In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 17-1136V
Filed: January 19, 2022
PUBLISHED

CAROLYN PIERSON, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	Special Master Horner Pneumococcal conjugate vaccine (Prevnar 13); Guillain-Barre Syndrome (GBS); Causation-in-fact

Jeffrey S. Pop, Jeffrey S. Pop & Associates, Beverly Hills, CA, for petitioner.
Austin Joel Egan, U.S. Department of Justice, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

On August 23, 2017, petitioner filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10-34 (2012),[2] alleging that the influenza (flu) vaccine she received on September 30, 2014, caused her to suffer Guillain-Barre Syndrome ("GBS"). (Pet., p. 1.) Petitioner later amended her petition to allege that she received the pneumococcal conjugate vaccination (Prevnar 13) on January 6, 2015, which caused in fact her GBS, instead of the flu vaccine. For the reasons set forth below, I conclude that petitioner is entitled to compensation.

I. Procedural History

Petitioner filed her petition *pro se* on August 23, 2017, alleging that she received a flu vaccination on September 30, 2014 which caused her to develop GBS. (ECF No.

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

[2] Within this decision, all citations to § 300aa will be the relevant sections of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

1.) This case was originally assigned to Special Master Millman who granted petitioner's motion to proceed *in forma pauperis*. (*See* ECF No. 7.) After an initial telephonic status conference, petitioner indicated that she was seeking representation. (ECF No. 8.) On January 16, 2018 a status conference was held and Special Master Millman ordered petitioner to file her medical records. (ECF No. 9.)

On March 12, 2018, petitioner's counsel filed a motion to substitute attorney. (ECF No. 10.) After petitioner secured representation, she filed an amended petition on April 12, 2018. (ECF No. 12.) Petitioner's amended petition now alleges that petitioner received a pneumococcal conjugate vaccination (Prevnar 13) on January 6, 2015 which caused her to develop GBS. (ECF No. 12.) On April 20, 2018 Petitioner filed her medical records, her declaration, and a statement of completion. (ECF Nos. 13-15.)

On June 11, 2018, respondent filed a status report requesting petitioner's pre-vaccination medical records and Special Master Millman ordered petitioner to file her medical records dating back three years prior to vaccination. (ECF Nos. 17-18.) On June 27, 2018, petitioner filed a status report indicating that she had filed all of her medical records, including primary care, emergency, and diagnostic testing records dating back to 2012. (ECF No. 19.) On July 30, 2018, respondent filed his Rule 4(c) report, arguing that the evidence presented did not meet petitioner's burden and recommending against compensation. (ECF No. 20.)

On January 23, 2019 petitioner filed an expert report from Dr. Lawrence Steinman and the accompanying medical literature. (ECF Nos. 22-24.) Petitioner filed updated medical records from Evergreen Family Medicine Center on February 14, 2019. (ECF No. 26.) Respondent filed a status report on March 18, 2019, indicating that he intended to file a responsive expert report. (ECF No. 28.) The case was reassigned to me on June 4, 2019. (ECF No. 30.) On July 1, 2019 respondent filed an expert report from Dr. Thomas Paul Leist and the accompanying medical literature. (ECF 32.) After reviewing the Rule 4 report, I ordered respondent to file a supplemental expert report responding to petitioner's proffered medical theory concerning molecular mimicry as well as any missing records from Mercy Medical Center, or a status report confirming their unavailability. (ECF No. 33.)

I granted petitioner's motion to issue a subpoena, and thereafter petitioner filed additional medical records from Mercy Medical Center on August 1, 2019. (ECF Nos. 35, 36.) The parties filed supplemental expert reports from Drs. Steinman and Leist and the accompanying medical literature on September 3, 2019 and March 20, 2020. (ECF Nos. 38, 42.) Petitioner filed additional medical literature on March 30, 2020. (ECF No. 44, 45.) On June 30, 2020, respondent filed a second supplemental expert report from Dr. Leist with additional medical literature. (ECF No. 49.)

On September 14, 2020, I scheduled a two-day entitlement hearing set to commence on November 17, 2021. (ECF No. 54.) On October 6, 2021, petitioner filed additional medical literature, a supplemental declaration, as well as declarations from David Pierson (petitioner's husband) and Laura Day (petitioner's co-worker and friend).

(ECF No. 59.) On November 3, 2021, petitioner filed a motion for leave to file additional medical literature out of time. (ECF Nos. 69, 70.) During a prehearing status conference on November 10, 2021, I granted in part and deferred in part petitioner's motion to file the additional medical literature out of time. (ECF 73.) I granted petitioner's motion to file Exhibits 64, 66, 68 and 70, while I deferred ruling on petitioner's motion with respect to Exhibits 63, 65, 67, 69. (*Id.*) I indicated that the relevance of the latter remaining exhibits remained unclear without expert explanation.[3] (*Id.*)

A two-day entitlement hearing was held remotely on November 17 and 18, 2021, via Webex. (*See* ECF Nos. 77-78, Transcript of Proceedings ("Tr"), filed 12/15/2021.) Thereafter, I ordered respondent to file a status report no later than December 3, 2021, indicating whether he wished to file a written response to any late-filed exhibits referenced during the hearing. (*See* Dkt. Text 11/18/2021.) On November 22, 2021, respondent filed a status report indicating that respondent did not wish to file a written response concerning Exhibits 63, 65, 67, and 69. On January 14, 2022, I granted petitioner's motion for leave to file out of time only with respect to Exhibit 69. (ECF No. 73 .) This case is now ripe for a decision on entitlement.

II. Factual History

a. As reflected in the medical records

Petitioner's pre-vaccination medical history is significant for headaches (Ex. 4, p. 11; Ex. 10, p. 13), arthritis (Ex. 3, p. 7), osteopenia (Ex. 4, p. 8), pyelonephritis (Ex. 10, p. 23), hypertension (Ex. 4, p. 57), and a history of hysterectomy and cholecystectomy (Ex. 3 at 7). Petitioner received the pneumococcal vaccine (Prevnar 13) on January 6, 2015 at Sav-On Pharmacy in Oregon. (Ex. 2.)

On January 21, 2015 petitioner presented to Eugene/Thurston Urgent Care to James Daskalos, M.D., with an ongoing unproductive cough since December 17, 2014. (Ex. 3, p. 1.) Additionally, petitioner complained of sneezing, congestion, wheezing, shortness of breath, and tingling. (*Id.*) Dr. Daskalos reported that "initial onset revealed no significant fever, chills, or myalgias" and noted that her cough was worse at night. (*Id.*) A physical exam revealed abnormal breath sounds—wheezing and scatter rhonchi bilaterally. (*Id.* at 2) Dr. Daskalos reviewed petitioner's x-ray which showed a right lower lobe infiltrate. (*Id.* at 2-3) He diagnosed petitioner with bronchopneumonia of an unspecified organism and prescribed doxycycline, Tessalon, and an inhaler. (*Id.*)

On February 3, 2015 petitioner returned to Eugene/Thurston Urgent Care to see Dr. Daskalos for an evaluation of her chronic cough. (Ex. 3, p. 11.) Petitioner complained of headache, tingling, numbness, cough, shortness of breath, and

[3] With regard to the exhibits for which I deferred ruling, I permitted petitioner to reference the exhibits during the hearing, but noted that I would not grant leave to file exhibits that ultimately were not accompanied by expert discussion by the close of the hearing. Respondent was permitted an opportunity to file a written response by his expert to any of these exhibit referenced during the hearing.

wheezing. (*Id.*) A physical exam revealed bilateral wheezing. (*Id.* at 12.) Dr. Daskalos diagnosed petitioner with acute bronchospasm, prescribed prednisone and an inhaler, and referred her to a pulmonologist. (*Id.* at 13.) Petitioner later cancelled her pulmonary appointment because she was "feeling much better." (*Id.*)

On February 26, 2015 petitioner returned for another follow-up appointment with Dr. Daskalos. (Ex. 3, p. 19.) Dr. Daskalos observed that petitioner showed "good improvement and was asymptomatic last week[,]" though "after completing the steroids [petitioner] then began having increasing symptoms of shortness of breath and cough-particularly with exertion" (*Id.*) Petitioner described no chest pain, though she experienced some left-sided thoracic posterior pain, but "no swelling of the lower extremities." (*Id.*) "Unrelated to her present complaints[,]" petitioner described symptoms of "carpal tunnel syndrome[,]" explaining that she is a cake decorator for Albertson's. (*Id.*) A review of systems confirmed chills, fatigue, sweats, shortness of breath, and wheezing related to her cough. The review of systems continued to indicate tingling, but also added neurologic weakness for the first time. (*Id.*) Petitioner's physical exam noted wheezing but was otherwise normal. (Ex. 3, pp. 20-21.)

On February 28, 2015 petitioner returned to Eugene/Thurston Urgent Care with a new symptom of mid-back pain and reported that she was using her husband's pain medication. (*Id.* at 36.) Petitioner reported her pain as an 8/10 and worse with movement and taking deep breaths. (*Id.*) Kerry Harrington, PA-C, noted no injury or trauma. (*Id.*) Petitioner described numbness and tingling in her hands, with a history of carpal tunnel syndrome. (*Id.*) Petitioner reported no leg pain or swelling. (*Id.*) Her physical exam revealed general distress due to pain, tenderness of her chest on palpation, and scattered wheezing. (Ex. 3, p. 27.) Petitioner was diagnosed with worsening acute bronchospasm, worsening cough, and backache. (*Id.* at 27-28.) Petitioner's d-dimer test was negative. (*Id.* at 28, 30.) She was prescribed Norco, Omnicef, and Flexeril; she was advised to alternate heat and ice and perform range of motion exercises; and cleared to return to work March 9, 2015.[4] (*Id.* at 28)

On March 1, 2015 petitioner again returned to Eugene/Thurston Urgent Care, complaining of "constant (but worse at times) numbness/tingling of the left hand and right hand[,]" since her previous visit. (Ex. 3, p. 36.) She also described "back pain, now related to numbness and tingling in her hands." (*Id.*) Matthew Driver, M.D., noted that petitioner had been given two courses of prednisone: the first relieved her pain, but she had breakthrough pain on the second course. (*Id.*) Petitioner also took Norco with no relief. (*Id.*) She was advised to go to the emergency department for a full evaluation. (*Id.*) Petitioner's physical exam indicated that petitioner was ambulatory, though she "rock[ed] back and forth in apparent pain[.]" (*Id.* at 37.) No detailed exam was performed, though Dr. Driver noted that "[petitioner's] face appears normal." (*Id.*) Petitioner was diagnosed with an unspecified backache. (*Id.*)

[4] As of this visit, Kerry Harrington, PA-C, notes "added an antibx" though her report does not specify any infection. (*See* Ex. 3, p. 25-28.)

Later that day petitioner presented to the emergency department at Mercy Medical Center with a questionable diagnosis of pneumonia. (Ex. 4, p. 38.) Her "main complaint [was] pain kind of at the bra line on the right side." (*Id*.) She described pain with twisting, turning, or coughing. (*Id.*) Petitioner reported no leg pain and Wade Fox, D.O., noted that "she is not really short of breath, not tachycardic." (*Id.*) Dr. Fox observed, "I think she has basically coughed herself to a musculoskeletal strain in the back." (*Id.*) Petitioner was prescribed more pain medication for her pain and cough. (*Id.*) Chest x-rays taken that day revealed no acute cardiopulmonary process. (Ex. 4, p. 49.) Petitioner was discharged and advised to follow-up with Jennifer Jarasa, M.D., as an outpatient. (*Id.* at 38.)

The next day, March 2, 2015, petitioner returned to Eugene/Thurston Urgent Care and was seen by PA Harrington. (Ex. 3, p. 42.) She complained of aching lower back pain, describing the severity as 10/10. (*Id.*) Petitioner reported that she had difficulty sleeping due to the pain; and that the Dilaudid did not reduce her pain. (*Id.*) She further complained of fatigue, sweats, chest pain/pressure, headache, light headedness, weakness, blurred vision, ongoing cough, congestion, shortness of breath and wheezing. (*Id.*) The physical exam described petitioner's rocking back and forth due to pain. (*Id.* at 43-44.) Petitioner was given a Dilaudid injection and prescribed Zofran. (*Id.* at 44.) She was advised to return to the emergency department. (Ex.3, p. 45.)

Later that day, petitioner saw David Rickman, M.D., reporting pain "mostly about her left upper back" that spread "all over her back" with "some pain in her hands and legs" that began one to one-and-a-half weeks prior. (Ex. 4, p. 58.) She described nausea without vomiting, ongoing cough, heaviness in her chest, and shortness of breath. (*Id.*) Petitioner denied having leg swelling, leg numbness, tingling, or weakness. (*Id.*) Dr. Rickman observed that petitioner "clearly [had] back pain which [was] somewhat intractable…although [he] [did] not see[] evidence of any more immediate or acute pathology." (*Id.*) Petitioner was given intravenous Zofran and Dilaudid twice. (*Id.*) Petitioner was discharged and instructed to follow-up with her primary care provider, Heidi McNulty, D.O. (*Id.*)

On March 3, 2015 petitioner saw Dr. McNulty who noted that petitioner contracted an upper respiratory infection in December and was seen multiple times in urgent care for her worsening cough, sudden acute pain in the bra line area as well as "new numbness and pain in the fingers and then in the toes and distal feet." (Ex. 5, p. 12.) Petitioner was diagnosed with thoracic spine pain, neuropathy, as well as climacteric arthritis of the hand. (*Id.* at 17.)

The following day, March 4, 2015, petitioner returned to Eugene/Thurston Urgent Care complaining of ongoing mid-back pain and requesting pain medication until she could be seen again by her primary care physician. (Ex. 3, p. 60.) Petitioner received Dilaudid and Phenergan injections. (*Id.* at 62.) Her diagnosis remained worsening backache unspecified, with her cough and bronchospasm improved. (*Id.*) Later that same day, petitioner followed up with Dr. McNulty who observed that petitioner had "a great deal of pain in the mid thoracic region and also in the lumbar area bilaterally" with

"burning pain" in her hands. (Ex. 5, p. 9.) Petitioner received an osteopathic manipulation and was prescribed hydromorphone. (*Id.* at 11.)

Petitioner was admitted to Mercy Hospital from March 5, 2015 to March 13, 2015. (Ex. 4, pp. 79-84.) The reason for admission described a one-week history of "upper and mid back pain, starting from mid chest to all the way down to [petitioner's] hips on both sides." (*Id.* at 79) Humayun Tufail, M.D., reported that "petitioner does not have any neurological symptoms" and had "no numbness, tingling in the legs." (*Id.*) More specifically, Dr. Tufail observed that "[h]er pain does not travel or radiate towards her legs, but is essentially from mid back up to her hip level." (*Id.*) Another report from the day of admission noted that petitioner of lower back pain radiating down to her legs complained for two weeks with "numbness in her feet and in her hands." (*Id.* at 87.) In her physical exam Tami Marriott, M.D., noted that petitioner "ha[d] a positive straight leg raise with both legs, just lifting her feet about 8 inches off the bed." (*Id.* at 88.) Dr. Marriott "d[id] not appreciate any numbness or tingling at this time" and concluded petitioner "ha[d] full strength." (*Id.*)

On March 7, 2015, petitioner was scheduled to be discharged when she had two large bowel movements with dark blood and clots. (Ex. 4, p. 75.) She was seen for abdominal pain and rectal bleeding by gastroenterologist, Petre Sorin, M.D., who ordered a colonoscopy. (*Id.* at 77.) That same day petitioner was seen by Bryan McVay, M.D., where petitioner reported that "her problems began during the winter holidays when she had a cough." (*Id.* at 72.) Petitioner made "no comment[s] regarding exacerbation or amelioration" except to say that the oral pain medications were ineffective, though the IV narcotics relieved her pain. (*Id.*) Petitioner was transferred to the intensive care unit for delirium and suspected ischemic colitis. (*Id.* at 72, 82.) Petitioner's colonoscopy revealed colon polyps, internal and external hemorrhoids (reason for bleeding), and colonic diverticulosis. (*Id.* at 163.) Petitioner was discharged from the ICU on March 8, 2015 and underwent a psychiatric evaluation for delirium. (*Id.* at 165-66.) Tamara Lee, PMHNP, concluded that the cause of petitioner's delirium was multifactorial, though likely attributable to a combination of medications, hospitalization, and lack of sleep. (*Id.*)

On March 12, 2015, Matthew Mason, D.O., observed that petitioner "may have Bell's palsy." (Ex. 6, p. 438.) The nursing staff reported that petitioner's facial droop appeared "much worse than it previously had," which prompted Dr. Mason to order another CT scan.[5] (*Id.*) The CT scan of petitioner's head was taken without contrast and showed no evidence of acute intracranial abnormality. (Ex. 4, p. 145.)

On March 13, 2015, James Guetzkow ordered a transfer to Sacred Heart Hospital where petitioner could be seen by a neurologist. (Ex. 4, p. 83.) Petitioner's

[5] It is unclear from petitioner's records the exact onset of her facial droop. This appears to be the first mention of facial droop. (Ex. 6, p. 438; *see also* Ex. 4, p. 145 (CT scan taken without contrast on March 12, 2015 notes history of "facial droop"); Ex. 6, p. 386 (hospital transfer on March 13, 2015 noting "RN stated [s]he is unable to move her legs or L arm, her L side of her face droops, her speech is slurred, CT scan is clear").)

discharge summary from Mercy Medical Center noted that petitioner "had an onset of an unusual illness[] during the month before admission." (*Id.* at 82.) Petitioner "developed pain in her thoracic spine with numbness and tingling in [her] hands and legs" and "had a cough for months with shortness of breath and chest heaviness, but no fever." (*Id.*) Her discharge diagnoses included: subacute flaccid paraparesis, acute peripheral neuropathy, acute right Bell's palsy, and thoracic back pain. (*Id.*) Petitioner was also diagnosed with gastroenteritis, hemorrhoids, and sigmoid diverticulosis as well as delirium and hallucinations. (*Id.*) On examination on the day of discharge, Dr. Guetzkow found "no strength in [petitioner's] extremities and no deep tendon reflexes or Babinski response." (*Id.* at 83.) Petitioner also complained of numbness in her hands, which "predated the onset of the weakness in the legs." (*Id.*) Petitioner was transferred via ambulance to Sacred Heart Hospital. (Ex. 4, p. 83, Ex. 6, pp. 383-387.)

Once petitioner was admitted at Sacred Heart Hospital, she was seen by neurologist Miguel Estevez, M.D. (Ex. 6, p. 227.) Petitioner's chief complaint listed "weakness." (*Id.*) Petitioner complained of pain distally in her hands and feet as well as right side peripheral cranial nerve VII palsy with difficulty closing her right eye and right upper and lower facial muscle weakness. (*Id.* at 228.) She further reported difficulty with swallowing, with weakness on the right lower part of her face "making it difficult to hold things in her mouth without great care." (*Id.*) Dr. Estevez described a "mixture of pathology" in petitioner's case—with peripheral nerve involvement and proximal muscle weakness. (*Id.* at 229.) Petitioner was ordered to receive IV fluids and undergo labs to rule out any rheumatologic pathology. (*Id.*) Dr. Estevez also ordered a lumbar puncture. (*Id.* at 229, 234.)

On March 14, 2015, petitioner underwent a brain MRI without contrast, which revealed no evidence of intracranial mass or abnormal enhancement, and no evidence of acute ischemia. (Ex. 6, p. 236.) Later that day, petitioner also underwent a cervical spine MRI which revealed multilevel cervical spondylosis, without evidence of abnormal epidural or intramedullary spinal cord enhancement; significant disc degeneration at C5-C6 resulting in moderate central stenosis and foraminal compromise; and asymmetrical foraminal facet on the left at C4-C5, second to hypertrophic arthropathy. (Ex. 6, p. 235.) On March 15, petitioner underwent a lumbar puncture which showed normal protein, elevated glucose, serum total of two nucleated cells, sixty-eight percent lymph, negative flow cytometry of the CSF, negative herpes simplex viruses, varicella zoster virus, and syphilis of the CSF. (Ex. 6, p. 226, 234.) Later that day, neurologist Elaine Skalabrin, M.D., ordered petitioner to receive five days of IVIG treatment. (*Id.* at 401.)

On March 21, 2015 petitioner saw neurologist Michael Balm, M.D., who diagnosed her with GBS. (Ex. 6, pp. 226, 391.) Dr. Balm noted that there was an atypical pattern of weakness, but that he was confident GBS was the correct diagnosis. (*See* Ex. 6, p. 391.) Petitioner was scheduled to follow-up with Dr. Balm in six weeks. (*Id.* at 390.)

