diseases. Resp't Ex. C, Tab 1 at 1. The paper describes the role of T and B cells in molecular mimicry:

> The fate of a T cell, whether it is productive expansion, tolerance, or death lies in the recognition by the T-cell antigen receptor of an antigenic peptide bound to a major histocompatibility-complex (MHC) molecule on the surface of an antigen-presenting cell. This recognition event is very flexible, giving T cells the potential to recognize a broad range of foreign antigens. However, this range of specificities also makes it possible for T-cell antigen receptors to cross-react with autoantigens. Protection against autoimmunity is provided by negative selection of self-reactive T cells in the thymus and induction of tolerance in T-cells in the periphery. In the thymus and in the periphery, the fate of a T cell is determined by the avidity of its antigen receptor for the peptide-MHC complex….However, some T cells are not deleted in the thymus or rendered tolerant to autoantigens or deleted periphery…Since these T cells do not recognize their cognate antigens, they are called "ignorant" T cells, and then antigens for which they are specific are referred to as "cryptic."
>
> Antibody responses, as well as cellular responses, are important in the development of autoimmune disease. The responses of antibodies reflect the antigenic specificity of B cells. Diversity exists among antibodies to maximize host defense, and mechanisms similar to those that allow T cells to survive may allow autoreactive B cells to survive. However, most productive B-cell responses depend on help from T cells. The development of autoimmunity suggests that tolerance to autoantigens has broken down, allowing previously quiescent, potentially autoreactive T and B cells to become activated.

Resp't Ex. C, Tab 1 at 2. Albert later explained that "experimental and clinical models...fall short of resolving the key issues in demonstration of molecular mimicry as a pathogenic

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[35] Albert, L. & Inman, R., *Molecular Mimicry and Autoimmunity,* 341 N Engl J Med 2068-74 (1999). [Resp't. Ex. C, Tab 1].

[36] Oldstone, M.B., *Molecular Mimicry, Microbial Infection, and Autoimmune Disease: Evolution of the Concept,* 296 Current Topics in Microbiol. Immunol. 1-17 (2005). [Resp't Ex. C, Tab 2].

[37] Rose, N., *Learning from Myocarditis: Mimicry, Chaos and Black Holes,* F1000 Prime Rept. 6-25 (2014). [Resp't Ex. C, Tab 3].

mechanism in autoimmune disease. For researchers in this area, challenges remain. Infection is common; autoimmunity is not. The frequency of shared peptide sequences and the flexibility inherent in immune recognition suggests that mimicry may be ubiquitous in biologic systems." *Id.* at 5.

The Oldstone paper summarized commentary following a symposium on the topic of molecular mimicry and Dr. McGeady interpreted the paper as providing some support for molecular mimicry, but it is an unproven theory. Tr. 276. Oldstone wrote "the most difficult step in the process is to definitively prove the relevance of molecular mimicry to human autoimmune disease," and that "hard data derived in experimental systems clearly indicate molecular mimicry as a mechanism for disease causation. For others, especially human disorders, the evidence can be strongly suggestive, but additional information is required before molecular mimicry can be accepted or rejected as biological reality." Resp't Ex. C, Tab 2 at 13. But Oldstone also explained that finding homologies between a host and a microbe can be done by using "immunologic agents, humoral or cellular, that cross-react with two protein structures (virus-host, virus-virus) or by computer searches to match proteins described in storage banks." *Id.* at 3. Further, Oldstone stated, "Regardless of the methods used for identification, it is now abundantly clear that molecular mimicry occurs between proteins encoded by numerous microbes and host self-proteins and is rather common." *Id.*

Dr. McGeady testified that the Rose paper indicates that beyond the examples of *c.jejuni* and GBS or rheumatic fever and myocarditis for molecular mimicry, "there is very little to go on." Tr. 277. On cross-examination, Dr. McGeady was asked if he would associate any vaccine with causing GBS, he stated that he would only associate the swine flu vaccine to GBS. Tr. 308. He stated that he "was not aware" of any other vaccines that could cause GBS. Tr. 309. Dr. McGeady was also unaware, as was Dr. Donofrio, that GBS after the flu vaccine was added to the Vaccine Injury Table. Tr. 312.

Regarding the specifics of Dr. Steinman's theory in this case, Dr. McGeady testified that there were no meaningful mimics between components of the Prevnar-13 vaccine and the nervous system that could cause GBS. Tr. 278. First, he addressed Dr. Steinman's molecular mimicry theory between the phosphoglycerol components in the vaccine and components in the myelin as potential causes of GBS. Resp't Ex. C at 3; Tr. 280. Dr. McGeady stated, "the prevalence of phosphocholine in the biological system…is present in multiple other tissues, in addition to the CNS," and that it is a "commonly encountered antigen," that the immune system "is not likely to be looking hard for phosphocholine as an invading process." Resp't Ex. C at 3; Tr. 280. Apparently agreeing with Dr. Steinman's assertion that an antigen which can be found widespread in the human body can be targets of auto-antibodies that result in different diseases, Dr. McGeady testified that "the same chemical grouping in different contexts can appear differently to the immune system," which is why exposure in one part of the body does not cause disease, but it can cause disease elsewhere. Tr. 281.

In his expert report, Dr. McGeady acknowledged that the Chang article demonstrates that the "phosphocholine radical was necessary for polysaccharide immunogenicity," but argued that it did not show an antibody was produced specifically to the phosphocholine only that it was needed to produce an antibody to the pneumococcal polysaccharide. Resp't Ex. C at 3. He

testified that the results in the Chang article show that the phosphoglycerol is not the primary epitope because there is some residual antigenicity when it is removed. Tr. 290. He stated that the residual antigenicity without the phosphoglycerol from the 18 saccharide demonstrates that it is important to hold the configuration together but is not the primary epitope targeted by antibodies. *Id.* In other words, the antibody is not made to the phosphoglycerol. Tr. 291.

Dr. McGeady also opined that Dr. Steinman's x-ray diffraction showing the phosphocholine molecule is the epitope bound by antibodies, regardless of the carrier molecule does not explain how the Prevnar-13 vaccine could cause GBS. Tr. 282. He testified that phosphocholine and phosphoglycerol are very small molecules and need carrier proteins to be recognized by the immune system. Tr. 283. Dr. McGeady stated that the Brown et al.[38] paper shows that phosphocholine are immunologically relevant only as part of a carrier molecule and that the carrier actually changes some things in the antibody as the reaction matures. Tr. 284. He stated that, "Even if antibody to phosphocholine in Prevnar 13 were to be generated, it would unlikely cross-react with phosphocholine [in the CNS]," because the configuration of the epitope is dependent on the surrounding structures. Resp't Ex. C at 3; Tr. 286. Dr. McGeady testified that the "phosphoglycerol is probably not going to look the same as it does in myelin," and there are "all kinds of mechanical differences are going to be there." Tr. 287.

With respect to Dr. Steinman's theory that there is molecular mimicry between CRM-197, the diphtheria toxoid carrier molecule, and contactin-1 found in the CNS, Dr. McGeady opined that this is also an unlikely cause for GBS. Tr. 292; Resp't Ex. C at 4. His criticism of this portion of Dr. Steinman's theory is that homology between microbes and human proteins is "commonplace," and that if molecular mimicry was a plausible theory for causing autoimmune diseases, then more people should have autoimmune diseases. Resp't Ex. C at 4; Tr. 295. Dr. McGeady criticized Dr. Steinman's reliance on the Raju paper, because Dr. Steinman overlooked the importance of the structure of amino acids in peptides, which may "differ considerably." Resp't Ex. C at 4; Tr. 294-95. Dr. McGeady read from the Raju paper:

> The results of the present study demonstrate that the molecular environment of a sequence region in the native protein antigen plays an important role in determination of the universal T-epitopes. Further attempts to predict the most immunogenic parts of protein antigen based on structural information should take into account not only primarily structural properties, but also molecular context of a different sequence regions within the three-dimensional structure of the antigen.

Pet'r Ex. 119 at 7. Dr. McGeady interpreted this section as meaning that "the sequence corresponding to something is not really what is important. It's how those things fit together in the context of an intact protein." Tr. 295. Essentially, Dr. McGeady argued that linear homology between proteins is not sufficient for molecular mimicry, but instead, structural homology is what can cause an autoimmune condition. *Id.*

Dr. McGeady opined that Dr. Steinman's adjuvant theory that the Prevnar-13 generated cytokines that resulted in GBS was also an unlikely mechanism. Tr. 296; Resp't Ex. C at 5. He

[38] Brown, M. et al., *The Structural Basis of Repertoire Shift in an Immune Response to Phosphocholine,* 191(12) J. Exp. Med. 2101-2112 (2000). [Resp't Ex. H].

stated that there is "no evidence of an overproduction of cytokines," and that while vaccines include adjuvants to generate cytokines, only a limited amount are produced. Tr. 296. In his expert report, Dr. McGeady stated that he does "not question the pro-inflammatory cytokines are involved in the pathophysiology of GBS, nor do I question the assertion that following injection of Prevnar-13 there is a limited production of pro-inflammatory cytokines IL-1β and IL-18," but that the amount and location of these cytokines was insufficient to lead to the development of GBS in the petitioner. Resp't Ex. C at 5. During the hearing he explained that there was no evidence that petitioner had a fever, which is often caused by the cytokine IL-1, and if it was present in any "significant amount," a patient would have a febrile response. Tr. 297. He also dismissed Dr. Steinman's argument that petitioner's fever may have been masked or the amount of IL-1 cytokines was reduced, by taking aspirin, and stated, "if it was that small, I doubt it would do much as far as altering the immune response." Tr. 298.

