In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: February 11, 2025

DORIS DIPONZIANO,	*	
Petitioner,	*	No. 17-1130V
v.	*	Special Master Gowen
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Entitlement; Pneumococcal Conjugate Vaccination ("Prevnar"); Guillain-Barré Syndrome ("GBS").
Respondent.	*	

Irene McLafferty, Mess and Associates, P.C., Philadelphia, PA, for petitioner.
Lynn Christina Schlie, U.S. Department of Justice, Washington, D.C., for respondent.

RULING ON ENTITLMENT[1]

On August 22, 2017, Doris DiPonziano ("petitioner") filed a petition for compensation under the National Vaccine Injury Compensation Program.[2] Petitioner filed an amended petition on August 24, 2017, alleging that the pneumococcal conjugate vaccine ("Prevnar 13" or "Prevnar") she received on July 11, 2016, was the cause-in-fact of her Guillain-Barre Syndrome ("GBS"). Petition (ECF No. 1); Amended Petition (ECF No. 9).

[1] In accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012), because this opinion contains a reasoned explanation for the action in this case, **this opinion will be posted on the website of the United States Court of Federal Claims**. This means the opinion will be available to anyone with access to the internet. As provided by 42 U.S.C. § 300aa-12(d)(4)B), however, the parties may object to the published Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has 14 days within which to request 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). **If neither party files a motion for redaction within 14 days, the entire opinion will be posted on the website and available to the public in its current form.** *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.

AUTHENTICATED U.S. GOVERNMENT INFORMATION GPO

Based on a full review of the evidence and testimony presented, I find that petitioner has established by a preponderance of the evidence that the Prevnar 13 vaccine caused her GBS, and therefore she is entitled to compensation.[3]

I. Procedural History

Petitioner filed a petition for compensation on August 22, 2017 and an amended petition on August 24, 2017, alleging that the Prevnar 13 vaccine she received on July 11, 2016, caused her to suffer GBS. Petition; Amended Petition. The amended petition was accompanied by medical records. Petitioner's Exhibits ("Pet'r Ex.") 1-6 (ECF No. 9). On April 26, 2018, respondent filed a status report stating that he intended to defend against the claim and that settlement discussions were not appropriate. Respondent's ("Resp't") Status Report ("Rept.") (ECF No. 18).

On June 12, 2018, respondent filed his Rule 4(c) report, recommending against compensation in this case. Resp't Rept. at 1 (ECF No. 21). Specifically, respondent stated that the medical records fail to establish a "more likely than not causal connection between petitioner's vaccination and the onset of her GBS," and that, while some of her treating physicians noted the temporal relationship, "none provided a causal theory beyond simply an alleged temporal association." *Id*. at 7.

Thereafter, petitioner filed an expert report from Robert Hyzy, M.D.,[4] and respondent filed an expert report from Brian Callaghan, M.D., M.S.[5] Pet'r Ex. 9 (ECF No. 33); Resp't Ex. A

[3] Pursuant to Section 300aa-13(a)(1), in order to reach my conclusion, I have considered the entire record including all of the medical records, statements, expert reports, and medical literature submitted by the parties. This opinion discusses the elements of the record I found most relevant to the outcome.

[4] Dr. Hyzy graduated from Kenyon College with a Bachelor of Arts Degree in Biology and Psychology in 1978. Pet'r Ex. 9.1 at 1. He graduated from New York University School of Medicine in 1982, followed by an internship in Internal Medicine from the University of Michigan in 1983. *Id*. He completed his residency in Internal Medicine at the University of Michigan in 1985. *Id*. Dr. Hyzy completed a fellowship in Pulmonary and Critical care Medicine also at the University of Michigan in 1989. *Id*. He is board certified in in Internal Medicine, Pulmonary Medicine, and Critical Care Medicine. *Id*. He was an instructor, lecturer, Clinical Assistant Professor in Internal Medicine, Associate Professor of Internal Medicine, and Professor of Internal Medicine in the University of Michigan Health System. *Id*. at 1-2. Dr. Hyzy has focused his research on pulmonology, internal medicine, and critical care. *See* Pet'r Ex. 9.1. Dr. Hyzy did not testify at the entitlement hearing.

[5] Dr. Callaghan graduated from the University of Michigan with a Bachelor of Science degree in 1996. Resp. Ex. B at 1. He graduated from the University of Pennsylvania Medical Center with a medical degree in 2004. *Id.* He remained at the University of Pennsylvania Medical Center for an internship in preliminary medicine from 2004 – 2005 and a residency in neurology from 2005 – 2008. *Id.* Afterwards, Dr. Callaghan completed a fellowship in neuromuscular medicine and a master's degree in clinical research design and statistical analysis at the University of Michigan Medical School. *Id.* In 2009, he was hired onto the Michigan faculty, where he is currently an associate professor in neurology. *Id.* Dr. Callaghan is also a clinical neurologist and director of the ALS Clinic at the Veterans Affairs Ann Arbor Health System. *Id.* at 1-2. He is board-certified in psychiatry and neurology as well as electrodiagnostic medicine. *Id.* Dr. Callaghan stated that his primary interest is in patients with neuropathy and neuralgic amyotrophy. Resp. Ex. A at 3. While Dr. Callaghan did not state what number or proportion of his patients have these disorders, his curriculum vitae reflects that he teaches, conducts research, publishes, and serves as an

(ECF No. 31). On April 11, 2019, I held a Rule 5 Status Conference, where I indicated that petitioner needed to provide further evidence to address the three prongs in *Althen*. Scheduling Order, Apr. 12, 2019 (ECF No. 37); *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005).

On July 26, 2019, petitioner filed additional expert reports from Robert Knobler, M.D., PhD[6] and Matthew Lee, M.D., RPh, M.S. [7] Pet'r Ex. 11; Pet'r Ex. 12 (ECF No. 43). On October 9, 2019, respondent filed a supplemental expert report from Dr. Callaghan. Resp't Ex. C (ECF No. 53). On October 28, 2019, respondent filed an expert report from You-Wen He, M.D., PhD.[8] Resp't Ex. D (ECF No. 55). After a second Rule 5 Conference and unsuccessful settlement negotiations, an entitlement hearing was set, and the parties filed pre-hearing briefs. Scheduling Order, Nov. 27, 2019 (ECF No. 56); Resp't Status Rept., May 12, 2020 (ECF No. 72); Hearing

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editor for numerous peer-reviewed journals focusing on peripheral neuropathy. *See generally* Resp. Ex. A. Dr. Callaghan was admitted as an expert in the subjects of neurology, and electrodiagnostic medicine. Tr. 319.

[6] Dr. Knobler graduated from the City College of New York with a BS in Biology in 1969. Pet'r Ex. 12 at 1. He graduated from the State University of New York with an M.D. and a PhD in Anatomy in 1975. *Id*. Dr. Knobler completed his residency in Neurology at Kings County Hospital Center in 1979. *Id*. He was a postdoctoral research fellow in the Department of Immunopathology at the Scripps Clinic and Research Foundation from 1979-1982, and was a clinical coordinator and co-director in the Multiple Sclerosis Research Center at Scripps Clinic and Research Foundation. *Id*. He has been an assistant professor, associate professor, adjunct professor, and professor at Thomas Jefferson University, Department of Neurology, from 1984 to 2002. *Id*. at 2. He was the Director of the Multiple Sclerosis Comprehensive Clinical Center at Thomas Jefferson University Hospital from 1996-1998. *Id*. His research area includes immunology and multiple sclerosis. *See* Pet'r Ex. 12. He has an active medical license in Pennsylvania and is a reviewer for a variety of journals in the fields of Neurology, Immunology, and Multiple Sclerosis. *Id*. at 3-5. Dr. Knobler was admitted as an expert in the field of neurology with a background in immunology and virology. Tr. 120.

[7] Dr. Lee graduated from Virginia Commonwealth University with a BS in Chemistry in 1992. Pet'r Ex. 11 at 2. He graduated from the Medical College of Virginia with a Bachelor of Science in Pharmacy in 1995, and a Master of Science in Pharmacology and Toxicology in 1999. *Id*. at 2. He received his M.D. from Virginia Commonwealth School of Medicine in 2004 and completed a post-doctoral internship in internal medicine in 2005. *Id*. at 2-3. He has been licensed to practice medicine and surgery in Virginia since 2005 and has been licensed to practice pharmacy in Virginia since 1995. *Id*. at 3. In 2016, he was appointed a consultant to the FDA advisory committee for pharmaceutical science and clinical pharmacology. *Id*. at 4. He is currently a primary care physician, a pharmacist, medical examiner, and veterans' evaluation services provider. *Id*. at 1. Dr. Lee was admitted as an expert in the field of pharmacology, internal medicine, and toxicology. Tr. 76.

[8] Dr. He graduated from the Fourth Military Medical University in Xian, China with an M.D. in 1986. Resp. Ex. E at 1. He Graduated from the Institute of Microbiology and Epidemiology from the Academy of Military Medical Science in Beijing in 1989. *Id*. He graduated from the Department of Microbiology & Immunology from the University of Miami School of Medicine in 1996. *Id*. Afterwards he was a Senior Fellow at the Howard Hughes Medical Institute in the Department of Immunology at the University of Washington. *Id*. He has been a Professor of Immunology in the Department of Immunology at Duke University Medical Center since 2000. *Id*. His research areas include innate and adaptive viral and bacterial immunity. *Id*. at 3-15. He has directed research on human immune responses to viral infections including influenza, HIV, HBV, and HCV. *Id*. He has been the Director of Immunology of Human Diseases at Duke University for the past five years and is the current Co-Principal Investigator for four clinical trials focusing on cancer immunotherapy. *Id.* at 3. He has served as a reviewer for over 20 different scientific journals and has published extensively in immunology. *Id*. at 9-17. Dr. He was admitted as an expert in the field of immunology. Tr. 227.

Order (ECF No. 77); Pet'r Pre-Hearing Brief (ECF No. 82); Resp't Pre-Hearing Brief (ECF No 83); Pet'r Reply to Resp't Pre-Hearing Brief (ECF No. 107).

An entitlement hearing was held on September 16 and 17, 2021. At the conclusion of Dr. Knobler's testimony on September 17, 2021, respondent requested a continuance to review the transcript and have an opportunity to prepare a response to Dr. Knobler's testimony. Tr. 184. I granted respondent's request and respondent filed supplemental expert reports from Drs. Callaghan and He. *Id.* at 184-85; Resp't Ex. F (ECF No. 100); Resp't Ex. G (ECF No. 100). The hearing concluded on October 21, 2021, and the parties thereafter filed post-hearing briefs. Pet'r Post-Hearing Brief (ECF No. 105); Resp't Post-Hearing Brief (ECF No. 106); Pet'r Post-Hearing Reply (ECF No. 107).

The matter is now ripe for adjudication.

II. Evidence Submitted

a. Summary of Petitioner's Medical History

Prior to petitioner's vaccination and GBS onset, petitioner and her husband shared the household responsibilities, doing "a lot of the shopping and running errands." *Id.* Both were retired by this point, and both could drive. *Id.* at 8, 15. Petitioner's brother-in-law, Mr. Tony Perez, testified that petitioner and her sister "got together often" for different activities such as "flower shows, different trips, shopping trips and things of that nature." *Id.* at 8. Petitioner was a "very healthy person" and "had a lot of energy." *Id.* Petitioner's husband, Mr. Carl DiPonziano noted that, prior to the vaccination, he and petitioner would shop together, visit with friends, and "do the normal things that people do." *Id.* at 30. Petitioner did the cleaning, laundry, and cooking in the house. *Id.* She was "very active" at this time, "she walked very fast," and was "just very busy all the time." *Id.* at 30.

On July 11, 2016, petitioner, a 79-year-old female, presented to Dr. Mary Monari-Sparks for a follow up for continued complaints of fatigue, two episodes of chest pain with exertion, and a skin lesion that was slow to resolve beneath her left breast. Pet'r Ex. 2 at 7. Petitioner's medical history at this time included, in part, gastroesophageal reflux disease, trochanteric bursitis, primary localized osteoarthritis of the lower leg, degenerative disc disease, shoulder joint pain, midline low back pain, and left leg pain. *Id.* at 8. Significantly for the issues in this case she was recorded as suffering from allergic rhinitis since at least 2015. *Id.* Petitioner noted at the hearing that she had "general" health issues and took Synthroid for hypothyroidism and Nexium for acid reflux. Tr. 50-51. Petitioner's husband, Carl DiPonziano testified that petitioner had allergies with symptoms including itching eyes and "running of the eyes." *Id.* at 30. Mr. Perez also noted that petitioner had allergies with "tearing of her eyes and itchy eyes from time to time. She would have some nasal discharge. She would blow her nose with some frequency, often going through several different boxes of tissues. Most of it seemed to be seasonal…[in the] spring, summertime." *Id.* at 9.

Petitioner's exam at the July 11, 2016 appointment was unremarkable aside from the lesion and rash beneath her breast and fatigue. Pet'r Ex. 2 at 13. Diagnoses at this appointment included precordial pain, unspecified hypothyroidism, right thumb pain, rash, and skin lesion. *Id.* at 15. She was referred to cardiology for the precordial pain and to dermatology for the skin issues. Petitioner also received the Prevnar 13 vaccine at this appointment. *Id*.

About one day after the vaccination, petitioner's arm became sore, "was very red," and "looked kind of crusty" at the injection site. Tr. 49. Petitioner's husband, Carl DiPonziano noted that there was swelling on the left arm that was about "two inches long by an inch wide" with redness. *Id.* at 32-33. A few days later, petitioner and her sister took a trip to Atlantic City, and petitioner recalled being concerned about her sore arm. *Id.* at 52. Mr. DiPonziano recalled that petitioner "was fine" when she left for this trip and was not coughing or otherwise sick. *Id.* at 33. Mr. Perez was unaware of any other symptoms, including fever or other issues, aside from swelling at the injection site and noted that that if petitioner "wasn't feeling well, she wouldn't have gone down to the shore, and [her husband] certainly wouldn't have let her go down to the shore." *Id.* at 9.