On March 24, 2015 petitioner was discharged from Sacred Heart Hospital. (Ex. 6, pp. 225-227.) Her discharge diagnoses were GBS resulting in bilateral lower extremity and upper extremity weakness and right peripheral seventh nerve weakness

as well as hyponatremia and neuropathic pain secondary to GBS. (*Id.* at 225.) During the course of her hospitalization, petitioner's MS panel revealed negative oligoclonal bands, but evidence of blood-brain barrier breakdown. (*Id.* at 226.) Additional serology showed negative mycoplasma, a low B6 level of unclear significance, negative paraneoplastic antibodies of the CSF, and negative Rickettsia antibodies of the serum. (*Id.*) Dr. Skalabrin explained that "[g]iven petitioner's progressive lower extremity greater than upper extremity weakness and essentially areflexic" she was given a "[preliminary][6] diagnosis of GBS." (*Id.*) In the last several days of her IVIG treatment petitioner showed significant improvement of her motor function; regained all of her normal strength in her upper extremities (with the exception of a mild decrease in grip); and a mild improvement of her facial droop with progressive improvement of her lower extremity weakness. (*Id.*) However, petitioner still had significant impairment of the proximal muscles, left worse than right. (*Id.*)

Petitioner was admitted for inpatient rehabilitation between March 24, 2015 and April 29, 2015. (Ex. 4, pp. 178-179; Ex. 6, pp. 1010-1012.) At this time petitioner presented with "significant neurologic deficits related to Guillain-Barre syndrome." (Ex. 4, p. 178.) Petitioner was scheduled to receive physical therapy and speech therapy, as well as rehabilitation nursing for bowel and bladder management. (*Id.*) Upon her discharge, petitioner's diagnoses included: "probable AIDP" (GBS) with predominant involvement of the lower extremities, neuropathic pain secondary to GBS, hypertension, hyponatremia (resolved), and osteoarthritis. (Ex. 6, p. 1011.) She was discharged home and instructed to follow up with outpatient physical therapy and occupational therapy at Mercy Medical Center and outpatient doctors' appointments. (*Id.*)

On July 7, 2015 petitioner saw Dr. Balm for an outpatient neurology appointment. (Ex. 9, pp. 6-10.) Petitioner described her condition as "95% better," though she reported some numbness in her feet and weakness of hip flexors and extensors, as well as some difficulty getting up from a chair and climbing stairs. (*Id.* at 6.) She no longer reported difficulties with speech or swallowing, though she complained of some mild residual right facial weakness. (*Id.*) Petitioner reported to Dr. Balm that "she did have combined Pneumovax and influenza vaccination sometime in late January, and had onset of significant, severe, deep lumbar aching pain (which she ha[d] never had before) within a few days after these immunizations."[7] (*Id.*) Petitioner underwent an EMG/NCV study which evidenced mild to moderate chronic axonal polyradiculoneuropathy, with no evidence of significant demyelination—consistent with the axonal variant of GBS. (*Id.* at 8- 9.) Dr. Balm expected petitioner would continue to have a gradual and slow improvement of her symptoms. (*Id.*)

[6] In fact, the record reads "pulmonary diagnosis of GBS," which appears to be a typographic error. Based on the record as a whole, and including to Dr. Balm's later confirmatory diagnosis, preliminary appears to best fit the meaning of the passage. (Ex. 6, p. 226.)

[7] Petitioner's vaccination record indicates that she received a Fluzone vaccine on September 30, 2014 and the Prevnar 13 vaccine on January 6, 2015. (Ex. 2.) There is no mention of an influenza vaccine in January. (*See id.*)

Later that day, petitioner saw Erik Stowell, M.D., for a follow-up appointment. (Ex. 8, pp. 5-6.) Petitioner described some residual nerve injury, as well as difficulty walking without assistive devices. (*Id.* at 5.) She rated her lower extremity strength at a 4 to 5/5, though she still experienced decreased sensation in her hands and feet. (*Id.*) Dr. Stowell recommended against petitioner returning to work and instructed her to "avoid immunization in the future due to the possible relationship between the flu vaccine and her developing AIDP."[8] (*Id.* at 6.)

On October 12, 2015 petitioner returned to Dr. Stowell to discuss her longer-term disability. (Ex. 8, p. 3.) Dr. Stowell reported petitioner's history of AIDP "came on after a flu vaccine with onset of symptoms sometime in January 2015." (*Id.*) As of this visit petitioner was no longer taking pain medications, though she continued to have weakness and fatigue and felt she could no longer return to her job as a cake decorator. (*Id.*) In his physical exam Dr. Stowell observed that petitioner continued to have lower extremity weakness, requiring the use of a cane, as well as mild incomplete ptosis of the right eye. (*Id.*) Dr. Stowell recommended against petitioner returning to work and recommended a follow-up appointment in six months. (*Id.* at 3-4.)

In April 2016 petitioner saw Dr. Stowell and Dr. Balm for follow-up appointments. (Ex. 8, p. 1; Ex. 9, p. 1.) On April 15, 2016, Dr. Stowell questioned whether petitioner suffered from CIDP. (Ex. 8, p. 1.) Petitioner then reported to Dr. Balm for "evaluation of CIDP from her rehab provider." (Ex. 9, p. 1.) Dr. Balm observed that petitioner "report[ed] no new symptoms, but continuation of chronic symptoms including numbness and tingling in her toes, fingertips, and perioral area." (*Id.*) His impression of petitioner was that "she is not recovered from [her initial syndrome] (can take a couple years to get back to complete normal if that happens), and she has been exercising, has been gaining weight, and has not been sleeping." (*Id.* at 4.) Dr. Balm explained that "[m]any patients report acral paresthesias[9] and perioral tingling," though he was unsure whether these symptoms would improve. (*Id.*)

On November 8, 2017, petitioner went to Centennial Medical Group to establish care with Shelli Flynn, M.D. (Ex. 33, p. 12.) She complained of pain in the bottom of her feet and feeling "pins and needles." (*Id.* at 14.) Dr. Flynn observed drooping of the right side of petitioner's mouth, and mild drooping of her right eyelid. (*Id.* at 15.) After several years, Dr. Flynn explained, "it is unlikely she will get much more improvement at this point." (*Id.* at 16.)

By May 7, 2018 petitioner returned to Centennial Medical Group for a follow-up on her weight and to request a prescription for sleeping pills. (Ex. 33, p. 6.) She reported that she continued to have "lots of pain in her legs and feet." (*Id.* at 8.)

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[8] Petitioner only received the Prevnar 13-vaccine in January 2015. (Ex. 2; *see supra* n. 5.)

[9] *See Acroparethesia,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=724&searchterm=acroparesthesia (last visited Jan. 10, 2022) ("paresthesia of limbs and tips of other extremities due to nerve compression at any of several levels, or polyneuritis[.]")

Petitioner was continuing to use diclofenac gel, and Dr. Flynn recommended to continue applying it daily. (*Id.* at 9.)

On July 16, 2020 petitioner presented to Evergreen Family Medicine for an annual wellness visit. (Ex. 49, pp. 9-13.) Petitioner indicated that she fell due to her neuropathy, though she did not report any injuries. (*Id.* at 12.) Petitioner's general appearance was active, alert, and no acute distress. (*Id.*) A fall risk assessment was completed with increased fall risk noted. (*Id.*)

b. Petitioner's declaration & supplemental declaration

Petitioner filed two declarations and also testified during the two-day entitlement hearing. (Exs. 1, 54; Tr. 16-98.) In her first declaration, petitioner provided a detailed account of her hospitalization and treatment. (Ex. 1, pp. 2-4.) During the hearing, however, petitioner testified that she has difficulty recalling portions of her hospitalization due to an acute onset of delirium. (Tr. at 44, 52, 83-84; *see also* Ex. 4, p. 82 (petitioner transferred to intensive care unit for delirium with hallucinations).)

In her first declaration, petitioner declares that she suffered from the following preexisting conditions: migraine headaches, arthritis, and high cholesterol. (Ex. 1, p. 1.) She states that she received a flu vaccine on September 30, 2014, "a few months before she received the pneumonia shot." (*Id.*) Petitioner further states that she does not recall having a primary care physician prior to her Prevnar 13 shot. (*Id.*) She was "generally in good health," and declares that before January 6, 2015 she did not have any tingling or numbness in her extremities, and she did not have any difficulty walking. (*Id.*)

On January 6, 2015, petitioner states that she received her Prevnar 13 vaccine at the pharmacy located inside of the Albertsons where she worked. (Ex. 1, p. 2.) Petitioner declares that on January 21, 2015 she went to the urgent care for a cough and congestion. (Ex. 1, p. 2.) She further states that she informed the doctor that she received "a pneumonia shot" a few weeks earlier. (*Id.*) Petitioner declares that she was diagnosed with bronchopneumonia, prescribed medication, and given an inhaler. (*Id.* (citing Ex. 3, pp. 1-10.)) During her testimony at the hearing, petitioner denied having pneumonia, congestion, or trouble breathing. (Tr. at 23, 76.) Petitioner testified that she recalled being prescribed an inhaler, though she didn't use it. (Tr. at 23-24; 93.) She further testified that she did not recall undergoing a chest x-ray on January 21, 2015. (Tr. at 24.) Petitioner testified that her husband attends all of her doctors' visits with her and typically fills out the paperwork. (Tr. at 67-68.)

Petitioner declares that she returned to Roseburg Urgent Care on February 3, 2015, still experiencing shortness of breath, cough, wheezing, and tingling. (Ex. 1, p. 2.) She was prescribed a prednisone taper and referred to a pulmonologist. (*Id.* (citing Ex. 3, pp. 11-18.)) Petitioner states that "around this time" she started developing "really horrible back pain." (*Id.*) She states that she "had never felt this kind of pain before," but put off going to the doctor because she thought her symptoms would

improve. (*Id.*) Petitioner declares that the tingling in her hands and legs increased to the point where she could no longer work. (*Id.*) Petitioner explains that she returned to urgent care on February 26, 2015 and was prescribed a second prednisone taper for her tingling and weakness. (*Id.*) During this visit, petitioner's records indicate, in part, that "[u]nrelated to her present complaints, [petitioner] [had] symptoms of carpal tunnel syndrome." (Tr. at 33; Ex. 3, p. 19.) Petitioner testified that she was never diagnosed with carpal tunnel syndrome. (Tr. at 33-34, 37.) When asked why her medical records indicated a history of carpal tunnel syndrome, petitioner testified "I don't know if it was put down that way or not, but I have no problem with my wrists." (Tr. at 71.)

Petitioner states that her back pain, weakness and tingling continued to intensify; and "[her] back pain spread to include [her] legs and hands." (Ex. 1, p. 2.) Over the course of the next week, petitioner states that she was seen "almost daily at the urgent care because of [her] pain despite being on pain medication and getting injections for the pain." (*Id.*) She states that she was sent to the ER twice for different tests but never diagnosed. (*Id.*) Petitioner's medical records indicate that she underwent a second chest x-ray on March 2, 2015. (Tr. at 38; Ex. 3, p. 35.) When asked about the x-ray petitioner testified during the hearing that she could not remember much from this period of time. (Tr. at 38; 41.) Petitioner declares that she established care with a family doctor, Dr. McNulty, for an evaluation and labs. (Ex. 1, p. 2.)

Petitioner declares that she went to the Mercy Medical Center emergency room on March 5, 2015 for possible hospital admission. (Ex. 1, p. 2 (citing Ex. 3, pp. 25-69; Ex. 4, pp. 38-39, 58-59; and Ex. 5, pp. 5-17.)) Petitioner states she was hospitalized between March 5, 2015 and March 13, 2015.[10] (*Id.*) During the hearing, petitioner testified that "[s]ome of this I can't remember…my mind was not working real good at that point." (Tr. at 44; *see also* Ex. 4, p. 82 (petitioner transferred to intensive care unit for delirium with hallucinations).) Petitioner testified that she could not recall suffering from rectal bleeding during her hospitalization, though she remembered undergoing a colonoscopy. (Tr. at 82-83.) Subsequently, she was transferred to Sacred Heart Hospital. (Ex. 1, pp. 2-3.) Petitioner testified that multiple doctors and nurses discussed the possibility that a vaccine caused her GBS. (Tr. 50-51.) Though she could not recall which doctor or nurse, she testified that her treating physicians inquired about her vaccinations while she was at Eugene at Riverbend (Sacred Heart Hospital). (*Id.*) Petitioner declares that she saw neurologist Dr. Estevez who observed her muscle weakness and ordered labs as well as a lumbar puncture. (Ex. 1, p. 3 (citing Ex 6, pp. 227-230).) On March 15, 2015, she began a five-day course of IVIG infusions. (Ex. 1, p.3; Tr. at 43.) Petitioner was ultimately diagnosed with GBS. (Tr. at 43; Ex. 1, p. 3.) Petitioner declares that she was discharged from Sacred Heart Hospital on March 24, 2015 and transferred to Oregon Rehabilitation Center. (*Id.*) Petitioner remained in rehabilitation for approximately six weeks. (Tr. at 44.)

[10] Petitioner further testified that she was paralyzed while at Mercy Medical Center before being transferred. (Tr. at 46.) Petitioner described an incident where she "tried to stand up, and [she] just completely went down." (Tr. at 46.)

Petitioner declares that she received inpatient care at Oregon Rehabilitation Center between March 24, 2015 and April 29, 2015, including daily physical therapy, speech therapy, and occupational therapy. (Ex. 1, p. 3.) At the time she was discharged, petitioner declares that she was able to walk 160 feet with a wheeled walker, and "able to make transfer alone." (*Id.*; Tr. at 44-45.) When she returned home, petitioner states that her husband built a ramp leading to their house for her wheelchair. (Ex. 1, p. 3.) For approximately one month, petitioner states that she slept on the first floor of her house and struggled climbing the stairs. (*Id.*) She also traveled to her mother's assisted living facility to use the handicap shower. (*Id.*; Tr. at 45.)

Petitioner declares that she established care with a family medicine doctor, Dr. Herbert, on May 1, 2015. (Ex. 1, p. 3.) At the time petitioner states that she used a wheeled walker to walk. (*Id.*) According to petitioner, Dr. Herbert told her to continue her pain management medications for her ongoing pain. (*Id.* (citing Ex. 7, pp. 10-14).) Then, between May 7, 2015 and June 12, 2015, petitioner states that she completed outpatient physical therapy sessions, and was discharged with a home exercise program. (*Id.*) Petitioner declares that she was unable to use a treadmill due to weakness and poor balance, though she was able to use a stationary bike for exercise. (*Id.*; Tr. at 45.) At a follow-up appointment with her pain management doctor on May 26, 2015, Dr. Stowell encouraged petitioner to continue physical therapy. (*Id.* at 4 (citing Ex. 9, pp. 7-9).)

On July 7, 2015, petitioner had an outpatient neurology appointment with Dr. Balm. (Ex. 1, p. 4.) Petitioner declares that she still had "numbness and weakness in [her] legs and feet and fatigued easily." (*Id.*) Petitioner describes "difficulty walking and going up and down stairs." (*Id.*) Petitioner states that she underwent a nerve conduction study; and that Dr. Balm informed her that the results were consistent with GBS. (*Id.* (citing Ex. 9, pp. 6-14.) That same day, petitioner had a follow-up appointment with Dr. Stowell, "who [told] her to continue my home exercise program and to avoid future vaccinations." (*Id.* (citing Ex. 8, pp. 3-4.))

By October 2015, petitioner states that she required a cane to walk, she could not walk far without tiring, and she "needed constant breaks" while grocery shopping. (Ex. 1, p. 4.) According to petitioner, Dr. Stowell confirmed that she was unable to return to work as a cake decorator. (*Id.* (citing Ex. 8, pp. 1-2; Ex. 9, pp. 1-5).

In April 2016 petitioner states that she returned to see Dr. Stowell and Dr. Balm. (Ex. 1, p. 4.) She declares that she continued to easily fatigue "but made improvements in [her] strength and no longer needed a cane to walk." (*Id.*) Petitioner states that Dr. Stowell "thought there was a possibility [she] could have CIDP but Dr. Balm's assistant confirmed [she] did not have CIDP." (*Id.* (citing Ex. 8, pp. 1-2; Ex. 9, pp. 1-5.)) Petitioner declares that she still suffered from numbness and tingling in her hands and feet. (*Id.*)

On February 24, 2017 petitioner established care with another family medicine doctor, Dr. Grady. (Ex. 1, p. 4.) She declares that she suffered from numbness in her

hands, feet, and tongue, and that it "felt like [she] had a film on my feet when [she] tried to walk." (*Id.*) According to petitioner, "Dr. Grad reaffirmed that all of these symptoms were caused by my GBS." (*Id.* (citing Ex. 10, pp. 6-11.)) In June 2017 Dr. Grady prescribed Voltaren gel for petitioner to apply to her feet and legs. (*Id.*)

Petitioner states that she still suffers the residual effects of GBS. (Ex. 1, p. 4; Tr. at 46.) Petitioner testified that she still has "slight tingling in [her] fingers and in [her] feet." (Tr. at 46.) She further testified that she takes a sleeping pill at night "because the tingling in my feet, [] wake me up, because I'll still get a little jolt every once in a while." (*Id.*) She also described residual "numbness in my tongue[.]" (*Id.*) Lastly, petitioner testified that she requires assistive devices for walking to the Coast or for distance. (*Id.*)

In her supplemental declaration, petitioner states that she began noticing some pain and tingling in her hands and feet in mid to late January 2015. (Ex. 54, p. 1.) She furthers states that within a week or two of noticing the tingling, petitioner noticed numbness in her hands and feet. (*Id.*) Petitioner describes the tingling sensations like "jolts of lightning." (*Id.*) These symptoms gradually worsened over the course of a month, when petitioner declares that she had to stop working. (*Id.*) Petitioner states that she complained regularly to her coworkers about the tingling and pain in her fingers. (*Id.*) The pain in her fingers "was different from previous stiffness in [her] hands that [she] would get from cake decorating." (*Id.* at 2.)

Petitioner further states that she went to urgent care several times to be evaluated, and told the doctor about the tingling and pain, "but the doctor was more focused on the cough that [she] had at the end of December." (Ex. 54, p. 2.) According to petitioner, if the doctor had not asked about a cough or illness, she would not have brought it up because she "did not feel like the cough was a big deal." (*Id.*)

Lastly, petitioner declares that the final stub she received from Albertsons covered the week of February 22, 2015 to February 28, 2015. (Ex. 54, p. 2.) She states that she had to stop working at this time because she "had a very intense and deep pain in [her] back in addition to the pain in [her] hands and feet." (*Id.*) Petitioner testified that based upon her final pay stub, she estimates that she quit working on February 25, 2015. (Tr. at 30-31.)

c. Declaration of David Pierson

Mr. Pierson, petitioner's husband, states that he and petitioner received "pneumonia shots" on January 6, 2015. (Ex. 55, p. 1.) He describes petitioner's cough as lasting as long as a "mild cold would last." (*Id.*) He states that petitioner's cough was gone before the start of the New Year. (*Id.*)

Mr. Pierson declares that when he would wake up during the night, he started noticing petitioner "sitting on the edge of the bed and rocking back and forth like she

was on a rocking chair."[11] (Ex. 55, p. 1.) He describes petitioner sitting "with her hands about a foot away from her face in a prayer-like position" and "[i]t looked like she was examining her hands." (*Id.* at 2.) When her husband asked what was wrong, petitioner "would tell [him] that her feet were aching but that she would be fine." (*Id.*) He states that "[t]his started happening more frequently when I would get up to go to the bathroom." (*Id.*) Subsequently, petitioner's husband states that petitioner started openly complaining about tingling in her hands and feet; and he observed her "downstairs sitting and rocking." (*Id.*)

Mr. Pierson further states that "around this time" petitioner developed pain along with the tingling in her hands and feet. (Ex. 55, p. 2.) As he describes it, "[a]ll these symptoms sort of developed together." (*Id.*) He declares that petitioner's tingling and pain had been "occurring for around a month by the time that it got so bad that she had to quit" her job. (*Id.*) According to her husband, petitioner's symptoms never went away, though now she is "steady on her feet but needs to concentrate closely when she walks" and "also needs to use handrails when she goes up and down the stairs." (*Id.*)

Mr. Pierson also testified at the hearing. (Tr. at 98-124.) His testimony was primarily the same as the statements contained in his declarations. (*See* Ex. 55.) As petitioner indicated in her testimony, her husband attends her doctors' visits with her and fills out the paperwork. (Tr. at 64, 67.) In his testimony, Mr. Pierson indicated that some of the handwriting on the written forms was likely his handwriting, though all of the signatures were that of petitioner. (Tr. at 119.) He testified that he visited petitioner every day while she was at Mercy Medical Center, arriving around 10:00 A.M. and leaving at approximately 7:00 P.M. (Tr. at 106.) He denied that petitioner had any difficulty walking at the time she was admitted to Mercy Medical Center. (Tr. at 105.) While at Mercy Hospital, he described an incident where petitioner fell trying to get out of bed unassisted.[12] (Tr. at 107-108.) By the time petitioner was transferred Sacred Heart Medical Center petitioner's husband testified that petitioner had no feeling below her waist. (Tr. at 107.) Regarding petitioner's carpal tunnel diagnosis, Mr. Pierson testified that she never indicated that she had carpal tunnel, and in fact "[s]he used her hands all the time, and she never ever complained about anything wrong with her hands." (Tr. at 111.)

d. Declaration of Laura Day

In her declaration, Laura Day describes working side-by-side with petitioner decorating cakes in the bakery. (Ex. 56, p. 1.) She states that petitioner was a "hard worker who never complained." (*Id.*) She further states that that petitioner started complaining of pain and tingling in her hands and feet, though "since she was not a big

[11] Mr. Pierson does not provide a date or timeline for the onset of these symptoms. (*See* Ex. 55, p. 1-2.) During the hearing, Mr. Pierson testified that petitioner began rocking on the bed "[p]robably in January." (Tr. at 120.)