Finally, Dr. McGeady addressed the onset of petitioner's symptoms and opined that an onset of 11 days post-vaccination would be "unusually brief," for the mechanism of molecular mimicry. Resp't Ex. C at 5. He testified, "From an immunologic point of view, when you start looking at something a person has not been exposed to before, when the immune system starts to react, it has to accumulate the cells. They have to proliferate…They have to elaborate proinflammatory factors like cytokines that we've been talking about. In GBS…the nerves are infiltrated by T cells and macrophages. This is not something that happens overnight, and I just think that eleven days is a bit of a stretch." Tr. 301. Dr. McGeady acknowledged that Dr. Donofrio opined that onset of seven to ten days post-vaccination was a medically acceptable timeframe to induce GBS, but argued, "…from an immunologic point of view, there is no way that a strictly immune response could cause physical disease in two or three days. I think it would be hard for it to happen in seven days, and I think it'd be hard for it to happen in 11 days, that the immune system would be activated, primarily active, replicate enough cells to carry out an attack and have the attack be so damaging to the tissue that you begin to see clinical signs." Tr. 299. Drawing a comparison of rheumatic fever and streptococcal infection, he testified that four weeks after infection to symptom onset would be an appropriate timeframe. Tr. 313. He stated that he would be "less skeptical" if symptom onset after vaccination was 14 to 21 days. Tr. 314.

IV. Legal Standard

The Vaccine Act was established to compensate vaccine-related injuries and deaths. Section 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 & Human Servs.,* 35 Fed. Cl. 1, 7 (1996) (quoting H.R. No. 908 at 3, *reprinted in* 1986 U.S.C.C.A.N. at 6287, 6344).

A petitioner bears the burden of establishing his or her entitlement to compensation from the Vaccine Program. The burden of proof is by a preponderance of the evidence. Section 13(a)(1).

a. Nature of Injury

The Federal Circuit established the test for actual causation of an off-Table injury in *Althen*, 418 F.3d at 1278. In that case: "There was no dispute as to whether the petitioner, Margaret Althen, actually suffered from a central nervous system demyelinating disorder. Therefore, the Federal Circuit was not presented with a case in which the diagnosis itself was questioned, but one in which causation of the injury by the vaccine was the issue in dispute." *Doe v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 597, 611 (2010) (citing *Althen*, 418 F.3d at 1282), *aff'd, Lombardi v. Sec'y of Health & Hum. Servs.*, 656 F.3d 1343 (Fed. Cir. 2011).

Special masters are generally not tasked with diagnosing injuries. In *Lombardi*, the Federal Circuit explained: "The function of a special master is not to 'diagnose' vaccine-related injuries, but instead to determine 'based on the record evidence as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the petitioner's injury.'" *Lombardi*, 656 F.3d at 1343, *citing Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1382 (Fed. Cir. 2009).

However, the Federal Circuit has determined that in certain instances, "if there is a dispute as to the nature of a petitioner's injury, the special master may opine on the nature of the petitioner's injury." *Contreras v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1363, 1368 (Fed. Cir. 2017), *citing Hibbard v. Sec'y of Health & Hum. Servs.*, 698 F.3d 1355 (Fed. Cir. 2012); *see also Locane v. Sec'y of Health & Hum. Servs.*, 686 F.3d 1375 (Fed. Cir. 2012); *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339 (Fed. Cir. 2010)).

In *Hibbard*, the Federal Circuit reasoned: "If a special master can determine that a petitioner did not suffer the injury that she claims was caused by the vaccine, there is no reason why the special master should be required to undertake and answer the separate (and frequently more difficult) question whether there is a medical theory, supported by 'reputable medical or scientific explanation,' by which a vaccine can cause the kind of injury that the petitioner claims to have suffered." 698 F.3d at 1365.

While the special master is not required to reach a specific diagnosis, the special master may appropriately evaluate at least the nature of petitioner's injury and whether that aligns with petitioner's theory. For example, in *Broekelschen*, the petitioner posited "transverse myelitis [which] is an inflammatory event caused by an immune response," while the respondent posited "anterior spinal artery syndrome, [which] is a vascular event caused by a blockage." 618 F.3d at 1346. The Federal Circuit observed: "Nearly all of the evidence on causation was dependent on the diagnosis" and because the injury itself [was] in dispute, the proposed injuries differ[ed] significantly in their pathology, and the question of causation turn[ed] on which injury [the petitioner] suffered." *Id.* Accordingly, the Federal Circuit held "it was appropriate… for the special master to first determine which injury was best supported by the evidence presented in the record before applying the *Althen* test so that the special master could subsequently determine causation relative to the injury." *Id.*

In contrast, in *Contreras*, the Court of Federal Claims held that the special master erred by diagnosing the petitioner's illness – as TM and not Guillain-Barré syndrome ("GBS") – before evaluating the *Althen* prongs. 107 Fed. Cl. 280, 292-93. The Court reasoned that the case contained "ample evidence that TM and GBS are similar diseases with similar pathologies" and the parties' "unified position [was] that an exact diagnosis of [the petitioner's illness] was not required to rule on causation." *Id.* at 293. The Court of Federal Claims articulated that "the general rule is that the special master should not conduct a differential diagnosis, at the outset of the causation analysis, to choose one diagnosis over another, or over a combination of diagnoses." *Id.*, *aff'd* 844 F.3d 1363; *see also Andreu*, 569 F.3d 1367, 1378 (holding that the special master need not determine whether an initial seizure was febrile or afebrile for purposes of assessing vaccine causation).

Relevant to this inquiry, the Vaccine Act provides that a special master must consider the record as a whole including any medical diagnosis contained therein. Section 300aa-13(b)(1). However, no diagnosis in the medical records is "binding on the special master." *Id.* Rather, "[i]n evaluating the weight to be afforded to any such diagnosis… the special master… shall consider the entire record and the course of the injury, disability, illness, or condition until the date of the judgment of the special master." *Id.* The special master shall also consider any expert opinions and additional medical scientific evidence in the record. *Id.*

b. Causation

A petitioner may prevail by proving either that (1) the vaccinee suffered an injury listed on the Vaccine Injury Table with onset beginning within a corresponding time period following receipt of a corresponding vaccine (a "Table Injury"), for which causation is presumed or that (2) the vaccinee suffered an injury that was actually caused by a vaccine. Under either method, however, the petitioner must also show that the vaccinee "suffered the residual effects or complications of the illness, disability, injury, or condition for more than six months after the administration of the vaccine." Section 11(c)(1)(D)(i).

In the present case, petitioner does not and cannot allege a Table injury. Thus, he bears the burden of establishing actual causation. To do so, he must "show by preponderant evidence that the vaccination brought about the injury by providing 1) a medical theory connecting the vaccination and injury; 2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and 3) a showing of proximate temporal relationship between vaccination and injury." *Althen v. Sec'y of Health & Human Servs.*, 418 F. 3d 1274, 1278 (Fed. Cir. 2005). There must be preponderant evidence for each *Althen* prong. *Caves v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 119, 132 (2011), *aff. per curiam*, 463 Fed. Appx. 932 (Fed. Cir. 2012).

Under *Althen* prong one, the causation theory must relate to the injury alleged. Thus, a petitioner must provide a "reputable" medical or scientific explanation that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355-56. The theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen*, 35 F.3d at 548. It must only be "legally probable, not medically or scientifically certain." *Id.* at 549. However, the theory still must be based on a "sound and reliable medical or scientific explanation." *Id.* at 548. The Federal Circuit explained in *Althen* that "while [that petitioner's claim] involves the possible link

between [tetanus toxoid] vaccination and central nervous system injury, *a sequence hitherto unproven in medicine*, the purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field *bereft of complete and direct proof of how vaccines affect the human body." Althen*, 418 F.3d at 1280 (emphasis added). Recently in *Doles*, the Federal Circuit clarified that a petitioner does not need to proffer a theory that is grounded in medical certainty and backed by medically certain (statistically significant) evidence. *Doles v. Sec'y of Health & Hum. Servs.*, No. 17-642, 2025 WL 1177875 (Fed. Cir. Apr. 23, 2025), (citing *Andreu ex rel. v. Sec'y of Health & Hum. Servs.,* 569 F.3d 1367, 1380 (Fed. Cir. 2009) ("In medical research, "attribution of causation is typically not made until a level of *very near certainty*—perhaps 95% probability—is achieved. In contrast, "determination of causation in fact under the Vaccine Act involves ascertaining whether a sequence of cause and effect is 'logical' and legally probable, not medically or scientifically certain.").

