In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: December 10, 2021

DONALD WINKLER,	*	PUBLISHED
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Petitioner,	*	No. 18-203V
	*	
v.	*	Special Master Nora Beth Dorsey
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Dismissal Decision; Tetanus-Diphtheria-Acellular Pertussis ("Tdap") Vaccine; Pneumococcal Conjugate ("Prevnar" or "Prevnar 13") Vaccine; Guillain-Barré Syndrome ("GBS").
Respondent.	*	

Michael Patrick Milmoe, Law Offices of Leah V. Durant, PLLC, Washington, DC, for petitioner.
Ryan Daniel Pyles, U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

I. INTRODUCTION

On February 9, 2018, Donald Winkler ("petitioner") filed a petition for compensation under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42 U.S.C. § 300aa-10 et seq. (2012).[2] Petitioner alleges that he suffered Guillain-Barré syndrome ("GBS") as the result of a tetanus-diphtheria-acellular pertussis ("Tdap") vaccination

[1] Because this Decision contains a reasoned explanation for the action in this case, the undersigned is required to post it on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). **This means the 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, upon review, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material from public access.

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

administered on April 26, 2017.[3] Petition at Preamble (ECF No. 1). Respondent argued against compensation, stating that "this case is not appropriate for compensation under the terms of the Act." Respondent's Report ("Resp. Rept.") at 2 (ECF No. 14).

After carefully analyzing and weighing the evidence presented in this case in accordance with the applicable legal standards, the undersigned finds petitioner is not entitled to compensation. Accordingly, petitioner's case must be dismissed.

II. ISSUES TO BE DECIDED

The parties agree petitioner suffered from GBS, although their experts disagree as to the subtype.[4] Petitioner's Motion for Ruling on the Record ("Pet. Mot."), filed Mar. 24, 2021, at 10 (ECF No. 49); Resp. Response to Pet. Mot. ("Resp. Response"), filed June 23, 2021, at 1-2, 11-12 (ECF No. 52); Pet. Exhibit ("Ex.") 9 at 2; Resp. Ex. C at 9-10.

The parties dispute causation. Petitioner alleges (1) the Tdap vaccine can cause GBS, (2) petitioner's GBS was caused by his Tdap vaccination on April 26, 2017, and (3) there is a proximate temporal relationship between petitioner's Tdap vaccination and his development of GBS. Pet. Mot. at 11-19; Pet. Reply to Resp. Response ("Pet. Reply"), filed July 23, 2021, at 2-9 (ECF No. 53). Thus, petitioner contends he has satisfied all three Althen prongs and is entitled to compensation. Pet. Mot. at 20; Pet. Reply at 6, 8-9. On the other hand, respondent asserts that petitioner is unable to satisfy his burden of proving causation under all three Althen prongs, and therefore, petitioner's case should be dismissed. Resp. Response at 1-2, 11-26.

III. BACKGROUND

A. Medical Terminology

1. Guillain-Barré Syndrome

GBS is defined as "an acute monophasic peripheral neuropathy." 42 C.F.R. § 100.3(c)(15)(i). It is a "rapidly progressive ascending motor neuron paralysis of unknown etiology, frequently seen after an enteric or respiratory infection." Guillain-Barré Syndrome, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=110689 (last visited Oct. 6, 2021). Typically, GBS first presents "with paresthesias of the feet, followed by flaccid paralysis of the entire lower limbs, ascending to the trunk, upper limbs,

[3] Petitioner received a pneumococcal conjugate ("Prevnar" or "Prevnar 13") vaccine two days later on April 28, 2017. Petitioner's Exhibit ("Pet. Ex.") 1 at 1. Although the petition does not allege the Prevnar vaccine played a part in the development of petitioner's GBS, petitioner's expert, Dr. Rinker, and respondent's expert, Dr. Chaudhry, both discuss the role of the Prevnar vaccine in this case. See Pet. Ex. 9 at 2, 4; Respondent's ("Resp.") Ex. C at 11-12, 15. Therefore, the undersigned considered all evidence surrounding both vaccines.

[4] Because the parties agree petitioner suffered from GBS, the undersigned will not opine as to the specific subtype.

and face; other characteristics include slight fever, bulbar palsy, absent or lessened tendon reflexes, and increased protein in the cerebrospinal fluid without a corresponding increase in cells." Id. Patients suffering from GBS typically reach nadir within four weeks following onset. Pet. Ex. 11 at 5, 7;[5] see also 42 C.F.R. § 100.3(c)(15)(i).

2. *Campylobacter*

Campylobacter is "a genus of bacteria of the family Campylobacteraceae, consisting of gram-negative curved, S-shaped, or spiral rods. . . . [T]hey are found in the oral cavity, intestinal tract, and reproductive organs. Some species are pathogenic." Campylobacter, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=7653 (last visited on Oct. 12, 2021). According to the Centers for Disease Control and Prevention ("CDC"),[6] a *Campylobacter* infection has an incubation period of two to five days. Pet. Ex. 34 at 1. *Campylobacter* infection can result in GBS. Id. The CDC "estimates *Campylobacter* are responsible for 5-41% of GBS illnesses." Id.

There are over 20 species of *Campylobacter* and approximately 90% of human *Campylobacter* illnesses are caused by *Campylobacter jejuni* ("*C. jejuni*"). Pet. Ex. 34 at 1. *C. jejuni* is "a species that is a common cause of enteric campylobacteriosis in humans." Campylobacter Jejuni, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=62516 (last visited on Oct. 12, 2021). Enteric campylobacteriosis or *Campylobacter enteritis* ("*C. enteritis*") is an "intestinal infection by a species of *Campylobacter*; characteristics include diarrhea that may be bloody, abdominal pain with cramps, and fever. The cause is usually ingestion of contaminated food or water." Enteric Campylobacteriosis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=62528 (last visited on Oct. 12, 2021); Campylobacter Enteritis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=73277 (last visited on Oct. 12, 2021). The "CDC estimates that 1.5 million people in the United States become ill from *Campylobacter* infection every year." Pet. Ex. 34 at 1.

B. Procedural History

Petitioner filed his petition on February 9, 2018 and filed medical records on April 9, 2018. Petition; Pet. Exs. 1-8. On February 15, 2019, respondent filed his Rule 4(c) Report, in which he recommended against compensation. Resp. Rept. at 2.

On August 19, 2019, petitioner filed an expert report from Dr. John R. Rinker. Pet. Ex. 9. This case was reassigned to the undersigned on January 21, 2020. Notice of Reassignment dated Jan. 21, 2020 (ECF No. 26). On February 7, 2020, respondent filed expert reports from Drs. J. Lindsay Whitton and Vinay Chaudhry. Resp. Exs. A, C.

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[5] Christiaan Fokke et al., Diagnosis of Guillain-Barré Syndrome and Validation of Brighton Criteria, 137 Brain 33 (2014).

[6] *Campylobacter* (Campylobacteriosis), Ctrs. for Disease Control & Prevention, https://www.cdc.gov/campylobacter/index.html (last reviewed Dec. 23, 2019).

The undersigned held a Rule 5 conference on April 2, 2020. Order dated Apr. 2, 2020 (ECF No. 31). The undersigned preliminarily found that there are three potential causes in this case, making it difficult to discern which cause was the most likely cause of petitioner's GBS. Id. at 1. Thereafter, the parties filed supplemental expert reports from Dr. Rinker and Dr. Chaudhry. Pet. Ex. 31; Resp. Ex. E.

On March 24, 2021, petitioner filed a motion for a ruling on the record. Pet. Mot. Respondent filed his response to petitioner's motion on June 23, 2021 and petitioner filed his reply on July 23, 2021. Resp. Response; Pet. Reply.

This matter is now ripe for adjudication.

C. Factual History

1. Medical History

Prior to the vaccination at issue, petitioner had a prior medical history including bilateral carpal tunnel syndrome, hearing loss, bilateral shoulder pain, left knee pain, and shortness of breath. Pet. Mot. at 2; Resp. Response at 3.

On April 26, 2017, at sixty-six years old, petitioner received a Tdap vaccination at Basin Medical Clinic ("Basin Clinic") after stepping on a wire. Pet. Ex. 1 at 1; Pet. Ex. 3 at 9; Pet. Ex. 5 at 7.

On April 28, 2017, two days later, petitioner visited Dr. Michael Olsen, his primary care physician, at Basin Clinic for a physical examination. Pet. Ex. 5 at 3. He "complain[ed] of itchy, tingling legs. He denie[d] burning or aching of the legs." Id. He also reported insomnia, urinary frequency of 6-7x daily with 1-2x at night, and left knee pain. Id. at 3-4. He denied diarrhea. Id. at 4. Physical examination was normal. Id. at 5-6. Assessment was daytime somnolence, fatigue, urinary frequency, hyperlipidemia, varicose veins, and proteinuria. Id. at 6. Dr. Olsen ordered labs and overnight oximetry. Id. Labs revealed an elevated creatinine level, high cholesterol, high mean corpuscular volume, high neutrophils, and low lymphocytes. Id. at 9-11. He found petitioner's "itching of legs most likely [] related to the varicose veins" and "recommended he see a specialist for evaluation and treatment." Id. at 6. Petitioner also received a pneumococcal conjugate ("Prevnar" or "Prevnar 13") vaccination at this visit. Id.; Pet. Ex. 1 at 1.

Petitioner returned to Dr. Olsen on May 3, 2017 "complain[ing] of feeling run down, fatigued, muscle aches, headaches, diarrhea, and urinary frequency x3 days." Pet. Ex. 5 at 2. He also reported chills, feeling feverish, sinus congestion, and a bloody nose. Id. Under review of systems, petitioner reported right upper quadrant abdominal pain, but no dyspepsia, heartburn, nausea, vomiting, or constipation. Id. He "had diarrhea x3 days up to 6x daily" and there "[m]ay have been melena or bright red blood per rectum with the diarrhea." Id. Physical examination was normal. Id. at 3. Dr. Olsen's assessment was fatigue, myalgia, urinary

frequency, diarrhea, and gastroenteritis.[7] Id. Petitioner was instructed to take Imodium and eat a bland diet. Id.

On May 11, 2017, petitioner presented to Ashley Regional Medical Center Emergency Room ("ER") complaining of diffuse weakness. Pet. Ex. 3 at 7. Petitioner reported difficulty standing, feeling unstable on his feet, and difficulty using his hands. Id. Petitioner could no longer pick up a bale of hay and he was having trouble getting off the toilet. Id. "He state[d] that last Friday he was feeling pretty normal but over the last 5 days he has noticed progressive weakness. . . . This morning it got so bad that he could not button up his pants." Id. Petitioner reported "considerable pain in his left calf intermittently," limping on his left leg, and his left leg "feeling much weaker." Id. He reported his "illness with vomiting and diarrhea as well as weakness about 2 weeks ago."[8] Id. Dr. Mitchell Melling noted petitioner "could not stand from a deep squat and had diffuse weakness" in the ER. Id.

Dr. Melling's physical examination found "[d]iffuse weakness with strength 2 to 3/5 bilaterally throughout in the proximal muscles. He also ha[d] considerable loss of coordination in his hands. He ha[d] 3 beats or clonus at the ankle and his deep tendon reflexes [were] a little brisk throughout." Pet. Ex. 3 at 8. Plan indicated progressive weakness with GBS as differential. Id. Petitioner was admitted, and a lumbar puncture and EMG were ordered. Id.

