In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 16-1592V

(to be published)

MARC HOWARD,	*	Chief Special Master Corcoran
Petitioner,	*	Filed: August 31, 2022
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Milton Clay Ragsdale, IV, Ragsdale LLC, Birmingham, AL, for Petitioner.

Naseem Kourosh, Department of Justice-Civil Division, Washington, DC, for Respondent.

ENTITLEMENT DECISION[1]

On November 30, 2016, Marc Howard filed a Petition under the National Vaccine Injury Compensation Program (the "Vaccine Program").[2] Mr. Howard originally alleged that as a result of receiving the tetanus-diphtheria-acellular pertussis ("Tdap") vaccine, he developed Guillain-Barré syndrome ("GBS") and/or Chronic Inflammatory Demyelinating Polyneuropathy ("CIDP"). Petition (ECF No. 1) ("Pet.") at 1–2. Petitioner has since amended his claim to assert only the causation-in-fact claim that his CIDP was vaccine-caused. ECF No. 61 at 3.

[1] This Decision will be posted on the Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012)). **This means that the Decision will be available to anyone with access to the internet.** As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the whole Decision will be available to the public. *Id*.

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755 (codified as amended at 42 U.S.C. §§ 300aa-10–34 (2012)) (hereinafter "Vaccine Act" or "the Act"). All subsequent references to sections of the Vaccine Act shall be to the pertinent subparagraph of 42 U.S.C. § 300aa.

On March 22, 2021, I issued a Prehearing Order in anticipation of a trial to be held in 2022 to resolve the claim. ECF No. 58. However, I noted at the time that my inclination was to decide this matter on the record, without live testimony, and that I would only hold a hearing if I determined that a fact issue had been presented that required live testimony. Both sides filed pre-hearing briefs in support of their respective positions—and in so doing also addressed the propriety of a trial. Petitioner's Pre-Hearing Memorandum, dated November 12, 2021 (ECF No. 61) ("Mot.") at 3, 17; Respondent's Pre-Hearing Memorandum, dated December 15, 2021 (ECF No. 62) ("Opp.") at 2, 21; Petitioner's Reply, dated January 11, 2022 (ECF No. 65) ("Reply"). I later determined that the case could in fact reasonably be decided on the papers. Scheduling Order, dated January 12, 2022 (ECF No. 66) ("Order").

Now, having considered the record evidence, expert opinions, and the parties' briefing, I deny entitlement. Petitioner has not preponderantly established that the Tdap vaccine can cause CIDP, or did so specifically to him.

I. Factual Background

Prior Medical History and Receipt of Vaccine

Mr. Howard was born on November 6, 1971. Ex. 1 at 1. His medical history prior to vaccination included asthma (Ex. 3 at 32), bronchospasm (Ex. 3 at 52), mild obstructive lung disease (Ex. 3 at 22, 34), and high blood pressure (Ex. 3 at 52). The month before the vaccination at issue, Petitioner presented to Urgent Care by the Bay in Daphne, Alabama on January 15, 2014, complaining of chest congestion, productive cough, and chills. Ex. 59 at 5. He denied fever but noted a history of bronchitis and asthma. *Id*. He was diagnosed with bronchitis and prescribed a five-day antibiotic regimen and a ten-day steroid treatment. *Id*. at 8.

One month later, on February 14, 2014, Petitioner presented for primary care. Ex. 3 at 7. It was noted he had not needed to use his inhaler for asthma in four days but was nonetheless currently experiencing asthma-related symptoms. *Id*. Coughing and wheezing were observed, but the physical exam was otherwise normal. *Id*. at 7–8. The treater assessment noted chest pain, asthma, and left knee pain. *Id*. at 8. Mr. Howard otherwise had no history of neurologic or neuropathic disorders. Ex. 3 at 7–8. He now received the Tdap vaccination in his right deltoid. *Id.* at 8; Ex. 1 at 1.

Onset of Injury

The record contains no evidence that Petitioner experienced any immediate vaccine reaction, and almost three weeks passed before Petitioner sought care again. On March 4, 2014, Mr. Howard was seen by Dr. Laura Hollensworth complaining of pain, tingling, burning, and

numbness in both feet and in his neck. Ex. 3 at 4. He reported his son had recently had strep throat, but rapid flu and strep tests came back negative. *Id*. at 4–5. A review of symptoms noted wheezing, elevated blood pressure, and back pain. *Id*. at 4. Petitioner's cranial nerve and motor exams produced normal results, he had normal strength and auscultation of his lungs, and he did not have a fever. *Id*. at 4–5. Mr. Howard was diagnosed with flu-like symptoms, cervicalgia, elevated blood pressure, and asthma. *Id*. at 4–6. An anti-inflammatory drug and steroid injection were administered, and Petitioner was instructed to go to the ER if his symptoms worsened. *Id*. at 6.

The following day (March 5th), Mr. Howard presented to Urgent Care by the Bay complaining of numbness and swelling of his feet that he now identified as having begun four days prior (or March 1st—16 days post-vaccination), plus finger tingling which he claimed had manifested a day before. Ex. 4 at 2. These symptoms were noted to be acute, and he was subsequently diagnosed with a peripheral neuropathy, and instructed to seek specialized neurologic care. *Id.* at 4. The next day, on March 6, 2014, Mr. Howard went to the Thomas Hospital Emergency Room in Fairhope, Alabama, for a "numb tingling feeling" that had begun four days ago in his right foot, and which had now progressed to his left foot and fingertips. Ex. 7 at 821. His cranial nerve and motor exam and physical exam were again all normal and he was noted to have normal strength. *Id*. at 822. No facial droop was observed. *Id*. Petitioner was discharged with a diagnosis of peripheral neuropathy. *Id*. at 818.