Under *Althen* prong two, petitioner must prove "a logical sequence of cause and effect showing that the vaccination was the reason for [her] injury." *Althen*, 418 F.3d at 1278. This prong is sometimes referred to as the "did it cause" test; i.e. in this particular case, did the vaccine(s) cause the alleged injury. *Broekelschen,* 618 F. 3d at 1345 ("Because causation is relative to the injury, a petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case"). Temporal association alone is not evidence of causation. *See Grant v. Sec'y of Health & Human Servs.,* 9556 F.2d 1144, 1148 (Fed. Cir. 1992). This sequence of cause and effect is usually supported by facts derived from petitioner's medical records. *Althen,* 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326; *Grant*, 956 F.2d at 1148.

Althen prong three requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen* at 1281. That term has equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is medically acceptable timeframe must align with the theory of how the relevant vaccine can cause an injury (*Althen* prong one). *Id.* at 1352.

The preponderance of the evidence standard requires the petitioner to demonstrate that it is "more likely than not" that the vaccine caused the injury. *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs.,* 931 F.2d 867, 873 (Fed. Cir. 1991). A petitioner must demonstrate 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 v. Sec'y of Health & Human Servs.,* 135 F.3d 1344, 1352-53 (Fed. Cir. 1999); *Pafford v. Sec'y of Health and Human Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006). Causation is determined on a case-by-case basis, with "no hard and fast *per se* scientific or medical rules." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). A fact-finder may rely upon "circumstantial evidence" which is consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F. 3d at 1280.

The petitioner often presents expert testimony in support of his or her claim. *Lampe v. Sec'y of Health & Human Servs.,* 219 F.3d 1357, 1361 (Fed. Cir. 2000). Expert testimony in the Vaccine Program is usually evaluated according to the factors set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594-96 (1993); *see also Cedillo,* 617 F.3d at 1339 (citing *Terran v. Sec'y of Health & Human Servs.,* 195 F.3d 1302, 1316 (Fed. Cir. 1999). A special master may use the *Daubert* framework to evaluate the reliability of expert testimony, but expert testimony need not meet each *Daubert* factor to be reliable. *Boatmon v. Sec'y of Health & Human Servs.*, 941 F.3d 1351 (Fed. Cir. 2019). The *Daubert* factors are "meant to be helpful, not definitive," and all factors "'do not…necessarily apply even in every instance in which the reliability of scientific testimony is challenged.'" *Boatmon,* 941 F. 3d at 1359 (citing *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 151, 119 S. Ct. 1167, 143 L.Ed.2d 238 (1999). Thus, for Vaccine Act claims, a "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly* at 1324. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Human Servs.,* 219 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe,* 219 F.3d 1357 at 1362).

If the petitioner makes a *prima facie* case supporting vaccine causation-in-fact, the burden shifts to respondent to show by a preponderance of the evidence that the injury is instead due to factors unrelated to the administration of the vaccine. *Deribeaux v. Sec'y of Health & Human Servs.*, 717 F.3d 1363, 1367 (Fed. Cir. 2013) (citing Section 13(a)(1)(B)). Respondent has the burden of demonstrating that: "[A] factor unrelated to the vaccination is the more likely or principal cause of injury alleged. Such a showing establishes that the factor unrelated, not the vaccination, was 'principally responsible' for the injury. If the evidence or alternative cause is seen in equipoise, then the government has failed in its burden of persuasion and compensation must be awarded." *Knudsen,* 35 F.3d at 551.

V. Entitlement

a. Petitioner's Diagnosis

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

I find that there is preponderant evidence that petitioner's diagnosis following vaccination was GBS. This finding is based on the opinions of petitioner's treating physicians, his clinical presentation, diagnostic testing, and the opinion of petitioner's expert, Dr. Steinman. While petitioner's multiple evaluations at emergency departments from April 11, 2017 through

April 19, 2017 initially appeared to cloud petitioner's ultimate diagnosis and treatment for GBS, a more careful review of these appointments indicate that petitioner appeared with signs and symptoms consistent with GBS throughout these initial presentations.

According to the medical literature filed by both parties, initial manifestations of GBS include weakness, paraparesis, ataxia, and/or areflexia. *See e.g.* Pet'r Ex. 77; Resp't Ex. A, Tab 1; Resp't Ex. E, Tab 2. The NIND GBS Fact Sheet states, "The first symptom of this disorder includes varying degrees of weakness or tingling sensations in the legs." Pet'r Ex. 77 at 1. Willison et al. states, "Weakness is classically described as ascending, and usually starts in the distal lower extremities, but can start more proximally." Resp't Ex. A, Tab 1 at 5. "In addition to weakness, patients might initially have sensory signs, ataxia, and features of autonomic dysfunction. Muscle pain or radicular pain, often but not always in the spinal region, is another frequent initial sign, which can complicate the diagnosis because pain can precede weakness in about a third of patients." *Id.* Asbury and Cornblath also endorse progressive motor weakness and areflexia as "features required for diagnosis" and explain that the rapid progression of symptoms by four weeks, relative symmetry between symptoms (although not absolute), and mild sensory symptoms or signs can be "features strongly supportive of the diagnosis." Resp't Ex. E, Tab 2 at 1.

When petitioner first presented to the emergency department on April 11, 2017, twelve days post-vaccination, he complained of a headache and "generalized weakness." Pet'r Ex. 4 at 9. Petitioner also reported numbness in his bilateral lower extremities, and difficulty walking secondary to weakness. *Id.* at 19. He demonstrated an abnormal finger-to-nose testing on the left side and fell to the left side while walking. *Id.* There was a concern for a stroke, and he was given a migraine cocktail. *Id.* At this same hospital visit, petitioner was examined by neurologist, Dr. Harsha Nagaraja, who noted petitioner had absent reflexes bilaterally in his lower extremities. Petitioner's paresthesias and gait imbalance improved with the migraine cocktail and he was discharged. *Id.* at 33. Even though petitioner was discharged with a diagnosis of "intractable migraine" and "generalized weakness: likely due to excessive fatigue and dehydration," Dr. Nagaraja wrote, "If any symptoms of ataxia and paresthesias in his hands and feet come back suggest spinal tap to rule out GBS given his examination is also significant for reduced reflexes in the bilateral lower extremities." *Id.*

At petitioner's second appearance to the emergency department on April 14, 2017, petitioner complained of "constant back pain," and again endorsed "bilateral foot numbness." Pet'r Ex. 4 at 247. Petitioner's examination was considered normal, he was given pain medication, and again discharged. Two days later, on April 16, 2017, petitioner went back to the emergency room stating that he still had back pain and numbness of his lower extremities, but this time he could not stand. *Id.* at 337. Petitioner was seen by Dr. Jesse Turley, and petitioner reported that he had "bilateral lower extremity weakness" and difficulty walking due to the weakness. *Id.* at 339. Dr. Turley wrote that petitioner "endorses weakness with attempted flexion and active straight leg raise," he also noted that petitioner had "reduced bilateral patellar reflex." *Id.* at 340. Petitioner again reported bilateral feet paresthesias. *Id.* at 341. Petitioner was discharged with pain medication and a prescription for prednisone for degenerative disc disease which was identified on an MRI. *Id.* at 338.

By April 19, 2017, petitioner's weakness had progressed so much, consistent with GBS, that he was unable to walk and that his "legs are paralyzed now." Pet'r Ex. 4 at 456. Dr. Andrew Wyman performed a physical examination and observed that petitioner had "mild ataxia to finger-nose testing," and "bilateral lower extremity ataxia, although this is limited secondary to weakness," along with absent patellar and Achilles reflexes. *Id.* Petitioner also had decreased sensation to vibration and "no appreciable sensation to vibration in bilateral feet." *Id.* Dr. Wyman reviewed petitioner's MRI and wrote that he had "a low suspicion that there is any acute [spinal] process," and that there was a concern for GBS or AIDP. *Id.* at 457. It was not until this assessment that petitioner was finally admitted, then transferred to CMC-Main for further evaluation, including a possible lumbar puncture. *See also* Pet'r Ex. 5. After petitioner's transfer to CMC-Main for evaluation of GBS, he was ultimately diagnosed with GBS, even after the lumbar punctures were unsuccessful. Petitioner was treated with five days of plasmapheresis and discharged to a rehabilitation facility with a diagnosis of GBS. *See* Pet'r Ex. 5 at 5.