Petitioner was also seen by Dr. Bruce A. Daniel in the ER on May 11, 2017. Pet. Ex. 3 at 26. Under history of present illness, Dr. Daniel documented that petitioner reported "2 weeks of progressively worsening weakness" that "started after a [Prevnar 13] vaccine and a bout of diarrhea, which [petitioner] had about the same time 2 weeks ago." Id. Petitioner reported his weakness had progressively gotten worse to where "he ha[d] no strength and [could not] even snap his pants close." Id. He reported his muscles were achy and his symptoms were "at least moderate to severe." Id. Dr. Daniel's physical examination revealed muscle weakness. Id. "[Petitioner] [was] able to lift against gravity easily with his extremities" and had no drift or asymmetry, and Dr. Daniel found petitioner's hand grip weaker than expected. Id. Petitioner was almost able to do a squat "but he really ha[d] to work hard to do it." Id. Additionally, his reflexes at the knee, patella, and Achilles were "normal to slightly decreased." Id. at 27. Dr. Daniel's differential diagnoses were GBS, fluid-electrolyte abnormality, hypothyroidism, and other autoimmune or inflammatory disease. Id. He noted petitioner's C-reactive protein was negative and his sedimentation rate was elevated at 25 (range 0-20). Id. at 27, 34, 36. Dr. Daniel opined petitioner had GBS. Id. at 27. He discussed the case with Dr. James D. White and Dr. Melling, and they agreed to admit petitioner and conduct further workup. Id. Petitioner was admitted to Dr. Melling's service. Id.

[7] Gastroenteritis is "inflammation of the lining of the stomach and intestines, characterized by anorexia, nausea, diarrhea, abdominal pain, and weakness." Gastroenteritis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=19818 (last visited Oct. 6, 2021). Causes of gastroenteritis include food poisoning, viral infections, and consumption of irritating food or drink. Id.

[8] It appears this quote was noted in the history of present illness section every day of petitioner's hospital stay. To avoid repetition, this statement will not be repeated.

A physical therapy ("PT") evaluation was conducted by Justin R. Watkins on May 11, 2017. Pet. Ex. 3 at 43-46. Petitioner reported "slowly getting weak over the past week," falling episodes, and having "a very hard time with fine motor tasks that involve his hands[,] and [] getting a lot of cramping in his calves when he walks." Id. at 43. Petitioner's grip strength was -4/5, his shoulder strength was 4/5, and his lower extremity strength was decreased. Id. at 44. Assessments included increased pain, decreased strength, decreased functional mobility, impaired activity tolerance, and fine motor deficits. Id. at 46.

On May 12, 2017, Dr. White provided a consultation and conducted electrodiagnostic studies.[9] Pet. Ex. 3 at 9-11; Pet. Ex. 6 at 48-51. He documented petitioner's history of present illness. Pet. Ex. 3 at 9. Dr. White wrote that petitioner reported that "[h]e had a [Tdap] shot and subsequently developed diarrhea (approximately 2 weeks ago). At around that time, he also had a [Prevnar 13] vaccine." Id. Petitioner indicated he was doing better that morning. Id. "He was able to squat 3 times" and he could pull up his pants, although with substantial difficulty. Id. Petitioner reported no shortness of breath, frequent urination, and weakness in the arms and legs. Id.

Dr. White's physical examination revealed petitioner's "reflexes [were] l+ at both the knees and the ankles" and no clonus at the ankle, wrist, or knee. Pet. Ex. 3 at 10. The Babinski and Hoffmann signs were negative bilaterally. Id. His strength was decreased for the extensor hallicus longus ("EHL") and anterior tibialis bilaterally at 4/5. Id. His "strength [was] symmetric for the gastrocnemius and [Dr. White] [was] unable to overcome gastrocnemius strength using [his] hands." Id. Petitioner's strength was also symmetric within normal range in his hamstrings, quadriceps, and gluteus medius. Id. For petitioner's upper extremities, petitioner had "neurogenic weakness in [abductor pollicis brevis ("APB")], the hand intrinsics, and the . . . flexors of all 4 fingers on each side" at 4/5, and well as "4/5 strength for the wrist flexors and extensors." Id. "[H]e ha[d] better strength for the biceps and triceps (4+) and for the external rotators strength [was] near normal." Id. Sensory examination revealed petitioner's "[t]hreshold to vibratory sensation [was] slightly decreased at the ankle." Id.

Dr. White found petitioner "ha[d] multiple abnormalities on nerve conduction studies . . . consistent with a diffuse neuropathic process." Pet. Ex. 3 at 11. Taking the electrodiagnostic findings, medical history, and physical examination together, Dr. White was "most strongly suspicious of acute inflammatory demyelinating polyneuropathy (AIDP, also known as [GBS])," with a differential diagnosis of early presentation of chronic inflammatory demyelinating polyneuropathy ("CIDP") and "diffuse peripheral neuropathy of other etiology." Id. He recommended checking petitioner's "spinal tap looking for elevated protein in the absence of an elevated white count which would add further evidence to the probability of AIDP." Id. If confirmed, he recommended IVIG treatment for five days. Id.

That same day, May 12, 2017, petitioner reported he still could not button his pants or open a sugar packet. Pet. Ex. 3 at 15. Physical examination by Dr. Melling revealed petitioner's

[9] Dr. White noted petitioner's extremities were cool prior to the study and he encountered difficulty maintaining an adequate temperature. Pet. Ex. 3 at 10.

clonus and hyperreflexia of his wrists and ankles resolved that morning. Id. Petitioner had "decreased reflexes in both upper and lower extremities," and "quite significant weakness throughout all 4 extremities." Id. After the EMG confirmed the likelihood of AIDP/GBS, petitioner received a lumbar puncture that day, which revealed an elevated protein at 49.4 (range 15-45) and confirmed petitioner's diagnosis. Id. at 15, 39, 42. Dr. Melling assessed petitioner with GBS (AIDP). Id. at 15. Petitioner was to remain in the hospital "for full treatment course or until his strength [was] sufficient to go home." Id. Petitioner started IVIG that afternoon. Id.

On May 13, 2017, petitioner was seen by Dr. Sara Daniel.[10] Pet. Ex. 3 at 16. Petitioner reported his legs felt much stronger, he could perform more than 10 deep squats, and he could button up his pants. Id. He also reported his bilateral hands were still weak and Dr. Daniel found he demonstrated a weak grip that improved as the day progressed. Id. Physical examination revealed weakness and normal strength. Id. at 17. Petitioner's bilateral hand strength was +4/5 "which improved throughout the day [but] continue[d] to remain weak," and his lower extremity strength "normalized" at +5/5. Id. Petitioner was to continue his IVIG treatment, and a PT evaluation[11] was ordered for his proximal muscle weakness. Id.

The following day, on May 14, 2017, petitioner reported "feeling much improved." Pet. Ex. 3 at 18. "He [was] now able to walk about without difficulty," and "[h]is hand strength [was] improving as well, but remain[ed] weak." Id. "[W]hile receiving his IVIG [petitioner] developed . . . hypotension," but "after slowing the transfusion rate and providing a 1 [liter normal saline] bolus, [petitioner] improved and was able to complete his treatment." Id. Petitioner remained in good, stable condition and comfortable throughout the remainder of the day. Id. Physical examination by Dr. Daniel revealed bilateral hand strength of +4/5 that "continue[d] to improve but remain[ed] weaker than baseline," and lower extremity strength of +5/5. Id. at 19. Petitioner was to continue with PT and IVIG. Id.

Petitioner reported continued improvement on May 15, 2017. Pet. Ex. 3 at 20. "He [was] able to care for himself and get dressed, however he continue[d] to worry that his hands [were] so weak," specifically his left hand more than his right. Id. Dr. Daniel's physical examination revealed +4/5 bilateral hand strength that "continue[ed] to improve but remain[ed] weaker than baseline," and +5/5 lower extremity strength. Id. at 21. Dr. Daniel noted petitioner would likely be discharged after his last IVIG treatment the following day. Id.

Dr. White provided a second consultation on May 15, 2017. Pet. Ex. 3 at 12. Petitioner was on his fourth day of IVIG and "[was] beginning to experience some increase in strength." Id. Petitioner reported "increased facility in performing functional abilities such as snapping of his pants" and "[h]e [was] now able to open his own orange juice and milk cartons in the hospital." Id. Physical examination revealed 1 to 2+ reflexes of knees and ankles, functional but decreased grip strength, 4 to 4+/5 strength in the hand intrinsics and long flexors of the fingers, 4+ to 5-/5 strength in the triceps, 5- to 5/5 strength in the biceps, 4-/5 decreased strength in EHL,

[10] The remaining references to Dr. Daniel are to Dr. Sara Daniel.

[11] The only PT record from petitioner's May 2017 hospitalization was an evaluation from May 11, 2017.

4/5 strength in the anterior tibialis, and good strength in the hamstrings and quadriceps. Id. Dr. White's impression was AIDP, but CIDP was to be ruled out over time. Id. He ordered petitioner to follow up with him one week after discharge. Id.

Petitioner was discharged on May 16, 2017. Pet. Ex. 3 at 13. His discharge diagnosis was GBS and proximal muscle weakness. Id. On discharge, petitioner could do a deep squat. Id. "His hand grip strength [was] still quite weak but all other muscle groups [] improved dramatically." Id.

On May 23, 2017, petitioner saw Dr. White at The Clinic at UBMC ("UBMC") for a follow up examination after his hospitalization for GBS/AIDP. Pet. Ex. 6 at 29. In a handwritten patient questionnaire, petitioner reported shortness of breath, loss of bladder control, diarrhea, hopelessness, numbness, tingling or burning sensations, and weakness over the past six months, as well as current aching pain in his calves. Id. at 26, 28. Petitioner reported that he did not believe he was doing better, but Dr. White noted petitioner "[was] now able to do 13 squats with no assistance and without difficulty." Id. at 29. Petitioner was also "able to do 12 toe raises before beginning to fatigue" and "duck walk normally on the right and with some drop in the foot on the left." Id. He had ongoing weakness in the EHL and anterior tibialis with a strength at 5-/5, and "he ha[d] normal or near normal strength in the hamstrings, gluteus medius[,] and quadriceps." Id. Dr. White found petitioner "still ha[d] rather remarkable weakness in the hand intrinsics," but "show[ed] improved strength in the APB at 4 to 4+/5, wrist flexion and extension [at] 4+/5, biceps and triceps [at] 4+ to 5-/5." Id. Dr. White added that petitioner was able to button up his pants, put on his shoes without assistance, and go fencing, although petitioner reported "he gets short of breath easily." Id. Petitioner believed his symptoms began approximately May 6, 2017, "or perhaps a little earlier than that." Id. Dr. White found petitioner's symptoms were "strongly suggestive of AIDP," but CIDP remained a differential diagnosis. Id. Dr. White ordered petitioner to return in 10 days. Id.

On June 2, 2017, petitioner visited Dr. White complaining of weakness. Pet. Ex. 3 at 2. Petitioner's bloodwork revealed a high erythrocyte sedimentation rate at 28 and a high ceruloplasmin ("CP") at 17 (range 0-15), and he tested negative for Lyme disease and antinuclear antibodies. Id. at 3-5; Pet. Ex. 6 at 20-23. Physical examination found weakness in hand intrinsics and APB. Pet. Ex. 6 at 13. Petitioner's wrist flexion and extension strength were 4+/5, his biceps and triceps strength was 5-/5, his anterior tibialis strength was 5-/5, and he had "near normal strength" in his hamstrings, gluteus medius, and quadriceps. Id. Dr. White also conducted an electrodiagnostic study and needle EMG. Id. at 13-18. Under indication for study, he noted that "[a]bout 4 weeks ago, [petitioner] developed diarrhea, 3 weeks ago he developed weakness and was diagnosed with [GBS] (most likely AIDP)." Id. at 13. Dr. White found petitioner's medical history "quite classic for [GBS]; he had a bout of diarrhea and one week later experienced significant weakness with suppressed reflexes." Id. at 14. Petitioner's "electrodiagnostic parameters [] improved for the greater part (with the exception of the left tibial motor amplitude, which [was] a little lower)." Id. Because the electrodiagnostic examination that day revealed significant axonopathy in petitioner's distal muscles, Dr. White

inquired whether petitioner had acute motor axonal neuropathy ("AMAN")[12] or acute motor-sensory axonal neuropathy ("AMSAN").[13] Id. He opined that AMAN or AMSAN were "less likely" because petitioner "had sensory involvement ruling out AMAN. Given his history and features, [Dr. White] [was] most suspicious of AIDP with axonal involvement," which petitioner had "in the more distal muscles of both upper and lower extremities." Id. at 14-15. Dr. White's impression was "[GBS] of the AIDP variety," with an axonal component. Id. at 15. He noted that "[t]he possibility of CIDP cannot entirely be ruled out at this point and time will reveal that if it is present." Id.