On the evening of July 22, 2016, petitioner was not "feeling good" and had "tingling in her hands and feet." *Id.* at 52-53. Early the next morning she "was not able to move very well" and her husband called 911. *Id.* Petitioner "did not feel as though she was sick in any way…even [with] a cold." *Id.* at 54. Her only symptoms at this point were "tingling and not feeling like [her]self." *Id.* Mr. DiPonziano testified that petitioner complained that she felt "kind of weird," noting tingling in her fingers and toes that "gradually got stronger." She was awake by 5:00 the next morning and could barely walk, requiring Mr. DiPonziano's assistance to the bathroom. *Id.* at 34. Mr. DiPonziano called 911, and petitioner was taken to the ED and transferred to the ICU at Cooper University Hospital. *Id.* at 35-36. Mr. Perez added more details about the onset of petitioner's symptoms during his testimony at the hearing, noting that petitioner did not complain of feeling unwell until July 22, 2016, the night before she was admitted to Cooper University Hospital. *Id.* At that point, she "was complaining that she wasn't feeling herself and she felt some numbness in her fingers and toes. By…early the next morning…she was hardly able to move." *Id.* at 10-11. Petitioner's husband called 911, and Mr. Perez and his wife met them at the Cooper University Hospital ED. *Id.* at 11.

i. Admission to Cooper University Hospital

On July 23, 2016, twelve days after vaccination, petitioner presented to the Cooper University Hospital Emergency Department ("ED") complaining of numbness and tingling in her hands and feet starting at about 10:00 p.m. the previous night "with progressive severe weakness." Pet'r Ex. 3 at 57, 60. Petitioner reported that she "felt weakness in her arms and legs bilaterally and 'could not walk'" when she woke up. *Id.* She also reported a red rash to the left upper arm over the past week that resolved. *Id.* at 56-57. The ED physician noted that petitioner was positive for recent upper respiratory infection ("URI") symptoms for four days, and that she recently received the pneumovax vaccine. *Id.* Mr. Perez testified that, during this time, "it was obvious that…[petitioner] was becoming more and more paralyzed. Tr. at 12.

On physical examination, petitioner had 2/5 strength in the bilateral upper extremities and 3/5 strength in the bilateral lower extremities. Pet'r Ex. 3 at 59. Petitioner could not hold her arms in the air but had "equal and strong grips" bilaterally. *Id.* at 56. She was unable to walk secondary to weakness. *Id.* at 59. Neurological symptoms included tingling, sensory change, and weakness, but the physical examination noted "no sensory deficit." *Id.* at 59. Petitioner's respiratory symptoms included a cough, but her pulmonary effort and breath sounds were normal. She had "no respiratory distress…no wheezes…no rales…[and] no tenderness." The examination of her mouth and throat recorded: "Uvula is midline, oropharynx is clear and moist and mucous membranes are normal. No oropharyngeal exudate, posterior oropharyngeal erythema or tonsillar abscesses." *Id.* at 57-58 The ED physician's assessment noted that petitioner was "a 79 [year old] female presenting with one day of acute onset bilateral weakness and paresthesias in [the upper extremity] and [lower extremity] with antecedent URI [symptoms]." *Id.* The differential diagnosis included "concern for" Guillain Barre Syndrome "given bilateral weakness and recent URI/vaccine." *Id*. The plan included lab work, head CT, lumbar puncture, and a neurology consultation. *Id.*

The ED physician performed another physical examination about two hours later due to petitioner's "progressive paralysis." *Id.* at 63. By this time, petitioner was positive for "mild [bilateral expiratory] wheeze" in the lungs. *Id.* at 62. Her neurological examination revealed 3/5 strength in the bilateral upper extremities and 4/5 strength in the bilateral lower extremities. *Id.* The physician was "unable to elicit patellar or ankle jerk reflexes," and petitioner was positive for bilateral pronator drift. *Id.* at 62. The "leading diagnosis" at this point was GBS given "the lack of bulbar" symptoms. *Id.* at 63. Immediate interventions included "imaging, emergent consultation with neurology and critical care, [and] intravenous immunoglobulin ("IVIG") initiation." *Id.*

About five hours later, petitioner was reassessed and had "persistent and worsening weakness bilaterally." *Id.* at 64. Petitioner's labs and head CT showed no abnormalities. *Id.* at 65. A lumbar puncture was performed and "showed no protein in fluid which would be consistent with GBS," if the disease was in the early stages. *Id.* The plan was to admit petitioner to the ICU with neurology to follow her, and petitioner was placed on a nasal cannula due to oxygen desaturation. *Id.* at 65-66.

The Critical Care history and physical noted that petitioner had a history of hypothyroidism and multiple allergies and presented "with acute rapidly progressive dysesthesia and paresis." *Id.* at 71. Petitioner reported tingling in her fingers followed by her toes the night before she presented to the ED, "rapidly followed by her inability to walk." *Id.* Petitioner denied "bowel/bladder incontinence, difficulty breathing, dizziness, [and] palpitations." *Id.* She also reported receiving "a pneumonia vaccine around 10 days [ago] which was followed by erythematous rash in her arm/shoulder region" at the injection site, and "URI symptoms for the past five days," including hoarseness over the past three to four days. *Id.* at 71, 77. The pulmonary exam was "clear to auscultation bilaterally" with "no rales or wheezes." *Id.*at 73. Assessment of the skin showed an "erythematous rash on [the] right shoulder" measuring 4 by 4 centimeters. *Id.* The neurologic exam revealed 2/3 strength in the right upper extremity, 3/3 strength in the left upper extremity, and 3/5 strength in the bilateral lower extremities." *Id.* at 74. Areflexia was present in both legs. *Id.* The Critical Care physician's impression was concern "for

GBS due to symmetrical involvement," and noted that "possible triggers include pneumonia vaccine, preceding URI." *Id.* The plan included a five-day course of IVIG and a low threshold for intubation in case of respiratory decompensation. *Id.*

The initial neurology consult on July 23, 2016, included a detailed timeline of the onset of petitioner's symptoms, noting that

> Last evening, around 6:00 p.m., [petitioner] began to experience numbness in her distal fingers. Numbness involved all five fingers in her bilateral hands. Later that evening the numbness was also present in her distal toes, again all five toes bilaterally. She reports around 9:00 p.m. she started to experience some generalized weakness. She was able to walk but felt as though she needed to hold on to chairs/the wall in order to feel stable. She went to bed but was having difficulty sleeping secondary to left arm and right leg pain. She awoke from bed in the middle of the night and walked to her recliner in her living room. Around 5:00 a.m. this morning she awoke and could not get out of her recliner. She called her husband and they called EMS and [she] was brought to the hospital. She reports her weakness is worsening over the few hours that she has been here. Initially she was able to stand and raise her arms and legs and now she is unable to raise her arms, and can only raise her legs slightly…She recently received the pneumovax on the 19th of this month. She reported a slight, confluent red rash on her left arm after the injection that has since resolved. She reports on Tuesday of this week she began to have a URI. She has had a dry cough, rhinorrhea, and post nasal drip.[9]

Id. at 108.

The motor examination performed during the neurology consult revealed 1/5 strength in the proximal right arm, 2/5 strength in the proximal left arm, 3/5 strength the distal right and left arms, 3/5 strength in the bilateral proximal lower extremities, and 4/5 strength in the bilateral distal lower extremities. *Id.* at 112. Petitioner's sensation was intact to light touch, pinprick, and vibration diffusely including the distal fingers and toes. *Id.* Her reflexes were diffusely absent, and the Babinski reflex was negative bilaterally. *Id.* Petitioner was unable to perform the finger to nose or heel to shin coordination tests due to weakness. *Id.* Her fine motor movement was intact, and rapid alternating movement was slow. *Id.* She could give a "very weak but symmetric grip and wiggle toes but [was] unable to move [her] arms or legs against gravity." *Id.* at 115. Neurology recommended admitting petitioner to the ICU for "close monitoring of hemodynamics and respiratory status," and IVIG treatment for five days. *Id.*

Petitioner received her first dose of IVIG on July 23, 2016, and completed IVIG treatment on July 27, 2016. *See id.* at 282, 301. A neurology consultation on July 27th noted "no significant improvement in [petitioner's] extremity weakness." *Id.* at 278. At the end of her IVIG

[9] Given the reference to days of the week in this neurology consult from July 23, 2016 it should be noted that the vaccine was actually administered on July 11, 2016. The onset of symptoms was Friday evening July 22, 2016 and the reference to the onset of URI symptoms on Tuesday would have been July 19, 2016 or three days before the onset of GBS symptoms.

treatment, petitioner was transferred from the ICU to the intermediate care unit but was transferred back to the ICU the following day due to increasing oxygen requirements. *Id.* at 268, 279. By July 29, 2016, petitioner's strength was 1-2/5 in all extremities, and she began taking gabapentin for neuropathic pain. *Id.* at 258-59. On August 2, 2016 petitioner was intubated and sedated due to respiratory distress. *Id.* at 123, 216. After failing an extubation attempt, she was re-intubated on August 7, 2016. *Id.* at 118. A tracheostomy procedure was performed on August 10, 2016. *Id.* at 116. Petitioner remained intubated throughout the rest of her hospitalization and was transferred to a rehabilitation hospital on August 13, 2016. *Id.* at 67. Her hospital course was further complicated by MSSA bacteremia and multifocal pneumonia. *Id.* at 67, 86, 207; Pet'r Ex 4 at 23. At the time of her discharge, petitioner's diagnoses included acute respiratory failure with hypoxia, on mechanically assisted ventilation, GBS, and unspecified hypothyroidism. Pet'r Ex. 3 at 68.

ii. Admissions to Long Term Care Facilities

On August 13, 2016, petitioner was transferred to Lourdes Specialty Hospital for ventilator weaning, where she stayed until September 9, 2016. Pet'r Ex. 4 at 17, 23, 187. Diagnoses upon admission included "ventilator-dependent respiratory failure/chronic respiratory failure, Guillain-Barre syndrome with respiratory compromise," pneumonia, and "methicillin-sensitive staphylococcus aures bacteremia." *Id.* at 25. Mr. Perez noted that, at the time of her transfer to Lourdes, petitioner was unable to walk. Tr. 14. She was weaned off mechanical ventilation after the pneumonia and bacteremia resolved. Pet'r Ex. 4 at 16-18. During this admission, petitioner had physical therapy ("PT"), occupational therapy ("OT"), and speech therapy. *Id.* at 284-319. She eventually regained the ability to feed herself. Tr. 14. At the time of her discharge, petitioner had been "successfully weaned from mechanical ventilation" and was decannulated. Pet'r Ex. 4 at 16. Petitioner was transferred to a rehabilitation facility on September 9, 2016. *Id.* at 16-17.

Petitioner was admitted to Marlton Rehabilitation Hospital on September 9, 2016, where she continued to have generalized weakness. Pet'r Ex. 5 at 41. Upon her admission, the right upper extremity had 3/5 strength, and the left upper extremity had 4/5 strength. *Id.* The lower extremity strength was "much decreased compared to the upper extremities," with petitioner demonstrating 1/5 strength in the right lower extremity and 2/5 strength in the left. *Id.* Petitioner also had bilateral foot drop. *Id.* During this admission, petitioner received PT, OT, and speech therapy "for progressive ambulation, [activities of daily living] training, strengthening and general conditioning, as well as transfer training, speech, swallowing, and cognitive evaluation." *Id.* at 47. She made "some progress" with the therapies by the time of her discharge to a subacute rehabilitation center on September 30, 2016. *Id.*

On September 30, 2019, petitioner was transferred to The Evergreens, a subacute rehabilitation facility for PT, OT, and speech therapy. Pet'r Ex. 6 at 59. By October 31, 2016, she "regained use of [upper extremities] but continue[d] to require assistance for transfers [and] toileting." *Id.* at 13. By January 5, 2017, petitioner had made "excellent progress" with physical therapy and could "function in her apartment." *Id.* at 153. However, she would "need home PT to continue progress toward maximal function." *Id.* Petitioner was discharged home on January 6, 2017. *Id.*

iii. Continued Treatment at Home

Mr. Perez described petitioner's home as a relatively small government-subsidized apartment. Tr. 16. She used a wheelchair, walker, and rollator in the home, and would "walk the hallways for her own physical therapy." *Id.* She also had a shower seat installed in the home. *Id.* at 17. Once petitioner was home, Mr. DiPonziano "had to do mostly everything for her," including putting her support stockings on, doing chores around the house, cooking, and cleaning. *Id.* at 39-40. Petitioner could transition out of the wheelchair into a chair or her bed with Mr. DiPonziano's help. *Id.* at 40. She had about five or six falls in the apartment in the few months after her discharge. *Id.* at 40, 45. On one occasion, she hit her head, but did not "have any damage." *Id.* at 41. She continued physical therapy treatment at home for approximately six weeks. *Id.* at 41.

At a follow-up neurology appointment on February 3, 2017, petitioner had "continued numbness in her fingertips" causing her to drop things. Pet'r Ex. 8 at 3. She also had "persistent right foot drop, curled left toes, and numbness in both feet." *Id.* She noted feeling unsteady with her walker and that her arms were sore when "holding on tight to her walker." *Id.* The motor examination demonstrated strength levels of 4+/5 bilateral upper extremities, 3/5 right hip flexion, 4-/5 left hip flexion, 4-/5 hip adduction and abduction, 4-/5 right knee extension, 4+/5 left knee extension, 2/5 right plantar flexion, 3/5 left plantar flexion, 2/5 right dorsiflexion, and 3+/5 left dorsiflexion. *Id.* at 7. Sensation was "intact throughout to all modalities" with "diminished light touch on the right lower extremity." *Id.*

Petitioner continued to see improvement throughout 2017 and into 2018. She received physical therapy in her home twice per week until June 6, 2019. Pet'r Ex. 14 at 36. During this time period, petitioner had several appointments with a new neurologist for an independent opinion on her prognosis. Pet'r Ex. 10 at 1. At one of these appointments, on September 26, 2017, petitioner arrived in a wheelchair and showed "substantial improvement since her last visit" four months earlier, as her left foot dorsiflexion strength was near normal. *Id.* at 4. At her last appointment on January 9, 2018, she was able to transfer and walk short distances without an assistive device. *Id.* at 6. She still had moderate right foot drop and mild left foot drop. *Id.*

Petitioner testified that she was not taking any medications related to GBS at the time of the hearing, though she was previously taking "a lot of gabapentin," approximately "600 milligrams…three time a day" which was eventually tapered. *Id.* at 67. She stopped physical therapy in 2019 and had not seen her neurologist since that time. *Id.* at 65. At the time of the hearing, petitioner was unable "to do the things she used to do prior to the GBS" but was able to do all of the cooking, could do some cleaning, and would occasionally join Mr. DiPonziano and a friend for shopping. *Id.* at 41. Petitioner had not received any treatment for GBS for the few years prior to the hearing. *Id.* at 43.

III. Expert Opinions Regarding Vaccine Causation

a. Opinions of Petitioner's Experts on Causation

i. Matthew C. Lee, MD, RPh, MS

Dr. Matthew Lee filed an expert report outlining his opinions in this case on July 26, 2019. Pet'r Ex. 11 (ECF No. 43). He was admitted and testified as an expert in pharmacology, toxicology, and internal medicine at the entitlement hearing. Tr. 20. Dr. Lee opined that the Prevnar-13 vaccine caused petitioner to develop GBS. Tr. 77-78. His overarching theory of causation was that the vaccine caused GBS "through the immune response" and the inability of the immune system to tell the difference between "the real bacteria" and "human host cells." Tr. 79, 80-81.