Despite petitioner presenting with signs and symptoms of GBS that progressed rapidly, Drs. Donofrio and Chaudhry asserted that petitioner's "evolution was not consistent with GBS." Resp't Ex. A at 14; Resp't Ex. E at 2. Drs. Donofrio and Chaudhry opined that petitioner's symptoms were caused by other conditions, such as rhabdomyolysis, vascular disease, or degenerative disc disease. Resp't Ex. E at 4-5. These opinions are not supported by the medical record and many of the assertions made by respondent's experts are contrary to petitioner's clinical course as documented by the records.

For example, Dr. Chaudhry states that petitioner's paresthesia improved with a migraine cocktail and "improvement with migraine cocktail of the noted paresthesias are not features of GBS." Resp't Ex. A at 16. But in the next three visits to the emergency department, petitioner consistently endorsed paresthesias in his bilateral lower extremities and there was no further report of migraine. On April 11, 2017, petitioner complained of "numbness in bilateral feet in stocking distribution to ankle," and then on both April 14th and 17th he reported numbness in his feet bilaterally. *See* Pet'r Ex. 4 at 247 ("Pt does endorse numbness in the soles of his [bilateral] feet intermittently."); Pet'r Ex. 4 at 337 ("…patient presented with lower back pain with numbness of the lower extremities…"). These symptoms presented bilaterally, consistent with GBS.

Dr. Donofrio also asserted that petitioner's presentations of weakness and absent reflexes were inconsistent on examinations and therefore, inconsistent with GBS. He testified, "The other thing that is important is that those features of GBS remain with the patient for at least a few days and usually for weeks. And you don't find weakness in four limbs and areflexia and then two hours or even the next day, a completely different examination." Tr. 188.

But petitioner's weakness and areflexia did not change over his initial presentation, from April 11-April 19, 2017. When petitioner was first examined by neurologist, Dr. Nagaraja, on April 11, 2017, petitioner had absent reflexes in the bilateral knees and ankles and although petitioner had normal strength on examination, petitioner expressed feeling weak. *See* Pet'r Ex. 4 at 33. Additionally, petitioner continued to describe feeling weak in the legs at the multiple times he went to the emergency room. *See* Pet'r Ex. 4 at 19 ("…associated numbness in his bilateral extremities, and difficulty walking secondary to leg weakness."); 339 ("…primary

complaint of low back pain and lower extremity weakness." and "…bilateral lower extremity weakness, difficulty ambulating secondary to weakness."). A nursing note from April 17, 2017 indicates that petitioner's "neurological symptoms" were "weakness" and that "[patient] reports being unable to bear weight on bilateral lower extremities." *Id.* at 416. When petitioner saw Dr. Wyman on April 19, 2017 in the emergency department, Dr. Wyman noted that petitioner had "*progressive* lower extremity weakness" and that petitioner had presented 3 times for weakness, and he was only seen by "neurology" one time. *See* Pet'r Ex. 4 at 456. Petitioner still had absent knee and ankle reflexes bilaterally. *Id.* The "History of Present Illness" by Dr. Wyman on April 19, 2017 clearly indicates that petitioner's weakness had progressed over a seven day period, consistent with GBS as described in all the medical literature filed in this case. *See e.g.* Resp't Ex. A, Tab 1 at 1 ("The acute progression of limb weakness…proceeds to its peak clinical deficit in 2-4 weeks."); Resp't Ex. G, Tab 1 at 1 ("Symptoms and signs of motor weakness develop rapidly but cease to progress by four weeks into the illness.").

Further, Dr. Donofrio incorrectly asserted that weakness needs to be present in all four limbs to meet the diagnostic criteria for GBS. Tr. 250-51. During the hearing, he was asked if the Asbury article actually stated that weakness needs to be present in all four limbs, and he replied, "It does not state that." Tr. 250. Instead, Asbury's GBS criteria states, "A) Progressive motor weakness of more than one limb. The degree ranges from minimal weakness of the legs, with or without mild ataxia, to total paralysis of the muscles of all four extremities and the trunk…." Resp't Ex. E, Tab 2 at 1.

Dr. Donofrio also relied upon Dr. Nagaraja's single notation from June 26, 2017, approximately three months after petitioner's hospitalization, as evidence that petitioner's symptoms were not related to GBS. Resp't Ex. E at 5. Dr. Nagaraja's wrote, "No objective evidence of GBS. He should have gotten better by now has been almost 2 months since onset of symptoms, if not more. Typically, this comes and goes within 4-6 weeks, particularly with him getting plasmapheresis which typically hastens recovery. I feel like his bilateral lower extremity pain is probably multifactorial potentially from neuropathy however also addition to severe lumbosacral spine disease." Pet'r Ex. 11 at 6. However, this notation is contradicted by the remainder of the medical records and the medical literature, which explains that GBS patients can have persistent, residual symptoms. *See* Resp't Ex. A, Tab 1 at 1 ("Symptoms peak within 4 weeks, followed by a recovery period that can last months or years."); Pet'r Ex. 77 at 2 ("In addition, recovery is not necessarily quick….patients usually reach the point of greatest weakness or paralysis days or weeks after the first symptoms occur….The recovery period may be as little as a few weeks or as long as a few years.").

Additionally, other causes of petitioner's symptoms were repeatedly ruled out from other physicians. For example, on April 19, 2017, petitioner was seen by neurologist, Dr. Sarise Freiman, who performed a physical examination of petitioner and reviewed his MRI and wrote:

> [Patient] has had progressive reflex loss in his lower extremities, upper extremities, and distal sensory loss in legs and arms, although patient has lumbar stenosis moderate at L4-L5 and nerve root compression from left L5 and right S1, and degenerative disease in his right hip, *I do not believe his findings are all explained by the above*. Guillain-Barre

> syndrome better known as acute inflammatory demyelinating polyneuropathy would best explain his clinical course.

Pet'r Ex. 4 at 482 (emphasis added). Dr. John Cunneen, wrote that petitioner's "MRI, CT and L-spine did not reveal any significant neural compression aside from a bulging disc with effacement of the L5 nerve root on the left that would not otherwise explain the patient's clinical symptoms." Pet'r Ex. 5 at 30. Petitioner's discharge summary also clearly states that petitioner's lumbar spondylosis and mild stenosis was not the "source of his bilateral lower extremity weakness." *Id.* at 5. During the hearing, Dr. Donofrio acknowledged that multiple doctors specifically *did not* attribute petitioner's symptoms of weakness, absent reflexes, or numbness to the findings on the spinal MRI. Tr. 89 ("Question: Do you see where it also discusses that [the MRI of the lumbar spine] was deemed that this was unlikely the source of his bilateral lower extremity weakness? Answer: That is what it states."). Finally, Dr. Nagaraja's notation where there was "no objective evidence of GBS" came prior to petitioner's EMG/NCS, done on July 3, 2017, which concluded:

> This is an abnormal study. There is electrophysiologic evidence of bilateral moderate median neuropathies at the wrist (i.e. carpal tunnel syndrome), bilateral on localized ulnar neuropathies, as well as a mixed mild demyelinating more than axonal mixed sensorimotor large-fiber length dependent peripheral neuropathy on this examination. *No obvious signs of a right lumbosacral radiculopathy were found.*

Pet'r Ex. 11 at 26 (emphasis added). As Dr. Steinman explained, the EMG/NCS results were consistent with GBS. Tr. 89-91. While Mr. Musick did have some L5 nerve root compression on the left, as his doctors recognized, this would not explain his *bilateral* lower extremity weakness or his *upper extremity* symptoms.

Despite the contention by Dr. Chaudry and Dr. Donofrio in their reports that based on the petitioner's elevated CPK levels and general weakness that his symptoms may have been caused by rhabdomyolysis, the evidence did not support rhabdomyolysis as an alternative diagnosis. Resp't Ex. A at 16; Resp't Ex. E at 2. During the hearing, Dr. Donofrio testified that petitioner was not diagnosed with rhabdomyolysis, and he acknowledged that plasmapheresis is not an appropriate treatment for rhabdomyolysis. Tr. 247, 261. Further, petitioner's treating neurologist, Dr. Freiman, acknowledged petitioner's elevated CPK levels and wrote, "I do not believe his findings are all explained by the above or increased CPK. Not only a myopathy. Guillain-Barré syndrome, better known as acute inflammatory demyelinating polyneuropathy, would best explain his clinical course." Pet'r Ex. 4 at 496-97. Petitioner's physicians also suspected that petitioner's acute kidney injury was related to his use of NSAIDs and decreased fluid intake. *Id.* at 454, 457.

Dr. Steinman provided further explanation that elevated CPK and rhabdomyolysis can be a feature of GBS not a separate diagnosis especially in patients who experience pain before weakness as was the case with petitioner. The Ropper article stated that elevated creatine kinase levels were found in 13 out of 16 GBS patients, who also experienced pain prior to the onset of weakness. Pet'r Ex. 98 at 5; Pet'r Ex. 107 at 2-3. Ropper observed that "serum [CPK]

concentrations were elevated between 50%-700% above normal levels," in GBS patients that were experiencing pain before the onset of weakness. Pet'r Ex. 107 at 2.