Petitioner next saw Dr. White on June 14, 2017. Pet. Ex. 6 at 11. Physical examination revealed normal strength in the quadriceps, gluteus medius, hamstrings, and anterior tibialis bilaterally. Id. Petitioner's strength in hand intrinsics was 4/5, APB was 4/5, wrist flexors and extensors were 4+/5, biceps and triceps were 5-/5, and external rotators were 5/5. Id. Dr. White's impression was "[GBS] (most likely AIDP) axonopathy noted distally in the upper and lower extremities on EMG at 3 weeks. [Petitioner] [was] steadily progressing." Id. Petitioner was ordered to follow up in two weeks. Id.

On June 26, 2017, petitioner followed up with Dr. White at UBMC for his GBS. Pet. Ex. 6 at 9. Petitioner reported he was able to do 20 squats with no difficulty, but continued to have ongoing weakness in his hands with symptoms he believed waxed and waned. Id. Physical examination revealed strength of 5-/5 in his biceps, triceps, wrist flexors, and wrist extensors, strength of 4+/5 in the long flexors of his fingers, and strength of 4/5 in hand intrinsics and APB. Id. Dr. White's impression was "[GBS] (most likely AIDP) with axonopathy noted distally in the upper and lower extremities . . . . [Petitioner] has had a good response in the lower extremities but ongoing weakness principally in the hands. Rule out CIDP." Id. Petitioner was to return in two weeks. Id.

Petitioner saw Dr. White at UBMC for a follow up examination for his GBS on July 12, 2017. Pet. Ex. 6 at 7. Petitioner reported he was continuing to improve, although "slower than he would like." Id. He could open the cap on a water bottle and squat 200 pounds. Id. Dr. White's physical examination found "ongoing weakness in the EHL bilaterally," and normal strength in the anterior tibialis, hamstrings, gluteus medius, and quadriceps. Id. Petitioner had ongoing weakness in his hand intrinsics with a grip strength of 4/5, wrist extensors strength of 5-/5, and wrist flexor strength of 4+/5. Id. Dr. White found petitioner's bicep and tricep strength good, but weak at 4+ to 5-/5. Id. Dr. White's impression remained "[GBS] (most likely AIDP) with axonopathy noted distally in upper and lower extremities." Id. Petitioner was ordered to return in one month. Id.

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[12] AMAN is "a subtype of [GBS] seen in China, caused by infection with [*C. jejuni*]." Acute Motor Axonal Neuropathy, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition? id=92651 (last visited Oct. 6, 2021).

[13] AMSAN is "a rare subtype of [GBS] involving primarily large sensory nerve fibers in the limbs, with paresthesias and weakness but not paralysis." Acute Motor-Sensory Axonal Neuropathy, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=92652 (last visited Oct. 6, 2021).

Petitioner returned to Dr. White on August 9, 2017. Pet. Ex. 6 at 3. Petitioner reported continued improvement but ongoing weakness with his grip. Id. Physical examination revealed improving grip strength and hand intrinsic weakness. Id. Petitioner had normal strength in his wrist flexors, wrist extensors, biceps, triceps, external rotators, anterior tibialis, hamstrings, gluteus medius, and quadriceps. Id. Dr. White noted "ongoing neurogenic weakness in the right greater than the left EHL." Id. He added that "although [petitioner's] strength is in the normal range for age, he is probably weak relative to his prior condition." Id. Dr. White's impression remained "[GBS], most likely of the AIDP variety, with axonopathy noted distally in the upper and lower extremities," and CIDP was to still be ruled out. Id. Dr. White directed petitioner to return in one month. Id.

Between August 18 and September 20, 2017, petitioner completed five PT sessions with Jerry Kulland. Pet. Ex. 2 at 2-9. Initial examination noted tightness, pain, and extreme weakness in petitioner's wrists and fingers, sharp pain that increases with activity, and a limitation in carrying objects. Id. at 9. By his last visit on September 20, 2017, petitioner "report[ed] he [was] doing good, getting better." Id. at 4.

On September 11, 2017, petitioner visited UBMC to follow up with Dr. White. Pet. Ex. 6 at 1. Petitioner reported continued improvement. Id. His grip strength was at the low normal range of 60 pounds (normal is 60-97 pounds for his age), but he had normal strength in his wrist flexors, wrist extensors, biceps, and triceps. Id. He was weak in the hand intrinsics bilaterally and "weak in the EHL bilaterally, but show[ed] good strength for the anterior tibialis, hamstrings[,] [] gluteus medius[,] and quadriceps." Id. Petitioner reported he was doing PT. Id. Dr. White's impression remained GBS, most likely AIDP, and he now included mild situational depression. Id. Petitioner was instructed to return in one month. Id. at 2. Dr. White noted he "may repeat electrodiagnostic studies thereafter depending on progress." Id.

Petitioner next returned to Dr. White on December 13, 2017. Pet. Ex. 6 at 76. Petitioner reported that his lower extremity strength is good, however his upper extremity strength was not satisfactory. Id. Physical examination revealed "slightly decreased" strength in hand intrinsics, APB, wrist flexors and extensors, biceps, and triceps. Id. Dr. White noted that "while [petitioner's] strength is within the normal range for a man his age, it is decreased relative to his prior history." Id. Dr. White's impression remained GBS, most likely AIDP. Id.

On January 10, 2018, petitioner presented for follow-up examination and for electrodiagnostic studies. Pet. Ex. 6 at 59-64. "[Petitioner] ha[d] a history of acute weakness coming in early May of 2017 and occurring 3 weeks after stepping on a wire, receiving a [Tdap] shot and developing diarrhea (he also had a [Prevnar 13] vaccine at that time)." Id. at 59. Dr. White documented that petitioner's symptoms had not relapsed. Id. Petitioner "complain[ed] of ongoing weakness primarily in the upper extremities." Id. Physical examination revealed "slightly decreased" strength in hand intrinsics, APB, wrist flexors and extensors, biceps, and triceps. Id. Dr. White found petitioner's history and electrodiagnostic studies consistent with GBS. Id. at 60. Also, petitioner's "electrodiagnostic parameters [were] improving over time, as [was] his strength. [Petitioner] has not had episodes of relapse and his strength ha[d] been steadily recovering." Id. Dr. White opined petitioner's "persistent weakness [was] secondary to

the axonal nature of his condition and the overall trend continue[ed] to be one of improvement." Id. Petitioner was directed to return in three weeks. Id.

Petitioner saw Dr. White on January 29, 2018. Pet. Ex. 6 at 54. On a handwritten document, petitioner indicated his pain was "about the same" since his last visit and he noted aching pain in his calves. Id. at 53. Petitioner complained of fatigue. Id. at 54. Dr. White indicated petitioner's clinical course was "most strongly reminiscent of AMSAN." Id.

No additional medical records have been filed.

2. Petitioner's Affidavit

On April 26, 2017, after stepping on a rusty nail, petitioner went to Basin Clinic and received a Tdap vaccination in his right arm. Pet. Ex. 7 at ¶ 1. At that visit, he made an appointment for a routine physical examination, which occurred two days later on April 28, 2017. Id. At his April 28, 2017 visit, he received a Prevnar vaccination and completed blood work. Id. His examination found "elevated cholesterol and itchy legs due to varicose veins." Id. He averred that "[he] was in great physical health. [He] routinely enjoyed activities such as water skiing with one board, riding horses, and cutting [his] own firewood." Id.

"By early May, [he] began feeling sick with aches and pains." Pet. Ex. 7 at ¶ 2. He stated his doctor told him he had the flu. Id. He continued to get worse and had "severe muscle aches and loss of energy." Id. By the morning of May 11, 2017, "[he] could no longer take the pain" and went to the ER. Id. He was admitted to the hospital, and after electrodiagnostic studies and a lumbar puncture, he was told he had GBS. Id. While in the hospital receiving IVIG treatments, "[he] experienced sharp pains in [his] arms and legs" and "had aching and numbness." Id.

Since discharge, he stated he has had a difficult time at home. Pet. Ex. 7 at ¶ 3. "Just waking up required an exceptional amount of energy that resulted in severe aches and pains. [He] had very little strength in [his] arms and hands," he "had difficulty picking up items," he "frequently dropped things," and he could not zip or snap his pants or open water bottles without assistance. Id. He became severely depressed. Id. He "was unable to perform [his] usual activities." Id. Before his GBS diagnosis, he was active and strong, and "enjoyed activities like riding horses, fixing [his] fencing, hauling hay, starting [his] lawn mower, cutting firewood, running power tools, water skiing, dancing, and pulling weeds in [his] garden." Id. However, after developing GBS, he "wasn't even strong enough to pick up [his] eight-month-old granddaughter." Id.

As of February 13, 2018, the day in which he executed his affidavit, he was still unable to do certain activities. Pet. Ex. 7 at ¶ 4. He could not ride a horse and had difficulty getting into a truck. Id. He continued to suffer from aches and numbness, as well as pain in his muscles and hands. Id. "The back of [his] legs tire easily." Id.

D. Expert Reports

1. Petitioner's Expert, Dr. John R. Rinker

a. Background and Qualifications

Dr. Rinker is a board-certified neurologist with a subspeciality in neuroimmunology. Pet. Ex. 9 at 1; Pet. Ex. 10 at 2. He received his M.D. from Medical College of Georgia in 2001. Pet. Ex. 10 at 2. Thereafter, he went to Washington University School of Medicine in St. Louis, Missouri for his internship, neurology residency, and additional postdoctoral training. Id. Dr. Rinker currently works as an Associate Professor of Neurology at the University of Alabama, Birmingham. Id.; Pet. Ex. 9 at 1. His "practice consists primarily of diagnosing and caring for patients with noninfectious, immune-mediated disorders of the nervous system." Pet. Ex. 9 at 1. He has "experience caring for patients with conditions presumed to have been triggered or aggravated by vaccines, including GBS, Acute Disseminated Encephalomyelitis (ADEM), and Susac's syndrome." Id. Dr. Rinker is a member of various professional societies, councils, committees, and editorial boards, has given numerous lectures, and has authored or co-authored over 30 articles. Pet. Ex. 10 at 3-4, 8-9, 13-16.

b. Opinion

i. Althen Prong One

Dr. Rinker opined that vaccines can cause GBS through the mechanism of molecular mimicry. Pet. Ex. 9 at 4. Dr. Rinker explained that when a person typically encounters a foreign agent, their adaptive immune system distinguishes foreign antigens from the host; however, in rare circumstances, "an infection or vaccination may inadvertently provoke the host to mount an immune response directed against self-antigens which can result in immune-mediated harm to otherwise healthy tissues." Id.

Quoting Tishler and Shoenfeld,[14] Dr. Rinker explained that with molecular mimicry, "antigenic determinants of the microorganisms are recognized by the host's immune system as similar to its own antigenic determinants and, because of the structural resemblance, antibodies and auto-reactive T cells[15] not only destroy the invading pathogen but can react with host tissues as well." Pet. Ex. 9 at 4 (quoting Pet. Ex. 37 at 3). Tishler and Shoenfeld further wrote that "[a]ccording to the mimicry hypothesis, it is possible that any microorganism that expresses

[14] Moshe Tishler & Yehuda Shoenfeld, Vaccines and Autoimmunity, in The Autoimmune Diseases 309 (Noel R. Rose & Ian R. Mackay eds., 4th ed. 2006).

[15] T cells, or lymphocytes, are "cells primarily responsible for cell-mediated immunity." T Lymphocytes, Dorland's Online Med. Dictionary, https://www.dorlandsonline.com/dorland/definition?id=87562 (last visited Oct. 15, 2021). "When activated by antigen, T lymphocytes proliferate and differentiate into T memory cells and the various types of regulatory and effector T cells." Id. Adaptive, not innate, immunity is "mediated by B and T lymphocytes following exposure to a specific antigen." Illustrated Dictionary of Immunology 18 (3d ed. 2009).

an epitope which could serve as a molecular mimic for an autoantigen could induce autoimmune disease." Pet. Ex. 37 at 3.