Dr. Lee explained that GBS is characterized "by the acute or subacute onset of varying degrees of weakness in limbs or cranial nerve-innervated muscles, [and] associated decreased or absent deep tendon reflexes." Pet'r Ex. 12 at 3. He further explained that "GBS is an immune-mediated polyneuropathy…or [occurs] when there [is] a stimulus for the immune system that evokes a response and the immune system actually attacks the nerves in the body." Tr. 75. He opined that petitioner's course at Cooper University Hospital, including respiratory failure, intubation, "and the further weakening of the nervous system," was consistent with GBS and that her case was "rather severe." *Id.* at 87.

Dr. Lee explained that the Prevnar vaccine is a "13-valent conjugate vaccine containing 13 pneumococcal serotypes," and exposure to the vaccine produces "an immune mediated response, that makes organisms more vulnerable to host defenses." Pet'r. Ex. 12 at 4. These "13 different strains of the strep pneumoniae bacteria …ha[ve] a coating on [them]" which is made up of proteins that the immune system recognizes "as a foreign material." Tr. 79. In other words, "the little pieces of these protein coats are put into the vaccine without the infectious part of the bacteria, and, that way, when the vaccine is administered, the body generates an immune response. So if it encounters that bacteria as a real bacteria and not as a vaccine, it will generate an immune response." *Id.* The Prevnar vaccine specifically "has another protein added onto it from the diphtheria [antigen] to evoke a larger immune response from the body." *Id.* at 75. The purpose of the protein is "to stimulate the immune system further and particularly [to stimulate] the…T cell immune-mediated response." *Id*. at 76.

Dr. Lee opined that the vaccine causes GBS "through the immune response" generated by the vaccine. *Id.* at 79. He further explained that the immune response "is to look for road signs" and that

> ideally, the road signs are on the bacteria. However, in this case, the nerve cells in the body also have similar road signs. So once the immune response is generated, the body can't tell the difference whether the road sign…is on the nerve or on the bacteria. So that's how the nerve cells are attacked by the body's immune system through that immune response created by the vaccine.

Tr. 79-80.

The body is unable to tell the difference between "the real bacteria" and "human host nerve cells" because the proteins that the body "looks for, or the road signs…on the bacteria are very similar to ones in the human body. So [the immune system] can't tell the difference just based on the road sign alone whether it's something in the human or something on the bacteria." *Id.* at 80. He defined "road signs" as "the epitope proteins which are proteins on the surface of bacteria, but also on the surface of human cells." *Id*. at 80-81. More specifically, "the epitopes are proteins on the surface of cells that the immune system is trained to recognize through vaccination. [If] those epitopes are similar between a bacteria and nerve cells, then the immune system will also attack the nerve cells that have similar epitopes as the bacteria." *Id.* at 81.

To support this theory, Dr. Lee referenced articles by Haber and Sejvar. *Id.* at 82. The Haber article is a vaccine reporting system post-licensure surveillance review which specifically discusses the Prevnar 13 vaccine and found that "in persons over the age of 65 that received Prevnar 13, there were 10 to 11 cases reported [to VAERS] for GBS." *Id.*; Pet'r Ex. 9.2 at 5.[10] According to Dr. Lee, the Sejvar article "describes the cross-reaction with the epitopes on peripheral nerve roots." Tr. 82; Pet'r Ex. 11.1.[11] The study notes that "vaccines are another antigenic stimulus for which potential associations with GBS have been reported" and that "with rare exceptions, the biological or epidemiological evidence for a causal association between GBS and antecedent infections or vaccination is equivocal." Pet'r Ex. 11.1 at 1-2.

Dr. Lee opined that there was a clear proximate temporal relationship of cause and effect between the vaccination and petitioner's injury given the timeline of vaccine administration and the onset of petitioner's symptoms. Tr. 84. In petitioner's case, it took her body 11 days "to generate the immune response and for the antibodies to attack the epitopes on her nerve cells." *Id.* He relied on the Haber article to support his opinion that 11 days falls within the accepted timeline for causation. *Id.* at 84-85. That article found that, in eleven "reports of possible GBS after PCV13 the median onset interval of symptoms was [nine] days," with a range of two to 34 days. Pet'r Ex. 9.2 at 4.

Finally, Dr. Lee addressed the theory of respondent's experts that petitioner had an upper respiratory infection ("URI"), which caused her to develop GBS as opposed to the vaccine. Tr. 85-86. He first disagreed that petitioner was diagnosed with a URI, noting that "she reported upper respiratory symptoms upon presentation to the ER but she had not undergone treatment or evaluation by a medical doctor to have that diagnosis." Tr. 86. Typical symptoms for a respiratory infection include "chest tightness, shortness of breath, wheezing, [and] sputum

[10] Penina Haber, et al., *Post-licensure surveillance of 13-valent pneumococcal conjugate vaccine (PCV13) in adults aged ≥ 19 years old in the United States, Vaccine Adverse Event Reporting System (VAERS), June 1, 2012 – Dec. 31, 2015*, 34 Vaccine 6330 (2016).

[11] James H. Sejvar, et al., *Population Incidence of Guillain-Barre Syndrome: A Systematic Review and Meta-Analysis*, 36 Neuroepidemiology 123 (2011).

production." *Id.* at 87. A URI is typically diagnosed based on history, onset, and symptomatology including presence of fever, cough, whether the cough is productive or nonproductive, runny nose, and chest tightness. *Id.* at 96. Other factors considered when diagnosing a URI include "the time of year…where [the patient] has been, if they have a history of allergies, if they've traveled, if they have other comorbid conditions, such as COPD…or diabetes or heart disease." *Id.* Referring to an examination by the ED provider at Cooper University Hospital, Dr. Lee opined that the review of systems and physical examination support the fact that petitioner "did not have an upper respiratory tract infection." *Id.* at 102-03; Pet'r Ex. 3.1 at 57. Dr. Lee also opined that, "if there was a URI present, [it] was not present long enough to generate the immune response that would be necessary to cause GBS." Tr. at 353. The medical record indicated URI symptoms for four days at the time of admission. *Id.* at 334. Dr. Lee noted that she was not treated for an upper respiratory infection at the hospital and that it appeared that the symptoms were not present at that time. *Id.* at 353. He testified that if untreated, a URI typically takes three to seven days to resolve, but "the exaggerated immune response that is responsible for GBS would take longer to develop than just the immune response against the pathogen causing the URI." *Id.* at 354-55.

ii. Robert L. Knobler, MD, PhD

Petitioner submitted an expert report from Dr. Knobler on July 26, 2019. Pet'r Ex. 11. Dr. Knobler was admitted and testified "as an expert in the field of neurology with special qualifications in neuroimmunology" at the entitlement hearing. Tr. 120. Dr. Knobler opined that petitioner "developed GBS following immunization with Prevnar 13." Pet'r Ex. 11 at 5; Tr. 122. He proposed two possible causal theories at the hearing as to how a vaccine can cause GBS, molecular mimicry and "collateral damage." Tr. 146-47. At the first hearing, Dr. Knobler opined that "that collateral damage" theory was more likely "the responsible mechanism" as opposed to molecular mimicry. *Id.* at 148. However, at the continuation of the hearing about a month later, he testified that the cause of petitioner's GBS more likely than not was due "to an element of molecular mimicry." *Id.* at 219.

Dr. Knobler testified that GBS "is a disorder that most frequently occurs following some type of immune perturbation disturbance that can be caused by a variety of different causes." Tr. 121. He further explained that "there is typically a time course that is involved between the precipitating event and the onset of clinical symptoms" which "involves the presentation of various neurological symptoms relating to the loss of the insulation of nerve fibers in the peripheral nervous system…" *Id.* In other words, GBS involves "a precipitating event, a timeline to which that leads to the loss of myelin, the insulation surrounding nerve fibers, and that there may be damage to the nerve fibers…and subsequently neurologic symptoms as a consequence of that pathological change." *Id.* at 121-22.

Dr. Knobler noted that "many of the components of the process by which" GBS develops "in any individual are highly variable" and "depends on circumstance." Tr. 197. To determine such mechanism, one must "search for what factors…have been associated with [GBS]." *Id.* at 197-98. He further explained that "factors such as infections and vaccinations are two of the most common causative agents that are associated with" GBS. *Id.* at 198. Temporal association

"meaning the timeline in which those events occur, have proven pivotal in terms of that association." *Id.* Moreover, Dr. Knobler cited to the same analysis by Haber as Dr. Lee to show that "there is an association between GBS and having received [the] Prevnar vaccine." *Id.* at 146.

Dr. Knobler explained that, with his collateral damage theory, "any vaccine has the potential in an individual of stimulating the immune system…and if it stimulates the immune system in a particularly susceptible individual…that stimulation of the immune system can lead to development of Guillain-Barre." Tr. 123-24. Importantly, "the immune system response can be misdirected in certain individuals and can lead to loss of tissue. One of the ways in which that happens is the development of GBS…" *Id.* at 125. Such misdirection can occur "in a variety of ways," one of which "is an immediate early type of response." *Id.* In this scenario, "when an antibody binds to a target, the Fc portion is left protruding, and a cell called a macrophage…attaches to the Fc portion of the antibody molecule and then it produces damage to the tissue." *Id.* at 125-26. In other words, "if there is binding of an antibody to a target, the Fc portion is then left to attract the macrophage, which is recruited to the area, and that activated macrophage will produce damage to the tissue that the antibody is attached to." *Id.* at 126. More specific to GBS, "if the antibody attaches to myelin, [the macrophage] will produce damage to myelin." *Id.* He noted that "when we look at GBS as an example, we look at how an antibody binds to a tissue and the time course that it takes for that antibody to be produced and the time it takes for the macrophages to produce damage." *Id.* at 126-27. Such damage can occur "anywhere from four days, at the absolute shortest if the system is primed, to usually somewhere closer to between seven and 14 days." *Id.* at 127.

Dr. Knobler explained that the Prevnar vaccine has elements of multiple "different strains of the pneumococcus bacteria and components of them that stimulate the immune system in order to provide a level of protection against infection…" *Id.* at 123. He explained the connection between the Prevnar vaccine and GBS response is "based on [the] general [immune system] response," noting that "there [are] a number of different [causal] mechanisms that have been investigated over the years." *Id.* at 127. He specifically referenced two such mechanisms, molecular mimicry and "nonspecific stimulation of the immune system." *Id.* at 127-28.

Dr. Knobler later characterized the "nonspecific stimulation of the immune system" as a "collateral damage hypothesis," which he defined as "immune sensitization and development of an immune response." *Id.* at 147, 159. When asked about the generality of the term "collateral damage," Dr. Knobler agreed that it could refer to "both the response of the innate and the adaptive immune system…when damage occurs." *Id.* at 159-60. He explained that collateral damage occurs when "the immune system responds by ingesting a target antigen, processing that target antigen, and then responding to it." *Id.* at 200. While the immune system is "meant to protect us…sometimes its impact is such that it can produce overwhelming damage." *Id.*

He referred to an article by Yuki and Hartung,[12] published in the New England Journal of Medicine, to support his theory that, under the collateral damage hypothesis, an "antibody binds to a target and then the activated macrophages swoop in" which "leads to damage of the tissue." Tr. 159-61. This study found "evidence of early complement activation, which is based on an antibody binding to the outer surface of the Schwann cell and deposition of activated

[12] Nobuhiro Yuki & Hans-Peter Hartung, *Guillain-Barre Syndrome*, 366 New England J. of Medicine 304 (2012).

complement components; such complement activation appears to initiate the vesiculation of myelin. Macrophage invasion is observed within one week after complement-mediated myelin damage occurs." Pet'r Ex. 12.5 at 4. This explanation by Yuki, Dr. Knobler testified, describes the general immune system response described in his testimony. Tr. 160-61.

Dr. Knobler explained that identification of a specific antigen is not needed to show how the Prevnar vaccine can cause GBS under his collateral damage theory, as only "stimulation of the immune system" is required. Tr. 147. In some instances, an adjuvant, such as the one used in the Prevnar vaccine, may be used to "stimulate a more vigorous immune response," which "is one of the ways in which collateral damage can occur." *Id.* at 147-48.

On questioning by the Court, Dr. Knobler stated that his theory in this case was consistent with the discussion in the case report by Ravishankar, which specifically discusses pneumococcal vaccines.[13] Tr. 177-78; Pet'r Ex. 12.3 at 1. The article explained that:

> there are two types of pneumococcal vaccines, plain and conjugated, that have different mechanisms…Conjugated vaccines elicit a T-cell dependent response. The polysaccharide conjugated to a carrier protein used MHC class-II dependent response to present the carrier protein to carrier-peptide-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.

Pet'r Ex. 12.3 at 2.

Citing to the Ravishankar article Dr. Knobler agreed with the author's conclusion that "it can be inferred that the conjugated [Prevnar] vaccine produces the enhanced B-cell immune response leading to autoimmune reaction to the peripheral nerves," which is consistent with his theory in this case. *Id.*

When specifically asked whether his collateral damage theory could be characterized as bystander activation, as respondent's expert, Dr. He suggested, Dr. Knobler explained that the antibody form of immune response is a humoral response or there could be a T cell response involving T cells and macrophages. In a bystander activation, the immune system is stimulated to provide a broad spectrum of responses, and, as a result, there can be an overwhelming activation of the immune system. Thus, he said, bystander reactions do occur. Collateral damage also occurs, but that does not negate the fact that specific pathogens can precipitate them. Tr. 201.

When asked to explain further in response to Dr. He's report, Dr. Knobler testified that a bystander activation is an example of the immune system's exuberance in a particular individual. The immune response is complex and it will respond to what it sees and to what it is genetically programmed to be able to do. There is variability from individual to individual. Some people are very high responders some are low responders. So, he testified, that when you administer an agent such as a vaccine, you are taking a risk that a person will have a broad response that is not expected, which is the bystander effect. Tr. 203-206.

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[13] Nidhi Ravishankar, *Guillain-Barre Syndrome Following PCV Vaccine*, 4 J. Neurology & Neurosurgery 134 (2017).

Dr. Knobler then addressed his molecular mimicry theory. He explained that while "the precise mechanism by which [GBS] is caused has not yet been fully clarified…one of the mechanisms proposed in some forms of GBS has been that of molecular mimicry, in which either the precise sequence or overall structure of a host cell and infectious agent coincide." *Id*. at 4. He testified that "the immune response directed against that target is similar…to a naturally occurring substance." Tr. 127. Further he explained that,

> molecular mimicry is a well-established mechanism in the laboratory and in nature. It has been documented in humans to exist where either the specific sequence of a substance or shape of a substance provides stimulation to the immune system, and that allows recognition of a target on an individual, and vulnerable targets, such as the myelin sheath in a disease like GBS, can be affected by that.

Id. at 128. Dr. Knobler further testified that "there can be components in a vaccine, as an example, in which…either the sequence or structure resembles a sequence or structure within the body. And so the immune response that is being stimulated by that vaccine is then going to target a comparable sequence or structure in the individual." *Id.* at 213. He said that is what molecular mimicry is in real life. *Id.* He further explained on rebuttal that his proposed molecular mimicry mechanism could be described an immune response directed against target antigens of potential agents that may cross-react with molecules in the nervous system. *Id.* at 358.