Lastly, petitioner's weakness did not resolve two weeks after onset of his symptoms, as asserted by Dr. Donofrio, to support his opinion that petitioner had rhabdomyolysis instead of GBS. *See* Resp't Ex. E at 4 ("Within 2 weeks of onset of symptoms, petitioner showed normal strength which would be very unusual in an illness such as GBS, where patients typically do not recover full strength for four weeks or longer."). During the hearing, Dr. Donofrio reviewed petitioner's physical therapy records from his stay at the rehabilitation hospital and acknowledged that petitioner was "judged to have weakness" by the physical therapists. Tr. 249. The records from petitioner's rehabilitation stay not only documented ongoing residual weakness post-treatment for GBS, but absent reflexes in the bilateral biceps, brachioradialis, triceps, patellar, and Achilles, along with continued numbness. *See* Pet'r Ex. 6 at 13-14.

In this case, the medical records provide well documented support for the diagnosis of GBS, which include documented signs and symptoms consistent with GBS as described in the medical literature. The opinions of treating physicians and neurologists' regarding petitioner's diagnosis, as well as results of EMG/NCS studies and the treatment provided to petitioner were consistent with GBS. The alternative diagnoses suggested by Drs. Chaudhry and Donofrio are not supported in the record in that the bilateral symptoms in upper and lower extremities are inconsistent with a nerve root explanation, and Dr. Steinman explained that elevated CPK and rhabdomyolysis can be a feature of GBS in patients who experience pain before weakness. Accordingly, petitioner has demonstrated by preponderant evidence that he suffered from GBS, beginning eleven to twelve days following receipt of the Prevnar-13 vaccination and progressing over the following weeks.

b. *Athen* prong one

Under *Althen* prong one, petitioner must provide a "reputable medical theory," demonstrating that the vaccine received can cause the type of injury alleged. *Pafford*, 451 F.3d at 1355-56. Such theory must only be "legally probable, not medically or scientifically certain." *Knudsen*, 35 F.3d 548-49. Petitioner may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *See Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). However, a "petitioner must provide a 'reputable medical or scientific explanation' for [her] theory." *Boatmon v. Sec'y of Health and Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019) (quoting *Moberly*, 592 F.3d at 1322). While the theory need not be medically or scientifically certain, "it must still be 'sound and reliable'" *Id.* (quoting *Knudsen*, 35 F.3d at 548-49). The petitioner must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." *Knudsen*, 35 F.3d at 548-49. Causation "can be found in vaccine cases…without detailed medical and scientific exposition of the biological mechanisms." *Knudsen*, 35 F.3d at 548-49.

For the reasons discussed below, I find that petitioner has provided by preponderant evidence a sound and reliable theory explaining how the Prevnar-13 vaccine can cause GBS, therefore, satisfying *Althen* prong one.

Dr. Steinman's theory involves molecular mimicry between two different components of the Prevnar-13 vaccine to host tissue, and that the immune response is also heightened by the inclusion of the adjuvant in the vaccine. *See* Pet'r Exs. 17 at 24. He proposes "two molecular mimics that are relevant to GBS in the composition of Prevnar-13, one from the phosphoglycerol sidechain linked to the pneumococcal polysaccharide antigen, and a second from the CRM-197 protein conjugate." Pet'r Ex. 17 at 6. He also opined that the adjuvant in the vaccine enhances the immune response and can contribute to the development of GBS through the heightened stimulation of inflammatory cytokines, particularly IL-18.

Respondent's experts accept molecular mimicry as a causal mechanism for inducing GBS or other autoimmune conditions in very limited circumstances. *See* Resp't Ex. A at 19-22; Resp't Ex. C at 2; Tr. 236; Tr. 275 (Dr. McGeady stating that molecular mimicry is a generally acceptable theory as a cause for certain autoimmune diseases for "a very limited, small number of diseases."). For example, both experts endorsed molecular mimicry as the causative mechanism for GBS following a *c.jejuni* infection and rheumatic heart disease and rheumatic fever after a streptococcal infection, but beyond specific diseases where studies have identified both the autoantibodies directed against human tissue and the mimics of the target antigen, respondent's experts contended that molecular mimicry is too speculative to be the causal mechanism for GBS post-Prevnar 13 vaccination. *See* Tr. 239, 275; Resp't Ex. C at 2. But respondent's experts' limited acceptance of molecular mimicry is based on the availability of direct proof and scientific certainty, where that is not the standard in the Vaccine Program, and requirement of such direct proof would impermissibly raise petitioner's burden of proof. "[T]he purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof of how vaccines affect the human body." *Althen*, 418 F.3d at 1280. "[T]o require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program." *Knudsen,* 35 F.3d at 549; *see also See Andreu ex rel.*, 569 F.3d at 1378 (citing *Capizzano v. Sec'y of Health & Hum. Servs.* 440 F.3d 1317, 1325-36 ("Requiring 'epidemiologic studies…or general acceptance in the scientific or medical communities….impermissibly raises a claimant's burden under the Vaccine Act.' ").

Dr. Steinman observed that even when molecular mimicry has been generally accepted and shown with scientific certainty, such as with Epstein Barr Virus and MS or *c.jejuni* and GBS, the infection is much more ubiquitous than the autoimmune disease, suggesting a likely multifactorial process initiated by molecular mimicry. Dr. Steinman acknowledged that there are many different antigens and self-tissues that have overlapping or structural similarity, and therefore it is likely that molecular mimicry is a necessary initiator of autoimmune disease in many cases, but that there are other factors such a genetic susceptibility or failure of the immune regulatory system to suppress an aberrant immune response is also necessary for autoimmunity to occur. Tr. 136-37. As explained in the Robinson paper, which demonstrated molecular mimicry between Epstein Barr Virus and Multiple Sclerosis:

> Nearly everyone is infected with EBV, but only a small fraction develops MS. Thus, other factors, such as genetic susceptibility, are important in MS pathogenesis. Certain genes, such as those encoding the antigen-presenting human leukocyte antigen (HLA) proteins, determine the portion of a protein that is presented o the immune system. Other genes control modifications in EBV-associated proteins, including phosphorylation. Such genes are critical for modulating molecular mimicry. *Thus, given these additional gating factors in MS pathogenesis, infection with EBV is likely to be necessary, but not sufficient to trigger development of MS. Infection with EBV is the initial pathogenic step in MS.*

Pet'r Ex. 73 at 2.[39]

This is also echoed in the Rose paper, which explains that there is a wide range of epitope mimicry between microorganisms and human cellular antigens and that the removal of self-reactive T or B cells is never complete, but instead kept from becoming pathogenic due to a regulatory system. Resp't Ex. C, Tab 3 at 4. Rose wrote that, "subtle regulatory factors make the pivotal difference between everyday harmless natural autoimmunity and a pathogenic autoimmune train wreck." *Id.* at 4. Finally, the Willison et al. article makes the same point about GBS. Resp't Ex. A, Tab 1 at 1. The article states:

> First, Guillain-Barré syndrome is usually preceded by infection or other immune stimulation that induces *an aberrant autoimmune response* that targets peripheral nerves and their spinal roots. Molecular mimicry between microbial and nerve antigens is clearly a major driving force behind the development of the disorder, at least in the case of *c.jejuni* infection. However, the interplay between microbial and host factors that dictates if and how the immune response is shifted towards unwanted autoreactivity is still not well understood.

Id. at 1.

Other, medical literature filed in this case also support molecular mimicry as a causal mechanism for the pathogenesis of GBS outside of *c.jejuni* or other identified specific mimics. Yuki states, "Some evidence supports the presence of molecular mimicry between gangliosides and antecedent infectious agents in patients with the Guillain-Barré syndrome." Resp't Ex. I at 6. Further, Yuki acknowledges that "autoantigens have yet to be unequivocally identified." *Id.* at 5. The Ravishankar article theorized that cross reaction to the Prevnar vaccine could cause GBS by molecular mimicry, stating, "The major mechanism resulting in the autoimmunity by adjuvanted vaccines has been proposed to be due to the epitopes of a vaccine that initiates the development of antibodies and/or T cells that could cross-react with epitopes on myelin or axonal glycoproteins." Pet'r Ex. 71 at 1-2.