Dr. Rinker added that vaccination can lead to GBS through molecular mimicry depending on the presentation of foreign antigens. Pet. Ex. 9 at 4. With GBS, "the immune system mounts an antigen-specific response against peripheral myelin gangliosides." Id. at 3. "[A]ntigen presenting cells ingest and process foreign proteins and molecules and present them in the context of molecules called Human Leukocyte Antigens (HLA)." Id. at 4-5. These "molecules are responsible for presenting foreign antigen[s] to immune cells, such as T cells, which in turn coordinate the immune response against the foreign agent." Id. at 5.

He cited various articles discussing how molecular mimicry can lead to GBS through various triggers including vaccination and infection. See, e.g., Pet. Ex. 12 at 4-5, 6 fig.2 (infection);[16] Pet. Ex. 14 at 5 (infection);[17] Pet. Ex. 22 at 4 (vaccination);[18] Pet. Ex. 23 at 21-25 (vaccination).[19] These articles describe molecular mimicry and the pathogenesis of GBS. See also Pet. Ex. 26 at 2 ("Molecular mimicry . . . [is] involved in the pathogenesis of GBS . . . ."). [20] These articles also note that molecular mimicry is thought to be the same mechanism at play for GBS post-*C. jejuni*. See, e.g., Pet. Ex. 12 at 4-5, 6 fig.2; Pet. Ex. 14 at 5; Pet. Ex. 26 at 3 fig.2.

Dr. Rinker acknowledged that two-thirds of GBS cases are preceded by an infection or illness, most commonly respiratory or diarrheal, within 4 weeks of onset. Pet. Ex. 9 at 3 (citing, e.g., Pet. Ex. 14 at 1). He agreed that *C. jejuni* is the most common infectious trigger of GBS, and noted that according to Jasti et al.,[21] "less than 0.1% of *C. jejuni* infections result in a case of GBS, suggesting that even though *C. jejuni* possesses immunological characteristics favorable to the development of GBS, the syndrome itself develops rarely." Id. at 5 (citing Pet. Ex. 39 at 10). Thus, he argued that "the rarity with which GBS occurs even following exposures to known triggers of the condition, should allow for the possibility that sporadic cases of GBS may occur

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[16] John A. Goodfellow & Hugh J. Willison, Guillain-Barré Syndrome: A Century of Progress, 12 Nature Revs. Neurology 723 (2016).

[17] B.C. Jacobs et al., The Spectrum of Antecedent Infections in Guillain-Barré Syndrome: A Case Control Study, 51 Neurology 1110 (1998).

[18] Nizar Souayah et al., Guillain-Barré Syndrome After Vaccination in United States: Data from the Centers for Disease Control and Prevention/Food and Drug Administration Vaccine Adverse Even Reporting System (1990-2005), 11 Neuromuscular Disease 1 (2009).

[19] Inst. of Med., Diphtheria and Tetanus Toxoids, in Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality 67 (Kathleen Stratton et al. eds., 1994).

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

[21] Anil K. Jasti et al., Guillain-Barré Syndrome: Causes, Immunopathogenic Mechanisms and Treatment, 12 Expert Rev. Clinical Immunology 1175 (2016).

following other immunological stimuli." Id.; see also Pet. Ex. 39 at 10 ("[W]e are convinced that GBS, similar to other inflammatory diseases, is the result of a permissive genetic background on which environmental factors, including infections, vaccination, and the influence of aging, lead to disease onset and the natural history of disease.").

Further, Dr. Rinker argued that vaccinations have also been implicated as triggering GBS. Pet. Ex. 9 at 3, 5; see, e.g., Pet. Ex. 21 at 1.[22] He cited to Schonberger et al.[23] and Salmon et al.[24] to demonstrate how the flu vaccine has been noted to cause GBS. Pet. Ex. 9 at 3. In Schonberger et al., the authors looked at 1,098 patients who developed GBS between October 1, 1976 and January 31, 1977 and found 532 of the patients received a A/New Jersey flu vaccination prior to onset of GBS. Pet. Ex. 42 at 1-2, 5. The data suggested there was "strong evidence . . . that A/New Jersey flu vaccination incited the onset of GBS in many adult vaccinees." Id. at 16. Similarly, Salmon et al. found a small increased risk of GBS after the flu A (H1N1) 2009 monovalent inactivated vaccine. Pet. Ex. 17 at 6.

Souayah et al. examined reports of GBS following vaccination in the Vaccine Adverse Event Reporting System ("VAERS") from 1990 to 2005. Pet. Ex. 22 at 1. Because studies showed an increased risk of GBS within six weeks after vaccination, the authors considered such cases suggestive of causal association. Id. at 2. The authors found 1,000 cases of GBS reported after vaccination, 773 of which were within six weeks of vaccination. Id. Of those 773 cases, 511 cases (the most common) were after flu vaccination, while 28 (the third-most common) were after tetanus and diphtheria toxoid vaccination and 14 were after a pneumococcal polyvalent vaccination. Id. at 2-3, 2 tbl.1. Additionally, 103 of the 773 cases were after a combination of two or more vaccines that were not specified. Id. They found "GBS is more strongly associated with vaccination for [flu] than for vaccination for other diseases. However, it is also apparent that [flu] vaccine is not the only one that presents a risk." Id. at 4. The study suggested that vaccines other than the flu vaccine can be associated with GBS. Id. at 5. The authors hypothesized that "GBS observed after vaccination may arise by [] molecular mimicry." Id. at 4. They acknowledged that their study had limitations, in part, due to the nature of VAERS.[25] Id. at 5.

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[22] Valérie Sivadon-Tardy et al., Guillain-Barré Syndrome and Influenza Virus Infection, 48 Clinical Infectious Diseases 48 (2009).

[23] Lawrence B. Schonberger et al., Guillain-Barré Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976-1977, 110 Am. J. Epidemiology 105 (1979). This article was also cited by Dr. Chaudhry, respondent's expert. See Resp. Ex. C, Tab 19.

[24] 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).

[25] The authors explained that VAERS, a passive surveillance system, "may be subject to underreporting, differential reporting, ascertainment bias, and variability in report quality and completeness." Pet. Ex. 22 at 5.

Using the Souayah et al. article for support, Dr. Rinker opined that the Tdap vaccine can cause GBS via molecular mimicry.[26] He also cited to a report issued in 1994 by the Institute of Medicine ("IOM"), now the National Academy of Medicine, who concluded that "[the] evidence favor[ed] a causal relation between vaccines containing tetanus toxoid (DT and Td) and GBS." Pet. Ex. 23 at 24. The IOM relied heavily on a case report by Pollard and Selby[27] of a 42-year-old patient who suffered three episodes of a demyelinating neuropathy, 21, 14, and 10 days following tetanus toxoid vaccinations, over a 14 years. Id. at 22-24; see Resp. Ex. A, Tab 17. Respondent's experts argued that the 1994 IOM report was outdated and superseded by a report from 2012. However, Dr. Rinker did not discuss or cite to the 2012 report.

Another article cited by Dr. Rinker was Baxter et al.,[28] which evaluated the relationship between GBS and vaccinations using retrospective data from Kaiser Permanente of Northern California from 1994 to October 2006. Pet. Ex. 30 at 2. Of the 896 potential cases of GBS, the authors included 415 in their study.[29] Id. at 3. In the 90 days preceding GBS onset, 277 (66.7%) cases had a respiratory or gastrointestinal ("GI") illness, 159 of which (38.3%) were respiratory, 77 (18.6%) were GI, and 41 (9.9%) were both. Id. at 4. Twenty-five of the 415 patients received a vaccine in the six weeks prior to GBS onset. Id. One received a Tdap vaccine, three[30] received a tetanus-diphtheria vaccine, and two received a 23-valent pneumococcal polysaccharide vaccine.[31] Id. at 5 tbl.1. The authors found "no evidence of an increased risk of GBS following any vaccination, as well as all vaccinations combined;" however, they concluded that they were "unable to exclude any possible association between vaccines and GBS." Id. at 5, 7.

For further support, Dr. Rinker cited to various case reports discussing incidents of GBS following a vaccines containing tetanus. In Newton and Janati,[32] for example, a 47-year-old man received a pure tetanus toxoid vaccine and developed numbness and weakness in both legs and

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[26] Although Dr. Rinker noted petitioner's Prevnar 13 vaccination as a potential trigger of petitioner's GBS, he did not opine as to how the Prevnar 13 vaccine specifically can cause GBS.

[27] J. D. Pollard & G. Selby, Relapsing Neuropathy Due to Tetanus Toxoid: Report of a Case, 37 J. Neurological Scis. 113 (1978). Petitioner did not file this article.

[28] Roger Baxter et al., Lack of Association of Guillain-Barré Syndrome with Vaccinations, 57 Clinical Infectious Diseases 197 (2013). This article was also cited to and discussed by respondent's experts. See Resp. Ex. A, Tab 16; Resp. Ex. C, Tab 11.

[29] Patients were excluded for various reasons including a lack of or insufficient medical records, subsequent diagnosis of CIDP, and a diagnosis of the Miller Fisher variant of GBS. Pet. Ex. 30 at 2-3.

[30] One of these patients also received a flu vaccine. Pet. Ex. 30 at 5 tbl.1.

[31] This is not the pneumococcal vaccine petitioner received.

[32] Norris Newton & Abdorassol Janati, Guillain-Barré Syndrome After Vaccination with Purified Tetanus Toxoid, 80 S. Med. J. 1053 (1987).

arms nine days later. Pet. Ex. 40 at 1. There was no prior history of infection, and no adverse reaction was noted following his prior tetanus vaccination. Id. "Immunologic studies showed a hypersensitivity to tetanus antigen." Id. at 1. Instead of molecular mimicry, the authors opined that the patient's GBS "appear[ed] to be an example of an autosensitivity disease in which the mechanisms of delayed T cell hypersensitivity predominate." Id.

In Ammar,[33] a 40-year-old man received a Tdap vaccine, and within one to two weeks, he developed weakness and numbness in his legs and was subsequently diagnosed with GBS. Pet. Ex. 28 at 1-2. Ammar noted the patient did not have diarrhea, fever, cough, or chills in the weeks preceding his illness, and the Tdap vaccination was the only recognized antecedent event. Id. at 2.

Bakshi and Graves[34] examined a 22-year old male who received a tetanus-diphtheria toxoid vaccination and developed bilateral tingling of the fingertips and toes four days later, which progressed to progressive proximal leg weakness over the following few days. Pet. Ex. 29 at 1. He was admitted to the hospital seven days after vaccination and diagnosed with GBS. Id. at 1-2. Although *C. jejuni* testing was not performed, he denied antecedent illness in the six months prior, and the authors noted no antecedent factors other than vaccination were identified as potential triggers. Id. Given other cases that reported GBS after tetanus toxoid vaccination, the authors "suspect[ed] that the tetanus portion of the vaccination produced the GBS," but acknowledged they could not provide proof. Id. They were also "unable to exclude that the GBS was secondary to the diphtheria portion of the vaccination or simply represented a coincidental occurrence." Id. The authors concluded "that the benefits of prevention of tetanus and diphtheria infection far outweigh the risk of GBS." Id.

Dr. Rinker concluded that the Tdap vaccine can cause GBS "[b]ased on case reports attesting to the possible causative relationship between tetanus vaccine and GBS, caution from the IOM about causative association between tetanus vaccines and GBS, and the biological plausibility of an idiosyncratic, immune-mediated reaction to Tdap causing GBS." Pet. Ex. 9 at 7.

ii. Althen Prong Two

Dr. Rinker opined that more likely than not, petitioner's Tdap vaccination caused him to develop GBS through the mechanism of molecular mimicry. Pet. Ex. 9 at 4, 7. He explained that petitioner's April 26, 2017 Tdap vaccine "triggered an idiosyncratic reaction in which his immune system mounted an autoimmune response directed towards peripheral myelin in his body." Id. at 6.