Initial Diagnosis of GBS

Mr. Howard saw Dr. Andrew Dukes on March 7, 2014, for numbness in his hands and feet that had been ongoing since March 2nd and had subsequently spread to his tongue, as well as extremity weakness and hypertension. Ex. 6 at 5. He was referred to neurology with a diagnosis of ataxia and neuropathy, where he was seen by Dr. Abdel Kasmia that same day. *Id*. at 6–7; Ex. 7 at 2. Petitioner's symptoms were reported to have begun five days prior in his right big toe, and it was noted he had experienced an upper respiratory infection ("URI") two or three weeks ago. *Id*.

Exam revealed hypersensitivity in Mr. Howard's distal extremities and a slightly diminished vibration sense in his lower extremities. Ex. 7 at 3. In particular, his distal strength was 4/5 and his deep tendon reflexes (DTRs) were absent at the Achilles tendon level and trace at the knee level, biceps, and triceps. *Id*. Ataxia was also observed. *Id*. Dr. Kasmia's impression was that Mr. Howard was suffering from the acute inflammatory demyelinating polyneuropathy variant of GBS, and hospitalization was recommended for further testing. *Id*. at 4.

Mr. Howard was subsequently admitted to the hospital complaining of gradually-ascending numbness, tingling, weakness, and gait difficulties that began five days ago. Ex. 7 at

571–74. He did not report any speech, swallowing, visual, or cranial nerve involvement. *See id*. His physical examination showed normal cranial nerves, as well as proximate and distal leg weakness, hyporeflexia/areflexia, and gait ataxia. *Id*. at 574. MRIs of his brain and cervical spine were normal and CSF cultures did not indicate any evidence of an infectious disease. *Id*. at 331–336, 569–570.

Mr. Howard was thereafter diagnosed with GBS. Ex. 7 at 571, 573, 575. His hospital stay was complicated by hypertension and hyponatremia, but these both resolved after treatment. *Id*. at 575. Moreover, his neurological symptoms progressed, which resulted in difficulty chewing and closing his eyes as well as some facial paralysis. *Id*. He was treated with IVIG for five days which improved his ability to chew, and he was eventually able to close his left eye. *Id*. Upon discharge on March 17, 2014, Mr. Howard required a walker to ambulate as well as assistance to stand, and he made the decision to have outpatient rehabilitation instead of inpatient. *Id*.

Second Hospitalization and Inpatient Rehabilitation

After being discharged, Mr. Howard became progressively weaker, and his wife could no longer care for him. Ex. 7 at 345. His primary care provider was unable to directly admit him to an inpatient rehabilitation facility, however, so he was readmitted to Thomas Hospital on March 21, 2014. *Id*. Mr. Howard's deep tendon reflexes ("DTRs") were diminished, he had poor balance, and his exam revealed some right facial nerve palsy. *Id*. at 346. He received five days of IVIG which improved his lower extremity and facial muscle strength, but developed a low-grade fever and hyponatremia, although his treaters noted this may be from the IVIG treatments. *Id*. at 363. Upon transferring to inpatient rehabilitation, he had decreased status for activities of daily living, decreased upper extremity strength, decreased endurance, decreased sensation, decreased self-care, and decreased fine motor control. Mr. Howard also required assistance with transfers. *Id*. at 376.

Petitioner was now transferred to Mobile Infirmary in Mobile, Alabama, for inpatient rehabilitation on March 27, 2014. Ex. 12 at 444. At this time, he was taking a muscle relaxant for truncal and abdominal spasms as well as a blood thinner for his deep vein thrombosis in his left gastrocnemius and tibial veins. *Id*. His symptoms improved with physical therapy, however, his status at the time of discharge on April 14, 2014, was modified independent with eating, grooming, upper and lower body dressing, bed mobility and transfers, and wheelchair mobility over 400 feet; minimum assist with toileting; and supervision with bathing, toileting, and shower transfers. *Id*. He was able to ambulate with a light gait over 400 feet with minimal assistance but was not tested on stairs. *Id*.

Follow-up Care and Third Hospitalization

Mr. Howard had a follow-up appointment with Dr. Andrew Dukes on April 21, 2014. Ex. 6 at 9. He reported that his strength was improving but he was still unable to close either eye completely. *Id*. He was still taking Xanax for paresthesia. *Id*.

The following month, however, Mr. Howard reported to the emergency room on May 3, 2014, with complaints of dizziness, weakness, and a drop in blood pressure after taking Zanaflex, a muscle relaxant. Ex. 7 at 262. He was prescribed Zanaflex in rehab for leg cramping. *Id*. He reported he had experienced GBS after taking the whooping cough vaccine. *Id*. at 266. His physical exam was negative for focal neurological deficits and facial droop. *Id*. at 265. He was discharged and diagnosed with an adverse drug reaction. *Id*. at 265, 279.

Mr. Howard returned to Dr. Dukes on May 9, 2014, and reported no significant improvement in strength despite attending physical therapy. Ex. 6 at 15. All labs were noted to be normal from his emergency room visit. *Id*. He was found to be hypotensive, and his medication was adjusted to address this. *Id*. at 17. He had another visit with Dr. Dukes three days later where he reported having a numb throat since May 10 which made swallowing difficult. *Id*. at 20. He also felt that his weakness was worsening. *Id*. This was noted as a possibility of CIPD. *Id.*

CIDP Diagnosis

Mr. Howard presented to the University of South Alabama ("USA") neurology department in Mobile on May 15, 2014. Ex. 5 at 7. He relayed that he had developed numbness, tingling, and sensory disturbances in his feet starting on March 2, 2014, which extended to his legs and hands within a few days. *Id*. Subsequently, he developed weakness in his limbs and became unable to ambulate shortly after that. *Id*. He also noted that he had received a whooping cough vaccination three weeks prior to the onset of these symptoms. *Id*.