Moreover, molecular mimicry has been accepted as a theory that has persuasively linked different vaccines to different demyelinating conditions, including GBS.
See e.g. See e.g., Salmins v. Sec'y of Health & Hum. Servs., No. 11-140V, 2014 WL 1569478 at *17 (Fed. Cl. Spec. Mstr. March 31, 2014) (finding that the HPV vaccine can cause GBS);

[39] Robinson, W. & Steinman, L., *Epstein-Barr Virus and Multiple Sclerosis,* Science (2022). [Pet'r Ex. 73]

Peugh v. Sec'y of Health & Hum. Servs., No. 99-638V, 2007 WL 15131666, at *17 (Fed. Cl. Spec. Mstr. May 8, 2007 (finding in an omnibus proceeding that the hepatitis B vaccine can cause GBS); *Whitener v. Sec'y of Health & Hum. Servs.*, No. 06-0477V, 2009 WL 3007380, at * 20 (Fed. Cl. Spec. Mstr., Sept. 2, 2009) (finding that the meningococcal vaccine caused GBS); *Mohamad v. Sec'y of Health & Hum. Servs.*, No. 16-1075V, 2022 WL 711604, at *9-18 (Fed. Cl. Spec. Mstr. Jan 27, 2022) (finding that the Tdap vaccine can cause GBS); *Pierson v. Sec'y of Health & Hum. Servs.*, No. 17-1136V, 2022 WL 322836, at *31 (Fed. Cl. Spec. Mstr. Jan. 19, 2022) (finding that the Prevnar-13 vaccine can cause GBS through molecular mimicry); *J.G. v. Sec'y of Health & Human Servs.*, 2023 WL 2752634, at *29-32 (finding that the Hep A vaccine can cause GBS).

In this case, Dr. Steinman's first theory of molecular mimicry between the phosphoglycerol components of the Prevnar-13 vaccine and myelin components is supported by the medical literature. Specifically, Ho, Nakos, Chang and Bryson, all provide additional support for this theory for how the Prevnar-13 vaccine could cause GBS through a cross-reaction between the components of the phoshoglycerol components and myelin, making this component of Dr. Steinman's theory sound and reliable.

Dr. Steinman explained that phospholipids are components in the myelin sheath, which are targeted by antibodies, resulting in GBS. Pet'r Ex. 17 at 9-10; Tr. 103. The Ho article, which Dr. Steinman was a senior author, found that in multiple sclerosis patients, autoantibodies target the phosphoglycerol and phosphocholine found in the polar head group of phospholipids in central nervous system myelin. Pet'r. Ex. 28 at 1; Tr. 104-05. The article explained that "lipids constitute 70% of the myelin sheath, and autoantibodies may contribute to the demyelination that characterizes MS." *Id.* The authors examined the lipid structures and found that "six of the seven targeted lipids had a phosphate group," and that antibodies in MS patients target the phosphoglycerol moiety of phospholipids, independent of the fatty acid side chains which are bound to the phosphoglycerol. *Id.* at 3. Ho et al. found that "myelin phospholipids are targeted by autoimmune responses in MS." *Id.* at 9. During the hearing, Dr. Steinman explained that while GBS is a disease of the peripheral nervous system and MS is a central nervous system disease, the structure of the phospholipids in the myelin sheath in both the central and peripheral nervous systems are similar. Tr. 106. Additionally, Nakos demonstrated that the serum of all nine GBS patients in the study had antiphospholipid antibodies directed against at least one lipid during the course of the disease, while no such antibodies were found in the controls. Pet'r Ex. 26. Nakos observed that while antibodies to gangliosides in GBS have been well studied only 15-20% of GBS patients develop antiganglioside antibodies.

Then utilizing the Prevnar-13 patent application and the Chang paper, Dr. Steinman demonstrated how an immune reaction to the phosphoglycerol component of the Prevnar-13 vaccine is critical to achieve immunogenicity. Chang found that preserving the phosphoglycerol component is critical for the immune system recognition and development of antibodies to the 18C antigen. Dr. McGeady agreed that Chang showed that the phosphoglycerol component of serotype 18C was a necessary component of the vaccine to confer immunogenicity but argued that Chang also found some "residual antigenicity," to the epitope, which suggests that the phosphoglycerol was not the "primary epitope" to which antibodies are generated. Resp't Ex C at 3; Tr. 289-90. Dr. McGeady suggested that the phosphoglycerol component was only

important to "hold the configuration" of the epitope together. Tr. 290. Dr. Steinman acknowledged that in the scientific experiment performed by Chang it was found that at very high concentrations of the polysaccharide antigen without the phosphoglycerol component, there was some minimal immunogenicity. Tr. 320-21. However, Dr. Steinman correctly observed that the experiment had to push the polysaccharide without the phosphoglycerol to a concentration 100-times higher to get an antibody response, which still supported the authors' conclusion that the retention of the phosphoglycerol is necessary to confer adequate immunogenicity to 18C through the vaccine. *See* Pet'r Ex 30 at 1.

The Bryson paper Dr. Steinman referenced, consistent with Chang, also demonstrates the antibody response to the phosphoglycerol component of the 23F antigen. According to Dr. Steinman, Bryson shows that the phosphoglycerol is at the center of the binding site for antibodies directed at 23F. Pet'r Ex. 55 at 11. Because the Prevnar-13 vaccine includes both 23F and 18C antigens and their necessary phosphoglycerol side chains, the immune response is to phosphoglycerol components, which can cross-react with myelin, leading to GBS. Pet'r Ex. 17 at 14; Tr. 105-06 ("…the human immune response to some of the components of the Prevnar 13 vaccine targets a common phosphoglycerol group.").

I have previously accepted Dr. Steinman's theory of molecular mimicry between the phosphoglycerol components of the Prevnar-13 vaccine and the phosphoglycerol components in the myelin as sound and reliable, as supported by much of the same literature he referenced in this case. *See Koller v. Sec'y of Health & Hum. Servs.,* No. 16-439V, 2021 WL 5027947, at *16-20 (Fed. Cl. Spec. Mstr. Oct. 8, 2021). His theory of molecular mimicry has also been accepted by other special masters in other GBS cases involving the Prevnar-13 vaccine. *See Pierson v. Sec'y of Health & Hum. Servs.,* No. 17-1136V, 2022 WL 322836, at *27-30 (Fed. Cl. Spec. Mstr. Jan. 19, 2022); *Maloney v. Sec'y of Health & Hum. Servs.,* No. 19-1713V, 2022 WL 1074087, at *30-31 (Fed. Cl. Spec. Mstr. Mar. 17, 2022); *Gross v. Sec'y of Health & Hum. Servs.*, 2022 WL 9669651, at * 35-36 (Fed. Cl. Spec. Mstr. Sept. 22, 2022); *Sprenger v. Sec'y of Health & Hum. Servs.*, No. 18-279V, 2023 WL 8543435, at *18-19 (Fed. Cl. Spec. Mstr. Nov. 14, 2023); *Parker v. Sec'y of Health and Hum. Servs.,* No. 20-411V, 2023 WL 9261248, at *20-22 (Fed. Cl. Spec. Mstr. Dec. 20, 2023); *Anderson v. Sec'y of Health & Hum. Servs.,* No. 18-484V, 2024 WL 557052, at *30-31 (Fed. Cl. Spec. Mstr. Jan. 17, 2024); *Cooper v. Sec'y of Health & Hum. Servs.*, No. 18-1885V, 2024 WL 1522331 (Fed. Cl. Spec. Mstr. Mar. 12, 2024); *Bartoszek v. Sec'y of Health & Hum. Servs.,* No. 17-1254V, 2024 WL 4263604 (Fed. Cl. Spec. Mstr. Aug. 27, 2024). Acceptance of molecular mimicry between the components of Prevnar-13 and the peripheral nervous system has not been universally accepted by all special masters. *See Deshler v. Sec'y of Health & Hum. Servs.,* 2020 WL 4593162, at *19-21; *Trollinger v. Sec'y of Health & Hum. Servs.*, No. 16-473V, 2023 WL 2521912, at *26 (Fed. Cl. Spec. Mstr. Feb. 17, 2023); *McConnell v. Sec'y of Health & Hum. Servs,* No. 18-1051V, 2022 4008238, at *9 (Fed. Cl. Spec. Mstr. Aug. 19, 2022). While these latter cases reach a different conclusion than I am reaching or that the majority of other Prevnar/GBS cases have reached, I continue to conclude that Dr. Steinman has presented a sound and reliable theory of Prevnar vaccine causation of GBS based on mimicry between the phosphoglycerol components in the vaccine and in myelin.

I also find that Dr. Steinman's theory of molecular mimicry between the CRM-197 (diphtheria toxin) and Contactin-1 to be sound and reliable. Dr. Steinman identified sequences of

shared homology between the proteins in the vaccine, specifically CRM-197, and Contactin-1. Pet'r Ex. 17 at 17; Tr. 113.

This part of his theory focused on a different component of the peripheral nerves that is thought to be involved in GBS. Dr. Steinman explained that Contactin-1 is a protein found in the peripheral nervous system at the nodes of Ranvier. Tr. 124. Mirua et al. explained, "In the peripheral nerves, the domain organization of myelinated axons depends on specific axo-glial contact between the axonal membrane and Schwann cells at nodes, paranodes, and juxtaparanodes." Pet'r Ex. 37 at 1. Mirua also found that in patients with CIDP, the more chronic form of GBS, IgG autoantibodies were directed against the nodes of Ranvier or the paranodal axo-glial apparatus." *Id.* Dr. Steinman was able to identify a "five out of ten amino acid sequence homology between Contactin-1 and CRM-197." Tr. 116; *see also* Pet'r Ex. 17 at 19. He opined that the cross-reactive immune response generated to the diphtheria toxin conjugate would then bind to the proteins in the nodes of Ranvier, resulting in GBS. Tr. 124. Raju demonstrated that one of the sequences that Dr. Steinman identified, beginning with WEQ, found in the diphtheria toxin, generated "the second strongest immune response in humans." Tr. 120; *see also* Pet'r Ex. 37 at 5. Then citing to the Mirua article, Dr. Steinman successfully demonstrated that anti-contactin-1 antibodies were found in five patients with GBS in that study. Pet'r Ex. 37 at 5.