Dr. Rinker explained that petitioner had two potential triggers that preceded the onset of his GBS: (1) a Tdap vaccination on April 26, 2017 and a Prevnar vaccination on April 28, 2017

[33] Hussam Ammar, Guillain-Barré Syndrome After Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine: A Case Report, 5 J. Med. Case Reps. 502 (2011).

[34] Rohit Bakshi & Michael C. Graves, Guillain-Barré Syndrome After Combined Tetanus-Diphtheria Toxoid Vaccination, 147 J. Neurological Scis. 201 (1997).

and (2) a diarrheal illness that began on or around May 1, 2017. Pet. Ex. 9 at 2, 4. He opined that "it is not possible to distinguish whether vaccination or the diarrheal illness alone was responsible for his GBS, or whether the two immunological stimuli worked in concert to provoke the immune response." Id. at 6.

He argued there is insufficient evidence to claim that the diarrheal illness was a more likely cause of petitioner's GBS than the Tdap vaccine. Pet. Ex. 9 at 6. In support, Dr. Rinker noted no microbiological tests were performed to identify a specific organism. Id. In his supplemental report, he argued that "while [petitioner] *may* have been affected by *C. jejuni* in the days leading up to the onset of his GBS, there [was] no confirmatory laboratory evidence to support this possibility as the organism was never identified, despite testing."[35] Pet. Ex. 31 at 1.

Next, he opined "it is possible" the diarrheal illness was not infectious, as "many transient diarrheal illnesses are caused by toxins produced by bacterial contaminants of food, rather than the bacteria directly, which are self-limited and resolve without inciting a significant immune response." Pet. Ex. 9 at 6.

Lastly, he added that "there are many other potential causes of gastroenteritis that could have produced [petitioner's] symptoms" since such illnesses are common, and their causes are rarely identified. Pet. Ex. 31 at 1. Dr. Rinker stated that according to the CDC, "only 0.2 to 1.7 in every 1,000 diagnosed and undiagnosed *Campylobacter* illnesses leads to GBS, but [the CDC] estimates *Campylobacter* are responsible for 5-41% of GBS illnesses." Pet. Ex. 34 at 1. Additionally, the CDC's Tdap Vaccine Information Statement[36] lists diarrhea as a possible adverse reaction. Pet. Ex. 33 at 2. However, Dr. Rinker acknowledged that he was unable to find medical literature to support the time period over which post-vaccination diarrhea may be expected to occur. Pet. Ex. 31 at 1-2.

Dr. Rinker opined that petitioner's Tdap vaccine, and not the diarrheal illness, was the more likely cause of petitioner's GBS. Pet. Ex. 31 at 1; Pet. Ex. 9 at 6-7. First, as explained in more detail in the following section, he opined that the latency period between vaccination and onset (9 to 10 days) and diarrhea and onset (4 to 5 days) "favors the vaccine as the more likely cause." Pet. Ex. 9 at 6-7. Next, he noted there was insufficient evidence to support Dr. Chaudhry's opinion that petitioner's diarrheal illness was the immunological trigger when (1) *C. jejuni* is an uncommon cause of gastroenteritis and (2) there was nothing in the record linking *C. jejuni* to petitioner's GBS. Pet. Ex. 31 at 2. Dr. Rinker found that "the mere presence of diarrhea before the onset of GBS, especially when *C. jejuni* was never identified, provides an unlikely cause of [petitioner's] GBS in comparison to the Tdap vaccination." Id.

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[35] After a review of the records, it does not appear that testing was done for *C. jejuni* or any related organisms. Additionally, in Dr. Rinker's first expert report, he noted "no microbiological reports were available." Pet. Ex. 9 at 6. It is not clear why Dr. Rinker notes testing was done in his supplemental report.

[36] Vaccine Information Statement, Tdap (Tetanus, Diphtheria, Pertussis) Vaccine: What You Need to Know, Ctrs. for Disease Control & Prevention, https://www.cdc.gov/vaccines/hcp/vis/vis-statements/tdap.html (last reviewed Apr. 1, 2020).

Dr. Rinker concluded that "[a]lthough documented cases of GBS following tetanus vaccination are rare, the biological plausibility of GBS following vaccination, and the multiple published case reports describing GBS following administration of tetanus vaccine, fit the definition of an idiosyncratic response to tetanus vaccination." Pet. Ex. 9 at 6. Thus, petitioner "more likely than not developed GBS as a consequence of his Tdap vaccination." Id. at 7.

iii. Althen Prong Three

With regard to timing, Dr. Rinker opined an "autoimmune response generated by an immunization is mediated by the adaptive immune system, which develops over a period of weeks following antigen exposure." Pet. Ex. 9 at 6. Such adaptive immune responses increase between 7 and 14 days following vaccination, "depending on whether the immunization is a primary or secondary exposure." Id. at 7. Citing Siegrist,[37] Dr. Rinker opined that "[s]ubsequent encounters with a foreign antigen typically result in more rapid adaptive immune response than an initial encounter." Id. (citing Pet. Ex. 20 at 9 fig.2.3).

Here, Dr. Rinker opined petitioner's onset was on May 5 or 6, 2017, or 9 to 10 days following petitioner's vaccinations, which he found was within the appropriate time frame. Pet. Ex. 9 at 2, 7. Although petitioner's diarrheal illness preceded the onset of his GBS by 4 to 5 days, Dr. Rinker opined that "[t]his time course [was] well below the median latency for *C. jejuni* infection." Id. at 6; see also Pet. Ex. 32 at 2 (noting "neurological symptoms of GBS that follow *C. jejuni* infection typically occur 1-3 weeks after the onset of diarrheal illness");[38] Pet. Ex. 34 at 1 (noting the incubation period of a *Campylobacter* infection is typically two to five days). He concluded that "the timing of GBS onset argues more strongly in favor of the vaccine as the causative immune stimulus rather than the diarrheal illness." Id. at 7.

He cited various articles that examined the timing between an antecedent immunological trigger and onset of GBS. First, Dr. Rinker cited Sivadon-Tardy et al., who examined 405 patients with GBS admitted to a French reference center between 1996 and 2004. Pet. Ex. 21 at 1. Of the 405 patients, a causing agent could not be identified in 234 patients (58%) while an identified cause was found in 171 patients (42%). Id. at 3. They found the median latency period between flu A and *C. jejuni* infections and GBS were 15 and 10 days, respectively, while the median latency period for unidentified causes was 6.5 days. Id. at 8 tbl.2. Of the 14 patients with evidence of a flu A or B infection prior to onset, one received the flu vaccine 15 days prior to onset. Id. at 4, 5 tbl.1.

Of the 532 patients in Schonberger et al. who received a flu vaccination prior to onset of GBS, 71% developed GBS within four weeks after vaccination, with 53% developing GBS in the second and third weeks after vaccination. Pet. Ex. 42 at 6. They found the largest percentage of cases (10%) occurred 16 and 17 days post-vaccination. Id. at 6-7, 7 fig.5. Similarly, Souayah et

[37] Claire-Anne Siegrist, Vaccine Immunology, in Plotkin's Vaccines 16 (7th ed. 2017).

[38] Ban Mishu Allos, *Campylobacter Jejuni* Infections: Update on Emerging Issues and Trends, 32 Clinical Infectious Diseases 1201 (2001).

al. found an onset peak in the first two weeks after any vaccination, including after tetanus and diphtheria toxoids and pneumococcal polyvalent vaccine. Pet. Ex. 22 at 3-4.

With regard to tetanus-containing vaccines specifically, Ammar discussed a 40-year-old man who received a Tdap vaccine, and developed GBS within one to two weeks. Pet. Ex. 28 at 1-2. Bakshi and Graves found a patient with a GBS onset of four days post-tetanus-diphtheria toxoid vaccination. Pet. Ex. 29 at 1. The patient in Pollard and Selby suffered three episodes of a demyelinating neuropathy, 21, 14, and 10 days following tetanus toxoid vaccination. Resp. Ex. A, Tab 17. The patient in Newton and Janati developed GBS nine days after a pure tetanus toxoid vaccine. Pet. Ex. 40 at 1. Lastly, Baxter et al. found one patient who received a Tdap vaccine and had an onset of GBS 45 days after vaccination, while three[39] patients received a tetanus-diphtheria vaccine and their onsets were eight, 12, and 41 days after vaccination. Pet. Ex. 30 at 5 tbl.1.

Baxter also noted two cases of GBS following a 23-valent pneumococcal polysaccharide vaccine,[40] with onsets of one day and 14 days. Pet. Ex. 30 at 5 tbl.1. The patient with a 14-day onset also received a flu vaccine, an inactivated (killed) polio vaccine, and a Japanese encephalitis vaccine. Id.

2. Respondent's Expert, Dr. J. Lindsay Whitton

a. Background and Qualifications

Dr. J. Lindsay Whitton received his B.Sc. in molecular biology, his M.B., Ch.B. in medicine, and his Ph.D. in herpesvirus transcription from the University of Glasgow in Scotland. Resp. Ex. B at 1. He also completed internships in medicine and surgery, and held various professor positions since 1986. Resp. Ex. A at 1; Resp. Ex. B at 1. He is currently a Professor in the Department of Immunology and Microbiology at Scripps Research Institute in California. Resp. Ex. B at 1. Dr. Whitton is a member of various professional societies and editorial boards. Id. He has authored or co-authored almost 200 publications. Id. at 2-15.

b. Opinion

i. Althen Prong One

Dr. Whitton opined that the evidence does not support Dr. Rinker's contention that the Tdap vaccine[41] can cause GBS through molecular mimicry. Resp. Ex. A at 7. Instead, "it is well-established that a recent GI infection can incite GBS." Id. at 12.

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[39] One of these patients also received a flu vaccine. Pet. Ex. 30 at 5 tbl.1.

[40] This is not the pneumococcal vaccine that petitioner received.

[41] Because the petition and Dr. Rinker focus solely on the Tdap vaccine, Dr. Whitton does not discuss the Prevnar vaccine in his expert report. Resp. Ex. A at 1.

He opined that GBS is an autoimmune disease thought to be triggered by molecular mimicry. Resp. Ex. A at 3; see also Resp. Ex. A, Tab 6 at 1-3 ("Molecular mimicry of pathogen-borne antigens, leading to generation of crossreactive antibodies that also target gangliosides, is part of the pathogenesis of GBS.").[42] He agreed that two-thirds of cases are "preceded by signs and/or symptoms of an infection, often of the respiratory or GI tracts," within the four weeks prior to onset of GBS. Resp. Ex. A at 4; see also Resp. Ex. A, Tab 1 at 2;[43] Resp. Ex. A, Tab 2 at 2;[44] Resp. Ex. A, Tab 5 at 3.[45]

Dr. Whitton explained that infectious diseases have an incubation period prior to the presence of symptoms, while vaccinations do not. Resp. Ex. A at 4. Therefore, an adaptive immune response can begin a few days after an infection has begun, but before any symptoms of such infection have appeared. Id. at 5. Because it is the infection and not the illness (symptoms) that trigger the adaptive immune response, this incubation period "makes it almost impossible to know exactly when the immune system was first triggered by an infection." Id. at 5, 10.

Dr. Whitton opined that several studies have failed to support a causal association between tetanus vaccines and GBS. Resp. Ex. A at 6-7. First, he cited Tuttle et al.,[46] a 1997 report on two active surveillance studies examining whether tetanus-toxoid-containing vaccines can cause GBS. Resp. Ex. A, Tab 11 at 1. Of the 213 adult cases and 93 children cases of GBS, the authors found only one adult and two children who developed GBS within six weeks of a tetanus-containing vaccine. Id. at 2-3. They concluded there was "no association of public health significance [] between tetanus-toxoid-containing vaccine and [GBS]." Id. at 4.