Partial peripheral right VII cranial nerve palsy and mild nystagmus on extreme later gaze were observed. Ex. 5 at 8. His upper extremity strength was 3–4/5; his lower extremity strength was 0/5; and his DTRs were 0/4, along with decreased sensation and being confined to a wheelchair. *Id*. An EMG showed severe primary demyelinating peripheral polyneuropathy, with associated extensive axonal loss. *Id*. Petitioner was diagnosed with "most likely chronic inflammatory demyelinating neuropathy (CIDP) despite an acute onset." *Id*. Additional IVIG treatment and physical therapy were recommended. *Id*.

Mr. Howard was discharged from occupational therapy on June 27, 2014, but he planned to increase the duration of his physical therapy sessions. Ex. 7 at 132. On August 27, 2014, Mr. Howard presented to USA neurology again. Ex. 5 at 11. He reported that his symptoms started

on March 2, that he was unable to walk by March 4, and that he was hospitalized on March 6. *Id*. He also reported ongoing pain in his feet, but the IVIG was improving his symptoms. *Id*. He was able to ambulate independently as of two weeks ago. *Id*. It was recommended he continue IVIG and physical therapy. *Id*. at 12.

Ongoing CIDP Symptoms and Care

Mr. Howard returned to USA Neurology December 19, 2014, for CIDP treatment. Ex. 5 at 5. He was now receiving IVIG every four weeks and regaining his strength and ability to ambulate. *Id*. He reported ongoing sensory disturbance in his feet and distal legs but no cranial or upper limb symptoms other than mild hand tingling and numbness. *Id*. at 4. He was diagnosed with CIDP, but it was noted that his symptoms were improving. *Id*.

Mr. Howard presented at Urgent Care by the Bay multiple times throughout January 2015 for unrelated matters. Ex. 4 at 6–10. No neurological issues were noted at these visits, however, and his physical exams were normal. *Id*. On April 13, 2015, Mr. Howard saw Dr. Dukes with complaints of a URI but did not report any neurological issues. Ex. 8 at 4–5. He did mention he was still receiving IVIG treatments. *Id*. Four days later, however, Mr. Howard returned to Dr. Dukes and complained of a burning sensation in the plantar aspect of his feet, as well as numbness and tingling in hands and feet. Ex. 10 at 4. He also reported occasional weakness on the right side of his face. *Id*. He stated that he felt he had improved overall. *Id*. He was instructed to continue IVIG. *Id*.

As of February 26, 2016, Mr. Howard was still receiving IVIG. Ex. 9 at 5. He reported ongoing foot paresthesia and hyperesthesia. *Id*. He noted the sensory symptoms in his arms had improved and that he no longer had weakness, gait problems, or incontinence. *Id*. His strength was 5/5 and his sensation was normal. *Id*. On August 24, 2016, and again on February 15, 2017, treaters recommended that Petitioner continue IVIG treatment every eight weeks for his CIDP, which was now deemed stable. Ex. 14 at 10–11; Ex. 17 at 5.

II. Expert Reports

A. *Kazim A. Sheikh, M.D.*

Dr. Sheikh filed two expert reports on behalf of Mr. Howard. Report, dated September 25, 2017, filed as Ex. 19 (ECF No. 31-1) ("First Sheikh Rep."); Report, dated May 20, 2018, filed as Ex. 60 (ECF No. 41-1) ("Second Sheikh Rep."). Dr. Sheikh opines that the Tdap vaccination Mr. Howard received on February 14, 2014, was a substantial factor in the causation of his CIDP. First Sheikh Rep. at 1.

Dr. Sheikh is a board-certified Neurologist. Curriculum Vitae, filed as Ex. 20 at 2 (ECF No. 31-2) ("Sheikh CV"). He is also board certified in psychiatry and neurology, muscle pathology, and clinical neuromuscular pathology. Sheikh CV at 2. Dr. Sheikh attended the Government College for his undergraduate education and King Edward Medical College for medical school, both in Lahore, Pakistan. *Id.* at 1. He then completed his residency at the Mayo Hospital in Lahore, Pakistan, followed by an internship at the Nassau County Medical Center in East Meadow, NY. *Id*. He subsequently completed his residency in Neurology with the Neurological Institute at Columbia University and a postdoctoral fellowship in peripheral nerve at John Hopkins University School of Medicine. *Id*.

Dr. Sheikh currently works as the Director of the GBS/CIDP Center of Excellence at the University of Texas along with being a tenured Professor of Neurology at the University. Sheikh CV at 1. He is also the Director of the Neuromuscular Program at the University of Texas Medical School, the Director of the Neuromuscular Disorders Center at the Mischer Neuroscience Institute at the Memorial Hermann-Texas Medical Center, and the Director of the Muscle and Nerve Laboratory. *Id*. He serves as an attending neurologist at the Memorial Hermann Hospital and Lyndon B. Johnson Hospital, along with being a staff neurologist at the Memorial Hermann Hospital. *Id.* at 2. He is also a member of the advisory board for the GBS/CIDP Foundation, and has been elected to the Board of Directors of Peripheral Nerve Society. Sheikh CV at 5. He has also authored or co-authored more than 150 peer reviewed articles, manuscripts, book chapters, abstracts, and patient education materials. *Id*. at 13–36.