Dr. McGeady's main disagreement with this aspect of Dr. Steinman's theory was based on a general skepticism of molecular mimicry and utilizing computer databases to identify sequence homology between epitopes in humans and in antigens/vaccines. Tr. 293. However, Dr. McGeady does not dispute the findings of Mirua, where autoantibodies to contactin-1 were identified in patients with GBS. Thus, given the medical literature cited by Dr. Steinman, I find that his opinion is more persuasive than Dr. McGeady's more non-specific argument against molecular mimicry.

The third theory Dr. Steinman offered was that the alum, the adjuvant in the Prevnar-13 vaccine, also contributes to the pathogenesis of GBS by stimulating proinflammatory cytokines IL-1 and IL-18. Pet'r Ex. 17 at 22-23; Tr. 125-29. According to this theory, the alum activates the proinflammatory cytokine, IL-18, which recruits certain T-helper cells that have been implicated in the pathogenesis of immune mediated demyelinating diseases, such as GBS. *See* Pet'r Ex. 43 at 1; Pet'r Ex 48 at 1,5; *see generally* Pet'r Ex. 49. Jander et al. found that activity of IL-18 was significantly increased in the nerve roots during the stage of active disease progression in experimental EAN, which parallelled T-cell infiltration, suggesting "a role for macrophage-derived IL-18 in the pathogenesis of Th1-mediated autoimmune demyelination in the [peripheral nervous system]." Pet'r Ex. 48 at 5. GBS patients also had significantly elevated IL-18 levels. *Id.* Dr. Steinman asserted this was a separate theory from his two molecular mimicry theories, suggesting that any one of them could cause GBS after the administration of the Prevnar-13 vaccine. Tr. 138.

While it is certainly true that the Prevnar-13 vaccine includes the alum adjuvant meant to increase the immunogenicity of the vaccine, and Dr. McGeady concedes that pro-inflammatory cytokines are involved in the pathophysiology of GBS, it is unclear based on the evidence provided if the alum in the Prevnar-13 vaccine alone is sufficient to induce GBS. As noted in the

Eisenbarth paper, "alum must be encountered simultaneously with an antigen *in vivo* for efficient priming to occur and suggests that the antigen might provide the first signal either directly, or indirectly by inciting the production of local pro-inflammatory cytokines from resident monocytes or specialized cells recruited by alum." Pet'r Ex. 43 at 4. According to Eisenbarth's theory, the alum provides the second signal for activation of inflammasome to produce IL-1β and IL-18. *Id.* Eisenbarth notes that the "two stimuli must be sensed by the same cell for effective immune activation, thereby increasing the specificity of an immune response and perhaps explaining why alum is such an effective adjuvant." *Id.* Given the implication that alum is meant to enhance the immune response to the antigens in the vaccine, the independent role of alum is not well understood in the pathogenesis of autoimmune diseases like GBS. Thus, this theory is the least persuasively presented by Dr. Steinman although it is recognized that the alum is meant to cause an enhanced immune response to the vaccine to stimulate the production of memory cells.

Finally, reliance on studies like Haber and Tseng offered by respondent's experts to demonstrate that the Prevnar-13 vaccine is not known to cause GBS is misplaced. Importantly, Dr. Donofrio conceded that Haber was using data from the passive reporting system, the Vaccine Adverse Effects Reporting System ("VAERS"), which is known to be subject to underreporting and the article, published in 2016, collected data from the time-period in which the Prevnar-13 vaccine was fairly new, which may explain limited case reports of GBS following administration of the Prevnar-13 vaccine. Nevertheless, the article still identified eleven cases of GBS after the Prevnar-13 vaccine was administered of which the authors accepted eight. Resp't Ex. E, Tab 6 at 4. The Tseng article, which studied adverse events following vaccination with the Prevnar-13 and Pneumococcal-23 ("PPV23"), found that there was "no greater incidence of GBS" following the Prevnar-13 vaccine compared to the PPV23. *See* Resp't Ex. E, Tab 9 at 7. However, a finding that there is no increased risk of an adverse event after vaccination with one vaccine compared to another is not evidence that adverse events do not occur, particularly in specific cases. Tseng merely demonstrates that in their study the incidents of GBS after the Prevnar-13 vaccine or the PPV23 were the same.

The question under *Althen* prong one is whether petitioner has presented preponderant evidence to support his *theory* that the Prevnar-13 vaccine can cause GBS, not to demonstrate causation by scientific certainty. *See Andreu*, 569 F.3d 1380 ("Medical literature and epidemiological evidence must be viewed, however, not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard: The standard of proof required by the [Vaccine Act] is simple preponderance of evidence; not scientific certainty…") (citing *Bunting v. Sec'y of Health & Hum. Servs.,* 931 F.2d 867,873 (Fed. Cir. 1991). Both Drs. Donofrio and McGeady, neither of whom acknowledged vaccine causation in any instance except after the 1976 swine flu vaccine, require something akin to scientific certainty to demonstrate causation, which impermissibly raises the burden on petitioner.

Petitioner, through Dr. Steinman, has presented two theories of molecular mimicry between the components of the Prevnar-13 vaccine and components of the peripheral nervous system. I find that his explanation of these theories with support from the medical literature is

persuasive and accordingly that he has presented a sound and reliable theory of vaccine causation, satisfying *Althen* prong one.

c. *Althen* prong three

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F. 3d at 1281. 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, is medically acceptable to infer causation." *Bazan v. Sec'y of Health & Hum. Servs.,* 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under *Althen* prong one). *Koehn v. Sec'y of Health & Hum. Servs.*, 773 F.3d 1239, 1243 (Fed. Cir. 2014); *Shapiro v. Sec'y of Health & Hum. Servs.,* 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.* 503 F. App'x 952 (Fed. Cir. 2013)

Petitioner received the Prevnar-13 vaccine on March 31, 2017. Pet'r Ex. 1. On April 11, 2017, petitioner sought treatment at the emergency department complaining of a headache, along with numbness and tingling in his hands and feet bilaterally that had begun approximately two days prior. Pet'r Ex. 4 at 30. Additionally, on April 11, examining physicians documented absent reflexes bilaterally in his lower extremities. *Id.* at 33. Consistent with the ruling above, the onset of petitioner's neurological symptoms of GBS appear to have begun nine to eleven days post-vaccination.

Dr. Steinman and Dr. Donofrio agreed that an onset of neurological symptoms between eight- and twelve-days post-vaccination is a medically acceptable timeframe to infer vaccine causation. *See* Pet'r Ex. 17 at 25; Tr. 240. Further, Drs. Steinman and Donofrio agreed that symptom onset between seven and twelve days is an acceptable time frame that coincides with the theory of molecular mimicry. Tr. 138-39; Tr. 242. However, Dr. McGeady opined that the onset of symptoms of GBS occurring seven to twelve days after exposure to an antigen is "a bit of stretch," suggesting that it would be too rapid of an onset to consider temporally appropriate. Tr. 298-300.

The medical literature filed in this case by both petitioner and respondent support Drs. Steinman and Donofrio's opinion. Haber et al. found 11 cases of GBS following the Prevnar-13 vaccine, with a median onset interval of nine days. Resp't Ex. E, Tab 6 at 4. The Schonberger et al. article, although it described GBS following the flu vaccine, found that fifty-two percent of vaccinated cases included an onset of within one-to-two weeks following vaccination. Pet'r Ex. 52 at 8. That percentage increased to seventy-one percent within four weeks following influenza vaccination. *Id.*

Additionally, an onset of GBS 11 days post-vaccination is also consistent with what has been found to be appropriate timing in other Vaccine Program cases in which molecular mimicry is the causal theory to explain how the Prevnar-13 vaccine can cause GBS. *See Diponziano v. Sec'y of Health & Hum. Servs.,* No. 17-1130V, 2025 WL 942744 (Fed. Cl. Spec. Mstr. Feb. 11,

2025) (finding an onset of 11 days after receipt of the Prevnar-13 vaccine was an "acceptable timeframe in which to infer causation"); *Maloney v. Sec'y of Health & Hum. Servs.,* 2022 WL 1074087, at *36 (finding onset of one to two weeks after the administration of the Prevnar-13 vaccine appropriate given the theory of molecular mimicry).