[12] Mr. Pierson did not provide the date of this fall. (*See* Tr. at 107-108.)

complainer she would keep working through her shift." (*Id.*) After several weeks of petitioner's complaints of pain, Ms. Day suggested she go home to rest. (*Id.*)

Ms. Day states that petitioner began having trouble writing on the cakes because of the pain and tingling in her hands, such that "[she] would write on the cakes to help her out." (Ex. 56, p. 2.) According to Ms. Day, the day petitioner stopped working,[13] she and petitioner started their shift around 7:00 or 8:00 A.M. but "[b]y midday, [petitioner] walked up and told [her] she could not do this anymore." (*Id.*) She states that petitioner left in the middle of the shift. (*Id.*) At this time, petitioner had been complaining to Ms. Day for about a month. (*Id.*) She states that "[h]er complaints were infrequent in the beginning but started to increase over the month." (*Id.*) Ms. Day declares that by the time petitioner stopped working, "she had tremendous pain and weakness in her hands and feet." (*Id.*)

Ms. Day's testimony during the hearing substantially reflected the statements in her declaration. (*See* Ex. 56.) Ms. Day testified that she did not know that petitioner had experienced carpal tunnel syndrome (as reflected in petitioner's medical records). (Tr. at 14.) Furthermore, Ms. Day testified that she did not notice petitioner coughing while at work. (*Id.*)

III. Expert Opinions

a. Petitioner's expert Lawrence Steinman, M.D., initial report, Exhibit 12

Dr. Steinman received his medical degree from Harvard in 1973. (Ex. 13.) He is currently a professor of the department of neurology at Stanford University. (Ex. 12, p. 1.) Dr. Steinman has treated patients, both adults and children, who suffered from various forms of autoimmune disease of the nervous system, including optic neuritis, acute disseminated encephalomyelitis (ADEM), inflammatory neuropathy, transverse myelitis, neuromyelitis optica (NMO), and multiple sclerosis (MS). (*Id.*) Dr. Steinman's research focuses on how the immune system attacks the nervous system and he has published on the subject of molecular mimicry. (*Id.* at 1-4; Ex. 13.) He holds over 50 American and European patents, including several U.S. patents relating to vaccines. (*Id.* at 4.)

Dr. Steinman opines that petitioner's Prevnar 13 vaccine triggered her GBS. (Ex. 12, p. 1.) Upon his review of petitioner's medical records, Dr. Steinman notes that petitioner's onset of neuroinflammation began January 21, 2015, with tingling, reported along with sneezing, congestion, cough, shortness of breath, and wheezing. (*Id.* at p. 4 (citing Ex. 3, p. 1.) On February 26, 2015 petitioner reported chills, fatigue, sweats, tingling, weakness, cough, shortness of breath, and wheezing. (*Id.* at p. 4 (citing Ex. 3, p. 19.) According to Dr. Steinman, tingling and weakness "are more likely than not indications of GBS." (Ex. 12, p. 4.) Later, in March 2015, Dr. Steinman observes that

[13] Ms. Day does not provide the exact date other than to say, "the day that [petitioner] stopped working." (*See* Ex. 56, p. 1-2.)

petitioner was diagnosed with subacute onset flaccid paraparesis, acute peripheral neuropathy, and Bell's palsy – all indicative of GBS. (Ex. 12, p. 5) Dr. Steinman opines that the onset of petitioner's inflammatory neuropathy began fifteen days after she received the Prevnar 13 immunization on January 6, 2015 – though he notes that petitioner's diagnosis of GBS occurred nine weeks later.[14] (*Id.*) Dr. Steinman bases his theory of how the Prevnar 13 vaccine can cause GBS through the concept of molecular mimicry. (*Id*. at 8-9.) He explains that molecular mimicry describes how shared structures on a virus or bacteria, or in a vaccine, can trigger a cross-reactive response to self. (*Id.* at 9.)

First Dr. Steinman notes that the Prevnar 13 vaccine contains a sterile suspension of saccharides of the capsular antigens of *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F, individually linked to non-toxic diphtheria CRM197 protein.[15] (*Id.* at 9 (citing *Prevnar-13 Prescribing Information* 1-43 (last revised July 2016) (Ex. 23).) Dr. Steinman suggests that antibodies to phospholipids are present in GBS patients. (*Id.* at 10 (citing B. Gilburd et al., *Autoantibodies to Phospholipids and Brain Extract in patients with the Guillain-Barre Syndrome: Cross-Reactive or Pathogenic?,* 16 AUTOIMMUNITY 23 (1993) (Ex. 24)).) Dr. Steinman's own research indicates that phospholipids are components of the myelin sheath in humans, and that they are targeted by antibodies in neuroinflammation in the central nervous system as well. (*Id.* (citing Jennifer Kanter et al., *Lipid microarrays identify key mediators of autoimmune brain inflammation,* 12 NATURE MEDICINE 138 (2006) (Ex. 25)).) In Ho et al., Dr. Steinman and his fellow researchers found that autoantibodies in MS target a phosphate group in phosphatidyl serine and oxidized phosphatidyl choline derivatives. (*Id.* (citing Peggy P. Ho et al., *Identification of Naturally Occurring Fatty Acids of the Myelin Sheath That Resolve Neuroinflammation,* 4 Sci. Translational Med. 137ra73 (2012) (Ex. 26)).) Notably, two of the six GBS patients tested in the Gilburd et al. study showed reactivity to phosphatidyl serine or phosphatidyl choline. (*Id.* (citing Gilburd et al, *supra,* at Ex. 24, p. 27.)) Based on these studies Dr. Steinman concludes that "in inflammation of the central nervous system, in humans with multiple sclerosis and in pre-clinical models of experimental autoimmune

[14] Dr. Steinman explains that chronic inflammatory Demyelinating Polyneuropathy (CIDP) is "closely related to GBS and it is considered the chronic counterpart of that acute disease." (Ex. 12, p. 8 (citing *Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) Information Page,* NINDS, http://www.ninds.nih.gov/disorders/cidp/cidp.htm (last updated Mar. 27, 2019, 16:20) (Ex. 21)).) He opines, however, that petitioner suffered from GBS and not CIDP. (Ex. 12, p. 8.) Dr. Steinman states that once petitioner was initially diagnosed and treated for her GBS with IVIg "she made a strong recovery." (*Id.*) Despite petitioner's ongoing, chronic symptoms of tingling and numbness in her toes, fingertips and perioral area, he explains that petitioner "never regressed to the point where she was at when she was first diagnosed with GBS." (*Id.*) Rather, her symptoms plateaued. (*Id.*) Dr. Steinman further adds that petitioner has only ever been diagnosed with GBS, and not CIDP. (*Id.*) Dr. Steinman notes, however, if petitioner did have CIDP "the same medical theory would apply to show that the Prevnar 13 immunization could similarly trigger CIDP." (*Id.*)

[15] "CRM197 is a nontoxic variant of diphtheria toxin isolated from cultures of *Corynebacterium diphtheriae* strain Cy (β197) grown in a casamino acids and yeast extract-based medium. CRM197 is purified through ultrafiltration, ammonium sulfate precipitation, and ion-exchange chromatography." (Ex. 12, p. 9 (citing *Prevnar-13 Prescribing Information, supra,* at Ex. 23).)

encephalomyelitis, as well as in inflammation of the peripheral nervous system there is evidence of an antibody response to phosphatidyl-choline structures." (*Id.* at 10-11 (citing Gilburd et al, *supra,* at Ex. 24; Kanter et al, *supra,* at Ex. 25; Ho et al., *supra,* at Ex. 26).)

In his initial report, Dr. Steinman concludes that these phospholipids are present in the Prevnar 13 vaccine. (Ex. 12, p. 11.) Looking at the Prevnar 13 package insert, Dr. Steinman observes that the phospholipid phosphorylcholine is expressed in the 19A component of Prevnar 13.[16] (*Id.* (citing *Prevnar-13 Prescribing Information, supra,* at Ex. 23; Yi-Ping Chuang et al., *Impact of the glpQ2 Gene on Virulence in a Streptococcus pneumoniae Serotype 19A Sequence Type 320 Strain,* 83 INFECTION AND IMMUNITY 682 (2015) (Ex. 27)).) Beginning with his first supplemental report, however, Dr. Steinman clarified that his theory pertains specifically to the phosphoglycerol component of the vaccine and acknowledges that the vaccine does not include phospholipids. (Ex. 35.)

In a perfect world, Dr. Steinman suggests that his theory would reach a higher level of certainty if petitioner's physicians had measured anti-phospholipid antibodies at the time of her injury—before immune therapy with IVIg was administered. (Ex. 12, p. 18.) Yet, Dr. Steinman opines that components of the Prevnar 13 vaccine administered to petitioner are immunologically cross-reactive with both myelin and axonal components. (*Id.*) Ultimately, the antibodies created to combat the vaccine's components mistakenly interact with myelin and axonal mimics – triggering GBS. (*Id.*) Even though petitioner's diagnosis of inflammatory neuropathy was construed as "chronic axonal polyradiculoneuropathy," Dr. Steinman maintains that petitioner's theory about "the potential immune targeting of phosphatidyl choline is robust." (*Id.* (citing Ex. 9, pp. 8-9.)) He explains that axons, like myelin, have the major membrane phospholipid phosphatidyl choline. (*Id.* (citing David J. Read et al., *Neuropathy Target Esterase Is Required for Adult Vertebrate Axon Maintenance,* 29 J. OF NEUROSCIENCE 11594 (2009) (Ex. 30.)).)

Finally, Dr. Steinman opines that the timing in petitioner's case is consistent with what has been reported for the onset of GBS. (Ex. 12, pp. 18-20.) He first notes that petitioner's inflammatory neuropathy began 15 days after receipt of the Prevnar 13

[16] Dr. Steinman opines that immunity to this phospholipid is involved in neuroinflammation in both the central and peripheral nervous systems. (Ex. 12, p. 11.) The enzyme for metabolizing lipids and producing phosphorylcholine is present in strains 3, 6B, 19A, and 19F. (*Id.* (citing Jonathan D. Kornspan and Shlomo Rottem, *The Phospholipid Profile of Mycoplasmas,* 2012 J. OF LIPIDS 1 (2012) (Ex. 28)).) Strains 3, 19A, and 19F are present in Prevnar 13. (Ex. 12, p. 11 (citing *Prevnar-13 Prescribing Information, supra,* at Ex. 23.)) Dr. Steinman also notes that he sought further clarification on the chemistry of the Prevnar vaccine from the CDC, who could not provide proprietary manufacturing information from the manufacturer. (*Id.* at 14-17.) Dr. Steinman also notes the well-known molecular mimicry between Campylobacter and components of the peripheral nerve axon, triggering the axonal variant of GBS. (Ex. 12, p. 17-18 (citing *Guillain-Barre Syndrome Fact Sheet,* NINDS, http://www.ninds.nih.gov/disorders/gbs/details_gbs.htm (last updated Mar. 16, 2020, 13:03) (Ex. 20)).) Dr. Steinman acknowledges that in petitioner's case the trigger is the phospholipids in Prevnar 13, "but the concept is congruent with the Campylobacter molecular mimic[.]" (*Id.* at 18.)

vaccine. (Ex. 12, p. 18.) Though petitioner's actual diagnosis and approved treatment for GBS was not made until approximately 9 weeks after the Prevnar 13 vaccination. (*Id.*) First, Dr. Steinman notes an increased incidence of peripheral neuroinflammation in GBS in this time frame in cases post-H1N1-vaccination in 1976. (*Id.* (citing Lawrence B. Schonberger et al., *Guillain Barre Syndrome following vaccination in the National Influenza Immunization Program, United States, 1976-1977,* 110 AM. J. OF EPIDEMIOLOGY 105 (1979) (Ex. 31)).) While Schonberger et al. does not cover Prevnar 13, Dr. Steinman suggests that it serves as a "surrogate in this case." (*Id.* at 20.) Second, Dr. Steinman cites the study from Haber et al., which showed that for a person of petitioner's age, GBS was the third most frequently reported adverse reaction following the Prevnar 13 immunization.[17] (*Id.* (citing Penina Haber et al., *Post-licensure surveillance of 13-valent pneumococcal conjugate vaccine (PCV13) in adults aged ≥ 19 years old in the United States, Vaccine Adverse Event Reporting System (VAERS), June 1, 2012-December 31, 2015,* 34 VACCINE 6330 (2015) (Ex. 32)).) Taken together, Dr. Steinman opines that the timing in petitioner's case is consistent with the onset of GBS.

b. Respondent's expert Thomas P. Leist, M.D., Ph.D., initial report, Exhibit A

Dr. Leist received his undergraduate degree from the University of Zurich in Switzerland in 1982. (Ex. B.) He received his Ph.D. in biochemistry from the University of Zurich in 1985. (*Id.*) Dr. Leist received his medical degree from the University of Miami in 1993. (*Id.*) He completed his residency in Neurology at the Cornell medical Center / Sloan Kettering Memorial Cancer Center in New York. (*Id.*) From 1997 to 2000 Dr. Leist was a clinical senior staff associate at NINDS at the NIH in Bethesda, Maryland. (*Id.*) He is board certified in Psychiatry and Neurology, Adult Neurology. (*Id.*) Dr. Leist is currently a professor of Neurology at Thomas Jefferson University and the Chief / Division of Clinical Neuroimmunology Director of the Comprehensive Multiple Sclerosis Center. (Ex. B.) He has participated as a researcher in multiple clinical trials and authored or co-authored over fifty medical articles peer-reviewed journals. (*Id.* at 6-11.)

Dr. Leist opines that no association has been established between the pneumococcal conjugate vaccines (Prevnar-13 and Pneumovax 23) and GBS; and the onset of petitioner's acute neurological symptoms occurred outside the typical onset of 42 days, considered plausible based on Langmuir et al.'s reanalysis of GBS cases following the 1976-1977 H1N1 flu vaccine. (Ex. A, p. 4 (citing Alexander D. Langmuir et al., *An Epidemiological and Clinical Evaluation of Guillain-Barre Syndrome Reported in Association with the Administration of Swine Influenza Vaccines,* 119 AM. J. OF EPIDEMIOLOGY 841(1984) (Ex. A, Tab. 2.)).)

[17] Table 2b in the Haber et al. study indicates that GBS was the third most frequently reported adverse reaction following the Prevnar 13 vaccination among person aged 65 years and older between 2013 and 2015. (Haber et al., *supra,* at Ex. 32, p. 4.) More specifically, Table 2b reports 10 individuals out of 138 total who reported an onset of GBS post-vaccination. (*Id.*)

Turning first to the association between the pneumococcal conjugate vaccines and GBS, Dr. Leist relies on two studies: Baxter et al. and Tseng et al. (Ex. A, pp. 4-5.) He stresses that both of these studies failed to find an association between Prevnar-13 and GBS. (*Id.* (citing Roger Baxter et al., *Lack of Association of Guillain-Barre Syndrome with Vaccinations,* 57 CLINICAL INFECTIOUS DISEASES 197 (2013) (Ex. A, Tab. 1); Hung Fu Tseng et al., *Pneumococcal Conjugate Vaccine Safety in Elderly Adults,* 2 OPEN FORUM INFECTIOUS DISEASES 100 (2018) (Ex. A, Tab. 3)).) Dr. Leist criticizes Dr. Steinman's theory, which he asserts does not offer evidence specifically linking the Prevnar 13 vaccine and GBS. (*Id.*) Dr. Steinman references an article by Haber et al., which Dr. Leist stresses found that there was no disproportionate reporting of GBS following Prevnar 13-vaccination. (*Id.*) In fact, Dr. Leist suggests that the authors of Haber et al. did not opine on the causality of the cases of GBS that were reported to VAERS based on temporal association. (*Id.*) Without more, Dr. Leist opines that there is no demonstrated causal link between the 13-valent conjugate pneumococcal vaccine and GBS. (*Id.*)

Regarding the onset of petitioner's symptoms, Dr. Leist opines that petitioner developed acute facial and lower extremity weakness on or about March 11 or 12, 2015 – or approximately sixty days after the administration of petitioner's Prevnar 13 vaccine. (Ex. A, p. 5.) Dr. Leist notes that petitioner was admitted for observation for her altered mental state due to narcotic pain medication (for severe low back pain) on March 5, 2012, but no neurological deficits were appreciated at the time. (*Id.* (citing Ex. 4, p. 87.)) She was scheduled to be discharged March 7, 2015 when she had two bowel movements with dark blood and clots, which prompted further evaluation. (*Id.* (citing Ex. 4, pp. 72-75.)) Dr. Leist next observes that petitioner had a brain CT on March 12, 2015, after developing right facial weakness. (*Id.* (citing Ex. 4.2, p. 83; Ex. 4.3, pp. 144-45.)) Reports from March 14, 2015 indicate that petitioner suffered "sudden onset [of] r[ight] side lower facial weakness approx[imately] 3 days ago after the colonoscopy [performed on March 8, 2015,] then developed upper r[ight] side facial/eye weakness subsequently." (*Id.* (citing Ex. 6.1, p. 192.)) Dr. Leist concludes, based on these records, that petitioner developed symptoms of GBS approximately sixty days post-vaccination. (*Id.*)

Dr. Steinman opined that the onset of petitioner's GBS began fifteen days post-vaccination, approximately January 21, 2015. (Ex. 12, p. 4.) Dr. Leist, however, stresses that petitioner's records from January 21, 2015 and February 2, 2015 note only the presence of "tingling." (Ex. A, p. 5-6.) Specifically, Dr. Leist emphasizes that petitioner's medical records do not elaborate on the term tingling, the records do not mention when the tingling started, whether it was continuous or intermittent, or whether there were aggravating factors (e.g., petitioner's work in decorating cakes). (Ex. A, p. 6.) Dr. Leist suggests that petitioner's history of carpal tunnel syndrome (Ex. 3, p. 19) or her reported hyperventilation, associated with shortness of breath, may have caused the tingling. (Ex. A, p. 6.) Moreover, Dr. Leist points to a two-to-three-week period where petitioner reportedly felt much better, which prompted her to cancel her appointment with a pulmonologist. (*Id.* (citing Ex. 3, pp. 13, 19.)) Dr. Leist

characterizes petitioner's records as "separate time periods of different symptoms rather than the crescendo of a single, extended episode of worsening sensory and motor complaints as would be expected were the dose of pneumococcal conjugate vaccine given on January 6, 2015 the inciting agent for the process." (Ex. A, p. 6.)

According to Dr. Leist, another alternative cause for petitioner's development of acute neurologic symptoms is the suspected infection she suffered on February 26, 2015. (Ex. A, p. 6.) Petitioner complained of chills, sweats, fatigue and left thoracic pain on February 26, 2015, which progressed to 8/10 mid back pain made worse with movement and breathing by February 28, 2015, resulting in 10/10 back pain with worsening numbness in the hands on March 1, 2015. (*Id.* (citing Ex 4, pp. 56, 61; Ex. 6, p. 38.)) According to Dr. Leist, "[c]hills and sweats suggest [the] presence of an infectious process and [petitioner] was started on cefdinir on February."[18] (Ex. A, p. 6.)

Dr. Leist also proposes that the accepted time interval for GBS following flu vaccination is informative. (Ex. A, p. 6.) According to Dr. Leist, that time interval is no less than three days and no longer than forty-two days. (*Id.* (citing references Langmuir et al., *supra,* at Ex. A, Tab. 2).) Dr. Leist opines that petitioner developed acute facial and lower extremity weakness on or about March 11 or 12, 2015 – or approximately sixty days after the administration of petitioner's Prevnar 13 vaccine. (Ex. A, p. 5.) He concludes that petitioner's onset falls outside the forty-two day time interval. (Ex. A, p. 6-7.)

c. Dr. Steinman's first supplemental report, Exhibit 35

In his first supplemental report, Dr. Steinman stresses that Baxter et al., a study relied upon by Dr. Leist, only studied Pneumovax 23 not Prevnar 13. (Ex. 35, p. 3 (citing Baxter et al., *supra,* at Ex. A, Tab. 1.) He adds that Tseng et al., the second study relied upon by Dr. Leist, reported a confidence interval[19] unadjusted at 1.22. (Ex. 35, p. 3 (citing Tseng et al., *supra,* at Ex. A, Tab. 3, p. 6.)).) Dr. Steinman explains that a confidence interval above 1 "is not an indication that [the Prevnar 13] vaccine in the elderly is 'totally safe.'" (Ex. 35, p. 3.) Based on the epidemiological studies available, Dr. Steinman states that while he may tell a patient that it is "highly unlikely" that the Prevnar 13 vaccine would cause a complication like GBS, he cannot tell that patient that it could not cause GBS. (*Id.*) Dr. Steinman also supplements his theory of molecular mimicry. (Ex. 35, pp. 4-11.) Dr. Steinman now proposes that there are two molecular

[18] Cefdinir is a "semisynthetic, third-generation cephalosporin effective against a wide range of bacteria, used in the treatment of otitis media, bronchitis, pharyngitis, tonsilitis, sinusitis, bacterial pneumonia, and skin and soft tissue infections; administered orally." *Cefdinir,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=13359 (last visited Oct. 21, 2021.) From my review of the record, it appears that petitioner was prescribed cefdinir on March 3, 2015. (Ex. 5, p. 2, 6.)

[19] A confidence interval is "a type of statistical interval estimated for an unknown parameter: a range of values believed to contain the parameter, with a predetermined degree of confidence. Its endpoints are the confidence limits, and it has a stated probability (the confidence coefficient) of containing the parameter." *Confidence interval,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=13359 (last visited Oct. 21, 2021.)

mimics that are relevant to GBS in the composition of Prevnar 13: one from the phosphoglycerol in the composition of the pneumococcal polysaccharide antigen, and a second from the CRM protein conjugate. (*Id.* at 4.)