First Report

Dr. Sheikh's first report began with a summary of Mr. Howard's medical history and treatment course. First Sheikh Rep. at 2–5. He took note of Mr. Howard's prior diagnoses of asthma, bronchospasm, mild obstructive lung disease, and high blood pressure, but emphasized that Mr. Howard had no history of neurologic or neuropathic disorders. *Id*. at 2. Dr. Sheikh did reference Dr. Hollensworth's acknowledgement (on the day Mr. Howard received the Tdap vaccine) of Mr. Howard's bronchitis diagnosis three weeks prior. *Id*. However, his first report downplayed the significance of this incident, in large part because (as of the time the first report was prepared) medical record evidence for its substantiation had not yet been filed or identified. *Id.* at 11.

Dr. Sheikh then focused on Mr. Howard's onset of neurological symptoms two weeks after receiving the vaccine, when he first reported pain and sensory disturbance. First Sheikh Rep. at 2. At this time, Petitioner tested negative for flu and strep, although he was then experiencing flu-like symptoms. *Id*. Dr. Sheikh described Mr. Howard's disease progression, initial diagnosis of GBS, and subsequent admission to the hospital where he was treated with IVIG. *Id*. He characterized Mr. Howard's worsening of symptoms upon discharge as a relapse, which resulted

in his readmission to the hospital for further IVIG treatment and eventual admission to an inpatient rehabilitation program. *Id*. Mr. Howard's improvement during inpatient rehabilitation was also noted. *Id*. at 3. Ultimately, Petitioner was diagnosed with CIDP, and Dr. Sheikh accepted that diagnosis as correct. *Id*. at 4–5.

GBS (here used interchangeably with acute inflammatory demyelinating polyneuropathy ("AIDP"), the most common GBS variant) and CIDP have much in common, Dr. Sheikh explained. First Sheikh Rep. at 5. Both fall under the umbrella of peripheral nerve disorders, with AIDP being the acute version and CIDP the progressive, chronic version (although CIDP can initially present acutely—as in this case). *Id*. Importantly, both are understood to be immune-mediated as well. *Id.* at 6. Therefore, "[i]t is believed that there is a temporal continuum between AIDP, the demyelinating form of GBS, and CIDP." *Id*.; R. A. Lewis, *Chronic Inflammatory Demyelinating Polyneuropathy: Etiology, Clinical Features, and Diagnosis*, UpToDate, 1, 2 (2016), filed as Ex. 23 (ECF No. 31-5) ("Lewis"). GBS/AIDP is the most common cause of acute flaccid paralysis, while CIDP is the most common chronic inflammatory/immune neuropathy. First Sheikh Rep. at 6.

There are, however, significant differences between the two. GBS does not typically progress beyond four weeks, although its subsequent recovery phase can be variable, resulting in significant residual deficits. First Sheikh Rep. at 5–6. In contrast, CIDP's progressive phase can last up to eight weeks, and patients may subsequently experience steady progression, remission and relapse, or little remission from symptoms thereafter. *Id*. at 6. Also distinguishing AIDP/GBS from CIDP are their "tempo, mode of transportation, prognosis, and responsiveness to immunosuppressants." *Id*.; M. Lunn & K. Sheikh, *Peripheral Neuropathies*, *in* N. Rose THE AUTOIMMUNE DISEASES 757, 766–69 (5th ed. 2014), filed as Ex. 21 (ECF No. 31-3) ("Lunn & Sheikh"); A. Hahn et al., *Chronic Inflammatory Demyelinating Polyradiculoneuropathy*, *in* P. J. Dyck & P. K. Thomas, eds. DISEASES OF THE PERIPHERAL NERVOUS SYSTEM 2221, 2222–23, filed as Ex. 22 (ECF No. 31-4); Lewis at 2.

Dr. Sheikh embraced the view that the primary differentiating factor between AIDP and CIDP are their durations. First Sheikh Rep. at 6. But he acknowledged that pathogenic pathways specific to CIDP might involve different autoantibodies or situses of attack on the peripheral nerves. As he noted, reliable scientific research indicates that "autoimmunity in CIDP is most likely mediated by antibodies directed against myelin sheath, axonal membranes, and/or the nodes of Ranvier."[3] *Id.* at 10; Lewis at 2-3. These antibodies have been found in patients with CIDP, and experimental animal models have also established that they likely contribute to CIDP's pathogenesis. *Id*.; A. Ilyas et al., *Antibodies to Acidic Glycolipids in Guillain-Barré Syndrome*

[3] The nodes of Ranvier are gaps in the neural axon's myelin. *Dorland's Medical Dictionary Online*, https://www.dorlandsonline.com/dorland/definition?id=93095&searchterm=nodes+of+Ranvier (last visited August 31, 2022).

and Chronic Inflammatory Demyelinating Polyneuropathy, 107 J. Neurological Scis. 111, 113–115, 118–120 (1992), filed as Ex. 31 (ECF No. 31-13) ("Ilyas"); W. Yan et al., *P0 Protein is a Target Antigen in Chronic Inflammatory Demyelinating Polyradiculoneuropathy*, 50 Annals Neurology 286, 286, 290–91 (2001), filed as Ex. 54 (ECF No. 31-36); L. Querol et al., *Antibodies to Contactin-1 in Chronic Inflammatory Demyelinating Polyneuropathy*, 73 Annals Neurology 370, 370–71, 374 (2013), filed as Ex. 55 (ECF No. 31-37); W. Yan et al., *Passive Transfer of Demyelination by Serum or IgG from Chronic Inflammatory Demyelinating Polyneuropathy Patients*, 47 Annals Neurology 765, 765, 770 (2000), filed as Ex. 56 (ECF No. 31-38).