As to whether the Prevnar vaccine caused petitioner's GBS, after explaining the theory of molecular mimicry, Dr. Knobler opined that, more likely than not, the vaccination was the precipitating event resulting in petitioner's development of GBS. Tr. 130, 219. His opinion was based on the time course in which petitioner was vaccinated and the development of symptoms within 10 days of the vaccination, leading to a GBS diagnosis and hospitalization. *Id.* at 217. He explained that this "is within the expected time course for such an event to occur, and there were no other documented events that occurred that would provide an alternative explanation for this." *Id.* at 130. Although at the initial hearing, he favored a more general theory of immune causation triggered by the vaccine which he called the collateral damage theory, at the continuation of the hearing on October 21, 2021, Dr. Knobler opined that, based on his clinical experience, laboratory experience, and his understanding of the medical literature, "the more likely than not explanation is that an element of molecular mimicry played a role in causation with respect to the vaccine." *Id.* at 219-20. He testified that he believed that molecular mimicry between the vaccine and the myelin was the most likely mechanism and that more likely than not it was molecular mimicry that was associated with the petitioner's GBS. *Id.*

Dr. Knobler also addressed the theory of respondent's experts that petitioner had an upper respiratory infection, which caused her to develop GBS, opining that, based on petitioner's examination in the Cooper University Hospital ED, "there was no indication…that [petitioner] had an upper respiratory infection" or any infectious process. Tr. 181-83; Pet'r Ex. 3.1 at 57. More specifically, he opined that the examination of petitioner's mouth and throat, where an upper respiratory infection would be located, showed no signs of infection. Tr. 183. Although the term "URI" was listed in petitioner's medical records, "there were no features of URI that were observed in the emergency department. There was no history of URI that occurred." *Id.* at 130.

Dr. Knobler agreed that "there were generic symptoms reported that could have been due to…anything," but "there was no fever; there was no sneezing; there was no runny nose, not even the simplest form of a URI." *Id.* Instead of a URI, Dr. Knobler opined that petitioner was most likely suffering from allergic rhinitis. *Id.* at 130. He explained that, given the time of year, "the likelihood of a cold or a flu or upper respiratory infection [is] far less likely simply because the infectious agents are not typically active in July." *Id.* at 131. He observed that petitioner had a history of allergies. He also noted that the timeline in petitioner's case "fits more appropriately and more closely, more directly with" the vaccination as opposed to a URI. *Id.* at 198, 217, 359. He testified that the timeline of 10 to 11 days strongly favored the vaccine as the causative agent as it generally takes seven to 10 days to mount the immune response. So even if she had a URI which he did not think likely the URI symptoms were not present long enough to generate the immune response that would be necessary to cause GBS. *Id.* at 353.

iii. Dr. Robert C. Hyzy, M.D.

Dr. Robert Hyzy, an internal medicine physician, did not testify at the hearing but submitted an expert report outlining his opinions. Pet'r Ex. 9. Dr. Hyzy opined that "the vaccination of [petitioner] was the cause of her GBS" and that there is "a logical sequence of cause and effect as the vaccination with Prevnar-13 was the reason for the injury and exhibited an appropriate temporal relationship between the vaccination and her injury." *Id.* at 2

Dr. Hyzy supported his conclusion with the Haber post-licensure surveillance study and noted that the article and the facts therein "clearly establish a causal relationship between the vaccination with Prevnar-13 and the onset of GBS." *Id.* He also noted that the article found a mean onset of symptoms of 9 days, with petitioner developing GBS eleven days after vaccination, "clearly within the expected range of onset of GBS following Prevnar-13." *Id.*

b. Opinions of Respondent's Experts on Causation

i. You Wen He, MD, PhD

Respondent filed two expert reports from Dr. You-Wen He, who was admitted and testified as an expert in immunology. Resp't Ex. D; Resp't Ex. G; Tr. 230. Dr. He did not dispute that GBS was the proper diagnosis in this case. Tr. 232. However, he opined that there was no "evidence, no mechanism that can link PCV 13 to GBS." *Id.* at 231.

Dr. He characterized GBS as "an inflammatory polyneuropathy characterized by an acute onset, rapid progression, symmetric muscle weakness, and hyporeflexia or areflexia." Resp't Ex. D at 2. He noted that the "incidence of GBS is 0.5-2 per 100,000 per year and it occurs during all seasons." *Id*. He agreed that GBS is an immune-mediated condition, which can be defined broadly as "immune cell participation." Tr. 232. Dr. He opined that infections are one of the most common causes of GBS and noted that "two-thirds of GBS" cases were seen in "patients with prior infection history, either URI or [gastrointestinal] tract." *Id.* However, he agreed that "vaccines are known …to cause GBS," and further explained that "the exact mechanism for [a] certain vaccine to cause GBS is unknown." *Id.* at 278. Whether a vaccine "has an effect on GBS…really boils down to what specifically the vaccine is." *Id.* at 249. When looking at the

Prevnar 13 vaccine, Dr. He found only weak evidence for an effect on GBS. *Id.* Dr. He also went through some of the medical literature filed by petitioner and testified that he does not believe any of the literature supports a link between the Prevnar vaccine and GBS, other than a temporal relationship. *See id.* at 260-71, 302-04. He agreed that, in the present case, petitioner had a temporal relationship between her vaccination and GBS. *Id.* at 308.

Dr. He primarily disputed Dr. Knobler and Dr. Lee's causation theories based on the strength of the vaccine and the type of immune response it generates. He agrees that vaccines can cause GBS, noting the 1976 swine flu vaccine as an example. However, he testified that when he looked at the PCV 13 vaccine he concluded that it is a relatively weak vaccine compared to others. He explained that the vaccine contains what he called very simple components or pathogen associated molecular patterns ("PAMPS"). The vaccine contains a polysaccharide conjugated to a carrier protein from diphtheria serum 1. He argued that using just the polysaccharide as an immune stimulant will not induce an antibody response that will last. He testified that the diphtheria component is necessary to stimulate a CD4 T helper response that is necessary for a lasting antibody response. Tr. 249. He acknowledged that the vaccine contains an adjuvant that is added to the vaccine to stimulate a more aggressive immune response and may also play a role in macrophage activation among other things. *Id.* at 250.

Dr. He discussed the difference in the "extent of the invasion" between a wild pathogen and a vaccine using the pneumococcus bacteria and Prevnar vaccine as an example. Tr. 238-41. The pneumococcus bacteria has "many different…pathogen-associated molecular patterns" which, in turn "will be sensed by so many different…receptors at the same time" giving a broad activation of the immune system. *Id.* at 238. The Prevnar vaccine, on the other hand, "only contains one type of molecular pattern" called polysaccharides, which "will engage one type of receptor, C-type lectin on [the] subsurface, [and] will not engage, for example, toll-like receptor 9." *Id.* at 238-39. Thus, when someone receives the pneumococcal vaccine, "they will have [the] antibody against the polysaccharide" whereas a patient who has the wild infection will have the antibody against the polysaccharide and other components of the bacteria. *Id.* at 240-41. He also derided Dr. Knobler's explanation of the immune system as being overly basic and out of date. *Id.* at 235. He was critical of the failure to discuss PAMPS and DAMPS and the roll of Toll Like Receptors. *Id.* at 236-37. He took particular issue with Dr. Knobler's testimony that tolerance was not important to the discussion in this case. *See, e.g.*, *id.* at 243. Dr. He explained this theory, noting that "for every type of positive force, there's a negative counterforce." *Id.* at 245. Part of the negative counterforce is "immune check point receptors," which "keep our immune system under control." *Id.* at 245. The Prevnar vaccine, for example, will "activate the dendritic cells and the macrophages, and those cells, once they're activated, [will] automatically start to express this counterforce called PD-1, PDL-1, and ligand adjuvant." *Id.* at 246.

Dr. He disagreed with Dr. Lee and Dr. Knobler's opinions that the immune response to a wild virus and the immune response to a vaccine are the same. Tr. 235-36. Consistent with his emphasis on the volume of the immune response he said infections are an uncontrolled process with unknown aim and components, whereas vaccines are controlled. *Id.* at 236. He explained that "pattern recognition receptors…have the ability to sense different patterns from the pathogen," and that petitioner's expert did not include this in his theory. *Id*. at 237-38. He further explained how pattern recognition receptors work with the following example:

> For example, Toll-like receptor 4 will see only one type of component from the pathogen called LPS, and Toll-like receptor 2 will sense…another one, called peptide ligand from Gram-positive bacteria and LPS is mostly from Gram-negative bacteria. And the virus will have [a] specific pattern for receptor 2…So for each component, we'll have a different type of pattern recognition receptors to sense it.

Id. at 237.

In response to Dr. Knobler's "collateral damage" theory of causation, Dr. He noted that "there is no such term called 'collateral damage' to refer to [an] autoimmune disease mechanism." Tr. 233. Rather, Dr. He characterized Dr. Knobler's theory as "a nonspecific activation of the immune system" resulting in damage caused by "nonspecific activated cells like macrophage[s]." *Id.* He testified that this nonspecific activation is termed "bystander activation," which "happens all the time." *Id.* He testified that bystander activation occurs every time "there is a foreign subject invading our body." *Id.* at 234. While bystander activation is "a common phenomenon," it is not common for it to cause damage leading to GBS. *Id.* at 234-35. He acknowledged that bystander activation can at times cause damage leading to an autoimmune disease. *Id.* at 233. Specific to vaccines, Dr. He explained that "when we receive a vaccine, we will have this bystander activation but" whether this bystander activation causes damage depends on the extent of the activation. *Id.* at 245. If the activation "is too much, [it] will cause damage. If it's not too much, our counterbalance, the central tolerance mechanism will come into play." *Id.* Dr. He also agreed that lectins in the body can bind to the polysaccharides in a vaccine and can stimulate an immune response which, when uncontrolled, can cause "collateral damage." *Id.* at 282-83. Whether or not lectin cells cause damage after activation by a carbohydrate requires a break of the "tolerance mechanism." *Id.* at 284. Dr. He argued that stimulation of the immune system by activated lectin cells would not cause GBS because of "immune control." *Id.* at 283. Importantly, however, he agreed that "in any case of GBS, the immune control system doesn't work," and further explained that "if the control works properly…you will not get GBS." *Id.*

In addressing petitioner's molecular mimicry theory, Dr. He agreed that "cross-reactive autoantibodies may play some role in…GBS development." Tr. 286. However, he argued that "cross-reactive antibod[ies] and cross-reactive T cell epitopes exist in our body all the time." *Id.* at 243, 286. This cross-reactivity is only "part of the molecular mimicry theory," though it is "the most important thing," as "cross-reactivity is needed to break [the] tolerance mechanism [and] cause damage." *Id.* at 287-88. However, these cross reactions are controlled through tolerance. *Id.* at 243-45. Dr. He agreed that "if there's a component in the [Prevnar] vaccine that cross-reacts with something in the Schwann cells or in the myelin, whether it's a strong vaccine or a weak vaccine, autoimmunity could occur in someone who's genetically susceptible and tolerance breaks down." *Id.* at 259. However, Dr. He explained that there is "no evidence…[that] PCV 13, the polysaccharide, has anything to do with any of the proteins involved in GBS." *Id.*

Dr. He highlighted petitioner's preceding URI symptoms as a possible alternative cause for her GBS, noting that "two thirds of [GBS] cases" relate to URIs or GI tract infections. Tr.

272. According to the article by Willison et al., [14] submitted by Dr. He, URI or gastrointestinal symptoms were reported within four weeks prior to onset of GBS in two thirds of patients. Resp't Ex. D-2 at 2. However, the same article recognized that other immune stimulation including by vaccines also causes aberrant autoimmune responses targeting peripheral nerves and their spinal roots. *Id.* at 1. He noted that the initial neurology consultation petitioner had at Cooper University Hospital noted that the GBS was "likely precipitated by [a] recent URI," and later agreed that the records also included the vaccine as a potential cause. *Id.* at 272, 301-02. Dr. He opined that petitioner had a URI at the time of her ED visit based on her symptoms, including "cough congestion…[and] runny nose." *Id.* at 279. He explained that these are "classic URI symptoms" but agreed that they could also be "symptoms of an allergic response to…a pollen allergy." *Id.* Regardless of whether petitioner had a URI, Dr. He did not believe that the Prevnar vaccine caused petitioner's GBS. *Id.* at 297-98. Dr. He agreed that, by ten- or eleven-days post vaccination, the vaccine would have generated an immune response and that by three to five days, if petitioner had a URI, the immune system would have generated a response to that as well. He agreed that it was possible that the combination of the two acting at the same time could have caused a sufficiently overwhelming response to cause autoimmunity. Tr. 312-13.

ii. Brian Callaghan, MD

Respondent filed three expert reports from Dr. Brian Callaghan, who was admitted and testified as an expert in neurology and electrodiagnostic medicine. Resp't Ex. A; Resp't Ex. C; Resp't Ex. F; Tr. 319. Dr. Callaghan's theory is that petitioner's "medically documented" URI constitutes a clear "nonvaccine cause" of her GBS and that there "is no evidence to support" a causal link between Prevnar and GBS. Tr. 321. While Dr. Callaghan generally agreed with Dr. He that there was no known evidence that Prevnar could cause GBS, the bulk of his testimony addressed the possible upper respiratory infection as a cause and will be addressed under the analysis of alternative cause below.

Dr. Callaghan disputed that petitioner's experts presented "a reliable or reputable theory for how the Prevnar 13 vaccine could cause petitioner's GBS" noting that "the theory has been very hard to get a cogent understanding of." Tr. 323. He understood Dr. Lee's theory as molecular mimicry and Dr. Knobler's theory to be molecular mimicry and "a nonspecific immune stimulation argument." *Id.* He did not think that either theory supports a causal connection between the Prevnar vaccine and GBS. *Id.* He noted that "molecular mimicry requires several steps of proof to determine that that's a causal mechanism" and that the nonspecific immune stimulation theory "could mean that any precipitant could cause any disease." *Id.* at 324.

Dr. Callaghan addressed the medical literature filed by petitioner's experts. He noted that the Yuki article discusses the 1976 swine flu vaccine and had "epidemiological literature to associate that vaccine with GBS," and he agreed that the swine flu vaccine was associated with GBS. Tr. 328. The rest of the article, he observed, discussed GBS generally and is not vaccine specific. *Id.* He noted that the pathogenesis of GBS discussed in the Yuki article and relied on by Dr. Knobler shows "what we don't know about GBS pathogenesis, because basically they're

[14] Willison et al., *Guillain Barre Syndrome*, 388 Lancet 717, 718 (2016).

invoking pretty much every piece of the immune system, whether it be…complement antibodies or T cells" and is more of a general description. *Id.* at 329.