Dr. Steinman identifies the phosphoglycerol component of the vaccine and explains that the phosphoglycerol is essential for the Prevnar 13 vaccine to be effective. (Ex. 35, pp. 4-11.) He notes that the polysaccharides in pneumococcus that are contained in the Prevnar vaccine are complex and allow for the chemical attachment of capsular polysaccharides via the glycerol moieties known as phosphoglycerol and phosphocholine (or phosphatidylcholine). (Ex. 35, p. 6.) In support, Dr. Steinman highlights diagrams and sections of the patent for Prevnar 13, showing the phosphoglycerol molecules. (*Id.* (citing United States Patent 9,492, 559 B2 (Ex. 36)).) The patent application provides, "[a]n important consideration during conjugation is the development of conditions that permit the retention of potentially sensitive non-saccharide substituent functional groups of the individual components, such as 0-Acetyl, phosphate or glycerol phosphate side chains that may form part of the saccharide epitope." (*Id.* (citing United States Patent 9,492, 559 B2, *supra,* Ex. 36, p. 34)).) Dr. Steinman stresses that the glycerophosphate and phosphorylcholine play a critical role in the immunogenicity of Prevnar 13. (*Id.* at 9 (citing Janoi Chang et al., *Relevance of O-acetyl and phosphoglycerol groups for the antigenicity of Streptococcus pneumoniae serotype 18C capsular polysaccharide,* 30 VACCINE 709007096 (2012) (Ex. 37); Czeslaw Lugowski and Harold J. Jennings, *Structural determination of the capsular polysaccharide of Streptococcus pneumoniae Type 18C,* 131 CARBOHYDRATE RES. 119 (1984) (Ex. 38); Junichiro Ohori et al., *Phosphorylcholine intranasal immunization with a 13-valent pneumococcal conjugate vaccine can boost immune response against Streptococcus pneumoniae,* 38 VACCINE 699 (2020) (Ex. 39)).) Dr. Steinman quotes the Chang et al. study to show that the glycerophosphate side chain must be preserved in the manufacturing process to conserve an adequate immune response to the 18C component. (Ex. 35, p. 8.) Lastly, Dr. Steinman cites a study, from Nakos et al., where phospholipid antibodies were found in patients with GBS. (Ex. 35, p. 10 (citing George Nakos et al., *Anti-phospholipid antibodies in serum from patients with Guillain-Barre syndrome,* 31 INTENSIVE CARE MED. 1401 (2005) (Ex. 40)).) The authors found that phosphatidylinositol, cardiolipin, phosphatidic acid, and phosphatidylcholine were the main antigens. (*Id.*)

The second area of molecular mimicry concerns a protein component, called CRM197. (Ex. 35, p. 11 (citing *Prevnar-13 Prescribing Information, supra,* at Ex. 23).) This protein component is used to conjugate the pneumococcal polysaccharides in the Prevnar 13 vaccine to an immunogenic protein carrier. (*Id.*) Dr. Steinman explains that Contactin-1 is "targeted in some cases of GBS." (*Id.* (citing Janev Fehmi et al., *Nodes, paranodes and neuropathies,* 89 J. OF NEUROLOGY, NEUROSURGERY, AND PSYCHIATRY 61 (2018) (Ex. 41); Constance Manso et al., *Contactin-I IgG4 antibodies cause paranode dismantling and conduction defects,* 139 BRAIN 1700 (2016) (Ex. 42); Yumako Miura et al., *Contactin I IgG4 associates to chronic inflammatory demyelinating polyneuropathy with sensory ataxia,* 138 BRAIN 1484 (2015) (Ex. 43)).) In order to test the components

of the Prevnar 13 vaccine, Dr. Steinman conducted BLAST searches[20] to align contactin-1 with the components of CRM197 in the Prevnar vaccine. (Ex. 35, p. 11) Dr. Steinman classifies his criteria for a molecular mimic as a run of 5 or more of 12 amino acids that are identical. (*Id.*) Based on his own published research, Dr. Steinman opines that the identity of 5 of 12 amino acids were sufficient to "trigger clinically relevant neuroinflammation with paralysis." (*Id.* at 13 (citing Anand Gautam et al., *A polyalanine peptide containing only five native myeline basic protein residues induces autoimmune encephalomyelitis,* 127 J. OF EXPERIMENTAL MEDICINE 605 (1992) (Ex. 46); Anand Gautam et al., *Minimum structural requirements for peptide presentation by major histocompability complex class II molecules: Implications in induction of autoimmunity,* 91 PROCEEDINGS OF THE NAT'L. ACAD. OF SCENCES OF THE U.S. OF AM. 767 (1994) (Ex. 47); Anand Gautam et al., *A viral peptide with limited homology to a self-peptide can induce clinical sign of experimental autoimmune encephalomyelitis,* 161 J. OF IMMUNOLOGY, 60 (1998) (Ex. 48)).) He also adds that the 5/12 amino acids that are identical need not be consecutive. (Ex. 35, p. 12.)

Dr. Steinman submitted his BLAST results in the Immune Epitope Database (IEDB)[21] to determine whether other researchers have identified the epitope(s). (Ex. 35, p. 16.) Dr. Steinman first tested the sequence WEQAKALSVE and determined that this sequence is found on human immune cells and it is also "an epitope in diphtheria toxin, which provide the basis for CRM197." (*Id.*) Dr. Steinman tested a second sequence, EYMAQACAGNRVRR, which also has "known cross-reactivity with epitopes described in humans and on the c. diphtheria microbe that is the basis for CRM197." (*Id.* at 17.) These results, Dr. Steinman explains, demonstrate a compelling theory that molecular mimics in the Prevnar 13 vaccine, received by petitioner, trigger inflammatory neuropathy culminating in GBS. (*Id.*)

d. Dr. Leist's supplemental reports, Exhibits C & D

In his first supplemental report, Dr. Leist opines that Dr. Steinman's theory regarding how an immune response against phospholipids causes GBS is not applicable to the Prevnar 13 vaccine because phospholipids are not a listed component of the vaccine. (Ex. C, pp. 1-2.) Dr. Leist explains that the polysaccharide preparations used in pneumococcal conjugate vaccines "are purified and the identity of the individual polysaccharides is ascertained by testing modalities including NMR, residual protein, antigenicity, and molecular weight (ADDC pamphlet)." (*Id.* (citing *Prevnar Prescribing Information,* 1-43 (last updated Aug. 2017) (Ex. C, Tab. 2); *Prevenar 13 suspension for*

[20] According to its own website, the Basic Local Alignment Search Tool (BLAST) "can be used to infer functional and evolutionary relationships between sequences as well as help identify members of gene families." *See* https://blast.ncbi.nlm.nih.gov/Blast.cgi (last visited Oct. 22, 2021).

[21] The IEDB "catalogs experimental data on antibody and T cell epitopes studied in humans, non-human primates, and other animal species in the context of infectious disease, allergy, autoimmunity, and transplantation. The IEDB also hosts tools to assist in the prediction and analysis of epitopes." *See* https://www.iedb.org/home_v3.php (last visited Sept. 1, 2021).

injection, EMC*,* https://www.medicines.org.uk/emc/product/453/smpc/ (last updated Mar. 2021) (Ex. C, Tab. 3)).) Additionally, Dr. Leist notes that the CRM197 carrier protein used in the Prevnar 13 vaccine is extensively purified. (*Id.*) Based on the filtration steps involving ultrafiltration, precipitation, chromatography, and centrifugation, Dr. Leist maintains that these components are not likely present in the vaccine beyond trace amounts. (*Id.*)

In his second supplemental report, Dr. Leist reiterates that alternative causes more than likely explain the onset of petitioner's tingling symptoms and her GBS generally. (Ex. D, p. 2.) Dr. Leist maintains that the tingling that petitioner reported in her January 21 and February 6, 2015 visits was likely related to carpal tunnel. (*Id.*) Dr. Leist highlights a note from petitioner's February 26, 2015 visit which reads: "[u]nrelated to [her] present complaints-patient having symptoms of carpal tunnel syndrome-[she] [*sic*] is a cake decorator for Albertson's-she does plan to retire in less than one year." (*Id.* (citing Ex. 3, p. 19.)) Moreover, Dr. Leist notes records from an emergency room visit on March 2, 2015 indicating that "[petitioner] has no leg numbness, tingling, or weakness" (Ex. 4, p. 58); records from March 5, 2015 where Dr. Marriott indicated petitioner's 10-point review of systems was negative and observed no numbness or tingling (Ex. 4, pp. 87-88)[22]; and records on March 7, 2015 where Dr. McVay recorded no focal deficits. (Ex. 4, p. 74.) Instead, Dr. Leist maintains that petitioner's new neurological symptoms appeared on or about March 11, and 12, 2015. (Ex. D, p. 2 (citing Ex. 4, p. 58.)) Dr. Leist highlights that

> GBS usually begins abruptly with distal, relatively symmetrical onset of paresthesias. Sensory disturbances are accompanied by or quickly followed by progressive weakness. Patients are able to identify a definite date of onset of sensory and motor disturbance. Progression is rapid, with about 50% of patients reaching clinical nadir by two weeks and more than 90% by 4 weeks.

(Ex. D, p. 2 (quoting Ted M. Burns, *Guillain-Barre Syndrome,* 28 SEMINARS IN NEUROLOGY 152 (2008) (Ex. D, Tab. 1)).) Not only does Dr. Leist stress that petitioner here did not experience symptom onset within the 42-day time interval, but he also maintains that an infectious condition is likely the proximate cause of her acute progression of symptoms. (Ex. D, p. 2.)

Dr. Leist also disagrees with Dr. Steinman's assertion that phospholipids are present in Prevnar-13. (Ex. D, p. 3.) While Dr. Steinman explains that phosphorylcholine is present in the 19A component of the vaccine, Dr. Leist stresses that the Chuang et al. article actually reports on the effect of the glgQ2 gene on virulence of streptococcus pneumoniae serotype 19A. (*Id.* (citing Chuang et al., *supra,* at Ex. 27.)) He emphasizes that "[t]he article does not provide information of the

[22] In the history of present illness, Dr. Marriott recorded that petitioner "states she does have numbness in both feet and hands" though upon Dr. Marriott's physical examination Dr. Marriott reports "I do not appreciate any numbness or tingling at this time. She has full strength." (Ex. 4, p. 87)

constituents of the Prevnar-13 vaccine." (Ex. D, p. 3.) In fact, Dr. Leist asserts that the Prevnar vaccine is a conjugate polysaccharide vaccine, and it does not contain streptococcus pneumoniae components other than polysaccharides. (*Id.* (citing United States Patent 7955605 Section 14 (Ex. D, Tab. 2.))

Regarding Dr. Steinman's theory regarding phosphoglycerol, Dr. Leist summarizes Dr. Steinman's theory as follows: "since select patients with Guillain-Barre syndrome have antibodies against phospholipids and since phosphoglycerol residues are a building block[] of phospholipids[,] substances containing phosphoglycerol residues such as select polysaccharides would…be expected to be able to induce antiphospholipid antibodies." (Ex. D, p. 5.) This theory, Dr. Leist explains, is based on "the inaccurate assumption that Prevnar-13 contains phospholipids and that phosphoglycerols and phospholipids can be considered as essentially the same." (*Id.* at 4.)

Finally, in response to Dr. Steinman's theory regarding the CRM197 carrier protein, Dr. Leist likewise agrees that antibodies to contactin-1 have been described in patients with GBS and CIDP. (Ex. D, p. 4.) However, Dr. Leist stresses that Dr. Steinman takes too great an analytical leap. Dr. Leist maintains that Dr. Steinman's BLAST search results do not provide any causal link to show that CRM197 protein-containing polysaccharides vaccines actually induce antibodies against contactin-1. (*Id.*) Nor does Dr. Steinman discuss why this theoretical mechanism is more likely to cause injury than the infection that Dr. Leist identified in petitioner's record in late February / beginning of March 2015. (*Id.* (citing Ex. 3, p. 43.))

e. Dr. Steinman's second supplemental report, Exhibit 50

Dr. Leist opines that petitioner showed a "[l]ack of progression of neurologic symptoms for well over a month" which he argues is inconsistent with the expected course of GBS. (Ex. D, p. 2.) In response, Dr. Steinman argues that petitioner's records show a progression of numbness and tingling more likely than not related to GBS. (Ex. 50, p. 1-2.) Dr. Steinman notes petitioner's symptoms of tingling and weakness appearing on February 26, 2015. (*Id.* at 1-2 (citing Ex. 3, p. 19).) At a follow-up on March 1, 2015, petitioner reported numbness and tingling in both hands since February 28, 2015. (Ex. 50 p. 2 (citing Ex. 3, pp. 36-41).) According to Dr. Steinman, these records show that "there was a progression of the numbness and tingling to involve symmetrically both hands." (Ex. 50, p. 2.) Dr. Steinman notes that petitioner presented to the ER at Mercy Hospital on March 2, 2015 reporting pain in her left upper back, which also spread to her hands and legs, though no leg numbness, tingling, or weakness was reported. (Ex. 50, p. 3 (citing Ex. 4, pp. 58-59).) According to Dr. Steinman, petitioner's discharge summary on March 13, 2015 reveals "further manifestations of inflammatory neuropathy." (Ex. 50 p. 3.) Quoting the discharge summary, Dr. Steinman notes that petitioner "**had an onset of an unusual illness the**

month before admission;"[23] she developed subacute flaccid paraparesis, acute peripheral neuropathy, Bell's palsy, and thoracic back pain. (Ex. 50. p. 3 (citing Ex. 4, pp. 82-84) (emphasis in original).) Taken together, Dr. Steinman seems to suggest that these records evidence a progression that is consistent with GBS. (*See id.*)

Dr. Steinman further disagrees with Dr. Leist's reliance on the Burns article. (*Id.*) Dr. Steinman proposes that the clinical course and onset described by Burns represents the typical onset, while petitioner's case was clearly "not of the 'usual' variety that Dr. Burns writes about." (*Id.*) Regarding Dr. Leist's opinion regarding alternative causes for petitioner's GBS, Dr. Steinman stresses that no infectious condition was ever diagnosed. (Ex. 50, p. 4.) Dr. Steinman states that the most commonly associated agent with GBS is *Campylobacter jejuni.* (*Id.* (citing Hans-Peter Hartung, *Infections and the Guillain-Barre syndrome,* 66 J. OF NEUROLOGY, NEUROSURGERY, AND PSYCHIATRY 277 (1999) (Ex. 51)).) Yet, Dr. Steinman explains that it is difficult to "invoke an infectious cause for a condition without evidence of the infection." (Ex. 50 p. 4.)

Finally, Dr. Steinman offers additional support in favor of his molecular mimicry theory relative to CRM197. (Ex. 50, p. 5.) He proposes an added step which he explains will further validate petitioner's causal theory. (*Id.*) Dr. Steinman reiterates that two regions of mimicry have been studied between contactin-1 and CRM in Prevnar 13 vaccine. (*Id.*) Citing a study by Raju et al., Dr. Steinman observes that humans have been shown to mount T cell responses to these regions of the diphtheria molecule: WEQAKLSVE and EYMAQACAGNRVRR. (*Id.* (citing Raghavanpillai Raju et al., *Epitopes for human CD4+ cells on diphtheria toxin: structural features of sequence segments forming epitopes recognized by most subjects,* 25 EUR. J. OF IMMUNOLOGY 3207 (1995) (Ex. 52)).) Dr. Steinman highlights the results of this study, which differ in only one amino acid from CRM, which he stresses provides "*actual detailed data* for molecular mimics in the CRM in the Prevnar 13 vaccine received by petitioner." (*Id.* at 6.)

f. Dr. Steinman's testimony

Dr. Steinman's testimony during the entitlement hearing was substantially similar to his expert reports. (Exs. 12, 25, 50; Tr. at 125-225; 319-331.) Consistent with his reports, Dr. Steinman explained that the "majority of cases of Guillain Barre that are associated with a microbe, they're known microbes." (Tr. at 132-33.) Among those cases, forty-five to sixty percent of cases are associated with Campylobacter, ten to fifteen percent of cases are associated with CMV, cytomegalovirus, and five to ten percent of cases are associated with Epstein Barr virus (EBV) infection. (Tr. at 133.) Regarding onset in these cases, I asked Dr. Steinman whether onset of infection occurred before the onset of GBS, or at some later point during the course of the disease. (Tr. 134-45.) Dr. Steinman testified that the infection "could have been at its tail end four weeks or one week before, or it could have been newly diagnosed at that

[23] Based on my review of the records, petitioner was admitted to the hospital on March 5, 2015. (Ex. 4, p. 79-80.) By Dr. Steinman's estimation above this would place petitioner's "onset of unusual illness the month before admission" at or around February 5, 2015.

point" but acknowledged that the exact timing of onset of infection remains unclear. (Tr. at 135.) At best, Dr. Steinman testified that "there was some evidence of a predated infection." (*Id.*)

In petitioner's case, Dr. Steinman testified that the onset and duration of petitioner's cough, and whether her cough evidences an infection, is difficult to interpret without a microbial diagnosis. (Tr. at 135-36.) Dr. Steinman testified that petitioner tested negative for several possible infectious causes of GBS (Tr. 137-40): Campylobacter (Ex. 6, p 211-12), c. difficile (*Id.*), Rickettsia and Leptospirosis (*Id.* at 213), and Borrelia (*Id.* at 215). Results for syphilis, herpes simplex virus, and the zoster virus were also all negative. (Ex. 6, pp. 215-16.) Petitioner was not tested for Epstein Barr virus ("EBV"). (Tr. at 140; *see* Ex. 6, pp. 211-223.) Dr. Steinman observed, however, that "[EBV is] one of the most common persistent viruses that we all pick up, usually somewhere in adolescence." (Tr. at 140.) Dr. Steinman further testified that petitioner's chest x-rays were normal and did not support a diagnosis of bronchopneumonia. (Tr. at 141.) Petitioner's cough, according to Dr. Steinman, was a nagging cough, one that was "unsolved and didn't amount to a pneumonia." (Tr. at 142.)

Concerning the typical course and onset of GBS, Dr. Steinman testified that he places the outermost medically appropriate onset date for vaccine-caused GBS at eight weeks, or 56 days, post-vaccination. (Tr. at 146, 200.) Dr. Steinman draws support for this time frame from the Schonberger article. (Tr. at 144 (citing Schonberger et al., *supra,* Ex. 31.)) Dr. Steinman testified that Figure 6 in Schonberger shows the expected incidence rate "remain[s] high, above that cross-hatched area, at eight weeks, and then they diminish a little more at nine and ten weeks, and then they finally blip down to the baseline at eleven weeks." (Tr. at 144 (citing Schonberger et al., *supra,* Ex. 31, p. 9.)) This, Dr. Steinman concludes, leads him to place "a cutoff somewhere around the end of week eight." (Tr. at 144-45.) Dr. Steinman's testimony regarding petitioner's symptoms reflected the same theory presented in his expert reports, placing onset of petitioner's GBS on approximately January 21, 2015. (Tr. at 147-152.) He testified that the nadir of petitioner's GBS occurred "somewhere in the first, second week of March, when [petitioner] was put on IVIG." (Tr. 152-53.)

Dr. Steinman's testimony concerning his theories of molecular mimicry were substantially the same as those expressed in his expert reports. (Exs. 12, 35, 50; Tr. at 154-188.) During his testimony, Dr. Steinman referenced a three-dimensional model from the Bryson exhibit (Exs. 58, 59) to identify the 23F carbohydrate, a component of the Prevnar 13 vaccine, as well as the Lys 100 (or Lysine), an antibody in humans that binds to the phosphate. (Tr. at 164.) Examining the same model, in the Lysine, Dr. Steinman identified the side chain as the phosphate head group. (*Id.*) Dr. Steinman also referenced Figure 2B and 2D in the Ho et al. article, where he identified on the diagram the phosphate head group in seven out of eight examples. (Tr. at 174-77; Ho et al., *supra,* Ex. 26, Fig. 2B, Fig. 2D, p. 4.) In addition to the presence of these antibodies, I asked Dr. Steinman about the significance of these specific antibodies demonstrating a cross reaction. (Tr. at 178.) Pointing to Table 2 in Gilburd et al., Dr.

Steinman testified that among six patients, two showed antibodies to phosphatidylethanolamine, one showed antibodies to phosphatidylserine, and one showed antibodies to phosphatidylcholine, while the remaining two patients showed antibodies to cardiolipin. (Tr. at 178-79 (citing Gilburd et al, *supra,* Ex. 24, Tab. 2, p. 26.)