Next, Dr. Whitton cited a letter from Nordin et al.[47] regarding Tdap and GBS. Resp. Ex. A, Tab 13 at 1. This letter discussed active surveillance results on the safety of the Tdap vaccine from a prior study[48] of 660,245 doses administered. Id. The authors re-examined the data after

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

[43] Pieter A. van Doorn et al., Clinical Features, Pathogenesis, and Treatment of Guillain-Barré Syndrome, 7 Lancet Neurology 939 (2008).

[44] Hugh J. Willison, The Immunobiology of Guillain-Barré Syndromes, 10 J. Peripheral Nervous Sys. 94 (2005).

[45] Richard A. C. Hughes & Jeremy H. Rees, Clinical and Epidemiologic Feature of Guillain-Barré Syndrome, 176 J. Infectious Diseases S92 (1997).

[46] Jessica Tuttle et al., The Risk of Guillain-Barré Syndrome After Tetanus-Toxoid Containing Vaccines in Adults and Children in the United States, 87 Am. J. Public Health 2045 (1997). This article was also cited by Dr. Chaudhry. See Resp. Ex. C, Tab 13.

[47] James D. Nordin et al., Tdap and GBS Letter, 29 Vaccine 1122 (2011).

[48] The original study was not filed.

reaching two million doses in the Vaccine Safety Datalink from 2005 to 2009. Id. After looking at patients who received a Tdap vaccine in the 42 days prior to onset of GBS, they "conclude[d] that there is no evidence that Tdap is associated with an increased risk of GBS within 6 weeks of vaccination." Id.

He also cited to Kuitwaard et al.[49] and Baxter et al.,[50] articles that focused on the risk of GBS recurrence after vaccination, especially flu vaccination. Resp. Ex. A, Tab 12; Resp. Ex. A, Tab 14. Of the 245 patients with GBS and 76 patients with CIDP in Kuitwaard et al.,[51] 23 GBS and eight CIDP patients reported a vaccination in the eight weeks preceding onset. Resp. Ex. A, Tab 12 at 3. The preceding vaccination in 3% was tetanus, while 7% received multiple unidentified vaccinations. Id. at 2 fig.1. In both articles, the authors found no cases of recurrent GBS after vaccination. Id. at 1; Resp. Ex. A, Tab 14 at 1.

However, Dr. Whitton cited literature acknowledging that vaccinations have been suggested to be associated with GBS. See, e.g., Resp. Ex. A, Tab 1 at 3; Resp. Ex. A, Tab 2 at 4; Resp. Ex. A, Tab 3 at 7;[52] Resp. Ex. A, Tab 6 at 3-4; Resp. Ex. A, Tab 14 at 1.

With regard to the case reports Dr. Rinker cited to support his theory, Dr. Whitton opined case reports are unreliable and "cannot be used to imply causality." Resp. Ex. A at 7. He argued Dr. Rinker's reliance on Souayah et al. and VAERS, like case reports, is misplaced because VAERS reports cannot prove causation. Id. at 9.

Dr. Whitton also criticized Dr. Rinker's use of outdated reports and recommendations, including the 1994 IOM report. Resp. Ex. A at 8. Dr. Whitton stated that (1) the vaccine at issue in the case was not licensed until 2005 and thus, was not considered by the 1994 report, and (2) the 2012 IOM report[53] superseded the 1994 report. Id. In particular, the 2012 IOM report found "[t]he evidence [was] inadequate to accept or reject a causal relationship between diphtheria toxoid-, tetanus toxoid-, or acellular pertussis-containing vaccines and GBS," as well as CIDP. Resp. Ex. A, Tab 15 at 35, 37. Additionally, the 2012 report noted the patient in Pollard and

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[49] Krista Kuitwaard et al., Recurrences, Vaccinations and Long-Term Symptoms in GBS and CIDP, 14 J. Peripheral Nervous Sys. 310 (2009).

[50] Roger Baxter et al., Recurrent Guillain-Barré Syndrome Following Vaccination, 54 Clinical Infectious Diseases 800 (2012).

[51] These patients were all members of the Dutch society of neuromuscular disorders who received and returned a questionnaire. Resp. Ex. A, Tab 12 at 1.

[52] Clarence C. Tam et al., Influenza, Campylobacter and Mycoplasma Infections, and Hospital Admissions for Guillain-Barré Syndrome, England, 12 Emerging Infectious Diseases 1880 (2006).

[53] Inst. of Med., Diphtheria Toxoid-, Tetanus Toxoid-, and Acellular Pertussis-Containing Vaccines, in Adverse Effects of Vaccines: Evidence and Causality 525 (Kathleen Stratton et al. eds., 2012).

Selby was "subsequently diagnosed with a spontaneously relapsing remitting neuropathy" after the patient "developed symptoms in association with acute viral infections." Id. at 36. The IOM noted "the authors did not rule out other possible causes and did not provide evidence beyond a temporal relationship with vaccine administration." Id. at 36-37. Therefore, they found the patient's "spontaneous development of peripheral neuropathy [made] it difficult to conclude that the tetanus toxoid vaccines were the causative agent." Id. at 37.

ii. Althen Prong Two

Dr. Whitton agreed that there are two proposed causes for petitioner's GBS: (1) GI infection and (2) Tdap vaccination. Resp. Ex. A at 11. He found a GI infection is a known trigger of GBS, while Tdap vaccination is not. Id. He opined that petitioner's GI infection, not his diarrheal symptoms or Tdap vaccination, initiated the adaptive immune response that may have caused petitioner's GBS, and thus, "the GI infection is the far likelier cause." Id. at 11-12.

He acknowledged that there is no proof that petitioner had *C. jejuni*; however, he argued that it is very common in GBS cases that an organism is not isolated, even those preceded by an infection. Resp. Ex. A at 6, 10; see, e.g., Resp. Ex. A, Tab 6 at 2 ("In about half of patients with GBS, a specific type of preceding infection can be identified."). Hughes and Rees, for example, noted that "[i]n most cases, the precise infection is not clear from the medical history and has often resolved by the time neuropathic symptoms develop. Viral or bacterial cultures are usually negative, and serologic tests may lack sensitivity and specificity." Resp. Ex. A, Tab 5 at 3. However, they also acknowledged that "stools from *C. jejuni*-infected patients may contain viable organisms for up to 4 weeks." Id. at 4-5.

iii. Althen Prong Three

Dr. Whitton opined petitioner's onset of GBS was on or around May 6, 2017, which is 10 days after his Tdap vaccination on April 26, 2017 and 6 days after the onset of his diarrhea on April 30, 2017. Resp. Ex. A at 6, 10. He found both intervals "fall squarely within the accepted range when considering the kinetics of the adaptive immune response." Id. at 10. However, he argued coincidental cases of GBS within 6 weeks of Tdap vaccination are inevitable and do not prove, more likely than not, that the Tdap vaccine caused petitioner's GBS. Id. at 11-12.

Dr. Whitton opined that petitioner's GI infection "most probably" began before, on, or near the date of vaccination. Resp. Ex. A at 6. With an infection like *Campylobacter*, for example, "onset of disease symptoms usually occurs 2 to 5 days after infection with the bacteria, but can range from 1 to 10 days."[54] Resp. Ex. E, Tab 2 at 2;[55] see also Resp. Ex. A at 4-5. If petitioner's diarrheal illness was caused by *C. jejuni*, Dr. Whitton explained "that [the] infection most probably began 2-5 days prior to the appearance of diarrhea," which would be around April

[54] According to literature filed by Dr. Chaudhry, there is a mean incubation period of three days (range one to seven days) with a *Campylobacter* infection. Resp. Ex. C, Tab 7 at 1.

[55] Campylobacter, World Health Org. (May 1, 2020), https://www.who.int/news-room/fact-sheets/detail/campylobacter.

25 to April 28, or around the date of petitioner's Tdap vaccination. Resp. Ex. A at 6. "[S]ince the incubation period for *C. jejuni* may be as long as 10 days, petitioner's GI infection may have begun as early as [April 20, 2017], 6 days prior to vaccination." Id. Thus, "[w]hen an incubation period is incorporated into the timing calculation, it is quite likely that the interval between stimulation of the adaptive immune system and GBS is longer for GI infection than it is for the Tdap vaccination." Id. at 10. However, he acknowledged that "the existence of an incubation period makes it almost impossible to know exactly when the immune system was first triggered by an infection." Id. at 5.

Winer et al.[56] examined the incidence of antecedent events and serological evidence of preceding infection in 100 patients with GBS. Resp. Ex. A, Tab 10 at 1. They found respiratory infection symptoms within one month of onset of neuropathic symptoms in 38% of GBS patients and 12% of controls, and GI infection symptoms in 17% of GBS patients and 3% of controls. Id. at 1-2. The authors also noted immunizations "were equally common in the patient and control subjects." Id. at 1. Serological evidence of a recent infection was identified in 31% of patients, with *C. jejuni* (14%) in significantly more patients than controls. Id. at 1, 3-4. Results showed a peak incidence of symptoms of an infection one to two weeks prior to neuropathic symptom onset, with the mean latency being shorter for GI infection. Id. at 2, 4. The authors concluded "the greatest relative risk of developing GBS is seen in the first 2 weeks following infection." Id. at 4. Additionally, the authors did not find an association between vaccination and GBS, but noted "[i]t [was] possible that the number of GBS patients surveyed was not sufficient to detect vaccine associated cases." Id. at 5.

Similarly, Hughes and Rees, looking at the association between *C. jejuni* and GBS, noted "an average of 10.5 days . . . between the onset of gastroenteritis and the onset of neuropathic symptoms." Resp. Ex. A, Tab 5 at 4.

3. Respondent's Expert, Dr. Vinay Chaudhry

a. Background and Qualifications

Dr. Vinay Chaudhry is board certified in neurology, neuromuscular diseases, electrodiagnostic medicine, and clinical neurophysiology. Resp. Ex. C at 1; Resp. Ex. D at 35. He received his M.B. and B.S. in India in 1980 and then completed an internship and various residencies and fellowships from 1980 to 1989. Resp. Ex. D at 2-3. He is currently a Professor of Neurology at Johns Hopkins University School of Medicine and the Co-Director of the Neurology EMG Laboratory at Johns Hopkins Hospital. Id. at 1. Dr. Chaudhry specialized in the field of neuromuscular diseases. Resp. Ex. C at 1. He has an active clinical practice where he sees over 2,000 patients per year. Id. He has authored or co-authored over 200 publications. Resp. Ex. D at 3-20.

[56] J. B. Winer et al., A Prospective Study of Acute Idiopathic Neuropathy. II. Antecedent Events, 51 J. Neurology Neurosurgery & Psychiatry 613 (1988).

b. Opinion

i. Althen Prong One

Dr. Chaudhry opined GBS is a post-infectious immune disorder and "molecular mimicry between an infectious agent and the nerve is the prevailing hypothesis." Resp. Ex. C at 12; see also Resp. Ex. C, Tab 2 at 1-2.[57] He agreed with Dr. Whitton that the Tdap vaccine is not an agent that would trigger GBS through the mechanism of molecular mimicry, and added that Prevnar is also not a triggering agent. Resp. Ex. C at 11-15.

Consistent with Dr. Rinker's and Dr. Whitton's opinions, Dr. Chaudhry cited various articles that support the finding that "[a]ntecedent infection precedes two-thirds of cases of GBS with symptoms of upper respiratory tract infection in 60% and of [GI] infection in 30%." Resp. Ex. C at 10-11; see also Resp. Ex. C, Tab 1 at 2;[58] Resp. Ex. C, Tab 2 at 2, 4; Resp. Ex. C, Tab 3 at 1;[59] Resp. Ex. C, Tab 9 at 2.[60] He noted that *C. jejuni* is the most predominant infection that leads to GBS, as it is found in 25-50% of GBS patients, but other infections are also associated with GBS. Resp. Ex. C at 11-12; see also Resp. Ex. C, Tab 7 at 4-5 ("*C. jejuni* infection has been established as a trigger of GBS . . . . It has been estimated that 30 to 40 percent of GBS illness is attributable to *Campylobacter* infection . . . .").[61]

Dr. Chaudhry acknowledged that GBS has been reported shortly after vaccinations like rabies and influenza A. Resp. Ex. C at 11, 13-14; see Resp. Ex. C, Tab 1 at 2; Resp. Ex. C, Tab 2 at 5-6. However, he argued not all vaccines are the same and there is no evidence of GBS occurring after Tdap or Prevnar 13 vaccination. Resp. Ex. C at 12-13, 15; Resp. Ex. E at 1. Yet, medical literature cited by Dr. Chaudhry acknowledged "epidemiological studies [that] have reported development of GBS following vaccinations," including those containing tetanus

[57] Francine J. Vriesendorp, Guillain-Barré Syndrome: Pathogenesis, UpToDate, https://www.uptodate.com/contents/guillain-barre-syndrome-pathogenesis/print (last updated Sept. 25, 2018).