Based on petitioner's medical records, the expert's opinions, and medical literature filed in this matter, I find that petitioner has provided preponderant evidence that the onset of petitioner's GBS occurred between 9- and 11-days post-vaccination and that such timing is medically appropriate. Further, the onset of petitioner's GBS coincides with petitioner's causal theory of molecular mimicry and the timing is consistent with most of the other Prevnar/GBS cases decided in the Program. Thus, petitioner has preponderantly established a "proximate temporal relationship" between the Prevnar-13 vaccine and his GBS, satisfying *Althen* prong three.

d. *Althen* prong two

Under *Althen* prong two, a petitioner must prove by a preponderance of the evidence that there is a "logical sequence of cause and effect showing that vaccination was the reason for the injury." *Capizzano,* 440 F.3d at 1324 (quoting *Althen,* 418 F.3d at 1278). The sequence of cause and effect must be "'logical' and legally probable, not medically or scientifically certain." *Althen,* 418 F.3d at 1278. The petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." *Capizzano,* 440 F.3d at 1325. Instead, petitioner may satisfy his burden by presenting circumstantial evidence and reliable medical opinions. *Id.* at 1325-26. "Evidence demonstrating petitioner's injury occurred within a medically acceptable time frame bolsters a link between the injury alleged and the vaccination at issue under the "but-for" prong of the causation analysis." *Capizzano,* 440 F.3d at 1326. There is a "logical overlap between the three *Althen* prongs, and that evidence that goes to one prong may also be probative for another prong." *Contreras,* 107 Fed. Cl. at 295.

As discussed above, the fact that petitioner has established that the Prevnar-13 vaccine can cause GBS and that the onset of petitioner's GBS, approximately 9 to 11 days post-vaccination, is a medically acceptable timeframe helps to establish that the Prevnar-13 vaccine was the but-for-cause of his condition. Petitioner's medical records, the opinions of petitioner's expert, and the medical literature, provide additional support to the finding that petitioner has demonstrated *Althen* prong two by preponderant evidence.

Eleven days after receiving the Prevnar-13 vaccine, petitioner presented with numbness and tingling, along with absent reflexes in his lower extremities. He reported that the numbness and tingling had been present for about two days. *See* Pet'r Ex. 4 at 4. While the diagnosis of GBS took repeated trips to the emergency department, he was finally admitted on April 19, 2017 as his symptoms progressed. *See* Pet'r Ex. 4 at 478. Neurologist, Dr. Freiman reviewed petitioner's previous MRIs and performed a physical examination, and wrote:

> [Petitioner] has had progressive reflex loss in his lower extremities, upper extremities and distal sensory loss in legs and arms. Although patient has lumbar stenosis moderate L4-

> L5 and nerve root compression left L5 and S1, and degenerative disease on his right hip, I do not believe his findings are all explained by the above. Guillain-Barre syndrome, better known as acute inflammatory demyelinating polyneuropathy, would best explain his clinical course.

Id. at 482. Petitioner was transferred to CMC-Main for treatment for GBS and began plasmapheresis treatment. Pet'r Ex. 5 at 5, 22. Petitioner was discharged to an inpatient rehabilitation facility on April 28, 2017, where he received both physical and occupational therapy. *See generally* Pet'r Ex. 6.

The progression from vaccination to onset of GBS in approximately nine to eleven days by the mechanism of molecular mimicry is logical based on the general understanding of immune cross reactivity and supported as to timing by the opinions of both Dr. Steinman and Dr. Donofrio. *See* Tr. 240 (Dr. Donofrio testifying, "…if somebody had symptoms of weakness, pain, tingling that started eight to twelve days after a vaccination," timing "would fit nicely for a vaccine onset."); Tr. 329; *see also* Resp't Ex. G, Tab 2 at 1 ("The acute progression of limb weakness, often with sensory or cranial nerve involvement 1-2 weeks after immune stimulation, proceeds to its peak clinical deficit in 2-4 weeks."). Additionally, as Dr. Steinman observed, petitioner had not experienced any other illness prior to the onset of his GBS that could have provided the immune stimulus to cause GBS. Even with the documentation of lumbar spine spondylosis on MRI, petitioner's treating physicians opined that the lumbar disease was unlikely the cause for the progression of petitioner's bilateral lower extremity weakness or sensory symptoms. *See e.g.* Pet'r Ex. 5 at 5 ("…an MRI of the lumbar spine was obtained which demonstrated multi lumbar spondylosis at L4-L5, left paracentral HNP, with moderate stenosis and right L5-S1 disc osteophyte complex with mild stenosis. It was deemed that this was the unlikely source of his bilateral lower extremity weakness….").

Even though petitioner's treating physicians did not engage in extensive discussion of a causal relationship between petitioner's GBS and the Prevnar-13 vaccine, there are several notations in his medical records that associate the onset of his symptoms with the pneumococcal vaccination (albeit some misidentified the Prevnar-13 vaccine as Pneumovax). For example, on April 24, 2017, Nurse Practitioner Traynor wrote, "62 y/o Caucasian male with recent flu and Pneumovax shots (approximately 3 weeks ago) with gradual painful ascending paresthesias/weakness in bilateral hands and feet s/p first Plex treatment." Pet'r Ex. 5 at 102. Again, petitioner's treating physician, Dr. John Cunneen documented that the onset of petitioner's ascending paralysis was "approximately 3 ½ weeks ago after he received his flu and Pneumovax vaccinations." *Id.* at 30; *see also* Pet'r Ex. 6 at 4. After petitioner's hospitalization and rehabilitation, Dr. Philip Iuliano wrote, "P/t had [Pneumococcal vaccine] in March. In April, he developed ascending paralysis, diagnosed with Guillain-Barré syndrome. Treated with plasmapheresis. Went to rehab." Pet'r Ex. 11 at 34. Dr. Steinman also observed that petitioner's physicians listed the "Pneumovax 23 (Guillain-Barré syndrome)" as an allergy, demonstrating some evidence that physicians were associating petitioner's GBS to the pneumococcal vaccine beyond a temporal association.[40] Tr. 96-98; *see also* Pet'r Ex. 11 at 35. "A treating physician's recommendation to withhold a particular vaccination can provide probative evidence of a causal link between the vaccination and injury a claimant has sustained."

[40] Some of petitioner's treating physicians misidentified the vaccination petitioner had received on March 31, 2017.

Andreu, 569 F. 3d at 1376-77; *see also e.g. Kelley v. Sec'y of Health & Hum. Servs.,* 68 Fed. Cl. 84, 100 (2005) (relying in part on petitioner's treater's reported hesitancy to administer further tetanus shots as evidence in support of the second *Althen* prong).

Further, petitioner's disease course and treatment were consistent with other cases in which petitioners' have demonstrated that the Prevnar-13 vaccine caused them to develop GBS. For example, in *Bartoszek*, the petitioner presented to the emergency room with acute back pain and numbness and tingling in his feet two weeks after receiving the Prevnar-13 vaccine. *Bartoszek v. Sec'y of Health & Hum. Servs.,* 2024 WL 4263604, at * 4-5. The petitioner in *Bartoszek* was diagnosed with GBS after neurological examinations revealed absent deep tendon reflexes in the lower extremities, treated with IVIG, went to inpatient rehabilitation, and experienced residual symptoms of diminished strength and continued numbness and tingling. *Id.*, at *5-6.

Respondent's arguments that petitioner may have suffered from rhabdomyolysis instead of GBS are inconsistent with petitioner's clinical course, as discussed above. While he initially had elevated CPK which can be a feature of rhabdomyolysis indicating muscle breakdown, the progression of his signs and symptoms, his ultimate diagnosis by treating physicians, based on many neurological examinations and the decision to treat with plasmapheresis were very consistent with GBS. Further, the Ropper article Dr. Steinman referenced, demonstrated that rhabdomyolyses with elevated CPK can be a feature of GBS, not a separate diagnosis. *See* Pet'r Exs. 108. Finally, Drs. Steinman, Donofrio, and McGeady agreed, plasmapheresis is used to treat GBS, and is not used for rhabdomyolysis. *See* Tr. 148; 222; 247.

As I found above, petitioner suffered from GBS, and the progression of his disease is consistent with an immune cross-reaction to the Prevnar-13 vaccine through the mechanism of molecular mimicry as proposed by Dr. Steinman. The onset of petitioner's disease, his progression of symptoms, treatment and residual symptoms are all consistent with GBS being induced by vaccination. Accordingly, petitioner has provided preponderant evidence of a logical sequence of cause and effect between the Prevnar-13 vaccine and his GBS, satisfying *Althen* prong two.

VI. Conclusion

After a review of the entire record and for the foregoing reasons, I find by preponderant evidence that petitioner suffered GBS caused-in-fact by the Prevnar-13 vaccination he received on March 31, 2017, with residual symptoms that continued to affect him as of the time of the hearing. As such he is entitled to compensation.

IT IS SO ORDERED.

s/Thomas L. Gowen
Thomas L. Gowen
Special Master