IV. Legal Standard

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

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, petitioner must prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Hum. Servs*., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); see also *Pafford v. Sec'y of Health & Hum. Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner who satisfies this burden is entitled to compensation unless respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B).

To receive compensation through the Program, petitioner must prove either (1) that she suffered a "Table Injury"— i.e., an injury listed on the Vaccine Injury Table — corresponding to a vaccine that she received, or (2) that he suffered an injury that was actually caused by a vaccination. *See* §§ 11(c)(1), 13(a)(1)(A); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1319-20 (Fed. Cir. 2006). Because petitioner does not allege that she suffered a Table Injury, she must prove that a vaccine she received caused her injury. To do so, she must establish, by preponderant evidence: (1) a medical theory causally connecting the vaccine and her injury ("*Althen* Prong One"); (2) a logical sequence of cause and effect showing that the vaccine was the reason for her injury ("*Althen* Prong Two"); and (3) a showing of a proximate temporal relationship between the vaccine and her injury ("*Althen* Prong Three"). § 13(a)(1); *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005). The causation theory must relate to the injury alleged. The petitioner must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." *Knudsen v. Sec'y of Health & Hum. Servs*., 35 F.3d 543, 548-49 (Fed. Cir. 1994). The Federal Circuit has reiterated that proof of causation does not "require identification and proof of specific biological mechanisms[.]" *Kottenstette v. Sec'y of Health & Hum. Servs.*, 861 F. App'x 433, 441 (Fed. Cir. 2021) (citing *Knudsen*, 35 F.3d at 549). Causation "can be found in vaccine cases…without detailed medical and scientific exposition of the biological mechanisms." *Knudsen*, 35 F.3d 543 at 548-49. It is not necessary for a petitioner to point to conclusive evidence in the medical literature linking a vaccine to the petitioner's injury, as long as the petitioner can show by a preponderance of

evidence that there is a causal relationship between the vaccine and the injury, whatever the details of the mechanism may be. *Moberly*, 592 F.3d at 1325.

Petitioner cannot establish entitlement to compensation based solely on his assertions; rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether petitioner is entitled to compensation, the special master shall consider all material in the record, including "any…conclusion, [or] medical judgment…which is contained in the record regarding…causation." § 13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in petitioner's favor when the evidence weighs in his favor. *See Moberly*, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); *Althen*, 418 F.3d at 1280 (noting that "close calls" are resolved in petitioner's favor).

In Vaccine Act cases, expert testimony may be evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594-96 (1993); *see also Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1325, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999)). In Vaccine Program cases, the *Daubert* analysis has been used in weighing scientific evidence actually proffered and heard rather than as a tool for the pre-trial exclusion of expert testimony. *Davis v. Sec'y of Health & Hum. Servs*., 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"), *aff'd*, 420 F. App'x 923 (Fed. Cir. 2011). The flexible use of the *Daubert* factors to determine the persuasiveness and/or reliability of expert testimony in Vaccine Program cases has routinely been upheld. *See, e.g*., *Snyder v. Sec'y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 742–45 (2009).

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 & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1362 (Fed. Cir. 2000)). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 (1997)). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs.*, 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

Close calls regarding causation must be resolved in favor of the petitioner. *Althen*, 418 F.3d at 1280 (holding that Congress created a system in which "close calls regarding causation

are resolved in favor of injured claimants"); *Knudsen*, 35 F.3d at 551 ("If the evidence (on alternative cause) is seen in equipoise, then the government has failed in its burden of persuasion and compensation must be awarded.").

V. Analysis

Petitioner's diagnosis of GBS was not contested by the respondent. Petitioner received the Prevnar 13 vaccine on July 11, 2016 and began experiencing the symptoms of GBS on July 22, 2016. All experts agreed that petitioner was correctly diagnosed with GBS and that GBS is generally considered to be an autoimmune disease. Thus, the only issue for determination is whether petitioner has established by a preponderance of the evidence that the Prevnar 13 vaccine she received on July 11, 2016 was a substantial factor in causing her subsequent GBS. *Shyface*, 165 F.3d at 1352.

a. *Althen* Prong One

Under *Althen* prong one, petitioner must provide a "reputable medical theory," demonstrating that the vaccine received can cause the type of injury alleged. *Pafford*, 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. In *Kottenstette*, the Federal Circuit reiterated that proof of causation does not "require identification and proof of specific biological mechanisms[.]" 861 F. App'x at 441 (citing *Knudsen*, 35 F.3d at 549). Causation "can be found in vaccine cases…without detailed medical and scientific exposition of the biological mechanisms." *Knudsen*, 35 F.3d at 548-49.

In their article entitled Guillain-Barre syndrome[15] filed by respondent, Hugh Willison and colleagues discussed the pathogenesis of GBS:

> First, Guillain-Barre syndrome is usually preceded by infection or other immune stimulation that induces an aberrant autoimmune response targeting 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 Campylobacter jejuni. 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. Furthermore, genetic

[15] Willison et al, *Guillain-Barre syndrome*, 388 The Lancet 717 (2016).

> and environmental factors that affect an individual ‘s susceptibility to develop the disease are unknown.
>
> Resp’t Ex. D-2 at 1.

Willison further noted that greater than 99% of people who are exposed to *C. jejuni* do not develop GBS which is associated with the pure motor axonal form of GBS (AMAN). He further noted that some infections such as Epstein Barr, influenza A virus and cytomegalovirus, which were not present in this case have been noted to have preceded GBS in some cases. Importantly, he noted that cases of GBS have also been reported shortly after vaccination. He referenced the rabies vaccine, the 1976 influenza vaccine, and the 2009 influenza vaccine which showed 1.6 excess cases of GBS per 100,000 people.

Willison addressed AIDP (acute inflammatory demyelinating polyneuropathy), the type of GBS that occurs most frequently in North America, and most likely the type that afflicted the petitioner.

> By contrast with acute motor axonal neuropathy, the immunological cascade involved in acute inflammatory demyelinating polyneuropathy is less well understood for various reasons. First, a wider range of immune stimulants cause AIDP compared with AMAN, which includes bacteria and viral infections, and vaccines. Second, biomarkers have yet to be characterized, despite widespread screening efforts to identify the putative nerve antigens. At present a wider range of anti-nerve autoantibodies directed at both proteins and glycolipids could be responsible for AIDP immunopathology than is the case for AMAN or Miller Fisher syndrome.

Id. Consistent with the state of knowledge about the cause of GBS, as explained by Willison, Dr. Knobler essentially presented alternative theories as to the cause of the petitioner’s GBS. These include bystander activation, which he referred to as the collateral damage theory, and ultimately pointing to molecular mimicry as the most likely mechanism. Dr. Lee presented the theory of molecular mimicry without using the term, by explaining the cross reaction of antibodies stimulated by the immune response to the vaccine. Both agreed that molecular mimicry or cross reaction triggered by the vaccine was the most likely mechanistic explanation for the occurrence of the petitioner’s GBS eleven days after receipt of the Prevnar 13 vaccine. Both pointed to the Haber article as finding 11 cases of post Prevnar GBS reported to VAERS with mean time of onset of nine days and a range of two to 32 days.

While only the flu vaccine is *presumed* to be a cause of GBS in the Vaccine program, petitioners have been found entitled to compensation for GBS caused by many other vaccinations, including Prevnar 13. *See* 42 U.S.C. § 100.3(a). *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); *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); *J.G. v. Sec'y of Health & Human Servs.*, 2023 WL 2752634, at *29-32 (finding that the Hep A vaccine can cause GBS).

Importantly for this case, which was one of the early Prevnar/GBS cases tried, there have now been multiple decisions by Special Masters finding that Prevnar was the cause of GBS based on a theory of molecular mimicry. *See, e.g.*, *Koller v. Sec'y of Health & Hum. Servs.*, No. 16-439V, 2021 WL 5027947, at *7-20 (Fed. Cl. Spec. Mstr. Oct. 8, 2021 (finding that the Prevnar 13 vaccine can cause GBS based on the mimicry between the essential phosphoglycerol component of the vaccine with the polar head group in the phospholipid membrane in the myelin of peripheral nerves.) (Gowen); *Byrd v. Sec'y of Health & Human Servs.*, No. 20-1476, 2024 WL 4003061 at *21-26 (finding that molecular mimicry based on the CRM 197 conjugate satisfied *Althen* 1) (Gowen). Similarly, other special masters have reached similar conclusions based on substantially similar theories of molecular mimicry. *See,* e.g., *Parker v. Sec'y of Health & Hum. Servs.*, No. 20-411V, 2023 WL 9261248 (Fed. Cl. Spec. Mstr. Dec. 20, 2023) (Dorsey); *Anderson v. Sec'y of Health & Hum. Servs.*, No. 18-484V, 2024 WL 557052 (Fed. Cl. Spec. Mstr. Jan. 17, 2024) (Dorsey); *Gross v. Sec'y of Health & Hum. Servs.*, No. 17-1075V, 2022 WL 9669651 (Fed. Cl. Spec. Mstr. Sept. 22, 2022) (Dorsey); *Sprenger v. Sec'y of Health & Hum. Servs.*, No. 18-279V, 2023 WL 8543435 (Fed. Cl. Spec. Mstr. Nov. 14, 2023) (Dorsey); *Maloney v. Sec'y of Health & Hum. Servs.*, No. 19-1713V, 2022 WL 1074087 (Fed. Cl. Spec. Mstr. Mar. 17, 2022) (Dorsey); *Simeneta v. Sec'y of Health & Hum. Servs.*, No. 18-1859V, 2024 WL 4881411 (Fed. Cl. Spec. Mstr. Oct. 31, 2024 (Dorsey); *Pierson v. Sec'y of Health & Hum. Servs.*, No. 17-1136V, 2022 WL 322836 (Fed. Cl. Spec. Mstr. Jan. 19, 2022) (Horner); *Bartoszek v. Sec'y of Health & Hum. Servs.*, No. 17-1254V, 2024 WL 4263604 (Fed. Cl. Spec. Mstr. Aug. 27, 2024) (Horner); *Cooper v. Sec'y of Health & Hum. Servs.*, No. 18-1885V, 2024 WL 1522331 (Fed. Cl. Spec. Mstr. Mar. 12, 2024) (Horner); *Tracy v. Sec'y of Health & Human Servs.*, No. 16-213V, 2022 WL 1125281, at *29-32 (Fed. Cl. Spec. Mstr. Mar. 30, 2022) (Sanders).

Some of these cases also accepted the theory of mimicry between the CRM197 protein in Prevnar with various nodal or paranodal components of the peripheral nerves either together with the phosphoglycerol theory or standing by itself as a likely source of GBS causing molecular mimicry. [16] *See e.g., Byrd*, No. 20-1476, 2024 WL 4003061 at *21-26. I have considered the

[16] Acceptance of this theory has not been unanimous among special masters. *Deshler v. Sec'y of Health & Hum. Servs.*, No. 16-1070V, 2020 WL 4593162 (Fed. Cl. Spec. Mstr. July 1, 2020) (Corcoran); *Trollinger v. Sec'y of Health & Hum. Servs.*, No. 16-473V, 2023 WL 2521912, at *26-31 (Fed. Cl. Spec. Mstr. Feb. 17, 2023) (Corcoran); *Bialek v. Sec'y of Health & Hum. Servs.*, No. 18-761V, 2023 WL 35509, at *33-37 (Fed. Cl. Spec. Mstr. Jan. 3, 2023) (Corcoran); *Gamboa-Avila v. Sec'y of Health & Hum. Servs.*, No. 18-925V, 2023 WL 6536207 (Fed. Cl. Spec. Mstr. Sept. 11, 2023) (Corcoran), mot. rev. den'd, No.18-925V (Fed. Cl. filed Feb. 26, 2024); *McConnell v. Sec'y of Health & Hum. Servs.*, No. 18-1051, 2022 WL 4008238 (Fed. Cl. Spec. Mstr. Aug. 19, 2022) (Moran); *Crosby v. Sec'y of Health & Hum. Servs.*, No. 18-1478V, 2021 WL 3464125 (Fed. Cl. Spec. Mstr. July 22, 2021) (Moran); *Morrison v. Sec'y of Health & Hum. Servs.*, No. 18-386V, 2024 WL 3738934 (Fed. Cl. Spec. Mstr. July 18, 2024) (Oler)

reasoning in these cases and consistent, with my prior opinions find the decisions favoring causation to be persuasive.

Petitioner presented the testimony of two physician experts and a third by an expert report. The third, Dr. Robert Hyzy, M.D. did little more than point to the post Prevnar GBS cases reported in the Haber study referenced above and opined that the timing of onset ten to eleven days after vaccination was sufficient to prove causation. He did not present a theory of pathogenesis and his opinion was almost entirely based on the cases reported in Haber and the temporal relationship between the vaccination and the onset of symptoms. While timing is an important consideration in evaluating causation it has never been sufficient to prove causation standing by itself. The cases reported to VAERS as detailed in Haber raise the issue of causation but do not explain it. Therefore, Dr. Hyzy's opinion is accorded little weight as to *Althen* prong one.

Dr. Knobler began his testimony with a general explanation of how vaccines, including the Prevnar vaccine work. He testified that the Prevnar vaccine contains strains of the "pneumococcus bacteria and components of them that stimulate the immune system in order to provide a level of protection against infection with these." Tr. 123. As to vaccines generally, Dr. Knobler explained that the purpose of vaccines "is to stimulate the immune system." The immune system is stimulated by a "combination of a number of different strains of bacteria" which provide "an immune response in order to provide protection from the actual bacteria." *Id.* In some susceptible individuals, however, "that stimulation of the immune system can lead to development of Guillain Barre" due to a misdirection of the immune response which "can lead to loss of tissue." *Id.* at 124-25.

At the entitlement hearing, Dr. Knobler testified that autoimmune diseases are common, that the tolerance system that Dr. He discussed is not infallible, and that the process of the development of an autoimmune disease such as GBS is multi-factorial. He said that autoimmune diseases are a reflection of the genetic background of the individual, interaction with an environmental agent – such as a vaccine – and the activation of the immune system. Tr. 196-97. He said that there is a certain amount of time in which the immune system is responsive to a particular stimulant and, in the case of petitioner, the timeline of 10-11 days between the administration of the Prevnar vaccine and the onset of her neurological symptoms fit most closely and more so than that with a possible URI occurring three to five days prior to onset. *Id.* at 198.