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

[59] *Campylobacter* (Campylobacteriosis): Guillain-Barré Syndrome, Ctrs. for Disease Control & Prevention, https://www.cdc.gov/campylobacter/guillain-barre.html (last reviewed Dec. 20, 2019).

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

[61] Ban M. Allos, Clinical Manifestations, Diagnosis, and Treatment of Campylobacter Infection, UpToDate, https://www.uptodate.com/contents/clinical-manifestations-diagnosis-and-treatment-of-campylobacter-infection/print (last updated Aug. 9, 2019).

toxoid. Resp. Ex. E, Tab 4 at 8-9.[62] Additionally, other literature noted cases of GBS after Prevnar 13 vaccination. See Resp. Ex. E, Tab 10 at 4.[63]

Like Dr. Whitton, Dr. Chaudhry relied on the 2012 IOM report, which found "[t]he evidence [was] inadequate to accept or reject a causal relationship between diphtheria toxoid-, tetanus toxoid-, or acellular pertussis-containing vaccines and GBS." Resp. Ex. C at 12 (quoting Resp. Ex. A, Tab 15 at 35). Dr. Chaudhry added that the 2012 IOM report reviewed several publications on the development of GBS after vaccines containing tetanus, diphtheria, and acellular pertussis antigens alone or in combination, some of which Dr. Rinker relied upon. Id. at 14 (citing Pet. Ex. 40; Pet. Ex. 29; Resp. Ex. A, Tab 17); see Resp. Ex. A, Tab 15 at 34. The IOM found these "publications did not provide evidence beyond temporality" and "did not contribute to the weight of mechanistic evidence." Resp. Ex. A, Tab 15 at 34-35.

Dr. Chaudhry also cited to Tuttle et al. to opine that the number of cases of GBS following administration of a tetanus-toxoid-containing vaccine is not greater than the number of GBS cases expected by chance alone. Resp. Ex. C at 13 (citing Resp. Ex. A, Tab 11). Thus, he argued "the risk for GBS after administration of tetanus toxoid is extremely low." Id. at 14.

With regard to pneumococcal vaccines, and Prevnar 13 specifically, Dr. Chaudhry cited studies finding no or minimal incidences of GBS following such vaccinations. Resp. Ex. C at 12. First, he cited to Haber et al., which found the incidence of GBS after Prevnar 13 vaccine "far lower" than the background incidence of GBS overall. Id. (citing Resp. Ex. C, Tab 10). Haber et al. evaluated all adverse events reported to VAERS from June 2012 to December 2015 following Prevnar 13 vaccination in individuals 19 years of age and older. Resp. Ex. C, Tab 10 at 2. Of the 2,976 reports to VAERS during this time period, the authors identified 11 reports of possible GBS following Prevnar 13 vaccination. Id. at 4. Ten of the 11 reports listed Prevnar 13 as the only vaccine administered, while one report also listed a flu vaccine was administered. Id. One case had an upper respiratory infection 16 days prior to GBS onset. Id. The authors found "no disproportionate reporting for GBS." Id. at 5.

He next cited to safety studies where no cases of GBS were reported. Resp. Ex. C at 12. In Jackson et al.,[64] the authors "conducted a randomized clinical trial to evaluate safety and immunogenicity of [Prevnar 13] compared to [23-valent pneumococcal polysaccharide vaccine] in adults aged 70 years and older who had been previously vaccinated with [23-valent pneumococcal polysaccharide vaccine]." Resp. Ex. C, Tab 15 at 2. The authors note one serious

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[62] Kishan Kumar Nyati & Roopanshi Nyati, Role of *Campylobacter Jejuni* Infection in the Pathogenesis of Guillain-Barré Syndrome: An Update, 2013 BioMed Rsch. Int'l 1.

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

[64] Lisa A. Jackson et al., Immunogenicity and Safety of a 13-Valent Pneumococcal Conjugate Vaccine in Adults 70 Years of Age and Older Previously Vaccinated with 23-Valent Pneumococcal Polysaccharide Vaccine, 31 Vaccine 3585 (2013).

adverse event (idiopathic thrombocytopenic purpura) that was considered related to vaccination. Id. at 5-6. In the follow-up study also authored by Jackson et al.,[65] "no vaccine related serious adverse events [] or deaths were reported." Resp. Ex. C, Tab 16 at 5.

Lastly, Dr. Chaudry cited to the Prevnar 13 package insert as well as efficacy and safety of Prevnar 13 from Pfizer. Resp. Ex. C at 12. Neither lists GBS as an adverse event. See Resp. Ex. C, Tab 14;[66] Resp. Ex. C, Tab 17.[67]

Dr. Chaudhry opined that a "*Streptococcus* pneumonia infection is not one of the infectious agents reported to precede GBS and hence pneumococcal vaccines against the bacteria *Streptococcus* pneumonia is unlikely to cause GBS." Resp. Ex. C at 12 (emphasis added).

ii. Althen Prong Two

Dr. Chaudhry opined that petitioner's Tdap and/or Prevnar vaccine did not play a causative role in the development of his GBS, and instead his GBS was secondary to his diarrheal illness. Resp. Ex. C at 11, 15; Resp. Ex. E at 1. He found that "[i]n the presence of a known preceding cause, a rare possible association [with the vaccines] is difficult to envisage." Resp. Ex. C at 14.

In support of his opinion that petitioner's GBS was preceded by a diarrheal illness, Dr. Chaudhry noted petitioner complained of fatigue, bloody stools, chills, and feeling feverish on May 3, 2017, and was subsequently diagnosed with gastroenteritis. Resp. Ex. C at 10-11, 15. Dr. Chaudhry found petitioner's presentation consistent with the most common symptoms of *Campylobacter* infection, which include cramping, abdominal pain, diarrhea, bloody stools, fever, headache, nausea, and vomiting. Resp. Ex. C at 10-11; Resp. Ex. E at 2-4; see Resp. Ex. C, Tab 7 at 1-2; Resp. Ex. E, Tab 2 at 2.

Dr. Chaudhry added that *Campylobacter* infection is the most common cause of diarrhea and gastroenteritis. Resp. Ex. E at 1-2; Resp. Ex. C at 11; see, e.g., Resp. Ex. C, Tab 6 at 5, 9;[68]

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[65] Lisa A. Jackson et al., Influence of Initial Vaccination with 13-Valent Pneumococcal Conjugate Vaccine or 23-Valent Pneumococcal Polysaccharide Vaccine on Anti-Pneumococcal Responses Following Subsequent Pneumococcal Vaccination in Adults 50 Years and Older, 31 Vaccine 3594 (2013).

[66] Prevnar 13, Pfizer, https://www.pfizermedicalinformation.com/en-us/prevnar-13 (last visited Jan. 20, 2020).

[67] Proven Efficacy and Safety, Pfizer, https://prevnar13adult.pfizerpro.com/efficacy-and-safety/proven (last visited Sept. 15, 2019).

[68] Ban M. Allos, Microbiology, Pathogenesis, and Epidemiology of Campylobacter Infection, UpToDate, https://www.uptodate.com/contents/microbiology-pathogenesis-and-epidemiology-of-campylobacter-infection/print?topicRef=2716&source=see_link (last updated Apr. 18, 2019).

Resp. Ex. E, Tab 1 at 1 ("Infection with [*C. jejuni*] is one of the most common causes of gastroenteritis worldwide.");[69] Resp. Ex. E, Tab 2 at 1.

Dr. Chaudhry also cited to statements by Dr. White and Dr. Melling, petitioner's treating physicians, where they considered petitioner's history of diarrhea. Resp. Ex. C at 15. Dr. White, for example, wrote petitioner's medical history was "quite classic for [GBS]; he had a bout of diarrhea and one week later experienced significant weakness with suppressed reflexes." Pet. Ex. 6 at 14. Petitioner's history of diarrhea was also noted by Dr. Melling. See Pet. Ex. 3 at 7. Dr. Chaudhry argued "the treating physicians considered the history of diarrhea relevant in making a diagnosis of GBS." Resp. Ex. C at 15.

Thus, due to petitioner's presentation on May 3, 2017, treating physician statements, and because *C. enteritis* is the leading cause of diarrhea, Dr. Chaudhry found it likely that petitioner suffered from a *C. jejuni* infection. Resp. Ex. C at 11.

Although petitioner was not confirmed to have *C. jejuni*, Dr. Chaudhry contended that (1) petitioner was never tested for such infection and (2) a majority of *C. jejuni* infections are likely undiagnosed. Resp. Ex. E at 2-3; see Resp. Ex. E, Tab 6 at 3.[70] Dr. Chaudhry found petitioner's clinical course and "the known [mechanism of] molecular mimicry are highly suggestive if not indicative of *C. jejuni* causing [petitioner's] GBS." Resp. Ex. E at 3. He concluded that "more likely than not," petitioner's GBS was caused by a *C. jejuni*-associated diarrhea, "a proven association," rather than his Tdap vaccination, "an unproven association." Id. at 4.

iii. Althen Prong Three

Dr. Chaudhry noted petitioner was admitted to the ER on May 11, 2017 complaining of a five-day history of diffuse weakness. Resp. Ex. C at 9. Relying on petitioner's medical records, he found petitioner's onset of weakness began on either May 5, 2017 or May 9, 2017. Id. (compare Pet. Ex. 3 at 7, 9, 13, 15, 20, with Pet. Ex. 6 at 7, 9). However, he then noted that "[o]ne day prior to the onset (5/4/2017) [petitioner] was able to go fishing and did not have any weakness." Id. (citing Pet. Ex. 3 at 9).

He found the onset of petitioner's diarrheal illness difficult to ascertain. Resp. Ex. C at 15. He cited medical records from petitioner's May 2017 hospital stay that documented a history of diarrhea two weeks prior to his admission on May 11, 2017. Id. at 9 (citing Pet. Ex. 3 at 7, 9, 13, 15, 17, 20). However, he also cited to medical records from May 3, 2017 where petitioner complained of diarrhea for three days and was diagnosed with gastroenteritis. Id. (citing Pet. Ex. 5 at 2-3).

Dr. Chaudhry opined that *C. enteritis* and diarrhea have been established as a trigger of GBS between one and two weeks following infection. Resp. Ex. C at 11. The CDC noted there

[69] Petitioner also cited this article. See Pet. Ex. 32.

[70] Noel McCarthy & Johan Giesecke, Incidence of Guillain-Barré Syndrome Following Infection with *Campylobacter Jejuni*, 153 Am. J. Epidemiology 610 (2001).

is a mean incubation period of three days (range one to seven days) with a *Campylobacter* infection, which "typically occurs between one and two weeks before the onset of neurologic symptoms." Resp. Ex. C, Tab 7 at 1, 4-5.

Studies have found onset of *C. jejuni*-associated GBS "typically occur[s] 1-3 weeks after the onset of diarrheal illness." Resp. Ex. E, Tab 1 at 1; see also Resp. Ex. E, Tab 4 at 1 ("Almost 25%-40% of GBS patients worldwide suffer from *C. jejuni* infection 1-3 weeks prior to the illness."). Similarly, Rees et al.[71] found "the median interval between the onset of diarrhea and neuropathic symptoms was 9 days (range, 2 to 20)." Resp. Ex. C, Tab 8 at 3.