In actuality, much of the general literature offered on these points was less supportive for the role certain autoantibodies might play in CIDP's progression than Dr. Sheikh suggested. Lewis, for example, identified certain specific antibodies to neurofascin-155 and contactin as *associated* with some versions of CIDP, but did not also find that they were triggers of it. Lewis at 2-3. Ilyas (a thirty year-old study) used human volunteers who had been diagnosed with GBS or CIDP, finding that (based on blood testing) eight of sixteen CIDP patients evaluated had tested positive for anti-acidic glycolipid antibodies, and in elevated amounts in comparison to controls. Ilyas at 112. However, Ilyas was primarily focused on identifying the presence of these antibodies in *GBS patients* (with more than 50 GBS patients considered in comparison to the limited number of CIDP cases), and moreover could do no more than propose that the identified antibodies might play some role in CIDP's disease pathogenesis, admitting that it was unclear if their existence constituted a "primary event" in encouragement of disease, or if they were merely "consequential" of it. *Id.* at 120. Ilyas also says nothing about what might cause these antibodies to appear in the first place.

A number of factors can influence the development of GBS, and in Dr. Sheikh's view, CIDP as well. First, innate host susceptibility is likely significant. First Sheikh Rep. at 8; K. Sheikh et al., *Campylobacter Jejuni Lipopolysaccharides in Guillain-Barré Syndrome*, 51 Neurology 371, 376 (1998), filed as Ex. 38 (ECF No. 31-20). In the context of CIDP, patients with autoimmune polyendocrinopathy syndrome type 1 (APS1) who possess a specific genetic mutation are particularly susceptible. First Sheikh Rep. at 8.

Second, various independent environmental factors can instigate an autoimmune process resulting in different forms of demyelinating diseases. It is medically-accepted, for example, that GBS can be triggered by an infection—or vaccination. First Sheikh Rep. at 6. Dr. Sheikh acknowledged that medical science was still debating CIDP's triggers or causal factors, due in part to CIDP's inherently slowly-developing and intermittent course (which renders it difficult to diagnose quickly). *Id*. Indeed—articles like Lewis clearly state that "antecedent events are more frequent with GBS than in CIDP," and that "specific *provoking* antigens have not previously been identified" for CIDP. Lewis at 2.

Nevertheless, Dr. Sheikh maintained that what is known about GBS's pathology (and specifically the things that can trigger it immunologically) is relevant to CIDP. To support this contention, he cited an animal model involving AIDP and CIDP referenced in one item of literature he offered. *Id*. at 6–7; Lunn & Sheikh at 769. Lunn & Sheikh is a chapter in a larger text regarding autoimmune diseases, and its authors determined that "where tolerance is circumvented, potentially pathogenic antibodies can be generated." *Id.* at 763. They made specific reference to a study that immunizing rabbits with "mixed bovine brain gangliosides or CM1 alone produced an acute flaccid paralysis in rabbits reminiscent of human disease." *Id.* (internal citation omitted). Of course, there is an obvious distinction between experiments in which protein antigens *known* to have similarity to the expected targets of an autoimmune cross-reaction are introduced (as opposed to vaccines *potentially* containing such antigens in vastly smaller amounts)—and in any event this research was not linked to CIDP as opposed to other, more general forms of peripheral neuropathies.

Based on this premise, Dr. Sheikh proposed that there are potentially "multiple, nonexclusive mechanisms," including infection or vaccination, that can contribute to the development of autoimmune processes—and in his opinion they apply equally to different neuropathy variants. First Sheikh Rep. at 7.[4] In GBS, for example, molecular mimicry is the dominant mechanism believed to mediate the aberrant immune response that leads to the disease. *Id*. Studies involving the axonal form of GBS have observed that the *Campylobacter jejuni* bacterium carries carbohydrate moieties that mimic gangliosides, and that individuals who experience a *C. jejuni* infection commonly display anti-ganglioside antibodies post-infection. *Id*. Some patients with AIDP and CIDP also have been demonstrated to possess anti-ganglioside antibodies (although as already noted the role those antibodies play in promulgating CIDP, as opposed to AIDP, is not well known). *Id*.; Ilyas at 111, 111, 113–115, 118–120.

Other reliable evidence, Dr. Sheikh maintained, supporting the conclusion that molecular mimicry is a probable pathogenic process for demyelinating diseases comparable to CIDP could be seen in the context of mycoplasma pneumoniae infections. First Sheikh Rep. at 7. As he explained, "[m]ycoplasma pneumonia express[es] glycolipid antigens that cross react with GalC, which is a glycolipid that is enriched in myelin sheath of Schwann cells in peripheral nerves." *Id*.; S. Kusunoki et al., *Anti-Gal-C Antibodies in GBS Subsequent to Mycoplasma Infection: Evidence of Molecular Mimicry*, 57 Neurology 736, 736–738 (2001), filed as Ex. 32 (ECF No. 31-14). Patients with a mycoplasma pneumoniae infection can test positive for anti-GalC

[4] Dr. Sheikh provided two non-identical lists of potential mechanisms in his report. First, he proposed more generally that autoimmune diseases (a broader category than GBS or CIDP) could occur via molecular mimicry, epitope spreading (in which damage caused by direct infection leads to secondary autoimmune response to self-tissue), "bystander activation" (where non-specific autoimmune cells are activated in the presence of an inflammatory environment), or "cryptic antigens." First Sheikh Rep. at 7. Later in his report, he focused more on the four mechanistic processes he deemed relevant to how CIDP would occur. *Id.* at 9-10. This second set of mechanisms also involved molecular mimicry, but was otherwise distinguishable—and it is the second set that is most relevant to Dr. Sheikh's ultimate opinion.