Dr. Knobler explained at the hearing that there are "a number of different mechanisms that have been investigated" for how vaccines can cause GBS, one being molecular mimicry and another which he referred to as "collateral damage." Tr. 127. Respondent, in his post-hearing brief, argued that Dr. Knobler's testimony regarding molecular mimicry was contradictory to his initial theory. Resp't Post Hearing Brief (ECF No. 106). During the initial hearing, Dr. Knobler testified that he believed "that collateral damage more likely than molecular mimicry is the responsible mechanism." *Id.* at 148. His use of the term "collateral damage" seemed to describe a result more than a theory, but in his explanation of it, as noted by Dr. He, it appeared that he was describing bystander activation, which is also one of the primary theories of autoimmune

causation. Dr. Knobler was asked to clarify this, and he testified that bystander activation occurs when the immune response, which includes inflammation, is greater than what was intended by the immune stimulation by a specific antigen such as in a vaccine. *Id.* at 204. He said that the immune response varies from person to person, and, in the vast majority of people, we see a very specific immune response directed against a very targeted antigen in order to achieve the desired effect. However, some people are high responders. In some people, the impact of the agents in the vaccine go beyond the intended result and that is where we get into problems such as the occurrence of GBS when an individual has a broad response based on the capacity of their immune system to respond. This explains how the bystander effect is capable of causing an unintended result when stimulated. *Id.* at 205-07. Dr. Knobler noted that collateral damage or bystander activation is the result of the immune system being keyed up or turned on. *Id.* at 147. He also noted that this hypothesis does not require a specific antigen and instead only needs stimulation of the immune system which occurs when a stimulant acts to juice up or amplify the response that the immune system is capable of making in a susceptible individual. *Id.* at 147-48. In this case, he opined that the Prevnar vaccine served as the immune stimulant that generated the strong immune response in the petitioner. *Id.* at 148. He stated that, "In neurology…we refer to the damage that we see as the final common pathway, and that there are multiple ways in which you can reach the damage that you see. In GBS, the final common pathway is the damage to the myelin that occurs at the nerve roots." *Id.* at 168.

Bystander activation has been recognized in other cases in the program. For example, in *Henley v. Sec'y of Health and Human Services*, Special Master Roth wrote:

> Another viable mechanism is bystander activation, which occurs when there is an exaggerated immune response to an exogenous agent that induces local tissue inflammation and stimulation of otherwise unaffected normal cells which can result in the release of normally sequestered self-antigens. The inflammation may activate previously dormant auto-reactive Th-1 cells that then react against the newly released self-antigens. Bystander activation cannot be seen clinically, but it is a mechanistic component of the process that triggers (autoimmune disease)
>
> No. 16-499V, 2024 WL 2272670 at *26 (Fed. Cl. Spec. Mstr. Apr. 25, 2024).

Indeed, bystander activation can act in conjunction with molecular mimicry as noted in *Cooper*, another Prevnar/GBS case in which Special Master Horner observed that Dr. Latov invoked both molecular mimicry and bystander activation, specifically noting that the two mechanisms can operate in conjunction. *Cooper*, No. 18-1885V, 2024 WL 1522331, at *13.

As to the molecular mimicry aspect of petitioner's theory specifically, prior to the entitlement hearing, Dr. Knobler provided an expert report in which he opined on causation as follows:

> Development of GBS is an unfortunate occurrence, it is a serious, potentially life-threatening disease. The precise mechanism by which it is caused has not yet been fully clarified. However, one of the mechanisms proposed in some forms of GBS has been that of molecular mimicry, in which either the precise sequence or overall structure of a host cell and infectious agent coincide. GBS has been reported, (Khatib) for the pneumococcal pneumonia infection. Pet'r Ex. 12 at 5

At the continuation of the hearing, Dr. Knobler focused on molecular mimicry and testified that, based on his laboratory experience and his understanding of the literature, molecular mimicry more likely than not "played a role in causation with respect to the vaccine." Tr. 219. He said that molecular mimicry with the Prevnar vaccine was the most likely mechanism of causation of petitioner's GBS. *Id.* As noted above, molecular mimicry and bystander activation mechanisms are not mutually exclusive and either may lead to "collateral damage" when there is a failure of tolerance.

Dr. Knobler testified that in GBS, an antibody binds to tissue, which then activates and recruits macrophages, and the macrophages damage the tissue the antibody is attached to. Tr. 126. Dr. Knobler described the mechanism, stating:

> And once the immune system is stimulated to react to that [antigen], you then get antibodies produced, you get activated cells of the immune system…there are helper cells that allow the antibody producing cells to function and give antibody producing cells a green light to function and that triggers the sequence of events that could yield to the demyelination.

Tr. 128-29. To support his theory, Dr. Knobler primarily relied on an article by Yuki, which described the pathogenesis of GBS. Tr. 151; Pet'r Ex. 12.5. Specifically, Dr. Knobler referred to a paragraph in that article which reads:

> The classic pathological findings in acute inflammatory demyelinating polyneuropathy are inflammatory infiltrates (consisting mainly of T cells and macrophages) and areas of segmental demyelination, often associated with signs of secondary axonal degeneration, which can be detected in the spinal roots, as well as in the large and small motor and sensory nerves. There is evidence of early complement activation, which is based on an antibody binding to the outer surface of the Schwann cell and deposition of activated complement components; such complement activation appears to initiate the vesiculation of myelin. Macrophage invasion is observed within 1 week after complement-mediated myelin damage occurs.

Pet'r Ex. 12.5 at 4. The Yuki article also explains that:

> [A]utoantibodies may bind to myelin antigens and activate complement. This is followed by the formation of a membrane-attack complex (MAC) on the outer

> surface of Schwann cells and the initiation of vesicular degeneration. Macrophages subsequently invade myelin and act as scavengers to remove myelin debris…Myelinated axons are divided into four functional regions: the nodes of Ranvier, paranodes, juxtaparanodes, and internodes. Gangliosides GM1 and GD1a are strongly expressed at the nodes of Ranvier, where the voltage-gated sodium (Nav) channels are localized. Contactin-associated protein (Caspr) and voltage-gated potassium (Kv) channels are respectively present at the paranodes and juxtaparanodes. IgG anti-GM1 or anti-GD1a autoantibodies bind to the nodal axolemma, leading to MAC formation. This results in the disappearance of Nav clusters and the detachment of paranodal myelin, which can lead to nerve-conduction failure and muscle weakness. Axonal degeneration may follow at a later stage. Macrophages subsequently invade from the nodes into the periaxonal space, scavenging the injured axons.

Pet'r Ex. 12.5 at 5. Notably, one reason why autoantibodies would bind to myelin antigens or to the outer surface of the Schwann cells, as discussed by Yuki, is through molecular mimicry. As Dr. Knobler explained, a vaccine can cause GBS via molecular mimicry and subsequently through the process described by Yuki because "there can be components in a vaccine…in which…either the sequence or structure resembles a sequence or structure within the body. And so the immune system response that is being stimulated by that vaccine is then going to target a comparable sequence or structure in the individual." Tr. at 213. Dr. Knobler further testified that molecular mimicry "has been documented in humans to exist where either the specific sequence of a substance or the shape of a substance provides stimulation to the immune system, and that allows recognition of a target on an individual…such as the myelin sheath in a disease like GBS…" *Id.* at 128. Dr. Knobler noted that "once the immune system is stimulated to react to that, you then get antibodies produced, you get activated cells of the immune system…" including "helper cells that allow the antibody-producing cells to function…" which "triggers the sequence of events that could yield the demyelination." *Id.* at 129. He further explained that his proposed molecular mimicry theory could be described as an immune response directed against target antigens of potential agents that may cross-react with molecules in the nervous system. *Id.* at 358. Such molecules would be those in the outer surface of the Schwann cells or myelin antigens, as described by Yuki.

This is consistent with Dr. Lee's explanation of molecular mimicry, in which he explained that the Prevnar 13 vaccine causes GBS "through the immune response generated by the vaccine," and that this immune response is to "look for road signs." *Id.* at 79. He explained that, typically, these "road signs are on the bacteria," but "the nerve cells in the body also have similar road signs." *Id.* In this case, "the body can't tell the difference whether the road sign…is on the nerve or on the bacteria. So that's how the nerve cells are attacked by the body's immune system through that immune response created by the vaccine." *Id.* at 80. He defined "road signs" as "the epitope proteins which are proteins on the surface of the bacteria, but also on the surface of the human cells." *Id.* at 80-81. Thus, "if those epitopes are similar between a bacteria and

nerve cells, then the immune system will also attack the nerve cells that have similar epitopes as the bacteria." *Id.* at 81.

Dr. Knobler explained that after the cross reaction between antigens in the vaccine and components of peripheral nerve occurs, the Fc portion of the antibodies provides a point of attachment for the invasion of macrophages and complement which cause damage to the cells, which Dr. Knobler termed "collateral damage," leading to GBS. Although Yuki did not specifically discuss vaccine causation this mechanism is consistent with his biological description of what Dr. Knobler opined is thought to occur in GBS after a vaccination.

Both Dr. Knobler and Dr. Lee referred to the Haber article to support their molecular mimicry theories. Tr. 82, 142-45; Pet'r Ex. 9.2. This article is a vaccine reporting administration post-licensure surveillance report to evaluate the safety of the PCV 13 vaccine. *Id.* at 1. Dr. Lee observed that the study found that "in persons over the age of 65 that received the Prevnar 13, there were 10 to 11 cases reported for GBS." Tr. 82. The study noted 11 verified reports of GBS "with symptom onset within 42 days of PCV vaccination with a reporting rate of 0.7 cases per million doses of vaccine distributed among adults aged" 19 or older. Pet'r Ex. 9.2 at 5. More specifically, the "median onset interval of symptoms" for these 11 cases was 9 days, with a range of 2-34 days after the vaccination, and the median age was 68 years with a range of 56-88. *Id.* Despite these findings, the authors concluded that the "data mining analysis identified no disproportionate reporting for GBS." *Id.*

Respondent's experts, Dr. He and Dr. Callaghan also noted that the authors of the Haber article, despite discussing 11 cases of post Prevnar GBS as reported to VAERS, concluded that this many cases were not sufficient to constitute a signal of a potential adverse event. *See* Tr. 264, 324-25. While Haber concluded that these cases did not identify a new safety signal, the fact that 11 cases of GBS within 42 days following vaccination with Prevnar 13 were identified nevertheless provides some circumstantial evidence of causation much as case reports do. For example, the article by Ravishankar reported in detail on a case of GBS following the administration of the Prevnar vaccine. *See* Pet'r Ex. 12.3. Moreover, as noted by other special masters, though Haber found "no disproportionate reporting for GBS," articles, such as Haber, which rely on VAERS data "are subject to significant limitations." *Pierson*, 2022 WL 322836, at *30; Pet'r Ex. 9.2. Notably, the Haber authors caution that the "limitations of VAERS…may include underreporting, varying quality of reports…and the lack of an unvaccinated comparison group." Pet'r Ex. 9.2 at 5. Haber also notes that such limitations make it "extremely difficult to determine causal associations between vaccines and" adverse events. *Id.* Perhaps more important than the number of VAERS reports found by the Haber authors in this 2016 article, is the fact that far more Prevnar/GBS cases with detailed records have been filed in the Vaccine Program. In fact, to date, there have been more reasoned decisions in the Vaccine Program than there were cases were found by Haber and there are many more cases pending on the docket. As an indication of the underreporting problem with VAERS data most cases filed in the Vaccine Program do not have filed VAERS reports.

Dr. He proposed three primary criticisms of the theories of Dr. Knobler and Dr. Lee. First, he contended that Prevnar was a weak vaccine, second that the tolerance system prevents autoimmune disease by training our immune cells not to attack self, and third that Dr. Knobler and Dr. Lee failed to provide a sophisticated discussion of immune mechanisms including Toll Like Receptors (TLRs), dendritic cells, C-lectin, PAMPS and DAMPS.[17] He also argued that the breadth of the immune response to a wild infection is much greater than to the components of a vaccine.

While Dr. He testified that Prevnar 13 was a weak vaccine, he did not explain why it would be considered weaker than other vaccines. In fact, the Sanford study[18] filed by the respondent detailing various comparative studies, described that Prevnar contains 12 serotypes in common with the Pneumococcal 23 vaccine and that Prevnar 13 provoked "a significantly greater immune response than PPV23 for 8 of 12 serotypes in common." Resp't Ex. G-7 at 5, 12. Dr. He testified that the Prevnar vaccine was "relatively weak" because it "contains very simple components" including "one type of PAMP called polysaccharide and a carrier protein…from diphtheria serum 1." Tr. 249. Despite this statement, Dr. He also agreed that the diphtheria protein conjugate and adjuvant in the Prevnar vaccine stimulate a more aggressive immune response than the PPV23 and may play a role in macrophage activation. *Id.* at 250. As Sanford reported the immune response to the conjugated vaccine with an adjuvant appears to be considerably stronger than the response to the PPV23 which does not contain CRM197 (the diphtheria carrier protein) or an adjuvant both of which were added to increase the immune response to the vaccine. Resp't Ex. C-7 at 12. An article by Pulendran and Ahmed entitled Immunological mechanisms of vaccination,[19] notes that vaccines such as the polysaccharide vaccine conjugated with the diphtheria antigen contains an adjuvant, alum, which has been shown to induce antibody responses independent of TLRs. Resp't Ex. G-3 at 3. Furthermore, the authors say, alum exerts a direct effect on IL-4 producing Gr-1 cells that are essential for priming and cloning expansion and optimal antibody production by B cells *in vivo. Id.* Thus, it would appear that the combination of the lipopolysaccharides (which also have an essential phosphoglycerol sidechain) combined with CRM 197 and the alum adjuvant has resulted in a considerably stronger vaccine than the prior pneumococcal vaccine which had been effective with adults.

While the role of tolerance in preventing attacks on self-antigens or structures is well recognized in general, Dr. He agreed that when a person develops an autoimmune disease such as GBS then the tolerance system has failed. Tr. 248. Thus, it follows that, as petitioner clearly developed a severe case of GBS, the tolerance and regulatory checkpoints, while important counterforces in general, failed in her case. While Dr. He testified that there is no such term as

[17] PAMPS stands for pathogen associated molecular patterns. DAMPS stander for danger or damage associated molecular patterns which are recognized by immune cells such as dendritic cells or TLRs.

[18] Mark Sanford, *Pneumococcal Polysaccharide Conjugate Vaccine (13-Valent, Adsorbed)*, 72 Adis Drug Profile (2012).

[19] Bali Pulendran & Rafi Ahmed, *Immunological mechanisms of vaccination*, 12 Nature Immunology 509 (2011).

collateral damage in immunology, the concept was recognized in an article he submitted. Tr. 233. The article by Wykes and Lewin,[20] filed by Dr. He, discussing immune checkpoint molecules, notes that such molecules "are crucial for maintaining self-tolerance and for modulating the length and magnitude of effector immune responses in peripheral tissues to minimize *collateral tissue damage*." Resp't Ex. G-2 at 1 (emphasis added). While I agree that the term collateral damage, as used by Dr. Knobler, immunologically was better understood to be describing bystander activation, the Wykes article recognizes the notion of collateral damage as a result to be avoided through the regulatory and tolerance systems. The collateral damage in this case was the resulting GBS when the tolerance and checkpoint systems did not work to prevent a cross reactive autoimmune attack in this particular patient.