Regarding the course of petitioner's GBS, Dr. Steinman testified that "the crescendo was very low, and it began to intensify about 30 days before the 5th day of March, and then it became deafeningly loud at the end of February and the first few days of March." (Tr. at 326.) Concerning petitioner's diagnosis of subacute flaccid paraparesis, I asked Dr. Steinman how he interpreted the characterization of "subacute." (Tr. at 326-37.) Dr. Steinman testified that while "subacute is not chronic," subacute can be "a few weeks," though he admitted that "I don't think it has a formal definition." (Tr. at 327.)

g. Dr. Leist's testimony

The testimony provided by Dr. Leist also closely resembled the opinions offered in his expert reports. (Exs. A, C, D; Tr. at 229-318.) Dr. Leist estimates that petitioner's onset of GBS occurred in or about early March 2015—based on petitioner's records indicating that she developed rapid lower extremity weakness on or about March 12, 2015. (Tr. at 236.) He testified that "[t]he rapid onset of flaccid paralysis is one of the cardinal features of Guillain-Barre syndrome."[24] (Tr. at 237.) Dr. Leist opines that petitioner's lower extremity weakness developed on or about March 12, 2015 based on a record from March 9, 2015. (*Id.* (citing Ex. 4, p. 165.) He testified that on March 9 petitioner "was moving all four extremities[,] [s]he wanted to get out of bed," and "she wanted to go to the chair." (Tr. at 238.) Dr. Leist interprets this record to mean that petitioner "was moving her extremities on that date, meaning that the later documented weakness in the lower extremities was not present on March 9, 2015."[25] (*Id.*) Taken together, Dr. Leist testified the fact that petitioner was "moving around March 9," she developed new neurologic symptoms around March 12 (lower extremity weakness), she was referred to a higher level of care, and the results of her lumbar puncture on March 15, all indicate that petitioner's onset of GBS "occurred around that period of time." (Tr. at 243.) I asked Dr. Leist, given the expected course of GBS and given that petitioner experienced her severest weakness in mid-March, whether it was reasonable to place her nascent symptoms of weakness as occurring as early as mid-February. (Tr. at 245.) Dr. Leist did not discount this possibility. (*See id.*) Dr. Leist opined that onset of GBS resembles a clear crescendo, as opposed to a variable course. (*See* Tr. at 246.)

[24] A *rapid* onset of flaccid paralysis, Dr. Leist testified, can be characterized as paralysis occurring over two weeks in 50 percent of cases and within four weeks in 90 percent of cases. (Tr. at 243 (citing Burns, *supra,* at Ex. D, Tab. 1, p. 153).)

[25] Dr. Leist acknowledged that GBS presents as ascending weakness and that it is not necessary for a person to be unable to move all four extremities in order to be diagnosed with an onset of GBS. (Tr. at 268.)

Dr. Leist further testified that petitioner's significant bowel event or the "recrudescence of respiratory complaints" at the end of February could have been a likely cause of petitioner's GBS. (Tr. at 246.) Though the stool culture was negative, Dr. Leist explained that stool cultures are invariable, due to the time difference between when the infection would occur and the actual onset of GBS. (Tr. at 247.) The stool culture, in his opinion, could not definitively rule out the presence of *C. jejuni*. (*Id.*) Dr. Leist further proposed that the antibiotics that petitioner was prescribed could have interfered with the detection of, or eliminated, the *C. jejuni* pathogen. (Tr. at 249.)

Dr. Leist testified that he disagrees with Dr. Steinman's molecular mimicry theory because it is based on "the inaccurate assumption that Prevnar-13 contains phospholipids[26] and that phosphoglycerol and phospholipids can be considered as essentially the same." (Tr. at 257.) Dr. Leist testified he "do[es not] think that lipids are a named constituent of the Prevnar 13" vaccine. (*Id.*) Therefore, Dr. Leist stresses that the applicability of the Ho et al. article is "at most tangential." (*Id.*) Dr. Leist also criticizes Dr. Steinman's reliance on Nakos, noting that the authors could not determine whether the antibodies at issue are "a sign of injury, or whether it was actually pathophysiologically important[.]" (Tr. at 260-61.) Overall, Dr. Leist testified that he agrees the individual steps in Dr. Steinman's theory are logical, though he opines that they don't connect.[27] (Tr. at 264-65.)

Looking at petitioner's discharge summary, Dr. Leist testified that petitioner was diagnosed with subacute flaccid paraparesis. (Tr. at 302.) Dr. Leist further testified that "subacute can be a day or two or so." (Tr. at 306.) While in contrast, he testified that acute would mean "less than a 24-hour period." (Tr. at 307.) Petitioner's discharge

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[26] In his initial report, Dr. Steinman opined that the "trigger is the phospholipids in Prevnar 13[.]" (Ex. 12, p. 18.) However, Dr. Steinman explained that after reviewing the Prevnar 13 vaccine patent he determined that the mimic is phosphoglycerol. (Tr. at 329.) This refinement in Dr. Steinman's opinion is also addressed in greater detail in the *Koller* decision. *Koller v. Sec'y of Health & Human Servs.,* No.16-439V, 2021 WL 5027947, *16-17 (Fed. Cl. Spec. Mstr. Oct. 8, 2021).

[27] Specifically, he testified

> So from that point of view, obviously there is a sequence homology. You also see some individuals who have these response, at least the individuals that were used for Exhibit 52 [Raju et al.], can have such a response without having illness. So in a certain way, it reminds me a little bit of the – it reminds me that there are individual arguments, but that the consequential steps in between so actually injury occurs as a consequence of this sequence homology or as a consequence of this – of an immune response that is present against a certain sequence, like in these healthy individuals that we just talked about, these steps are not there. So in a certain way, the way almost would have to be the opposite way around. Take patients that have – if they exist, which I would think would be difficult to do – that have alleged injury secondary to the Prevnar, and then show that they developed – that they developed immune response on the other side. I mean, Dr. Steinman proposes individual steps, that individually look logical, but they don't connect…I view them as speculative, so from that point of view, they don't connect in what I would consider a reliable theory.

(Tr. at 264-65.)

summary was authored on March 13, 2015. (Tr. at 306; Ex. 4, p. 83.) Therefore, Dr. Leist estimates that petitioner's onset was likely on or about March 12, 2015—according to his definition of subacute. (Tr. at 306-307.) According to Dr. Leist, his interpretation is also supported by the record as showing that "on [March 9], [petitioner] was not flaccid" because she was able to move all four extremities. (Tr. at 306.)

IV. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations, including showing that an individual received a vaccination covered by the statute; received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury. In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table. If so, the Table Injury is presumed to have been caused by the vaccination, and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300 aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B).

In many cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table. In such instances, an alternative means exists to demonstrate entitlement to a Program award. That is, the petitioner may gain an award by showing that the recipient's injury was "caused-in-fact" by the vaccination in question. § 300aa-13(a)(1)(B); § 300aa-11(c)(1)(C)(ii). In such a situation, of course, the presumptions available under the Vaccine Injury Table are inoperative. The burden is on the petitioner to introduce evidence demonstrating that the vaccination actually caused the injury in question. *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines v. Sec'y of Health & Human Servs.*, 940 F.2d 1518, 1525 (Fed. Cir. 1991). In this case, petitioner alleges that she suffered GBS, which is not listed on the Vaccine Injury Table relative to Prevnar 13. Accordingly, petitioner must satisfy this burden of proof for a cause-in-fact claim.

The showing of "causation-in-fact" must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); *see also Althen*, 418 F.3d at 1279; *Hines*, 940 F.2d at 1525. Under that standard, the petitioner must show that it is "more probable than not" that the vaccination was the cause of the injury. *Althen*, 418 F.3d at 1279. The petitioner need not show that the vaccination was the sole cause of the injury or condition, but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition, and was a "but for" cause. *Shyface v. Sec'y of Health & Human Servs.*, 165

F.3d 1344, 1352 (Fed. Cir. 1999). Thus, the petitioner must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury;" the logical sequence must be supported by "reputable medical or scientific explanation, *i.e.*, evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F.3d at 1278; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner may not receive a Vaccine Program award based solely on his or her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1).

In what has become the predominant framing of this burden of proof, the *Althen* court described the "causation-in-fact" standard, as follows:

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury. If Althen satisfies this burden, she is entitled to recover unless the [government] shows, also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine.

Althen, 418 F.3d at 1278 (citations omitted). The *Althen* court noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279-80. That expert's opinion must be "sound and reliable." *Boatmon v. Sec'y of Health & Human Servs.*, 941 F.3d 1351, 1359-60 (Fed. Cir. 2019) (citing *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548-49 (Fed. Cir. 1994)). The *Althen* court also indicated, however, that a Program fact-finder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." 418 F.3d at 1280.

V. Additional Background and Program Case Law

Guillain-Barre syndrome is an acute-onset, monophasic, polyneuropathy. (Burns, *supra,* Ex. D, Tab. 1, p. 1); (Baxter et al., *supra,* Ex. A, Tab. 1, p. 1.) GBS is generally considered an autoimmune condition and is associated with a number of triggers, including infections and vaccination. (Baxter et al., *supra,* Ex. A, Tab. 1, p. 1.) Among published case series, approximately two-thirds of all cases are preceded by a gastrointestinal or respiratory infection within three months prior. (*Id.*; Hartung, *supra,* Ex. 51, p. 277.) *Campylobacter jejuni*, cytomegalovirus (CMV), Epstein-Barr virus, and *Mycoplasma pneumoniae* are known precipitants of GBS, with other infections occurring no more often in GBS than in controls. (Hartung, *supra,* Ex. 51, p. 1.) The infection most commonly associated with GBS is *Campylobacter jejuni.* (*Id.*)

A small but significant increase in the number of GBS cases post-vaccination was observed with the 1976 swine influenza vaccine. (Baxter et al., *supra,* Ex. A, Tab. 1, p. 1.) Several studies assessing the risk of GBS post seasonal influenza vaccines since 1976 have shown either no risk, or a small attributable risk, approximately 1 case per million doses. (*Id.* at 1-2.) Studies assessing the risk of GBS following the 2009 H1N1 monovalent influenza vaccines in the United States found an attributable risk ranging from 1 to 5 per million doses. (*Id.* at 2.)

It is generally accepted that GBS results from molecular mimicry. This is most clearly demonstrated in the case of Campylobacter jejuni. (Tr. at 170; Nakos et al., *supra,* Ex. 40, p. 1; Burns, *supra,* Ex. D, Tab. 1, p. 4.) The theory of molecular mimicry describes how shared structures on a virus or bacteria, or components of a vaccine, can trigger a cross-reactive response self. (Ex. 12, p. 9.) "Such mimicry works by showing the immune system stretches of amino acids that look like self." (Lawrence Steinman, *Autoimmune Disease,* SCI. AM. 107 (1993) (Ex. 22, p. 3).) Anti-ganglioside[28] autoantibodies are most commonly suspected as the vehicle for molecular mimicry in cases of GBS; however, this has not been definitively established and other autoimmune targets have also been proposed. (Nakos et al., *supra,* Ex. 40, p. 2; Gilburd et al., *supra,* Ex. 24, p. 1.)

Molecular mimicry is a well-established theory in the Vaccine Program and has been persuasively linked to several autoimmune conditions. *See e.g.*, *W.C. v. Sec'y of Health & Human Servs.,* No. 07-456V, 2011 WL 4537877, at *11-12 (Fed. Cl. Spec. Mstr. Feb. 22, 2011), (finding that molecular mimicry is a well-regarded theory in some contexts but finding against molecular mimicry in the context of flu vaccine causing or worsening MS), *mot. for rev. denied*, 100 Fed. Cl. 440 (2011), *aff'd*, 704 F.3d 1352 (Fed. Cir. 2013); *Swaiss v. Sec'y of Health & Human Servs*., 15-286V, 2019 WL 6520791 (Fed. Cl. Spec. Mstr. Nov. 4, 2019) (finding that Petitioner's small fiber neuropathy variant of GBS was more likely than not caused by molecular mimicry following the Tdap vaccine); *H.J. v. Sec'y of Health & Human Servs*, No. 11-301V, 2015 WL 6848357 (Fed. Cl. Spec. Mstr. Nov. 6, 2015) (finding Tdap vaccine caused Petitioner to develop rheumatoid arthritis via molecular mimicry); *Salmins v. Sec'y of Health & Human Servs*., No. 11–140V, 2014 WL 1569478 (Fed. Cl. Spec. Mstr. Mar. 31, 2014) (finding that HPV vaccine caused Petitioner to develop GBS via molecular mimicry); *Roberts v. Sec'y of Health & Human Servs*., No. 09-427V, 2013 WL 5314698 (Fed. Cl. Spec. Mstr. Aug. 29, 2013) (finding that Tdap vaccine led Petitioner to develop transverse myelitis via molecular mimicry); *Hayes v. Sec'y of Health & Human Servs*., No. 06-738V, 2010 WL 2985632 (Fed. Cl. Spec. Mstr. July 12, 2010) (finding that, by the process of molecular mimicry, the flu vaccine was a substantial cause of Petitioner's transverse myelitis, ADEM, bilateral optic neuritis, and developmental delay). In particular, the association between the flu vaccine and GBS has been well-established in the Program. 42 C.F.R.

[28] "[A]ny of a group of glycosphingolipids in which the polar head group on ceramide is a sialic acid–containing oligosaccharide linked via a glucose residue; they occur predominantly in tissues of the central nervous system." *Ganglioside,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=19729&searchterm=ganglioside (last visited Jan. 4, 2022.)

§ 100.3(a); *see also Chinea v. Sec'y of Health & Human Servs.*, No. 15-095V, 2019 WL 1873322 at *29 (Fed. Cl. Spec. Mstr. Mar. 15, 2019); *Strong v. Sec'y of Health & Human Servs.*, No. 15-1108V, 2018 WL 1125666 (Fed. Cl. Spec. Mstr. Jan. 12, 2018); *Stitt v. Sec'y of Health & Human Servs.,* No. 09-653V, 2013 WL 3356791 (Fed. Cl. Spec. Mstr. May 31, 2013); *Stewart v. Sec'y of Health & Human Servs.*, No. 06-777V, 2011 WL 3241585, at *16 (Fed. Cl. Spec. Mstr. July 8, 2011); *see also Barone v. Sec'y of Health & Human Servs.,* No. 11-707V, 2014 WL 6834557 (Fed. Cl. Spec. Mstr. Nov. 12, 2014).

Flu vaccine-GBS cases often rely upon the theory of molecular mimicry, specifically proposing that antibodies produced by B cells in response to the vaccine's viral antigen components cross-attack the myelin sheath (where the target antigen and gangliosides of the myelin sheath share structural homology), causing demyelination of peripheral nerves. *See Chinea,* 2019 WL 1873322, at *15. Nonetheless, this does not explain all cases of GBS and other known triggers of GBS do not have established homologies. (Nakos et al., *supra,* Ex. 40, p. 2; Gilburd et al., *supra,* Ex. 24, p. 23.) GBS was added as a Table Claim in 2017 for the flu vaccine, though it is not recognized for the pneumococcal vaccine at issue in this case. 42 C.F.R. § 100.3(a).

While molecular mimicry "is a generally accepted scientific principle, mere invocation of the scientific term does not carry a petitioner's burden in a Program case." *Deshler v. Sec'y of Health & Human Servs*., No. 16-1070V, 2020 WL 4593162, at *20 (Fed. Cl. Spec. Mstr. July 1, 2020) (citing *Forrest v. Sec'y of Health & Human Servs.*, No. 14-1046V, 2019 WL 925495, at *3 (Fed. Cl. Spec. Mstr. Jan. 18, 2019)). This is because "the finding of sequence homology does not necessarily mean the similarity has significance to the immune system." *Tullio v. Sec'y of Health & Human Servs.*, No. 15-51V, 2019 WL 7580149, at *15 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), *aff'd,* 149 Fed. Cl. 448 (2020); *see also Caredio v. Sec'y of Health & Human Servs.,* No. 17-0079V, 2021 WL 4100294, at *31 (Fed. Cl. Spec. Mstr. July 30, 2021) ("*demonstration of homology alone is not enough to establish a preponderant causation theory*") (emphasis in original) (citing *Schultz v. Sec'y of Health & Human Servs.,* No. 16-539V, 2020 WL 1039161, at *22 n.24 (Fed. Cl. Spec. Mstr. Jan. 24, 2020) ("[m]ere demonstration of theoretical homology alone, based on computer-driven searches involving databases of amino acid sequences, does not carry the day")), *mot. for rev. denied,* 2021 WL 6058835 (Fed. Cl. Dec. 3, 2021).

In a decision often cited in cases of molecular mimicry, *W.C. v. Secretary of Health & Human Services*, the Federal Circuit outlined the reasons why that petitioner's theory of molecular mimicry was insufficient to prove petitioner's flu vaccine caused multiple sclerosis, finding, "[p]etitioner provided no evidence that the portions of the influenza virus shown by Wucherpfennig to mimic myelin basic protein were present in the influenza vaccine Petitioner received," and "[p]etitioner also did not provide evidence that any peptide from the influenza vaccine he received was cross-reactive with myelin basic protein-specific T-cells." 704 F.3d at 1360-61 (citing decision below). The Federal Circuit further found that the epidemiologic studies cited by the Special Master, which showed that MS was not exacerbated by the influenza vaccination, were more

persuasive than petitioner's expert's theory and affirmed the denial of compensation by the Special Master. *See id.* at 1361.

Similarly, Judge Horn affirmed the Special Master's decision in *Tullio v. Secretary of Health & Human Services,* finding that although petitioner's theory of molecular mimicry provided some evidence, petitioner failed to provide evidence that any peptide from the influenza vaccine he received was cross-reactive with the specific T cells. 149 Fed.Cl. 448, 468 (citing *W.C. v. Sec'y of Health & Human Servs.,* 704 F.3d at 1360-61; *Broekelschen v. Sec'y of Health & Human Servs.,* 618 F.3d 1339, 1351 (Fed. Cir. 2010)). Finding that the four studies petitioner presented on tetramers lacked persuasive value, petitioner was left supporting his claim with epidemiologic studies and his expert's BLAST searches. *See Tullio,* 149 Fed.Cl. at 469-70. Regarding the BLAST searches, Judge Horn outlined the reasons why these searches were insufficient, quoting the Special Master's decision, explaining that because all proteins "'are built from the same 20 amino acids, it is inevitable that some sequences of amino acids will repeat.'" *Id.* at 471 (citing decision below). Thus, "'the finding of sequence homology does not necessarily mean the similarity has significance to the immune system.'" *Id.* (citing decision below). Though not dispositive, the Special Master found the epidemiologic studies did not support petitioner's hypothesis. *Id.* at 473-75. Taken together, the Special Master's decision was not arbitrary or capricious. *Id.* at 478.

As the above caselaw illustrates, a petitioner must offer more than superficial invocation of molecular mimicry as the causal mechanism. "It also cannot be enough that a medical expert can simply identify homologous peptides from a generic BLAST search that are not, in any way, linked to the biological process that is dysfunctional or has suffered injury." *Brayboy v. Sec'y of Health & Human Servs.,* No. 15-183V, 2021 WL 4453146, at *19 (Fed. Cl. Spec. Mstr. Aug. 30, 2021).[29] Ultimately, "[t]he line must be drawn somewhere between speculation and certainty." *Id.* Preponderant evidence under *Althen* prong one exists where a petitioner can identify "a cross-reaction between components of the vaccine and proteins in the body that are directly responsible for the health and productivity of the organ at issue." *Id*. On the other hand, while direct,

[29] *See also Forrest v. Sec'y of Health & Human Servs*., No. 14-1046V, 2019 WL 925495 at *4 (Fed. Cl. Spec. Mstr. Jan. 28, 2019) (finding that Dr. Steinman's theory that a flu vaccine caused TM via molecular mimicry was not sufficiently developed to meet Petitioner's burden under *Althen* prong one because Dr. Steinman had "not investigated his hypothesis[,]" other than through computerized homologies revealing "some overlap in sequences of amino acids[.]"). In that case, the special master discredited Dr. Steinman's theory, in part, because he "appear[ed] to have made errors in proclaiming the degree of similarity [in the homologies] that he found[.]" *Id*. There have also been instances where Dr. Steinman's use of BLAST searches has been found to help support a finding of vaccine causation. *See E.M. v. Sec'y of Health & Human Servs.,* No. 14-753V, 2021 WL 3477837, at *36-39 (Fed. Cl. Spec. Mstr. July 9, 2021) (finding persuasive Dr. Steinman's evidence of "numerous examples of sequences in the 2011 Fluarix vaccine and between earlier seasonal flu vaccines, that share similar homologies with the [protein] alpha3 nicotinic AChR, which is associated with small fiber neuropathy"); *White v. Sec'y of Health & Human Servs.,* No. 15-1521, 2019 WL 7563239, at *24 (Fed. Cl. Spec. Mstr. Dec. 19, 2019) (crediting Dr. Steinman's molecular mimicry theory and BLAST searches where there were "sufficient homologies between the basic myelin protein and two of the strains of the HPV L1 strains…and between MOG and all four HPV antigens in the vaccine[,]" which could cause TM).

testable evidence of pathology may be the strongest scientific evidence, this level of certainty goes beyond petitioner's preponderant burden in this Program.[30] In the Vaccine Program, it is well understood that petitioners are not obligated to prove the precise mechanism of injury as a component of their causation theory. *Kottenstette v. Sec'y of Health & Human Servs.*, 861 F. App'x 433, 441 (Fed. Cir. 2021); *Knudsen v. Sec'y of Health & Human Servs.,* 35 F.3d 543, 548 (Fed. Cir. 1994).

Although the flu vaccine stands alone as being presumed to cause GBS within this Program, cases concerning GBS have also concluded that vaccines other than the flu vaccine can cause GBS. *See Salmins v. Sec'y of Health & Human Servs.*, No. 11-140V, 2014 WL 1569478 at *14 (Fed. Cl. Spec. Mstr. March 31, 2014) (accepting Dr. Souayah's opinion that the HPV vaccine (Gardasil) "can cause" GBS although there was no published medical literature demonstrating homology); *Peugh v. Sec'y of Health and Human Servs.,* No. 99–638V, 2007 WL 1531666 (Fed. Cl. Spec. Mstr. May 8, 2007) (hepatitis B vaccine caused GBS)[31]; *Whitener v. Sec'y of Health & Human Servs.,* No. 06-0477V, 2009 WL 3007380 (Fed. Cl. Spec. Mstr. Sept. 2, 2009) (meningococcal vaccine found causal of GBS); *but see Isaac v. Sec'y of Health & Human Servs.*, 108 Fed. Cl. 743 (2013) (denying review where petitioner alleged that the tetanus vaccine caused GBS), *aff'd without opinion,* 540 Fed. App'x. 999 (Fed. Cir. 2013).