With regard to the vaccinations at issue here, Haber et al. found 11 cases of possible GBS following Prevnar vaccine with a median onset interval of 9 days (range 2-34 days). Resp. Ex. C, Tab 10 at 4. Other articles cited by Dr. Chaudhry that note or discuss onset were cited by Dr. Rinker and/or Dr. Whitton and are discussed above.

IV. DISCUSSION

A. Standards for Adjudication

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

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). The petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006). Instead, petitioner may satisfy his burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

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

[71] Jeremy H. Rees et al., *Campylobacter Jejuni* Infection and Guillain-Barré Syndrome, 333 New Eng. J. Med. 1374 (1995).

prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B). However, if a petitioner fails to establish a prima facie case, the burden does not shift. Bradley v. Sec'y of Health & Hum. Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

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

B. Causation

To receive compensation through the Program, petitioner must prove either (1) that he suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that he received, or (2) that he suffered an injury that was actually caused by a vaccination. See §§ 11(c)(1), 13(a)(1)(A); Capizzano, 440 F.3d at 1319-20. Because petitioner does not allege he suffered a Table Injury, he must prove a vaccine he received caused his injury. To do so, petitioner must establish, by preponderant evidence: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen v. Sec'y of Health & Hum. Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005).

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

evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in petitioner's favor).

V. CAUSATION ANALYSIS

A. Althen Prong One

Under Althen Prong One, petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1375 (Fed. Cir. 2009); Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by a "sound and reliable" medical or scientific explanation. Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1359 (Fed. Cir. 2019); see also Knudsen, 35 F.3d at 548; Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioner relies upon a medical opinion to support his theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen v. Sec'y of Health & Hum. Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better than the soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

Here, the experts agree that molecular mimicry is not a disputed theory as it relates to GBS. They also agreed that two-thirds of GBS cases are preceded by a respiratory or GI infection or illness, with a *C. jejuni* infection being the most common GI infection. And all of the experts cited literature discussing how *C. jejuni*, in particular, can cause GBS via molecular mimicry. They did not dispute that a GI illness can cause GBS. However, they do dispute whether the vaccines at issue here can cause GBS.

Due to the facts and circumstances of this case, specifically the fact that petitioner had a preceding GI illness prior to his GBS, the undersigned's determination as to causation turns on an analysis of Althen Prong Two. Assuming that petitioner has proven a sound and reliable causal mechanism under Althen Prong One, the undersigned finds petitioner did not provide preponderant evidence of a logical sequence of cause and effect under the facts of this case where petitioner had a GI illness at the same time as his vaccinations. Thus, the undersigned turns her focus to Althen Prong Two. See Vaughan ex rel. A.H. v. Sec'y of Health & Hum. Servs., 107 Fed. Cl. 212, 221-22 (2012) (finding the special master's failure to rule on Althen prong one not fatal to his decision because Althen prong two was fatal to petitioner's case); Hibbard v. Sec'y of Health & Hum. Servs., 698 F.3d 1355, 1364 (Fed. Cir. 2012) ("discern[ing] no error in the manner in which the special master chose to address the Althen [prongs]" when he focused on Althen prong two after "assuming the medical viability of [the] theory of causation").

B. Althen Prong Two

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

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting Althen, 418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras v. Sec'y of Health & Hum. Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). The petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, petitioner may satisfy his burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

To summarize petitioner's clinical course, petitioner received a Tdap vaccination on April 26, 2017. Two days later, on April 28, 2017, petitioner received a Prevnar vaccination. On May 3, 2017, petitioner "complain[ed] of feeling run down, fatigued, muscle aches, headaches, diarrhea, and urinary frequency x3 days." Pet. Ex. 5 at 2. He "had diarrhea x3 days up to 6x daily" and there "[m]ay have been melena or bright red blood per rectum with the diarrhea." Id. He was diagnosed with gastroenteritis. On May 11, 2017, petitioner presented to the ER complaining of diffuse weakness for five days. Petitioner reported vaccination and diarrhea "about the same time" prior to GBS onset. Pet. Ex. 3 at 26. Subsequent diagnostic testing, including a lumbar puncture, confirmed petitioner's GBS diagnosis.

On May 11, 2017, Dr. Melling noted petitioner reported his "illness with vomiting and diarrhea as well as weakness about 2 weeks ago." Pet. Ex. 3 at 7. Dr. Melling did not associate petitioner's vaccinations with his GBS. That same day, Dr. Bruce Daniel documented that petitioner reported "2 weeks of progressively worsening weakness" that "started after a [Prevnar 13] vaccine and a bout of diarrhea, which [petitioner] had about the same time 2 weeks ago." Id. at 26. On May 12, 2017, Dr. White wrote that petitioner reported that "[h]e had a [Tdap] shot and subsequently developed diarrhea (approximately 2 weeks ago). At around that time, he also had a [Prevnar 13] vaccine." Id. at 9.

After discharge, petitioner continued to see Dr. White. At a visit on June 2, 2017, Dr. White noted that "[a]bout 4 weeks ago, [petitioner] developed diarrhea, 3 weeks ago he developed weakness and was diagnosed with [GBS] (most likely AIDP)." Pet. Ex. 6 at 13. Dr. White found petitioner's medical history "quite classic for [GBS]; he had a bout of diarrhea and one week later experienced significant weakness with suppressed reflexes." Id. at 14. On

January 10, 2018, Dr. White documented, "[petitioner] ha[d] a history of acute weakness coming in early May of 2017 and occurring 3 weeks after stepping on a wire, receiving a [Tdap] shot and developing diarrhea (he also had a [Prevnar 13] vaccine at that time)." Id. at 59.

The experts devoted substantial time to the issue of whether petitioner had a *C. jejuni* or other GI infection that led to his development of GBS. From the records provided, it does not appear that testing was done to confirm whether petitioner had a specific infection, such as *C. jejuni*. Dr. Whitton acknowledged that a specific organism was not isolated in petitioner, but he explained that is common with GBS cases. Dr. Chaudhry agreed. Dr. Chaudhry also found petitioner's presentation on May 3, 2017 consistent with the most common symptoms of *Campylobacter* infection. He also argued petitioner's treating physicians considered petitioner's history of diarrhea relevant when treating and diagnosing him with GBS. Dr. Chaudhry found petitioner's clinical course and "the known [mechanism of] molecular mimicry are highly suggestive if not indicative of *C. jejuni* causing [petitioner's] GBS." Resp. Ex. E at 3.

Dr. Rinker acknowledged that petitioner's diarrheal illness was a potential trigger of his GBS. He opined that "it is not possible to distinguish whether vaccination or the diarrheal illness alone was responsible for his GBS, or whether the two immunological stimuli worked in concert to provoke the immune response." Pet. Ex. 9 at 6. However, Dr. Rinker did not explain how the vaccines and GI illness could work together in concert to cause GBS. And he did not support this statement with medical literature or other evidence.

Further, Dr. Rinker argued there was insufficient evidence to claim that the diarrheal illness was a more likely cause of petitioner's GBS. However, in his supplemental report, he found there was sufficient evidence that petitioner's Tdap vaccination was the more likely cause for petitioner's GBS. Dr. Rinker's opinion that a vaccine was more likely than a GI illness to cause petitioner's GBS is not supported by the evidence.

Dr. Rinker attempted to argue that the temporal association between vaccination and GBS onset favored the vaccines as the more likely cause. However, literature cited by Dr. Rinker notes there is an incubation period with *Campylobacter* infections, consistent with Dr. Whitton's opinion and literature cited by both Drs. Whitton and Chaudhry. Taking into account the incubation period between infection and symptom onset would place the date of infection before or approximately the date of petitioner's vaccination. Thus, this argument fails.

Dr. Rinker then argues that "the mere presence of diarrhea before the onset of GBS, especially when *C. jejuni* was never identified, provides an unlikely cause of [petitioner's] GBS in comparison to the Tdap vaccination." However, as previously stated, no testing was conducted. This argument does not explain how the Tdap vaccine is the more likely cause of petitioner's GBS.

The undersigned is not persuaded by petitioner's arguments, given petitioner's clinical course, treating physician statements, and the experts' opinions and supporting medical literature. The undersigned acknowledges that petitioner is not required to eliminate other potential causes in order to be entitled to compensation. See Walther v. Sec'y of Health & Hum. Servs., 485 F.3d 1146, 1149-52 (Fed. Cir. 2007) (finding petitioner does not bear the burden of

eliminating alternative independent potential causes). However, she finds it reasonable to consider "evidence of other possible sources of injury"—here, petitioner's GI illness—in determining "whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question." Stone, 676 F.3d at 1379.

In this case, "the presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the vaccination." Pafford, 451 F.3d at 1358-59; see also Walther, 485 F.3d at 1151 n.4 ("Where multiple causes act in concert to cause the injury, proof that a particular vaccine was a substantial cause may require the petitioner to establish that the other causes did not overwhelm the causative effect of the vaccine."). As such, the undersigned finds petitioner failed to prove that the Tdap and/or Prevnar vaccines were the "but for" cause of petitioner's GBS.

For all of the reasons described above, the undersigned finds that petitioner has failed to provide preponderant evidence of a logical sequence of cause and effect required under Althen Prong Two.

C. Althen Prong Three

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

Based on the most contemporaneous-in-time medical records, and consistent with the experts' opinions, the undersigned finds petitioner's GBS onset to be on or about May 5 or 6, 2017.

Dr. Rinker opined petitioner's GBS onset was May 5 or May 6, 2017. Dr. Whitton agreed that petitioner's GBS onset was on or around May 6, 2017. Dr. Chaudhry noted the medical records supported a GBS onset of May 5, 2017.

Even though the experts agree as to GBS onset, they disagree as to whether timing is appropriate given their proposed triggers at play. Dr. Rinker opined that here, with an adaptive immune response, the timing for vaccine-caused GBS is appropriate. He cited articles supporting a timeframe between four days and four weeks after vaccination.

Dr. Whitton agreed that this interval between vaccination and GBS "fall[s] squarely within the accepted range when considering the kinetics of the adaptive immune response," but

argued the interval between infection and GBS is also appropriate. Resp. Ex. A at 10. Because the onset of disease symptoms with *Campylobacter* infections occurs one to ten days after exposure to infection, he found petitioner's GI illness "most probably" began before, on, or near the date of vaccination. He acknowledged that "the existence of an incubation period makes it almost impossible to know exactly when the immune system was first triggered by an infection," but maintained that "[w]hen an incubation period is incorporated into the timing calculation, it is quite likely that the interval between stimulation of the adaptive immune system and GBS is longer for GI infection than it is for the Tdap vaccination." Id. at 5, 10.

Dr. Chaudhry agreed with Dr. Whitton that the timing is appropriate for the GI infection as the cause of petitioner's GBS. Both Drs. Whitton and Chaudhry cited literature to support an onset of neurological symptoms one to three weeks following infection.

Petitioner's GBS onset of May 5 or May 6, 2017 was 9-10 days after petitioner's Tdap vaccination, 7-8 days after petitioner's Prevnar vaccination, and 5-6 days after his diarrheal illness onset. All of these intervals are appropriate given the undersigned's knowledge and experience with the adaptive immune system and molecular mimicry, and respondent's experts' opinions. Dr. Rinker does not discuss whether the interval between petitioner's GI illness and GBS onset is appropriate. He only argues that the timing is more appropriate for the Tdap vaccine as the prevailing trigger.

Therefore, the undersigned finds the temporal association is appropriate given the mechanism of injury and petitioner has satisfied the third Althen prong. However, temporal association alone is insufficient for petitioner to show vaccine causation for his alleged injury, and thus, petitioner is not entitled to compensation.

VI. CONCLUSION

For the reasons discussed above, the undersigned finds that petitioner has not established by preponderant evidence that his vaccinations caused his GBS. Therefore, petitioner is not entitled to compensation and his petition must be dismissed. In the absence of a timely filed motion for review pursuant to Vaccine Rule 23, the Clerk of Court **SHALL ENTER JUDGMENT** in accordance with this Decision.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master