Importantly, Dr. He acknowledged that the occurrence of GBS necessitates the breaking of tolerance or the control mechanisms of the immune system. *Id.* at 283. Dr. He testified that "if the control means work properly…you will not get GBS." Moreover, Dr. He agreed that *if* there is "a component in the [Prevnar 13] vaccine that cross-reacts with something in the Schwann cells or in the myelin, whether it's a strong vaccine or a weak vaccine, autoimmunity could occur in someone who [is] genetically susceptible and [in whom] tolerance breaks down." *Id.* at 259.

I agree that the explanation of molecular mimicry provided by petitioner's experts in this case was not as sophisticated as theories presented in other cases. However, the explanation from petitioner's experts is consistent with that of Willison who indicated that molecular mimicry is likely a significant mechanism in the development of GBS, but that the specific antigens in question are not well understood to date except in the case of *C. jejuni* in the AMAN form of GBS. Willison emphasized that in AIDP there is a larger list of likely mimics whether the foreign antigen is an infection or a vaccine. In the Vaccine Program the Federal Circuit, as noted above, has held that the petitioner is not required to provide a detailed biological explanation as long as she provides a sound and reliable theory. Moreover, 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. *Andreu*, 569 F.3d at 1378-79 (citing *Capizzano*, 440 F.3d at 1325-26). The theory provided in this case invoked two well recognized theories of autoimmunity – molecular mimicry and bystander activation – supported by the appropriate timing of the immune response to the vaccine. Dr. He also agreed that the petitioner's checkpoint or tolerance system had failed as evidenced by the onset of GBS, and that in a genetically susceptible person an element of a vaccine could cross react with the myelin in the peripheral nerves and cause GBS.

While Dr. He and Dr. Callaghan propose a standard of proof requiring medical literature showing direct biological evidence of the mechanism of autoimmunity linking the Prevnar 13 vaccine to GBS, the Federal Circuit has held that requiring medical literature directly on point "contravenes section 300aa-13(a)(1)'s allowing medical opinion as proof. [Requiring specific medical literature] prevents use of circumstantial evidence envisioned by the preponderance

[20] Michelle Wykes & Sharon Lewin, *Immune checkpoint blockade in infectious disease*, 18 Immunology 91, 91 (2018).

standard…" *Althen*, 418 F.3d at 1280. Scientific certainty or biological specificity, the standard applied by Dr. He and Dr. Callaghan, is not petitioner's burden of proof in the Vaccine Program, particularly when the state of medical knowledge is not sufficient to provide such specificity. As held by the Federal Circuit in *Althen*, "While this case involves the possible link between TT 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 F3d 1274 at 1280.

Molecular mimicry has been accepted in numerous program cases as a cause of GBS. Multiple cases have also found molecular mimicry in the immune response to the Prevnar vaccine to be the cause of GBS. *See, inter alia*, *Koller, Anderson, Gross, Pierson, Cooper, Bartoszek, Byrd*, *supra* p. 24. "In fact, given the nature of the condition, molecular mimicry has been accepted as a theory of causation for GBS even in the absence of *any* demonstration of homology and cross-reaction." *Salmins*, 2014 WL 1569478 at *14; *Bartoszek*, 2024 WL 4263604, at *16.

Petitioner's theory that the Prevnar 13 vaccine can act as an immune stimulant causing molecular mimicry, leading to cell damage and GBS is sound and reliable and is consistent with the holdings in multiple other cases involving Prevnar and GBS, as detailed above. The respondent's experts do not dispute that the Prevnar 13 vaccine is an immune stimulant. Moreover, they do not dispute that cross-reactions may happen particularly in genetically susceptible individuals. The medical literature provided by both parties explained the process by which damage can occur leading to GBS while recognizing that the field is bereft of complete and direct proof of how vaccines or infections cause GBS. Petitioner has presented a theory of molecular mimicry and or bystander activation which has been recognized and accepted as a sound and reliable theory in Prevnar/GBS cases as well as in the cases of other vaccines and GBS. Petitioner is not required to provide proof of specific epitopes or proven biological mechanisms to satisfy prong one. Although articles, such as Haber, cited by petitioner's experts have limitations, I find that after consideration of all the evidence presented in this case, including the expert reports, expert testimony, and medical literature filed, I find that petitioner has provided preponderant evidence of a sound and reliable medical theory and has satisfied *Althen* Prong one.

b. *Althen* Prong Two

To satisfy *Althen* prong two, petitioner must show by a preponderance of the evidence that there was a "logical sequence of cause and effect showing that the vaccine was the reason for the injury." *Capizzano*, 440 F.3d at 1324 (quoting *Althen*, 418 F.3d at 1278). "Petitioner must show that the vaccine was the but for cause of the harm…or in other words, that the vaccine was the 'reason for the injury.'" *Pafford*, 451 F.3d at 1356. In evaluating whether this prong is satisfied, the opinion and views of treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326. Medical records and medical testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether

there is a logical sequence of cause and effect. *Althen*, 418 F.3d at 1280; *see also Capizzano*, 440 F.3d at 1326. 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 medical community to establish a logical sequence of cause and effect." *Capizzano*, 440 F.3d at 1325. Petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. *Id.*

As I previously concluded that petitioner has satisfied *Althen* prong one, the analysis next turns to whether the Prevnar 13 vaccine petitioner received caused her GBS. Performing such inquiry requires analysis of the appropriateness of the diagnosis, the course of petitioner's illness, and the logic of the explanation building upon the conclusion under *Althen* prong one that the vaccine can cause GBS. In this case, all experts agreed that petitioner was appropriately diagnosed with GBS and that her symptoms began about 11 days after her vaccination. There was, however, disagreement among the experts as to whether an upper respiratory infection ("URI") alternatively caused petitioner's GBS. While respondent may present evidence relating to an alternative cause to demonstrate the inadequacy of petitioner's evidence supporting her case in chief, petitioners are not required to eliminate alternative causes "where the other evidence on causation is sufficient to establish a prima facie case." *Walther v. Sec'y of Health & Hum. Servs.*, 485 F.3d 1146, 150 (Fed. Cir. 2007); *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1353 (Fed. Cir. 2008).

The fact that petitioner has satisfied *Althen* prongs one and three (as will be discussed below) is significant to the *Althen* prong two analysis. *See Capizzano*, 440 F.3d at 1326. Both of petitioner's experts opined that there was a logical sequence of cause and effect between petitioner's vaccination and the development of GBS. Dr. Lee testified that "the temporal nature of the vaccine administration as well as the development of symptoms" provided evidence of such logical sequence. Tr. 83. He further explained that, in the Haber study, "the reported time frame for the development of GBS after Prevnar was 2 to [42] [sic] days, average being 9. In [petitioner's] case, it was 11 days, so within that timeframe." *Id.* Moreover, Dr. Lee's expert report notes that "Vaccines are antigenic stimuli and are associated with GBS. Administration of Prevnar-13 to [petitioner] was directly causal to her development of GBS. Were it not but for the administration of Prevnar-13, [petitioner] would not have developed GBS." Pet'r Ex. 11 at 5. Dr. Knobler similarly testified that the fact that onset occurred within 11 days of the vaccination and that, in his opinion, there were no alternative explanations for petitioner's GBS creates a logical sequence of cause and effect.

The cause of GBS within this time frame is well supported by the mechanism of molecular mimicry or bystander activation in that program cases have frequently recognized a time frame including eleven days to be an appropriate interval for the onset of GBS caused by a cross reaction stimulated by the vaccine. Thus, while the petitioner's experts pointed heavily to the timing of the onset in relation to receipt of the Prevnar vaccine, when understood in terms of the time in which a cross reaction caused by molecular mimicry can occur it is sufficient to demonstrate a logical sequence of cause and effect between the vaccine and the petitioner's GBS.

Petitioner's medical record likewise support a logical sequence of cause and effect between the vaccination she received and her GBS. Petitioner received the Prevnar 13 vaccine on July 11, 2016. Twelve days later, she presented to the ED with complaints of numbness and tingling in her hands and feet starting the night before. Pet'r Ex. 3 at 57, 60. Her treating providers immediately noted that she received the Prevnar vaccine prior to the onset of her symptoms. Her treating providers also consistently listed the vaccine as a potential cause of her GBS along with a preceding URI.

Most of Dr. Callaghan's testimony addressed the issue of a possible URI in the petitioner prior to the onset of GBS. He argued that an upper respiratory infection is statistically more likely to be a cause of GBS. I will address his opinion in detail under "alternative cause" below.

Dr. He agreed that there would have been an active immune response to the vaccine ten to eleven days after vaccination and if the petitioner had a URI there would also have been an immune response to that three or four days after onset. He agreed that the combined effect of the immune response to the vaccine and to a possible URI could have caused an overwhelming immune response leading to her GBS. Tr. 312-13. Thus, even if she did have an upper respiratory infection, the evidence for which, as addressed below, is equivocal, the combined immune response to the vaccine and to an infection could have combined as substantial factors in causing the petitioner to develop GBS. *See*, *Shyface*, 165 F.3d at 1352-53.

Where there is conflicting evidence in the record which neither compels nor precludes a finding of viral alternate causation, then compensation must be awarded. *Knudsen*, 35 F.3d at 550. As will be addressed below, I have concluded that the evidence does not establish that a virus acted as the sole cause of the petitioner's GBS.

With diagnosis and onset established and undisputed and the evidence for a URI being at best equivocal, the fact that petitioner has satisfied *Althen* prongs one and three is significant to the *Althen* prong two analysis. *See Capizzano*, 440 F.3d at 1326. The progression from vaccination to onset of GBS in 11 days as caused by molecular mimicry or bystander activation is logical based on the general understanding of immune cross reactivity. It is reinforced by the timing of onset found by Haber of 2-42 days with a median of nine days. The petitioner's onset was quite close to the median of this range.

The testimony and reports of petitioner's experts, and the repeated notations by petitioner's treating providers that the vaccine was a potential cause of her GBS, provide preponderant evidence of a logical cause and effect between the Prevnar vaccine and the affliction of the petitioner with GBS. Therefore, I find that petitioner has shown preponderant evidence of a logical sequence of cause and effect between the vaccination and her injury, and has thus, met her burden under *Althen* prong two.

c. *Althen* Prong Three

Althen prong three requires petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. This phrase is further defined as a "medically acceptable temporal relationship." *Id.* A petitioner must offer

"preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understating of the disorder's etiology, it is medically acceptable to infer causation-in-fact." *de Bazan*, 539 F.3d at 1352. Although a temporal association alone is insufficient to establish causation, under the third prong of *Althen*, a petitioner must show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d at 1278. The special master cannot infer causation from temporal proximity alone. *Thibaudeau v. Sec'y of Health & Hum. Servs.*, 24 Cl. Ct. 400, 403-04 (1991); *see also Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144 (Fed. Cir. 1992) ("[T]he inoculation is not the cause of every event that occurs within the ten-day period…[w]ithout more, this proximate temporal relationship will not support a finding of causation.").

Dr. Knobler noted in his report that "the time period between the vaccination and the onset of symptoms (July 22, 2016) was noted as 11 days." Pet'r Ex. 12 at 3. There is in fact no dispute that petitioner received the Prevnar 13 vaccine on July 11, 2016 and developed the initial symptoms of GBS on the evening of July 22. These symptoms developed rapidly into full blown GBS through the day of July 23 and resulted in a prolonged hospitalization/inpatient rehabilitation and significant disability. The fact that petitioner's onset of GBS occurred 11 days after vaccination was not contested by respondent's experts. Dr. Callaghan, in his report and his testimony, indicated that petitioner "developed GBS 11 days after [the] Prevnar vaccination and 8 days after an upper respiratory infection." Resp't Ex. A at 1. Such timing from vaccination to onset of symptoms is also consistent with petitioner's testimony and medical records. The medical records indicate that petitioner received the Prevnar 13 vaccine on July 11, 2016. Pet'r Ex. 2 at 15. Petitioner testified that, about a day later, her arm became sore, "was very red," and "looked kind of crusty at the injection site." Petitioner's husband described the area as about "two inches long by an inch wide with redness." *Id.* at 32. About 11 days after vaccination, on July 22, 2016, petitioner was "feeling good" but had "tingling in her hands and feet." *Id.* at 52-53. By the next morning, petitioner was unable to move, and Mr. Diponziano called 911. Petitioner was taken to the Cooper University Hospital Emergency Department complaining of numbness and tingling beginning at about 10:00 p.m. the previous night "with progressive severe weakness." Pet'r Ex. 3 at 57, 60. Based on this record, petitioner's onset occurred on July 22, 2016, or 11 days after she received the Prevnar vaccine.

During the entitlement hearing, Dr. Lee testified that the onset of symptoms 11 days after the vaccination fits with petitioner's theory because "the administration of the vaccine and then the time for the body to react and have that immune response where it's producing the antibody to make the vaccine…takes time and [is] different from individual to individual." Tr. 83-84. In petitioner's case, "11 days is the time that it took her body to generate the immune response and for those antibodies to attack the epitopes on her nerve cells." *Id.* at 84. Dr. Lee referred to the Haber article to support his opinion that such timeline is appropriate, noting that the reported timeframe in the study "for the development of GBS after Prevnar was 2 to 42 days, [with the] average being 9." Tr. 83. Dr. Knobler similarly testified that 11 days from vaccination to onset of petitioner's GBS "is within the expected time course for such events to occur." Tr. 130.

An onset of GBS 11 days after vaccination is also consistent with what has been found to be appropriate timing in other cases in the Vaccine Program in which molecular mimicry is the causal theory for Prevnar vaccine causation of GBS. *See e.g., Koller*, 2021 WL 5027947 at *23

(finding that onset of GBS 12 to 14 days after receipt of the Prevnar-13 vaccine was "an acceptable timeframe in which to infer causation."); *Byrd v. Sec'y of Health & Hum. Servs.*, No. 20-1476V, 2024 WL 4003061, at *28-29 (Fed. Cl. Spec. Mstr. July 8, 2024) (accepting onset about four days after receipt of the Prevnar vaccine as a medically appropriate timeframe); *Anderson*, 2024 WL 557052, at *34 (finding onset of 10 days to be appropriate.).