Recently, two decisions regarding GBS alleged to have been caused-in-fact by the Prevnar 13 vaccine have reached opposing conclusions. In *Deshler v. Secretary of Health & Human Services,* petitioner alleged that she suffered from GBS as a result of receiving the Prevnar 13 vaccine in 2015. 2020 WL 4593162, at *1. Petitioner in that case presented two similar theories, the first regarding a molecular mimic involving the polysaccharides of *S. pneumoniae*, a known infectious cause of GBS, and a second

[30] In *Tullio v. Secretary of Health and Human Services,* Judge Horn observed that, to the extent that the Special Master required experts to "conduct[] experiments about molecular mimicry" the Special Master's "Testability" portion of the decision was inconsistent with the Program's role which is "not to be seen as a vehicle for ascertaining precisely how and why…vaccines sometimes destroy the health and lives of certain children while safely immunizing most others." 149 Fed.Cl. at 477-78 (quoting *Knudsen v. Sec'y of Health & Human Servs.,* 35 F.3d 543, 549 (Fed. Cir. 1994)). *But compare Terran v. Sec'y of Health & Human Servs.,* 41 Fed. Cl. 330, 336 (1998) *aff'd*, 195 F.3d 1302 (Fed. Cir. 1999) (indicating that special masters may consider whether an expert's opinion is and has been "tested") *with, Andreu v. Sec'y of Health & Human Servs.,* 569 F.3d 1367, 1380 (Fed. Cir. 2009) (quoting *Bunting v. Sec'y of Health & Human Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991) (observing that petitioners do not have to prove their cases with scientific certainty).

[31] On October 13-14, 2004, former Special Master Sweeney held a hearing—which became known as the "Hepatitis B – Neurological Demyelinating Omnibus Proceeding"—to determine whether a causal association exists between the Hepatitis B vaccine and several demyelinating illnesses (multiple sclerosis, TM, chronic inflammatory demyelinating polyneuropathy, and GBS) alleged in four paradigm cases. *Stevens v. Sec'y of Health & Human Servs.,* No. 99-594V, 2006 WL 659525 (Fed. Cl. Spec. Mstr. Feb. 24, 2006); *Werderitsh v. Sec'y of Dept. of Health & Human Servs.*, No. 99-310V, 2006 WL 1672884 (Fed. Cl. Spec. Mstr. May 26, 2006); *Peugh,* 2007 WL 1531666; *Gilbert v. Sec'y of Dept. of Health & Human Servs.,* No. 04-455V, 2006 WL 1006612 (Fed. Cl. Spec. Mstr. Mar. 30, 2006). These cases were then reassigned to former Special Master Laura Millman, who found that in all four cases, the Hepatitis B vaccine was causal. *Peugh*, 2007 WL 1006612, at *1, *17–18.

theory suggesting that the diphtheria conjugate component (CRM197) was a key factor in triggering GBS. *Id.* at *20. Petitioner in that case failed to meet her burden under *Althen* prong one because petitioner's experts could not present evidence of a shared structural homology between the polysaccharides contained in the pneumococcal vaccine and self-structures of the peripheral nervous system. *Id.* at *20-21. Both of petitioner's experts in that case drew comparisons to the *C. jejuni* bacterium, and GBS' autoimmune etiology generally—which fell short where Dr. Levy acknowledged that the underlying pneumococcal bacterial strains in the Prevnar-13 vaccine "were not *themselves*…associated with GBS (unlike, for example, *C. jejuni*)." *Id.* at *5. The Chief Special Master was further persuaded by respondent's expert's testimony in that case, where Dr. Whitton opined that the pathogenic nature of CRM197 "could not be conflated with what was known about the diphtheria toxoid used as a conjugate in other vaccines." *Id.* at *20 (internal citation omitted.) Thus, petitioner's *Althen* prong one theory was left relying on epidemiologic studies and a temporal relationship to the vaccine. *Id.* at *19-21. The Chief Special Master found that the epidemiologic studies cited by Dr. Souayah in that case, Baxter, Haber, and Cordonnier, failed to preponderantly show that the Prevnar-13 vaccine can cause GBS. *Deshler v. Sec'y of Health & Human Servs.*, No. 16-1070V, 2020 WL 4593162 at *21 (Fed. Cl. Spec. Mstr. July 1, 2020).

In *Koller v. Secretary of Health & Human Services,* petitioner also alleged that the Prevnar 13 vaccine he received in 2015 caused his GBS. No. 16-439, 2021 WL 5027947 at *1 (Fed. Cl. Spec. Mstr. Oct. 8, 2021). Petitioner's expert in that case, Dr. Steinman, theorized that a molecular mimic existed between a component of the Prevnar 13 vaccine and the myelin sheath of the peripheral nervous system, causing petitioner's GBS. *Id.* at *8. Unlike in *Deshler,* Dr. Steinman proposed a mimic involving phosphoglycerol, a key component of phospholipids which make up seventy percent of the myelin. *Id.* According to his theory, the immune reaction to the phosphoglycerol in the vaccine induces an attack on the phosphoglycerol attached to the phospholipids in the myelin. *Id.* Respondent's expert, Dr. Leist, criticized Dr. Steinman's theory for failing to identify a single amino acid, or side chain, sufficient for molecular mimicry. *Id.* at *16. Dr. Leist further stressed that the presence of a naturally occurring amino acid in a protein was insufficient to invoke molecular mimicry. *Id.* at *16. Support for Dr. Steinman's theory in that case was grounded in three key pieces of medical literature: Chang et al., Ho et al., and Gilburd et al., as well as the Prevnar 13 vaccine patent application. *Id.* at *16-18, 20. In particular, Dr. Steinman offered the Ho et al. article to demonstrate that the phosphate group in phospholipids in myelin was targeted by autoantibodies in MS patients, thus triggering demyelination. *Id.* at *20. Dr. Steinman proposed that the Prevnar 13 vaccine triggers the same cross-reactive mechanism, which can cause similar demyelination in the peripheral nerves, causing GBS. *Id.* Under *Althen* prong one, the Special Master concluded that requiring "definitive proof or epidemiology would impermissibly raise the petitioner's burden of proof." *Id.*

Prior decisions, including those discussed above, do not control the outcome of this case. *Boatmon v. Sec'y of Health & Human Servs.,* 941 F.3d 1351, 1358-59 (Fed. Cir. 2019); *Hanlon v. Sec'y of Health & Human Servs.,* 40 Fed. Cl. 625, 630 (1998).

Federal Circuit holdings regarding legal issues are binding on special masters. *Guillory v. Sec'y of Health & Human Servs.,* 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. App'x. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Human Servs.,* No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014). However, decisions by other special masters or by the Court of Federal Claims are not binding. *Hanlon*, 40. Fed. Cl. at 630. Nor, for that matter, are special masters obligated to distinguish decisions reaching a different result. *Boatmon,* 941 F.3d at 1358. The discussion above is provided only to provide context given that both GBS and molecular mimicry are commonly encountered within this Program while this specific combination of vaccination and injury is rare by comparison. *See, e.g. Doe v. Sec'y of Health & Human Servs.,* 76 Fed. Cl. 328, 338-39 (2007) ("[o]ne reason that proceedings are more expeditious in the hands of special masters is that the special masters have the expertise and experience to know the type of information that is most probative of a claim").

VI. Discussion

As explained above, petitioner's burden is to demonstrate by preponderant evidence each of the three *Althen* prongs for determining causation-in-fact (i.e. a medical theory, a logical sequence of cause and effect, and a proximate temporal relationship). *Althen*, 418 F.3d at 1278. Provided petitioner can affirmatively meet this burden, she bears no burden of eliminating alternative causes. *Walther v. Sec'y of Health & Human Servs.*, 485 F.3d 1146, 1150 (Fed. Cir. 2007); *de Bazan v. Sec'y of Health & Human Servs.,* 539 F.3d 1347, 1352 (Fed. Cir. 2008). Importantly, however, respondent may present evidence relating to an alternative cause to demonstrate the inadequacy of petitioner's evidence supporting her case in chief. *de Bazan,* 539 F.3d at 1353.

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 v. Sec'y of Health & Human Servs.*, 451 F.3d 1352, 1355–56 (Fed. Cir. 2006) (citations omitted). Such a theory must only be "legally probable, not medically or scientifically certain." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548-49 (Fed. Cir. 1994). 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 v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano v. Sec'y of Health & Human Servs.,* 440 F.3d 1317, 1325–26 (Fed. Cir. 2006)). However, "[a] petitioner must provide a 'reputable medical or scientific explanation' for [her] theory. While it does not require medical or scientific certainty, it must still be 'sound and reliable.'" *Boatmon v. Sec'y of Health & Human Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019) (quoting *Knudsen*, 35 F.3d at 548-49).

Here, consistent with much of the above discussion regarding GBS, Dr. Steinman proposes that the Prevnar-13 vaccine can cause GBS via molecular mimicry. He opines that there are two molecular mimics that are relevant to GBS in the composition of Prevnar 13: one from the phosphoglycerol in the composition of the pneumococcal polysaccharide antigen, and a second from the CRM protein conjugate. (Ex. 35, p. 4.)

1. Phosphoglycerol

Although antiganglioside antibodies have primarily been suspected as causal in GBS, Dr. Steinman observes that two prior studies have shown GBS patients to have autoantibodies to phospholipids. First, Gilburd et al. (1993) sought to investigate autoantibodies in GBS by testing the reactivity of GBS sera with various phospholipids—those that are known constituents of myelin that also serve as autoantigens in other autoimmune conditions. (Gilburd et al., *supra,* Ex. 24, p. 1.) Their results indicated that six out of sixteen GBS sera studied had antibodies to one of more of the phospholipid antigens. (*Id.* at 5.) At the time, the authors theorized that these results "may be produced by a cross reaction of autoantibodies to [a] yet unidentified myelin constituent." (*Id.* at 5-6.) However, Gilburd et al. did not find a significant association between the presence of any specific antiphospholipid antibodies or anti-DNA antibodies in GBS when compared to controls. (*Id.* at 6.) The authors ultimately concluded that the autoantibody production was "more likely the result of myelin damage and the liberation of various myelin antigens into circulation." (*Id.*) Dr. Steinman testified that this study shows that many of the antibodies in GBS target phospholipids. (*See* Tr. at 169.) While the authors "didn't have enough insight at the time or they never asked what part of the phospholipid is being targeted[,]'" Dr. Steinman testified that some of the same phospholipids were demonstrated by a later study, Ho et al (discussed further below), as being targeted in the context of multiple sclerosis. (*Id.*) Thus, while the authors' data was not conclusive, Dr. Steinman explained that the later discoveries published in Ho et al. allowed him to reevaluate the Gilburd et al. data.

Second, the results from Nakos et al. (2005) also reveal that phospholipid antibodies were found in patients with GBS. (Nakos et al, *supra,* Ex. 40, p. 1405.) The authors observe that many earlier studies attempted to evaluate the clinical relevance of anti-phospholipid antibodies, but with conflicting results. (*Id.* at 5.) In their study, Nakos et al. obtained four blood samples before and after treatment for GBS, testing the samples for IgM, IgA, and IgG antibodies to phosphatidylcholine, phosphatidylinositol, cardiolipin, phosphatidic acid, phosphatidylserine, phosphatidylglycerol, phosphatidylethanolamine, sphingomyelin, and gangliosides. (*Id.* at 1.) Anti-phospholipid antibodies of the IgM, IgA and IgG families were detected in all of the GBS patients, and none of the controls. (*Id.* at 5.) The authors found that phosphatidylinositol, cardiolipin, phosphatidic acid, and phosphatidylcholine were the main antigens. (*Id.* at 1.) Soon after the administration of γ-globulin IgG antibodies to

phosphatidylcholine, phosphatidylinositol, phosphatidic acid, and cardiolipin were significantly increased—Nakos et al. posit that this increase could be related to the antiphospholipid activity in the infused γ-globulin (in which significant levels of IgG anti-phospholipid antibodies were detected). (*Id.* at 6.) According to Nakos et al., their results demonstrate that there is a more extensive immune reaction occurring in GBS beyond the well-known anti-ganglioside production, though "it is not well understood whether these anti-phospholipid antibodies play a role in the pathogenesis of the polyneuropathy or represent a part of a more extensive immunoreaction that takes place in the GBS." (*Id.* at 6-7.) These results, Dr. Steinman testified, show that in GBS patients "a lot of the anti-phospholipid antibodies are being made, and they include, again, some of the phospholipids that [Ho et al.] studied in the MS patients, the [phosphatidylcholine,] the [phosphatidylserine,] the phosphatidylethanolamine[.]" (Tr. at 170.)

Although these studies are insufficient on their own to establish these autoantibodies as injurious, Dr. Steinman additionally cites his own prior study, Ho et al., which shows in a different context – multiple sclerosis – that phospholipids within myelin can be the target of autoimmune attack. Ho et al. (2012) describes how the autoantibodies against phospholipids contribute to demyelination in multiple sclerosis, and how the autoantibodies target a phosphate group attached to the lipids. (Ho et al., *supra,* Ex. 26, p. 3.) In cases of MS, the immune system attacks the phosphate headgroup—a component of the phospholipids in the myelin. (*Id.* at 9.) The authors explain that "[w]hereas the polar head groups are the lipid components targeted by the antibodies, the fatty acid side chains are the components that mediate the lipids' anti-inflammatory effects." (*Id.*)

Dr. Steinman persuasively explains that Ho et al. demonstrates how the immune system could likewise attack the phosphate headgroup on the phospholipids in the myelin in the context of GBS. (Tr. at 166-70.) In that regard, Dr. Steinman also points to Gilburd to suggest that that paper demonstrates not merely the presence of relevant autoantibodies among the GBS patients, but also provides at least some reason to suspect that these autoantibodies cross react. (Tr. at 178.) During the hearing Dr. Steinman referenced six patients in the study, two of which had antibodies to phosphatidylethanolamine. (*Id.*) One patient also showed antibodies to phosphatidylcholine, which Dr. Steinman explained "which we also saw in the paper by Ho." (*Id.*) Though it was a small study, he explained that Gilburd et al. looked at many of the same molecules, each of which contained phosphoglycerol (cardiolipin, phosphatidylethanolamine, phosphatidylcholine, and phosphatidylserine). (Tr. at 178-79.)

This leaves the critical remaining question of whether this proposed cross-reaction can be linked to the Prevnar 13 vaccine. Dr. Steinman has identified a phosphoglycerol component present in the vaccine that is essential for the Prevnar 13 vaccine to be effective. (Ex. 35, pp. 4-11.) Specifically, the polysaccharides in

pneumococcus that are contained in the Prevnar vaccine "allow for the chemical attachment of capsular polysaccharides via the glycerol moieties" known as phosphoglycerol and phosphocholine (or phosphatidylcholine). (Ex. 35, p. 6.) The glycerophosphate and phosphorylcholine play a critical role in the immunogenicity of Prevnar 13. (*Id.* at 9 (citing Chang et al., *supra,* at Ex. 37; Lugowski and Jennings, *supra,* at Ex. 38; Ohori et al., *supra,* at Ex. 39.) [32] Dr. Steinman explained that the homology to the phosphoglycerol in the vaccine exists at the polar head group for this specific phospholipid, as well as phosphatidylserine. (Tr. at 173-74.) This is significant because the Ho et al. study demonstrates that phospholipids cross-react at the polar headgroup. (Ho et al., *supra,* at Ex. 26, pp. 3, 9.) Moreover, Dr. Steinman points out that Ho et al. shows that among the phospholipid polar headgroups within the myelin tissue that cross-react are those that contain a phosphoglycerol chain. (Tr. at 166-67.)

Dr. Leist disagrees with Dr. Steinman's theory because it is based on "the inaccurate assumption that Prevnar-13 contains phospholipids[33] and that phosphoglycerol and phospholipids can be considered as essentially the same." (Ex. D, p. 4; *see also* Tr. at 257 ("[I] was of the impressions that Dr. Steinman was inferring that Prevnar 13 included phospholipids . . . .").) Dr. Leist testified he "do[es not] think that lipids are a named constituent of the Prevnar 13" vaccine. (Tr. at 257.) Therefore, Dr. Leist stresses that the applicability of the Ho et al. article is "at most tangential." (*Id.*) However, Dr. Steinman has persuasively explained that his theory does not merely rely on phospholipids broadly, but involves molecular mimicry between phosphoglycerol, attached to the phospholipids, and the same phosphate group contained within the polar head of the phospholipids in myelin. (*See* Tr. at 167-68 (Dr. Steinman's description of the phosphate headgroup in the Ho et al. article (*supra,* Ex. 26, at Fig. 2, p. 4.)) Dr. Leist also criticizes Dr. Steinman's reliance on Nakos, noting that authors could not determine whether the antibodies examined were pathophysiologically important or merely a sign of injury. (Tr. at 260-61.) Dr. Steinman acknowledged this conclusion by Nakos et al., though he countered that in light of the findings in Ho et al., the data in Nakos et al. can now be reexamined and reconsidered. (Tr. at 176-78; 212-13.)

Overall, Dr. Leist testified that he agrees the individual steps in Dr. Steinman's theory are logical, though he opines that they don't connect. (Tr. at 264-65.) Yet, this is consistent with petitioner's burden of proof under *Althen* insofar as a petitioner can establish causation through expert opinion and rely on circumstantial evidence so long

[32] The question of how Dr. Steinman established the presence of phosphoglycerol is explained in greater detail in the Special Master's decision in *Koller. See Koller,* 2021 WL 5027947 at *8-10. Dr. Steinman has presented the same theory in both cases.

[33] In his initial report, Dr. Steinman opined that the "trigger is the phospholipids in Prevnar 13[.]" (Ex. 12, p. 18.) However, Dr. Steinman explained that after reviewing the Prevnar 13 vaccine patent he determined that the mimic is phosphoglycerol. (Tr. at 329.) This refinement in Dr. Steinman's opinion is also addressed in greater detail in the *Koller* decision. *Koller,* 2021 WL 5027947 at *16-17.

as the opinion is based on sound and reliable scientific explanation. *Boatmon*, 941 F.3d at 1359-60; *Althen,* 418 F.3d at 1280. "The assessment of whether a proffered theory of causation is 'reputable' can involve assessment of the relevant scientific data. Medical literature and epidemiological evidence must be viewed, however, not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Andreu*, 569 F.3d at 1380. That is, the fact that petitioner's medical theory is novel does not preclude a finding that it is nonetheless preponderantly established based on sound and reliable scientific explanation. *Accord Kottenstette v. Sec'y of Health & Human Servs*., 861 F. App'x 433, 441 (Fed. Cir. 2021); *Knudsen,* 35 F.3d at 548-59. *Accord Althen,* 418 F.3d at 1280 (The Federal Circuit explaining that "[w]hile this case involves the possible link between [tetanus toxoid] vaccination and central nervous system injury, a sequence hitherto unproven in medicine, the purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof of how vaccines affect the human body.")

Although epidemiologic evidence has not detected a statistically significant association between GBS and the Prevnar 13 vaccine, researchers and clinicians remain interested in the possibility of a causal relationship and have reported this in the medical literature through case reports. (Nidhi Ravishankar, *Guillain-Barre Syndrome Following PCV Vaccine,* 4 J. OF NEUROLOGY AND. NEUROSURGERY 134 (2017) (Ex. 66); Chad Conner et al., *13-Valent Pneumococcal Conjugate Vaccine-Induced Guillain-Barre Syndrome,* 158 ALLERGY AND AIRWAY A59 (Ex. 64).)[34] "[C]ase reports 'do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value'…. [but] 'the fact that case reports can by their nature only present indicia of causation does not deprive them of all evidentiary weight.'" *See Paluck v. Sec'y of Health & Human Servs.,* 104 Fed. Cl. 457, 475 (2012) (quoting *Campbell v. Sec'y of Health & Human Servs*., 97 Fed. Cl. 650, 668 (2011), *aff'd* 786 F.3d 1373 (Fed. Cir. 2015)). Standing alone these case reports would be far too weak to support petitioner's claim. In the present case, however, they provide some limited support for the idea that Dr. Steinman, though presenting a novel theory, is not isolated in the relevant medical community in believing there can be a connection between this particular vaccine and injury. *Contra Boatmon*, 941 F.3d at 1360-61 (rejecting petitioner's *Althen* prong one showing in part because "[i]t would be an extension of the Triple Risk Model to include vaccination-induced cytokine activity in the list of

[34] Dr. Steinman acknowledged that "there's a paucity of case reports. There's a couple that have been cited to, [] I would say, [they're] weak evidence…[f]or the bacterium itself" *S. pneumoniae*. (Tr. at 217.) Ravishankar is a case report highlighting a woman who developed severe respiratory failure from GBS after receiving a PCV13 vaccine in January 2015 and a second dose of PPSV23 in August 2015. (Ravishankar, *supra,* at Ex. 66, p. 1.) Dr. Steinman testified further that Ravishankar has a "tarnished history" because the author published the article in two different places, which he explained affects its "academic purity, but I don't think it breaks any laws." (Tr. at 217-18.) Dr. Steinman also acknowledged that the case report from Conner et al. was not a paper, but instead a medical student presentation. (Tr. at 218-19.)

exogenous stressors as Dr. Miller proposes. Dr. Miller himself concedes that, outside of Vaccine Act litigation, vaccinations have not been identified as an exogenous stressor for SIDS.")