antibodies, and often later develop AIDP. First Sheikh Rep. at 7–8; M. Samukawa et al., *Clinical Features in Guillain-Barré Syndrome with Anti-Gal-C Antibody*, 337 J. Neurological Scis. 55, 55 (2014), filed as Ex. 33 (ECF No. 70-1). Experimental animal studies also support this notion. *Id*.; K. Saida et al., *In Vivo Demyelination Induced by Intraneural Injection of Anti-Galactocerebroside Serum*, 95 Am. J. Pathology 99, 99, 105, 107 (1979), filed as Ex. 34 (ECF No. 31-16) ("Saida"). Saida, an animal model using rabbits, "demonstrated that intraneural injection of anti-serum to galactocerebroside can produce *in vivo* primary demyelination in a circumscribed area of the recipient peripheral nerve." Saida at 105. Saida's authors maintained that anti-GC antibodies (generated in reaction to the introduction of the antigens injected into the animal subjects) are responsible for such demyelination. *Id.*

There are also studies and articles suggesting possible vaccine/infectious triggers for CIDP, although by Dr. Sheikh's admission there is far more robust evidence associating GBS/AIDP with vaccines. For example, melanomas or melanoma vaccines have been observed to be associated with CIDP, possibly causing it to occur via the mechanism of molecular mimicry. First Sheikh Rep. at 8; M. Weiss et al., *Molecular Mimicry in Chronic Inflammatory Demyelinating Polyneuropathy and Melanoma*, 51 Neurology 1738, 1738, 1741 (1998), filed as Ex. 35 (ECF No. 31-17); G. N. Fuller et al., *Demyelinating Neuropathies Triggered by Melanoma Immunotherapy*, 44 Neurology 2404, 2405 (1994), filed as Ex. 36 (ECF No. 31-18). Melanomas and melanoma vaccines can cause the expression of anti-ganglioside antibodies in patients. First Sheikh Rep. at 8. This, Dr. Sheikh maintained, provided at least "'proof of principle' for molecular mimicry in rare cases of CIDP," even though he acknowledged that the specific findings in these articles were not all that strong. *Id*.

Nevertheless, Dr. Sheikh maintained that tetanus-containing vaccines were likely equally causal of GBS or CIDP. First Sheikh Rep. at 9; K. Nyati & R. Nyati, *Role of Campylobacter Jejuni Infection in the Pathogenesis of Guillain-Barré Syndrome: An Update*, 2013 BioMed Rsch Int'l 1, 8–9 (2013), filed as Ex. 41 (ECF No. 31-23) ("Nyati & Nyati"); N. Souayah et al., *Guillain-Barré Syndrome after Vaccination in the United States: Data from the Centers for Disease Control and Prevention/Food and Drug Administration Vaccine Adverse Event Reporting System (1990–2005)*, 11 Neuromuscular Disease 1, 2–5 (2009), filed as Ex. 42 (ECF No. 31-24) ("Souayah") (GBS); K. L. Gable et al., *Distal Acquired Demyelinating Symmetric Neuropathy After Vaccination*, 14 Neuromuscular Disease 1, 1, 5 (2013), filed as Ex. 43 (ECF No. 31-25)[5] ("Gable"); J. D. Pollard & G. Selby, *Relapsing Neuropathy Due to Tetanus Toxoid*, 37 J. Neurological Scis. 113, 113, 117, 123–124 (1978), filed as Ex. 44 (ECF No. 31-26) ("Pollard & Selby"); R. A. C. Hughes, et al., Letter to the Editor, *Immunization and Risk of Relapse of*

[5] Petitioner's filed version of Gable does not include its original page numbers, so it is being cited in filed pagination order from 1–6.

Guillain-Barré Syndrome or Chronic Inflammatory Demyelinating Polyneuropathy, 19 Muscle & Nerve 1230, 1230–31 (1996), filed as Ex. 45 (ECF No. 31-27) ("Hughes").

The case report evidence was, however, not especially probative of causation when reviewed carefully. Pollard & Selby is over 40 years old, did not involve a specifically-diagnosed case of CIDP (although it is possible that the CIDP designation might reasonably be applied in retrospect), and (most importantly) involved a clearly-established pattern of "rechallenge,"[6] and thus strong evidence of causation *for the single individual in question.* Pollard & Selby at 117. Hughes identified only three instances of post-vaccination GBS *or* CIDP based on an internet database search for publications over a *thirty*-year period, adding that of 110 UK patients followed since 1984, only two had experienced a symptoms relapse (as opposed to new onset). Hughes at 1231. None of these instances were specifically associated with a tetanus-containing vaccine; at most, Hughes's authors noted the risk of post-tetanus vaccination relapse for individuals *previously* diagnosed with GBS or CIDP. *Id.*[7] There is no evidence in this case that Mr. Howard experienced either illness in the past.

Relying on the foregoing, Dr. Sheikh proposed four non-exclusive mechanisms he deemed medically plausible that might explain the pathologic course for Tdap-caused CIDP. First Sheikh Rep. at 9–10. All four, he maintained, rely on the well-established interaction vaccines have with the "innate and adaptive immune system to boost reactivation of memory B-cells," which increases the number of antibodies that have a "higher affinity" for target antigens. *Id*. at 9.

Dr. Sheikh primarily focused on molecular mimicry involving the inactivated tetanus toxin component of the vaccine as the mechanism most likely applicable to CIDP, in a manner comparable to how AIDP is believed to occur in some instances—but with an important distinction specific to Tdap. First Sheikh Rep. at 9. Even though the tetanus toxin included in Tdap has been inactivated into a less-dangerous "toxoid,"[8] it can retain some binding capability

[6] A challenge-rechallenge has been defined as "when a person (1) is exposed to one antigen, (2) reacts to that antigen in a particular way, (3) is given the same antigen again, an (4) reacts to the antigen similarly. Typically, the second reaction is faster and more severe." *Nussman v. Sec'y of Health & Hum. Servs.*, 83 Fed. Cl. 111, 119 (Fed. Cl. 2008) (internal citations omitted) (quoting *Nussman v. Sec'y of Health & Hum. Servs.*, No. 99-500V, 2008 WL 449656, at *9 (Fed. Cl. Spec. Mstr. Jan. 31, 2008).