Based on petitioner's medical records, the expert reports, medical literature, and the expert testimony, I find that petitioner has presented preponderant evidence that petitioner's onset of GBS occurred 11 days after her Prevnar vaccination and that such timing is medically acceptable and fits with petitioner's causal theory of molecular mimicry. Thus, petitioner has preponderantly established a "proximate temporal relationship" between the vaccination and her injury and has satisfied *Althen* prong three. As such petitioner has established a prima facie case of vaccine causation.

d. Alternative Cause

Respondent's expert, Dr. Callaghan, opined that petitioner had a preceding URI that was the more likely cause of her GBS as opposed to the Prevnar vaccine. Dr. Callaghan testified that GBS can be a post-infectious condition, meaning "that infections can trigger the immune system to cause patients to have GBS." *Id.* at 321. This occurs "mostly with upper respiratory tract infections and gastrointestinal illnesses, particularly Campylobacter" which the petitioner did not have. *Id.* He stated that when GBS is suspected to be secondary to an infection, the antecedent infection is "very rarely identified" and is not looked for with URIs. *Id* at 321-22. Dr. Callaghan testified that, to determine whether a patient's GBS is post-infectious, one looks to "whether there is medical evidence" and "if someone has a temporal association." *Id.* at 322. According to Dr. Callaghan, a URI within "a handful of weeks of the" onset of GBS would lead to the conclusion that the GBS is post-infectious.

In order to establish alternate causation, once petitioner has satisfied the three *Althen* prongs, the government must provide "proof that some other factor was the actual cause…by identifying a particular such factor (or factors) and presenting sufficient evidence to establish that it was the *sole* substantial factor in bringing about the injury." *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1354 (Fed. Cir. 2008)(emphasis added). While true that respondent need not identify a specific *type* of viral infection to establish alternate causation, if conflicting evidence on the record neither compels nor precludes a finding of alternate causation, then "the government has failed in its burden and compensation must be awarded." *Andreu*, 569 F.3d at 1378 (citing *Knudsen*, 35 F.3d at 550). Moreover, where there are two potential causes for an illness, a petitioner is not required to eliminate the other potential cause in order to be entitled to compensation. *Walther v. Sec'y of Health & Hum. Servs.*, 485 F.3d 1146, 1150 (Fed. Cir. 2007) (ruling that "Petitioner does not bear the burden of eliminating alternative independent potential causes."); *Pafford*, 451 F.3d at 1358-59. Case law instructs that where two causes combine to cause a vaccine-related illness, and it is not possible to determine which of the causes was most responsible, it is appropriate to find in favor of compensation. *Shyface*, 165 F.3d at 1352-1353 (finding in favor of petitioners where both a vaccine and an *Escherichia coli* infection contributed to the death because concurrent forces may bring about a single harm.); *Zamora v.*

Sec'y of Health and Hum. Servs., No. 19-1718V, 2023 WL 6180857 (Fed. Cl. Spec. Mstr. Aug. 28, 2023).

In petitioner's case, Dr. Callaghan opined that petitioner "had an upper respiratory tract infection eight days before GBS, which he said is a reasonable timeframe" and, based on this, concluded that petitioner's GBS was post-infectious. Tr. at 322. He based his opinion that petitioner had a URI on reports of a cough or run00ny nose which the record indicated began about four days before the onset of GBS. However, an upper respiratory infection was not observed or treated by medical personnel. He testified that URIs are "almost always diagnosed purely on clinical history." *Id.* at 323. According to Dr. Callaghan, petitioner had "some of the most common symptoms of an upper respiratory tract infection," and he argued that "was the judgment of her medical providers." *Id.* The medical records which mentioned symptoms such as cough or congestion appeared to be based on answers to questions about recent history and not to findings on physical examination. It did not appear that any physician actually diagnosed an upper respiratory infection after performing multiple physical examinations that included the respiratory system, albeit a URI was mentioned as part of her history. Dr. Callaghan pointed to one note by Dr. Michael Weston, M.D. who did a neurology consult on the afternoon of July 23. Dr. Weston in his plan indicated that Ms. Diponziano likely has GBS based on diffuse symmetric weakness and a lack of reflexes. He said, "likely precipitated by recent URI." Pet'r Ex 3 at 114. A review of the history that he took indicated the onset of numbness and tingling in her fingers followed by her toes during the evening of July 22. She had difficulty sleeping and woke up in the middle of the night and again at 5 AM when she could not walk. He noted that she had received the pneumovax on the 19th which was in error as she received it on July 11. "She reported a slight confluent red rash on her left arm after the injection that has since resolved. She reports on Tuesday (which was the 19th and four days before onset) she began to have a URI. She has had a dry cough, rhinorrhea, and post nasal drip. She denies any abdominal pain." *Id* at 80, 108. There was no indication that Dr. Weston conducted any examination of her respiratory tract and was understandably focused on her loss of strength and reflexes.

The history from Cooper University Hospital fairly uniformly listed a cough as having occurred about four days prior or as beginning on Tuesday which was four days before the onset of GBS on Friday, July 22, 2016 or at least in the range of three to five days prior. Physical exams performed by other providers found no evidence of a URI. On the day of admission at 8:49 AM, the examiner recorded oropharynx is clear and moist and mucous membranes are normal. No oropharyngeal exudate, posterior oropharyngeal erythema or tonsillar abscesses. Pulmonary and chest: Effort normal and breath sounds normal. No respiratory distress. She has no wheezes. She has no rales. She exhibits no tenderness. *Id*. at 57.

A critical care note from later that day noted that petitioner had multiple allergies and she states that she took a pneumonia vaccine around 10 days back which was followed by an erythematous rash in her R arm/shoulder region. She has also had URI symptoms for the past 5 days. The rash was noted to be 4 x 4 cm. The ENT exam was normal, and her pulmonary exam was clear to auscultation bilaterally, no rales or wheezes. *Id.* at 44. Treating physicians did not find any evidence supportive of an active viral infection in petitioner's chest x-ray, blood work, or physical examination.

Petitioner's medical history verified that she did have a history of seasonal allergies which was confirmed by her husband's testimony. The symptoms described of a cough with postnasal drip is certainly consistent with allergy symptoms which Dr. Knobler testified would be more likely to occur in the summer. She had not sought any treatment and remained active through the week preceding her hospitalization including taking a trip to Atlantic City with her sister.

In terms of possible causes of GBS most entries in the hospital chart listed "PPV vaccine/uri" or just "vaccine/uri."*See, e.g.*, Pet'r Ex. 3 at 58 ("Guillain Barre-concern for given bilateral weakness and recent uri/vaccine."). Dr. Peterson wrote at 5:38 PM July 23, "79 year old female Jehovah's witness with [history of] hypothyroidism, multiple allergies presents with rapidly progressive ascending paresis and dysesthesias. Concerning for GBS due to symmetrical involvement. Possible triggers include pneumonia vaccine, preceding URI." *Id* at 75. Dr. Peterson also wrote, "The patient had a PNA vaccine (left deltoid) with rash-non-spreading. Over the last 3-4 days she has had hoarseness. Denies dyspnea." *Id*. at 76 Her chest x-ray showed no infiltrate. *Id.* Patient received IVIG x 5 for GBS secondary to vaccine vs. uri. *Id.* at 78. Another note by critical care physician Haney Mallemat, M.D. on July 25 noted concern for GBS possibly triggered by recent PNA vaccine/URI. No respiratory distress currently, afebrile no leukocytosis. *Id.* at 101, 129. Similar notes appeared at multiple other pages of the Cooper University Hospital record indicating GBS possibly triggered by PNA vaccine/uri. *Id.* at 134, 140, 146, 158, 169 and 176.

While it is difficult to discern the level of thought process in attributing either or both of these as the possible cause of her GBS, it did appear that most of the physicians at Cooper did consider both the Prevnar vaccine and a possible URI as possible causes of the petitioner's GBS. In fact, it appeared that the history of the vaccination and the URI quickly elevated GBS to the top of the differential diagnosis shortly after admission.

Dr. Knobler and Dr. Lee opined that there was no convincing evidence of an upper respiratory infection and that in a person who suffered from allergies as does petitioner, it is more likely that she may have had allergic rhinitis that would have explained her symptoms. They noted that she had no treatment for a URI and did not have a fever. The ENT and pulmonary exams as well as the chest x-ray in the hospital were normal. The lay witnesses at the hearing indicated that petitioner had been active all week, including going on a trip to Atlantic City with her sister indicating that at most she had minimal symptoms.

Dr. Callaghan cited to an article by Grief,[21] which found that "nasal congestion is seen in 80 to 100 percent of patients with URI, cough in 40 percent, fatigue and malaise in 20 to 25 percent, and fever in only 21 percent." Tr. 330. He used this data to dispute Dr. Knobler's opinion that petitioner's lack of fever supported the fact that she did not have a URI, noting that "only one in a thousand people with URIs have fever." *Id.* This testimony was given despite his reference indicating that 21% of people with URI have fevers. He also disputed Dr. Knobler and Dr. Lee's opinions that the lack of treatment for URI supports the fact that petitioner did not have one, explaining that treatment of a URI with antibiotics is "the exception, not the rule." *Id.* He

[21] Samuel Grief, *Upper Respiratory Infections*, 40 Primary Care Clinical Office Practice 757 (2013).

indicated that more than 90 to 95 percent "of URIs are treated symptomatically with mostly time but also…treatments…to help you with your cough or your runny nose." *Id.* Dr. Callaghan opined that petitioner's symptoms were not consistent with allergic rhinitis because malaise and fatigue are atypical for allergies, and cough is less commonly associated with allergies. *Id.* at 336. Thus, Dr. Callaghan concluded that "petitioner clearly has the constellation of symptoms" for a URI and that "her providers correctly diagnosed with a URI." *Id.* at 330. He further noted that this is particularly relevant "because we have really strong epidemiologic data linking URIs with GBS." *Id.* at 330.

Dr. Callaghan presented two articles, one by Greene[22] and another by Galeotti,[23] to support the contention that "a causal association between an upper respiratory infection and GBS is more common than the association between vaccines and GBS." *Id.* at 338; Resp't Ex. A-3; Resp't Ex. A-4. The two articles found that "the odds of developing GBS after upper respiratory tract infection were much higher than after the flu…vaccine." *Id.* at 338. These studies did find a significantly higher number of GBS cases associated with gastrointestinal and respiratory illnesses but as in Galeotti there was still a relative risk of 2.1 associated with the studied influenza vaccine. In another article, filed by respondent, by van den Berg et al,[24] referring to the influenza vaccine from 2009 the authors said, "but extensive national and international studies found that vaccination was associated with only a small attributable risk of GBS. 1.6 excess cases of GBS per 1,000,000 vaccine recipients, a frequency similar to that for all seasonal vaccines. Resp't Ex. D-1 at 4. Notably, however, "the fact that epidemiological evidence point[s] to a virus rather than [the vaccine] as a trigger for the [injury] is insufficient to preclude recovery." *Andreu*, 569 F.3d at 1378 (citing *Knudsen*, 35 F.3d at 550).

Thus, although it can be fairly concluded that infections medically documented before the onset of GBS are more common causes of GBS, none of the articles either assert that the infections are the sole cause or that they explain all cases of GBS. Galeotti and van den Berg both identified some excess relative risk secondary to vaccines. All of the articles consider vaccination as a possible cause of GBS even as the risk is less than for example from the flu itself.

Significantly, Dr. He agreed that the Prevnar vaccine administered 11 days prior to onset and a possible URI occurring three to four days prior would both have been generating an immune response at the time of onset and that it was possible that the combination of the two acting at the same time could have caused a sufficiently overwhelming response to cause autoimmunity. Tr. 312-13; *See Shyface*, 165 F3d at 1353. Special Master Millman, in *Mulvaney,* noted, "the Federal Circuit emphasized that the vaccine does not have to be the predominant

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[22] Sharon Greene et al., *Guillain-Barre Syndrome, Influenza Vaccination, and Antecedent Respiratory and Gastrointestinal Infections: A Case-Centered Analysis in the Vaccine Safety Datalink, 2009-2011*, PLoS ONE, June 2013.

[23] Francesca Galeotti et al., *Risk of Guillain Barre syndrome after 2010-2011 influenza vaccination*, 28 Pharmaco-Epidemiology 433 (2013).

[24] Van den Berg et al., *Guillain-Barre syndrome: pathogenesis, diagnosis, treatment and prognosis*, 10 Nature Reviews, Neurology 469 (2014).

factor in order for petitioner to prevail." *Shyface* instructs that proof of a substantial factor satisfies the requirements of the Vaccine Act. *Id.* at 1353.

At the outset, it is important to note that the evidence that petitioner actually had a URI is scant. No physicians noted any signs of an active infection in petitioner's blood work, on physical examination, or in her chest x-ray. The only indication that petitioner may have had a URI is based on her reported symptoms of a cough and congestion in the days prior to her hospitalization. The mild upper respiratory symptoms described in the hospital record as being reported could readily have been caused by allergic rhinitis particularly in a patient with an allergy history and occurring in the summer months when an allergy attack would be more likely than a respiratory infection. The physical examinations performed by various physicians in the hospital did not find any indication of a respiratory infection and in fact documented a clear respiratory tract. They did note that the petitioner said that she had a cough or hoarseness for several days. All but one of the treating physicians in the hospital listed both the Prevnar vaccine and the URI as possible triggers of the GBS. As Dr. Callaghan indicates that URIs are often rather loosely diagnosed based on history alone, it would appear that the reference to a URI may also be rather loosely made in that the types of symptoms reported by Ms. DiPonziano could just as easily be caused by allergies. Furthermore, there were multiple examinations made of her respiratory tract which found no evidence of a URI upon admission to the hospital.

Although a recent URI was mentioned in the records at multiple locations based on a history of a cough and congestion, the evidence on causation is, at most, in equipoise. These symptoms could readily have been explained by allergies as testified by Dr. Knobler. Additionally, respondent's expert, Dr. He agreed that, in the event there was a mild URI in the interval between the vaccine and the onset of GBS, the vaccine and an infection, acting in concert, could have caused the overwhelming immune response leading to autoimmunity. Although the possible occurrence of a mild upper respiratory infection prior to the onset of the petitioner's GBS cannot be disregarded, neither can the possible allergic rhinitis explanation or the fact of the two acting in concert to cause GBS.

When there are two potential causes for an illness, a petitioner is not required to eliminate the other potential cause in order to be entitled to compensation. *Walther v. Sec'y of Health & Hum. Servs.*, 485 F.3d 1146, 1150 (Fed. Cir. 2007) (ruling that "Petitioner does not bear the burden of eliminating alternative independent potential causes."). Moreover, in order for the government to meet its burden, it must provide preponderant evidence that a particular agent or condition unrelated to the vaccine was the "sole substantial factor in bringing about the injury." *de Bazan*, 539 F.3d at 1354. Given my conclusion that the evidence of the URI as an alternative cause is at best, in equipoise, the government has failed in its burden of persuasion to demonstrate an alternative cause by a preponderance of the evidence. *Knudsen*, 35 F.3d at 551 ("If the evidence [on alternative cause] is seen in equipoise, then the government has failed in its burden of persuasion and compensation must be awarded."). Accordingly, the petitioner is entitled to compensation.

VI. Conclusion

After a review of the entire record and for the foregoing reasons, I find that petitioner has established by preponderant evidence that the Prevnar 13 vaccine she received more likely than not caused her Guillain-Barre syndrome. Thus, petitioner is entitled to compensation. A separate damages order will be issued.

IT IS SO ORDERED.

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