In contrast, respondent cites Baxter et al. (2013), a large retrospective study assessing the risk of GBS following the Pneumovax 23 vaccine – notably, a different vaccine.[35] (Baxter, *supra,* at Ex. A, Tab. 1, pp. 1-2.) The authors did not find any association between Pneumovax and the development of GBS within six weeks following vaccination. (*Id.* at 7.) Haber et al. (2016) assessed adverse events following Prevnar-13 vaccination, as recorded in the Vaccine Adverse Event Reporting System ("VAERS"). (Haber et al., *supra,* at Ex. 32, pp. 1-2.) That study verified 11 GBS reports, with a reporting rate of 0.7 cases per million doses of the vaccine among adults (above the age of 19). (*Id.* at 5.) The authors did not identify any new safety signals when reviewing the VAERS reports. (*Id.*) (Petitioner acknowledges the overall Haber findings, but stresses the 11 verified cases of post-Prevnar GBS as, in effect, case reports. (Tr. at 216).)

Petitioners in the Vaccine Program are not required to present epidemiological evidence to establish their causation burden under *Althen. Moberly v. Sec'y of Health & Human Servs*., 592 F.3d 1315, 1325 (Fed. Cir. 2010).[36] On balance, neither Baxter et al. nor Haber et al. significantly undermines petitioner's theory. Baxter et al. found no increased risk of GBS following vaccination, though the study involved a different, unconjugated version of the vaccine. (Baxter et al., *supra,* at Ex. A, Tab. 1.) Although the vaccines may be related, Dr. Steinman has supported his theory with specific investigation into the immunogenicity of components of the Prevnar-13 vaccine specifically. Haber et al. found "no disproportionate reporting for GBS," though as other special masters have observed, articles relying on VAERS data are subject to significant limitations.[37] Specifically, the authors of the Haber et al. study caution that

[35] The pneumococcal conjugate vaccine (PCV13 or Prevnar13) "includes purified capsular polysaccharide of 13 serotypes of *Streptococcus pneumoniae* (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F, 18C, and 23F) conjugated to a nontoxic variant of diphtheria toxin known as CRM197." While the pneumococcal polysaccharide vaccine (PPSV23 or Pneumovax23) "includes purified preparations of pneumococcal capsular polysaccharide. PPSV23 contains polysaccharide antigen from 23 types of pneumococcal bacteria." *Types and Composition of Pneumococcal Vaccines,* CDC, https://www.cdc.gov/vaccines/vpd/pneumo/hcp/about-vaccine.html (last visited Jan. 11, 2022).

[36] However, "[n]othing in *Althen* or *Capizzano* requires the Special Master to ignore probative epidemiological evidence that undermines petitioner's theory." *D'Tiole v. Sec'y of Health & Human Servs.*, 726 F. App'x 809, 811 (citing *Andreu*, 569 F.3d at 1379 ("Although *Althen* and *Capizzano* make clear that a claimant need not produce medical literature or epidemiological evidence to establish causation under the Vaccine Act, *where such evidence is submitted*, the Special Master can consider it in reaching an informed judgment as to whether a particular vaccination likely caused a particular injury." (emphasis added)); *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148-49 (Fed. Cir. 1992) (considering negative epidemiological studies).

[37] *See Bender v. Sec'y of Health & Human Servs.,* No. 11-693V, 2018 WL 3679637, at *31 (Fed. Cl. Spec. Mstr. July 2, 2018) ("[b]ecause it is a passive reporting system, VAERS database findings … cannot be reasonably interpreted to suggest causation. For this reason, special masters do not typically

"[i]t is important to the note the limitations of VAERS, which may include underreporting, varying quality of reports (for example reports may lack details, contain errors or be missing information), and the lack of an unvaccinated comparison group." (Haber et al., *supra,* Ex. 32, p. 5.)

Furthermore, petitioner's *Althen* prong one theory is generally consistent with this Program's overall understanding of GBS and its causes. That is, as explained above, it is well established that GBS represents an autoimmune condition, likely resulting from molecular mimicry, but with multiple suspected triggers many of which do not have definitively identified homologies. Moreover, while molecular mimicry is most often discussed in the context of proteins and amino acids, the common example of molecular mimicry in GBS is with *c. jejuni,* which is a molecular mimic to ganglioside sugar structures within myelin. *See, e.g.*, *Chinea v. Sec'y of Health & Human Servs.*, No. 15-095V, 2019 WL 1873322 (Fed. Cl. Spec. Mstr. Mar. 15, 2019); *Stitt v. Sec'y of Health & Human Servs.,* No. 09-653V, 2013 WL 3356791 (Fed. Cl. Spec. Mstr. May 31, 2013). And, in any event, prior cases have found that GBS can be causally linked to vaccines other than the flu vaccine via molecular mimicry even in the absence of direct proof of homology and cross-reaction. *See, e.g., Salmins v. Secretary of Health & Human Servs.,* 11-140V, 2014 WL 1569478 at *14 (Fed. Cl. Spec. Mstr. Mar. 31, 2014).

Here, Dr. Steinman does purport to demonstrate a homology between the phosphoglycerol within the Prevnar vaccine and the phosphate head group attached to the phospholipids in myelin. Moreover, in relying on Ho, et al, he further purports to demonstrate cross-reaction to myelin in the context of a different, though also demyelinating, condition. His extrapolation occurs in relying on Gilburd et al., Ho et al., and Nakos et al, to circumstantially demonstrate how this proposed homology and cross-reaction can be pathophysiologically relevant in the specific context of post-Prevnar GBS, relying primarily on the fact that relevant autoantibodies have been detected among those suffering GBS. Especially given the overall understanding of GBS and its causes, this extrapolation is sound and reliable, as well as consistent with petitioner's preponderant burden of proof.

2. CRM197

Dr. Steinman's second proposed molecular mimic concerns a protein component of the vaccine called CRM197, which is used to conjugate the pneumococcal polysaccharides in the Prevnar 13 vaccine to an immunogenic protein carrier, and Contactin-1, an axonal adhesion molecule that is targeted in some cases of GBS.[38]

afford great weight to VAERS data in determining causation") (citing *Analla v. Sec'y of Health & Human Servs.,* 70 Fed. Cl. 552, 558 (2006) ("the Court [of Federal Claims] uniformly has upheld the Chief Special Master's concerns about the reliability of VAERS data")).

[38] Dr. Leist likewise agrees that antibodies to contactin-1 have been described in patients with GBS and CIDP. (Ex. D, p. 4.) Citing a study by Raju et al., Dr. Steinman observes that humans have been shown to mount T cell responses to regions of the diphtheria molecule: WEQAKLSVE and EYMAQACAGNRVRR. (Ex. 50, p. 5 (citing Raju et al., *supra*, at Ex. 52.).) According to Dr. Steinman,

(Ex. 35, p. 11 (citing Fehmi et al, *supra,* at Ex. 41; Manso et al., *supra,* at Ex. 42; Miura et al., *supra,* at Ex. 43.) On this record, Dr. Steinman's CRM197 theory of molecular mimicry is much less developed than his theory pertaining to phosphoglycerol. Because I have concluded that petitioner has satisfied *Althen* prong one based on the phosphoglycerol theory, I do not reach the question of whether the theory that CRM197 can cross react with Contactin-1 to cause GBS could potentially be preponderantly established.

b. *Althen* prongs two and three

Having shown that the Prevnar-13 vaccine can cause GBS, petitioner must also establish that it did cause GBS in this specific case. *Pafford v. Sec'y of Health & Human Servs*., 451 F.3d 1352, 1356 (Fed. Cir. 2006). This latter aspect of petitioner's *prima facie* showing is generally broken down into two further questions pursuant to *Althen* prongs two and three. The second *Althen* prong requires proof of a logical sequence of cause and effect usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Human Servs*., 956 F.2d 1144, 1148 (Fed. Cir. 1992). The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs*., 539 F.3d 1347, 1352 (Fed. Cir. 2008).

In this case, petitioner's ultimate diagnosis is undisputed. Petitioner's treating physicians and both experts agree that petitioner suffered from GBS. (Ex. 6, p. 225; Ex. 12, p. 5; Ex. A, p. 5.) However, determining the onset of petitioner's GBS is complicated by the fact that during the relevant period she appears to have been suffering several complaints or conditions that may have obscured the onset of what was ultimately diagnosed as GBS, including: a prolonged cough, suspected carpal tunnel syndrome, severe back pain, and delirium during her hospitalization. Given petitioner's complex presentation, the parties disagree as to the initial onset of petitioner's GBS as well as

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the results of this study differ in only one amino acid from CRM, which provides "*actual detailed data* for molecular mimics in the CRM in the Prevnar 13 vaccine received by petitioner." (*Id.*) However, Dr. Leist criticizes Dr. Steinman's reliance on Raju et al. Dr. Leist testified that the T cell clones that were utilized in the study were derived from seven healthy humans of different histocompatibility complex haplotypes. (Tr. at 261-62.) According to Dr. Leist, the fact that these healthy individuals developed T cell responses goes to show that simply identifying sequence homologies doesn't necessarily indicate that the homologies are pathophysiologically important for susceptibility to the disease. (Tr. at 262.) Dr. Leist points out that CRM is a protein commonly used in other vaccines as well. (Tr. at 263-64.) "[I]f CRM would be a major source of cross-reactive immune response of this pathophysiological importance that leads to GBS," Dr. Leist suggests that "the conglomeration of CRM-containing vaccines would have stood out as causing th[is] injury." (Tr. at 264.)

her time-course to the nadir of her condition. Both of these issues affect whether petitioner's GBS can fairly be considered to be post-vaccinal relative to her Prevnar vaccination. Accordingly, *Althen* prongs two and three intersect in that the medical understanding of the evolution of petitioner's condition pre-diagnosis informs the timing of onset, which then informs both the logical sequence of cause and effect and the temporal relationship to vaccination.

With respect to the appropriate timing for a post-vaccinal GBS, the parties have filed two seminal papers by Schonberger and Langmuir respectively addressing the timing of onset of GBS following the 1976 swine flu vaccine. (Ex. 12 pp. 18-20; Ex. A, p. 6; Tr. at 147; 284.) Both experts utilize these papers as a reasonable, albeit imperfect, proxy for assessing the appropriate timing for GBS to be attributable to the pneumococcal vaccine at issue in this case. (*Id.*) Schonberger is an epidemiologic study evaluating over 1,000 individuals who were diagnosed with GBS in the 1976-77 timeframe. (Schonberger, *supra,* at Ex. 31.) Schonberger observed that the expected peak onset occurred 16 to 17 days post-vaccination (among the population of cases considered), though the majority of all GBS cases considered in the chart began within four weeks. (Schonberger, *supra,* Ex. 31, pp. 6-7.) However, Schonberger observed a statistically significant increase in reported cases as far out as nine to ten weeks post-vaccination.[39] (Schonberger, *supra,* at Ex. 31, pp. 1, 9.) While Schonberger et al. does not cover Prevnar 13, Dr. Steinman suggests that it serves as a "surrogate in this case." (Ex. 12, p. 20.) Dr. Leist explained, however, that the Schonberger article was re-examined by Langmuir et al. (Tr. at 259.) Dr. Leist testified that Langmuir et al. indicates that an association between the then-marketed vaccines and GBS could be observed "between – up to 42 days later." (Tr. at 284; Langmuir et al., *supra,* Ex. A, Tab. 2, at p. 865.) While Dr. Leist is correct that Langmuir expressed preference for the 42-day onset period, the authors of Langmuir et al. reported that their results support an association "for at least six [weeks] and may have continued at a low level of increased risk as long as eight [weeks], but not longer." (Langmuir et al., *supra,* Ex. A, Tab. 2, at p. 25.) Dr. Steinman is therefore persuasive in placing the outermost medically appropriate onset date for vaccine-caused GBS at eight weeks, or 56 days, post-vaccination. (Tr. at 146.)

Here, petitioner received her Prevnar 13 vaccine on January 6, 2015. (Ex. 2.) Thus, the 56-day timeline proposed by Dr. Steinman would require onset of petitioner's GBS to occur no later than about March 3, 2015, in order for it to be considered causally-related to her prior Prevnar-13 vaccination.[40] During that period, petitioner

[39] Dr. Steinman testified that Figure 6 in Schonberger shows the expected incidence "remain[s] high, above that cross-hatched area, at eight weeks, and then they diminish a little more at nine and ten weeks, and then they finally blip down to the baseline at eleven weeks." (Tr. at 144;citing Schonberger et al., *supra,* Ex. 31, p. 9.) This, Dr. Steinman concludes, leads him to place "a cutoff somewhere around the end of week eight." (Tr. at 144-45.)

[40] Note, however, that the Federal Circuit holding in *Paluck v. Secretary of Health & Human Services,* cautions against setting "hard and fast deadline[s]" for onset. *See*, 786 F.3d 1373, 1383-84 (Fed. Cir. 2015) (stating that "[t]he special master further erred in setting a hard and fast deadline" for onset and noting that the medical literature filed in the case "do not purport to establish any definitive timeframe for

sought care on multiple occasions, primarily at urgent care, beginning on January 21, 2015. She was later hospitalized beginning on March 5, 2015. Flaccid paralysis was confirmed by no later than March 13, 2015, and she was ultimately diagnosed with GBS on March 21, 2015. (Ex. 6, pp. 391, 226)

Dr. Steinman proposes that petitioner's onset of neuroinflammation began January 21, 2015, when petitioner reported tingling along with her symptoms of sneezing, congestion, cough, shortness of breath, and wheezing. (Ex. 12, p. 4 (citing Ex. 3, p. 1.)) Then on February 26, 2015 petitioner additionally reported weakness along with her ongoing tingling and constitutional symptoms of chills, fatigue, sweats, cough, shortness of breath, and wheezing. (*Id.* at p. 4 (citing Ex. 3, p. 19.) According to Dr. Steinman, the tingling and weakness "are more likely than not indications of GBS." (Ex. 12, p. 4.) Dr. Steinman observes that later, in March 2015, petitioner was diagnosed with subacute onset flaccid paraparesis, acute peripheral neuropathy, and Bell's palsy – all indicative of GBS. (Ex. 12, p. 5.) Thus, Dr. Steinman opines that the onset of petitioner's inflammatory neuropathy began with tingling on or about January 21, 2015, or fifteen days after she received the Prevnar 13 immunization on January 6, 2015 – though he notes that petitioner's diagnosis of GBS occurred nine weeks later. (*Id.*)

While petitioner's earliest reports of tingling are potentially consistent with GBS, they do not in themselves provide preponderant evidence supporting Dr. Steinman's opinion that the onset of petitioner's neuroinflammation began January 21, 2015. Petitioner's medical records do not elaborate on the nature of the reported tingling, including when the tingling started or whether it was continuous or intermittent, but do suggest there were other aggravating factors (e.g., petitioner's work in decorating cakes). (*See* Ex. A, p. 6.) Specifically, a record from February 26, 2015 by Dr. Daskalos at Eugene/Thurston Urgent Care states: "[u]nrelated to her present complaints-patient having symptoms of carpal tunnel syndrome-she[] is a cake decorator for Albertson's-she does plan to retire in less than one year." (Ex. 3, p. 19.) Two days later, February 28, 2015, PA Kerry Harrington at Eugene Thurston Urgent Care also observed that petitioner "ha[s] history of carpal tunnel syndrome."[41] (Ex. 3, p. 25.) Petitioner also appears to have suffered from arthritis prior to her Prevnar 13 vaccination (Ex. 6, p. 14), which Dr. Leist testified could be another explanation for intermittent numbness and tingling in the hands. (Tr. at 69-70 ("I have like swollen knuckles…[j]ust working in a bakery, you know, using my hands and stuff, I had swollen knuckles"); *see also* Ex. 3, p. 7; Ex. 5, p. 2 (petitioner diagnosed with climacteric arthritis

onset of clinical symptoms."). Notwithstanding Langmuir's disagreement, there is some limited, albeit not preponderant, evidence from Schonberger to suggest onset could potentially exceed eight weeks.

[41] Relevant to this specific notation, petitioner denied ever having been diagnosed with carpal tunnel syndrome. (Tr. at 33.) Upon my review of the record, petitioner's medical records do not contain any *diagnosis* of carpal tunnel syndrome. However, a careful reading of Dr. Daskalos' record suggests that he recorded an impression of petitioner's reported symptoms both as being consistent with carpal tunnel syndrome and as being unrelated to her other complaints. This impression stands on its own terms irrespective of any previously established carpal tunnel syndrome diagnosis.

of the hand[42].) Moreover, if petitioner experienced her first symptoms of GBS by January 21, 2015, and did not reach the nadir of her condition until Mid-March, that would be an unusually prolonged period from first manifestation to nadir of GBS. (Burns, *supra,* at Ex. D, Tab. 1. p. 2.)

However, in contrast to these earlier records, on March 1, 2015, petitioner was noted to have tingling that was reportedly "constant" and "severe" that began on February 28, 2015. (Ex. 3, p. 36.) Additionally, when petitioner was ultimately diagnosed with GBS by Sacred Heart Medical Center, ongoing neuropathic hand and foot pain was identified as a symptom relevant to her GBS diagnosis. (Ex. 6, p. 225-27.) The first report of hand and leg *pain* occurred at petitioner's March 2, 2015 emergency department encounter, shortly after she first reported onset of severe and constant tingling. (Ex. 4, p. 58.) Thus, although petitioner's initial reports of tingling are themselves inconclusive, if neuropathic pain was the first symptom of petitioner's GBS, it was likely evidenced in the medical records by no later than March 2, 2015, which falls within 56-days of her vaccination.

In contrast, Dr. Leist opines that the onset of petitioner's GBS occurred more than sixty days post-vaccination based on the onset of her lower extremity weakness. (Ex. A, p. 5.) Dr. Leist notes that petitioner was admitted for observation for her altered mental state due to narcotic pain medication (for severe low back pain) on March 5, 2012, but no neurological deficits were appreciated at the time. (*Id.* at 5 (citing Ex. 4, p. 87.)) She was scheduled to be discharged March 7, 2015 when she had two bowel movements with dark blood and clots, which prompted further evaluation. (*Id.* (citing Ex. 4, pp. 72-75.)) Dr. Leist observes that petitioner had a brain CT scan on March 12, 2015, after developing right facial weakness. (*Id.* (citing Ex. 4, p. 83; Ex. 4, pp. 144-45.)) Reports from March 14, 2015 indicate that petitioner suffered "sudden onset [of] r[ight] side lower facial weakness approx[imately] 3 days ago after the colonoscopy [performed on March 8, 2015,] then developed upper r[ight] side facial/eye weakness subsequently." (*Id.* (citing Ex. 6, p. 192.)) Thus, Dr. Leist opines that petitioner developed acute facial and lower extremity weakness on or about March 11 or 12, 2015 – more than sixty days after the administration of petitioner's Prevnar 13 vaccine. (*Id.*)

The idea that petitioner's weakness heralded her GBS harmonizes petitioner's own clinical course with the diagnostic standards in that extremity weakness is a key diagnostic aspect of GBS[43] and onset of petitioner's weakness is consistent with the

[42] "[A] condition sometimes seen in women at menopause, due to ovarian hormonal deficiency and marked by pain in the small joints, shoulders, elbows, or knees; called also climacteric a." *Menopausal arthritis, ,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=58975 (last visited Dec. 20, 2021.)

[43] The Brighton criteria, used for clinical case definitions of GBS, includes both bilateral and flaccid weakness of the limbs and decreased or absent reflexes at levels one, two and three as important diagnostic considerations. (Daniel A. Salmon et al., Association between Guillain-Barré syndrome and influenza A (H1N1) 2009 monovalent inactivated vaccines in the USA: a meta-analysis, 381 LANCET 1461 (2013) (Ex. 70, p. 3); Tr. at 244.) Dr. Steinman explained that the Brighton group and the American Academy of neurology have created criteria for diagnosing GBS. (Tr. at 153.) However, these criteria were designed to be used in studies so that "a group of more homogenous cases are done." (*Id.*)

understanding that GBS develops acutely, typically with no more than a four-week period between initial onset and nadir. (Burns, *supra*, Ex. D, Tab 1, p. 2.) Importantly, however, even accepting Dr. Leist's opinion that extremity weakness should be the first sign of petitioner's GBS, Dr. Leist is not persuasive in interpreting the medical records as definitively demonstrating full strength until at least March 11, 2015. Instead, Dr. Steinman is persuasive in noting as part of his overall opinion that extremity weakness was reported in the medical record by no later than late February 2015. (Ex. 50, p. 1 (citing Ex. 3, p. 19.))

Dr. Leist is correct that petitioner was evaluated by Dr. Marriott as having full strength in the Mercy emergency department upon admission on March 5, 2015.[44] (Tr. at 269; *see* Ex. 4, pp. 87-88 (petitioner has positive straight leg raise with both legs and full strength).) However, the record as a whole presents conflicting reports regarding the onset of petitioner's "weakness." Petitioner's first report of weakness appears to be on February 26, 2015, when petitioner returned for a follow-up appointment with Dr. Daskalos—complaining of chills, fatigue, sweats, tingling, shortness of breath,

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Whether, or to what extent, this limits the applicability of the Brighton criteria to petitioner's diagnosis in this case, Dr. Steinman did not say. (*See id.*) However, he maintained that "the loss of reflexes, the symmetry, the motor and sensory findings are all kind of cornerstones of a diagnosis of Guillain Barre." (Tr. at 153-54.) The Brighton criteria are frequently referenced in the Program in cases of GBS regarding diagnosis. *See Swaiss v. Sec'y of Health & Human Servs.,* No. 15-286V, 2019 WL 6520791, at *13 (Fed. Cl. Spec. Mstr. Nov. 4, 2019) ("[t]he Brighton group developed its criteria for the purpose of researching whether different vaccines might cause or contribute to GBS"); *Lapierre v. Sec'y of Health & Human Servs.*, No. 17-227V, 2019 WL 6490730, at *8 n.12 (Fed. Cl. Spec. Mstr. Oct. 18, 2019); *Harrington v. Sec'y of Health & Human Servs.*, No. 15-752V, 2018 WL 1125831, at *5 (Fed. Cl. Spec. Mstr. Jan. 19, 2018), *mot. for review den'd* 139 Fed. Cl. 465 (2018).