[7] Other items of case report literature were not specific to CIDP, and are thus inherently of less probative value. Nyati & Nyati looked at the association of *C. jejuni* with GBS. Nyati & Nyati at 2. Its authors determined that the "evidence favored an association between oral polio vaccine and tetanus toxoid-containing vaccines and GBS." *Id.* at 9. Souayah discussed GBS post-vaccination using VAERS data. Souayah at 1. The analysis found 1,000 cases of GBS post-vaccination, with 32 total cases after receipt of the Tdap vaccine. *Id.* at 2–3. The article concluded that vaccines in addition to influenza could be causal of GBS. *Id.* at 5.

[8] A toxoid is "a modified or inactivated bacterial exotoxin that has lost toxicity but retains the properties of combining with, or stimulating the formation of, antitoxin." *Dorland's Medical Dictionary Online*, https://www.dorlandsonline.com/dorland/definition?id=50428&searchterm=toxoid (last visited Aug. 31, 2022).

to complex gangliosides expressed on the muscle cell surface as well as the nerve fibers innervating muscles. *Id*.; E. Habermann & J. Tayot, *Interaction of Solid-Phase Gangliosides with Tetanus Toxin and Toxoid,* 23 Toxicon 913, 913 (1985), filed as Ex. 50 (ECF No. 31-32); J. Müthing & M. Čačić, *Glycosphingolipid Expression in Human Skeletal and Heart Muscle Assessed by Immunostaining Thin-Layer Chromatography*, 14 Glycoconjugate J. 19, 19–20, 22, 24 (1997), filed as Ex. 51 (ECF No. 31-33). As a result, "antigen processing cells in the milieu of the vaccination site [may] process toxoid-ganglioside complexes for the generation of aberrant immune response against the gangliosides." First Sheikh Rep. at 9–10.

Thus, in a process believed to be "the most common autoimmune effectors" in the context of GBS, autoantibodies produced as a result of the antigenic presentation of the toxoid to the muscle and nerve receptors would in turn attack the ganglioside structures of the nerves as well, resulting in autoimmune disease. First Sheikh Rep. at 10. Dr. Sheikh did not, however, identify medical or scientific literature establishing the likelihood that the Tdap vaccine could actually cause these antibodies to generate, relying on the aforementioned case reports plus his prior contentions about the discovery of certain antibodies in CIDP patients, coupled with what is thought to be known about how they encourage neuropathic injury. *Id.*

Three alternative potential disease mechanisms were also proposed, but with less overall evidentiary support. First Sheikh Rep. at 10. The second mechanism Dr. Sheikh discussed was based on the contention that the intramuscular administration of the Tdap vaccine might cause a break in immune tolerance and a subsequent autoimmune attack. *Id.* Because muscles are "richly innervated with twigs of peripheral nerve fibers," the Tdap vaccine adjuvants (included in it to boost immunogenicity) "could lead to an aberrant immune response to self-antigens contained in the intramuscular nerves," which could then mediate nerve injury. *Id*. A third possible mechanism amounted to a "catch all," in which autoimmunity would be propagated by one of the general autoimmune mechanisms he mentioned earlier in his report, like bystander activation. *See id.* at 7. And then Dr. Sheikh mentioned a fourth possibility: the "fertile field" model, in which exposure to a viral infection (or, Dr. Sheikh proposed, vaccination) could promote, for a limited timeframe, an environment favorable to destructive, autoreactive immune cells capable of inducing autoimmune disease in otherwise-susceptible individuals. *Id*. at 10; M. von Herrath et al., *Microorganisms and Autoimmunity: Making the Barren Field Fertile?*, 1 Nature Revs. Microbiology 151, 151, 154–55 (2003), filed as Ex. 57 (ECF No. 31-39) ("von Herrath").[9] None of these three alternative mechanisms, however, were as substantiated in Dr. Sheikh's first report as molecular mimicry.

Finally, Dr. Sheikh highlighted the overarching circumstances from Petitioner's medical history that he deemed consistent with his causation theory. First Sheikh Rep. at 10. The vaccine

[9] Importantly, von Herrath says nothing about the propensity of vaccination to either create the circumstances for the hypothesized "fertile field," or to interact with it once an independent infectious process created it in the first place.

was the only triggering event that could be identified, as the bronchitis diagnosis noted by several of Petitioner's treating physicians was not supported by the medical records (at least as of the time of the preparation of Dr. Sheikh's first report). *Id*. at 11. And Petitioner personally denied any preceding illness when he was admitted to the hospital. *Id*. Dr. Sheikh also deemed a two-week timeframe between vaccination and onset to be medically acceptable for a post-vaccination auto-immune complication. *Id*. at 12. Indeed, the acute onset of Petitioner's symptoms made it easier to identify the triggering event than in most cases of CIDP (which by its nature can be slow to progress, and often is characterized by an intermittent, stuttering course). *Id*.

Second Report

In his second report, Dr. Sheikh responded to some of the contentions contained in the report of Respondent's expert, Dr. Vartanian. First, he argued that the lack of epidemiologic evidence in support of a CIDP/Tdap association was not enough to rule out the possibility of causation. Second Sheikh Rep. at 1. Epidemiologic studies can never account for individual characteristics that may increase one's risk of developing an autoimmune disease after vaccination, and therefore can fail to detect rare complications. *Id*. at 2. He maintained instead that biologic plausibility should be the test of whether his causation theory was evidentiarily sufficient. *Id*.