[44] There may be some reason to give less weight to this emergency room assessment as it would pertain to signs of GBS. *Tenneson v. Sec'y of Health & Human Servs.*, 142 Fed. Cl. 329, 340 (2019) (observing that "the purpose of an emergency room visit is to receive emergency treatment, not a comprehensive health check-up"). Importantly, it is an initial emergency encounter that was focused on a history of intractable back pain that was noted to have broken through multiple types of pain medication. (Ex. 4, pp. 87-88.) For example, at the time of this evaluation, petitioner reported numbness in her hands and her feet. (Ex. 4, p. 87.) In fact, this symptom was noted to be the impetus for seeking treatment at the emergency department. (*Id.*) This symptom was also documented both in petitioner's earlier treatment records and her later treatment records. (Ex. 3, p. 25 (2/28/15); Ex. 3, p. 36 (3/1/15); Ex. 5, p. 12 (3/3/15; Ex. 9, p. 9 (7/9/2015); Ex. 9, p. 1 (4/19/2016).) In fact, her discharge summary from the same hospital confirms this symptom predated her weakness. (Ex. 4, p. 83.) Yet, Dr. Marriott documented an inability to appreciate numbness or tingling on exam and ultimately petitioner's back pain was the reason for admission. (*Id.* at 88.) And, indeed, the positive straight leg raise recorded by Dr. Marriott is a test intended to detect lower back pain. *See Straight-leg—raising test,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=112992 (last visited Jan. 5, 2022). Additionally, to the extent the examination would have required petitioner's cooperation, she ultimately was assessed with delirium in the course of this same hospitalization and her altered mental state was noticed on the date of admission. (Ex. 4, p. 79.) Also of note, the primary reason petitioner was discharged from Mercy Hospital to another hospital on March 13, 2015 was because Mercy Hospital lacked inpatient neurology consultation services. (Ex. 4, p. 83.) Whereas Dr. Marriott noted a positive straight leg raise, subsequent notations regarding neurologic evaluation at Mercy Hospital are less explicit. For example, Dr. Tufail noted only the absence of focal deficits without describing his neurologic examination. (Ex. 4, p. 80.)

wheezing, and weakness. (Ex. 3, p. 19.) At that time, Dr. Daskalos added weakness, not merely as a constitutional symptom, but as a neurologic sign under his review of systems. (*Id.*) On March 2, 2015 petitioner was seen by PA Harrington in Urgent Care, complaining of similar symptoms and again noted weakness. (Ex. 3, p. 42.) Yet, later that day, petitioner saw Dr. Rickman reporting pain "mostly about her left upper back" that spread "all over her back" with "some pain in her hands and legs," though she reportedly "[had] no leg numbness, tingling, or weakness." (Ex. 4, p. 58.)

It should also be noted that the Mercy hospital records are in themselves inconsistent. While Dr. Marriott documented normal strength upon initial admission, petitioner's discharge record documents that petitioner's weakness was evident upon her arrival at the emergency department and was evidenced by a collapsing episode.[45] (*Compare* Ex. 4, pp. 87-88, *and* Ex. 4, pp. 82-83, 177.) Moreover, whereas the discharge summary documents the onset of petitioner's Bell's palsy as occurring during hospitalization, it does not separately identify an onset of extremity weakness as occurring during the course of hospitalization even though that weakness was confirmed at the time of discharge. (Ex. 4, pp. 82-83.) When petitioner was subsequently admitted to Sacred Heart Medical Center on March 13, 2015, with a chief complaint of weakness, her neurological evaluation noted that petitioner was presenting "from Mercy Hospital after an approximately 6-week course of increasing weakness." (Ex. 6, p. 227.) At that time petitioner reported that onset of her weakness occurred approximately two weeks prior to her hospitalization at Mercy Hospital. (*Id.*) Thus, this record places onset of petitioner's weakness sometime in February of 2015.

In reaching his overall assessment of the medical records, Dr. Leist relied heavily during the hearing on a record dated March 9, 2015, which he interpreted as showing petitioner "moving all four extremities." (Tr. at 238.) The inpatient consult dated March 9, 2015 at Mercy Medical Center states in part that petitioner "wanted to get out of her recliner and wanted to go upstairs and trying to get out of the Posey vest restraint, occasionally trying to pull her IV or Foley." (Ex. 4, p. 165.) Petitioner also became agitated, "slapping at the nurse that she wanted out of the chair[.]" (*Id.*) Dr. Leist testified that petitioner:

> wanted to get out of bed. She wanted to go to the chair. Obviously she was confused. So my interpretation of this one as it pertains to the case at hand is the fact that she was moving her extremities on that date, meaning that the later documented weakness in the lower extremities was not present on March 9, 2015.

[45] Mr. Pierson likewise recalled that petitioner fell at some point during her hospitalization at Mercy, although he did not indicate when this occurred. (Tr. 105-08.) However, to the extent petitioner may have been weak at the time of admission, Mr. Pierson did not recall her having difficulty walking at that time. (*Id.*)

(Tr. at 238 (citing Ex. 4, p. 165.)) However, contrary to Dr. Leist's interpretation, this record does not actually indicate petitioner was moving all four extremities. (*See id.*) Apart from her "wanting" to leave, petitioner is described only as pulling and slapping while in a restraint; nothing in this record suggests petitioner was moving her lower extremities. Nor, for that matter, are those experiencing weakness necessarily entirely incapable of moving their extremities.[46] Dr. Leist acknowledged that GBS presents as ascending weakness and that it is not necessary for a person to be unable to move all four extremities in order to be diagnosed with an onset of GBS.[47] (Tr. at 268.) This record also raises the question of whether the fact of petitioner being restrained due to her delirium and confusion may have impeded the opportunity for hospital staff to observe increasing lower extremity weakness based on natural movement.

Dr. Leist also disputes Dr. Steinman's interpretation of petitioner's onset of paralysis based on the monophasic nature of GBS. Dr. Leist testified that "[t]he rapid onset of flaccid paralysis is one of the cardinal features of Guillain-Barre syndrome." (Tr. at 237.) A *rapid* onset of flaccid paralysis, Dr. Leist testified, can be characterized as paralysis occurring over two weeks in 50 percent of cases and within four weeks in 90 percent of cases. (Tr. at 243 (citing Burns, *supra,* at Ex. D, Tab. 1, p. 2.) In that regard, both experts in this case relied on petitioner's Mercy Hospital discharge summary, specifically the diagnosis of "subacute flaccid paresis." (Ex. 4, p. 82.) However, the experts offered opposing interpretations of the term "subacute." (Tr. at 306, 327).

Dr. Leist testified that "subacute can be a day or two or so." (Tr. at 306.) Petitioner's discharge summary was authored on March 13, 2015. (*Id.;* Ex. 4, p. 83.) Therefore, Dr. Leist estimates that petitioner's onset was likely on or about March 12, 2015—according to his definition of subacute. (Tr. at 236, 243.) In contrast, Dr. Steinman testified that while "subacute is not chronic," subacute can be "a few weeks," though he admitted that "I don't think it has a formal definition." (Tr. at 327.) "A few weeks" prior to petitioner's March 13, 2015 discharge would be consistent with the first reports of weakness recorded on February 26, 2015, by Dr. Daskalos. (Ex. 3, p. 19.)

There are several reasons why Dr. Leist is less persuasive on this point. According to Dr. Leist, his interpretation is also supported by his interpretation the record as showing that "on [March 9], [petitioner] was not flaccid" because she was able to move all four extremities. (Tr. at 306.) However, for the reasons discussed above, I did not find that interpretation persuasive. Additionally, Dr. Leist's own reliance materials indicate that in the context of GBS "acute" or "rapid" onset is considered to occur over the course of two to four weeks, suggesting that Dr. Leist's interpretation of

[46] The fact that she was in a restraint to keep her from leaving does suggest at least some concern that she had some degree of mobility.

[47] Dr. Balm later described petitioner's pattern of weakness as "atypical," though he felt "confident [GBS] is the correct diagnosis." (Ex. 6, p. 391.)

subacute is overly stringent. (Burns, *supra*, at Ex. D, Tab 1, p. 2.) I asked Dr. Leist, given the expected course of GBS and given that petitioner experienced her severest weakness in mid-March, whether it was reasonable to place her nascent symptoms of weakness as occurring as early as mid-February. (Tr. at 245.) Dr. Leist did not discount this possibility.[48] (*See id.*) Furthermore, with regard to this specific record, use of the term "subacute" contrasts with several of petitioner's other discharge diagnoses, which characterize conditions arising during the course of her hospitalization, including bell's palsy and delirium, as "acute." (Ex. 4, p. 82.)

Ultimately, Dr. Leist persuasively testified that GBS exhibits a clear crescendo, as opposed to a variable course. (*See* Tr. at 246.) Dr. Steinman, however, explained that in petitioner's case, "the crescendo was very low, and it began to intensify about 30 days before the 5th of March, and then it became deafeningly loud at the end of February and the first few days of March." (Tr. at 326.) Ultimately, although I am not persuaded by Dr. Steinman's reliance on earliest notations of tingling, I do find that it is more likely than not, based on consideration of the medical records as a whole, that petitioner suffered nascent symptoms of weakness by no later than February 26, 2015, neuropathic pain by no later than March 2, 2015, and thereafter demonstrated a steady decline culminating in her hospitalization with frank weakness and absent reflexes documented by the time of discharge from Mercy Hospital on March 13, 2015.

This is also consistent with the fact witness testimony. Although petitioner struggled at work for a period of time, especially with the finer hand work of cake decorating, she specifically testified that it was her weakness and pain in her hands *and feet* that ultimately caused her to abruptly stop working. (Tr. 31.) The record evidence, including petitioner's final pay stub and witness testimony, indicates this occurred on or around February 25, 2015. (Tr. 29-31 (discussing Ex. 11.) Her medical records confirm that her absence from work was discussed with her doctor on February 28, 2015, as part of her plan of care. (Ex. 3, p. 28.)

Thus, while petitioner was not in perfect health in the months leading up to her GBS diagnosis, the record as a whole reflects a clear change in her health beginning not later than late February of 2015 with onset of symptoms of weakness and neuropathic pain consistent with her subsequently diagnosed GBS. This places the initial onset of GBS within the 56-day post-vaccination onset timeline identified by Dr. Steinman, which I find establishes a proximate temporal relationship between petitioner's January 6, 2015 Prevnar 13 vaccination and her GBS.

None of petitioner's treating physicians attributed her GBS to her Prevnar 13 vaccination, though some attributed her diagnosis to a flu vaccine and warned against

[48] Dr. Leist pointed to Salmon et al., which describes a "monophasic character of the illness," which he explained "doesn't indicate a plateauing of symptoms, arresting at a certain level and then progressing." (Tr. at 245-46.) However, that point speaks to Dr. Steinman's assessment of onset beginning over a longer course with tingling in January of 2015 and also assumes Dr. Leist's own interpretation of the medical records subsequent to February 26, 2015, is the best.

future vaccinations generally.[49] (Ex. Ex. 8, pp. 3-6.) The treating physicians did not otherwise identify any cause for petitioner's GBS at all. (*See* Ex. 6, pp. 225-27, 391.) Thus, in addition to temporality, petitioner stresses that the exclusion of alternative etiologies establishes a logical sequence of cause and effect under *Althen* prong two. (ECF No. 67, pp. 23-26.) Respondent, however, contends that an infection beginning about February 26, 2015, is a more likely cause of petitioner's GBS. (ECF No. 65, p. 13.)

The records indicate that petitioner complained of chills, sweats, fatigue and left thoracic pain on February 26, 2015, which progressed to 8/10 mid back pain made worse with movement and breathing, and fatigue and sweats by February 28, 2015. (Ex. 3, pp. 19, 25.)) According to Dr. Leist, "[c]hills and sweats suggest [the] presence of an infectious process and [petitioner] was started on cefdinir [in] February."[50] (Ex. A, p. 6.) Notably, however, despite these subjective reports, petitioner did not have a fever. (Ex. 3, p. 20 (vitals recording temperature of 97.7°F).) Importantly, however, Dr. Leist's opinion that these symptoms may be indicative of an underlying cause of petitioner's GBS is premised on his identification of GBS onset occurring on March 11, 2015, or about two weeks following petitioner's chills and sweats. (Ex A, pp. 6-7.) As explained above, however, the medical records when viewed as a whole preponderate in favor of neurologic weakness consistent with GBS occurring as early as February 26, 2015, contemporaneous to petitioner's report of these constitutional symptoms, with evidence of neuropathy occurring by no later than March 2, 2015.

Petitioner's records further indicate that she was diagnosed with "bronchopneumonia organism unspecified" on or about January 21, 2015. (Ex. 3, pp. 1-3.) In that regard, Dr. Leist testified that while the petitioner's chest x-ray was negative, he could not "exclude a viral illness." (Tr. at 282.) However, Dr. Steinman disagreed

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[49] The possible causal relationship between a flu vaccination and petitioner's GBS, as contemplated by Drs. Balm and Stowell is unsurprising. As discussed above, the association between the flu vaccine and GBS has been well established in this Program. *See, e.g.*, *Chinea v. Sec'y of Health & Human Servs.*, No. 15-095V, 2019 WL 1873322 (Fed. Cl. Spec. Mstr. Mar. 15, 2019); *Strong v. Sec'y of Health & Human Servs.*, No. 15-1108V, 2018 WL 1125666 (Fed. Cl. Spec. Mstr. Jan. 12, 2018); *Stitt v. Sec'y of Health & Human Servs.,* No. 09-653V, 2013 WL 3356791 (Fed. Cl. Spec. Mstr. May 31, 2013); *Stewart v. Sec'y of Health & Human Servs.*, No. 06-777V, 2011 WL 3241585, at *16 (Fed. Cl. Spec. Mstr. July 8, 2011); *see also Barone v. Sec'y of Health & Human Servs.,* No. 11-707V, 2014 WL 6834557 (Fed. Cl. Spec. Mstr. Nov. 12, 2014). Petitioner's records indicate that she received a Fluzone vaccine on September 30, 2014 and the Prevnar 13 vaccine on January 6, 2015. (Ex. 2.) There is no mention of an influenza vaccine in January. (*See id.*) Given that the association between the flu vaccine and GBS is far better known generally, the fact that some physicians attributed petitioner's GBS to the more remote flu vaccine neither adds nor detracts significantly from petitioner's *Althen* prong two showing.

[50] Petitioner was prescribed Omnicef on February 28, 2015. (Ex. 3, p. 28.) Omnicef is a trademark name for a preparation of cefdinir. *Omnicef,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=13359 (last visited Dec. 22, 2021.) Cefdinir is a "semisynthetic, third-generation cephalosporin effective against a wide range of bacteria, used in the treatment of otitis media, bronchitis, pharyngitis, tonsilitis, sinusitis, bacterial pneumonia, and skin and soft tissue infections; administered orally." *Cefdinir,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=13359 (last visited Dec. 22, 2021.)

that petitioner's medical records supported a diagnosis of bronchopneumonia. (Tr. at 141.) Dr. Steinman testified that determining whether or not petitioner's cough was pneumonia, and whether an infection could have alternatively caused her GBS, is difficult to interpret without a microbial diagnosis. (Tr. at 135-36.) In that regard, further testing showed that petitioner was negative for mycoplasma pneumonia.[51] (Tr. at 137; Ex. 6, 223.) Dr. Steinman also stressed that petitioner tested negative for several other possible infectious causes of GBS (Tr. 137-40): Campylobacter (Ex. 6, p 212), c. difficile (*Id*.), Rickettsia and Leptospirosis (*Id*. at 213), and Borrelia (*Id*. at 214). Results for syphilis, herpes simplex virus, and the zoster virus were also all negative.[52] (Ex. 6, pp. 215-16.) Nonetheless, Dr. Leist testified that he could not rule out an infectious cause in petitioner's case of GBS. (Tr. at 279.) Specifically, Dr. Leist noted that the stool culture, in his opinion, could not definitively rule out the presence of *C. jejuni* due to the time difference between when the infection would occur and the actual onset of GBS. (Tr. at 247.) Dr. Leist further proposed that the antibiotics that petitioner was prescribed could have interfered with the detection of, or eliminated, the *C. jejuni* pathogen. (Tr. at 249.)

Respondent may present evidence relating to an alternative cause to demonstrate the inadequacy of petitioner's evidence supporting her case in chief. *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1353 (Fed. Cir. 2008). However, "the Vaccine Act does not require the petitioner to bear the burden of eliminating alternative causes where the other evidence on causation is sufficient to establish a prima facie case." *Walther v. Sec'y of Health & Human Servs.*, 485 F.3d 1146, 1150 (Fed. Cir. 2007). The Court of Federal Claims has also similarly observed that petitioners do not bear a burden to "discount *every* potential cause that exists within the entire realm of possibility." *Pafford v. Sec'y of Health & Human Servs.*, 64 Fed. Cl. 19, 35 (2005) (emphasis original), *aff'd* 451 F.3d 1352 (Fed. Cir. 2006). Here, there is not preponderant evidence that petitioner suffered pneumonia in January or February of 2015 and to the extent she may have had constitutional symptoms suggestive of an unspecified infection, that possible infection remains unidentified despite petitioner having been tested for a number of possible infections that could be implicated as causes of GBS.

Accordingly, for all the reasons discussed above, I find that petitioner has met her burden under both *Althen* prong two and three. That is, the timing of onset of petitioner's GBS is appropriate to infer it was vaccine caused and a logical sequence of cause and effect supports that causal relationship.

[51] Dr. Steinman further stressed the lack of IgM antibodies which would have suggested an acute infection.

[52] Petitioner was not tested for Epstein Barr virus ("EBV"). (Tr. at 140; *see* Ex. 6, pp. 211-223.) Dr. Steinman observed, however, that "[EBV is] one of the most common persistent viruses that we all pick up, usually somewhere in adolescence." (Tr. at 140.)

c. Analysis of factors unrelated to vaccination

Based on the analysis above, petitioner has presented a *prima facie* case that her GBS was, more likely than not, caused by her Prevnar 13 vaccination by demonstrating each of the three *Althen* prongs by preponderant evidence. Once petitioner has satisfied her own burden pursuant under the *Althen* test, the burden shifts to respondent to demonstrate that her injury was caused by factors unrelated to vaccination. § 300aa-13(a)(1)(B); *Deribeaux v. Sec'y of Health & Human Servs.*, 717 F.3d 1363, 1367 (Fed. Cir. 2013).

In order to meet his burden, respondent must demonstrate by preponderant evidence "that a particular agent or condition (or multiple agents/conditions) unrelated to the vaccine was in fact the sole cause (thus excluding the vaccine as a substantial factor)." *de Bazan*, 539 F.3d at 1354. As with petitioner's burden under *Althen*, respondent must show a logical sequence of cause and effect linking the injury to the proposed factor unrelated. *Deribeaux*, 717 F.3d at 1369. It need not be scientifically certain but must be legally probable. *Id*. Conditions or other factors that are "idiopathic, unexplained, unknown, hypothetical, or undocumentable" cannot defeat a petitioner's claim. § 300aa-13(a)(2); *Knudsen*, 35 F.3d at 548. Significantly, the Federal Circuit has rejected the contention that the presence of a viral infection can *per se* be considered a factor unrelated to vaccination. *Knudsen*, 35 F.3d at 548-50. Rather, respondent bears a burden of proving not only that there was a viral infection, but also that the infection was principally responsible for causing petitioner's injury. *Id*.

Among published case series, approximately two-thirds of all cases of GBS are preceded by a gastrointestinal or respiratory infection within three months prior. (Hartung, *supra,* Ex. 51, p. 1.) *Campylobacter jejuni*, cytomegalovirus (CMV), Epstein-Barr virus, and *Mycoplasma pneumoniae* are known precipitants of GBS, with other infections occurring no more often in GBS than in controls. (*Id.*) However, Dr. Leist's testimony that he cannot rule out the possibility of an infectious cause (Tr. at 279) does not meet respondent's burden in showing that a particular agent unrelated to the vaccine was in fact the sole cause of petitioner's GBS, and thus excluding the vaccine as a substantial factor. *de Bazan*, 539 F.3d at 1354. Respondent bears the burden of proving not only that there was a viral infection, but also that the infection was principally responsible for causing petitioner's injury. Respondent has not demonstrated preponderant evidence that petitioner suffered from a microbial infection at the time of her onset, nor has he shown that an infection principally caused her GBS.

VII. Conclusion

Accordingly, for all the reasons described above, I find that petitioner is entitled to compensation. Specifically, I find that petitioner has established by preponderant evidence that her GBS was caused-in-fact by her January 6, 2015 Prevnar-13 vaccination. A separate damages order will be issued.

IT IS SO ORDERED.

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