In this regard, Dr. Sheikh disputed Dr. Vartanian's interpretation of the Institute of Medicine's (the "IOM") findings relevant to Tdap (which Dr. Vartanian had argued were unsupportive of causation). Second Sheikh Rep. at 2; Committee to Review Adverse Effects of Vaccines, *Adverse Effects of Vaccines: Evidence and Causality*, 477–78, 480 (K. Stratton et al. eds., 2011), filed as Ex. 61 (ECF No. 41-2) ("Stratton"). The IOM in fact did not fully reject an association, even if it had found no compelling evidence in support. Stratton at 480. And he relatedly questioned the probative value of the "Pubmed"[10] search Dr. Vartanian reported to have conducted, and which allegedly produced no results establishing published literature supporting a Tdap vaccine/CIDP association. Second Sheikh Rep. at 8. In Dr. Sheikh's view, Pubmed's search methodology is not all that sensitive, and therefore the absence of relevant articles surfacing after a specific search is not proof that they do not exist. *Id*.

Second, Dr. Sheikh attempted to rebut Dr. Vartanian's argument that molecular mimicry stemming from the tetanus toxoid's purported capacity to bind to muscle receptors (as opposed to a reaction with nerve receptors directly). Second Sheikh Rep. at 3. Dr. Sheikh maintained in response that muscles possess polysialogangliosides to which the tetanus-derived vaccine antigens could attach (and for support he referenced his own research). *Id*.; K. Sheikh et al., *The*

[10] "Pubmed" is an online database put forth by the National Institutes of Health that "comprises more than 34 million citations for biomedical literature from MEDLINE, life science journals, and online books." National Library of Medicine, Pubmed.gov, https://pubmed.ncbi nlm nih.gov/ (last visited Aug. 31, 2022).

Distribution of Ganglioside-like Moieties in Peripheral Nerves, 122 Brain 449, 449, 456–57 (1999), filed as Ex. 64 (ECF No. 41-5) ("Sheikh II"). Sheikh II determined that antibody binding sites (specifically "*Gal(β–3)*, *GalNAc*, and TTC) all are present on the surface of a mature myelinated muscle fiber. Sheikh II at 456. As a result, Sheikh II theorized that antibodies formed against these receptors "might injure paranodal Schwann cells and cause demyelination." *Id.* at 457. But (like other articles previously offered to substantiate the role autoantibodies might play in causing CIDP), Sheikh II is not specific to CIDP—and it does not confirm the capacity of vaccines containing tetanus toxoid to cause these autoantibodies to spring into existence. *Id.* at 456–57. Dr. Sheikh otherwise maintained that even if the cross-reaction did not occur directly at the situs of muscle ganglioside structures, his theory was not rebutted, since he *also* maintained that an autoimmune cross-reaction was occurring at ganglioside structures in the peripheral nerves (and such nerves were found intermingled among muscle fibers). Second Sheikh Rep. at 3.

Relatedly, Dr. Sheikh rejected Dr. Vartanian's assertion that the tetanus toxoid cannot be available for antigen presentation at motor nerve terminals since it gets rapidly internalized shortly after vaccination. Second Sheikh Rep. at 5. On the contrary, the study Dr. Vartanian relied upon for this contention indicated that almost *all* the injected toxoid escapes this mechanism of internalization. *Id*.; U. Weller et al., *Quantitative Comparison Between Tetanus Toxin, Some Fragments and Toxoid for Binding and Axonal Transport in the Rat*, 24 Toxicon 1055, 1061 (1986), filed as Ex. Q (ECF No. 35-5) ("Weller"). In addition, tetanus toxoids in human vaccines undergo a much more stringent toxoiding process, further reducing their internalization capacity (even if this also renders them less likely to bind to polysialogangliosides otherwise). *Id*.; B. Metz et al., *Physicochemical and Immunochemical Assays for Monitoring Consistent Production of Tetanus Toxoid*, 41 Biologicals 231, 231 (2013), filed as Ex. 65 (ECF No. 41-6). Thus, it remains likely that the toxoid could bind to polysiagangliosides to induce an autoimmune response. Second Sheikh Rep. at 5.

Third, Dr. Sheikh addressed in greater detail the record evidence of Petitioner's pre-vaccination URI, and its potential causative impact. He now conceded that Petitioner *had* suffered a URI prior to vaccination and CIDP onset, but maintained that the vaccine remained the most likely proximate trigger. Second Sheikh Rep. at 5, 6. Dr. Sheikh also argued that it would be medically impossible to distinguish between post-infectious and post-vaccination forms of CIDP—and thus in a context in which both could be explanatory, neither could be ruled out as more likely causal. *Id*. at 6–7. Moreover, the "fertile field" mechanistic model he had proposed in his first report as an alternative to molecular mimicry essentially described circumstances in which a preexisting URI could synergistically interact with a subsequent vaccination, resulting in conditions sufficient for a peripheral neuropathy autoimmune disease to occur. *Id*. at 7.

B. *Timothy Vartanian, M.D., Ph.D.*

Dr. Vartanian filed two expert reports on behalf of Respondent. Report, dated December 15, 2017, filed as Ex. A (ECF No. 33-1) ("First Vartanian Rep."); Report, dated October 2, 2018, filed as Ex. W (ECF No. 43-1) ("Second Vartanian Rep."). Dr. Vartanian opined that the theory of Tdap vaccine-induced CIDP, mediated by molecular mimicry, is implausible, and that an antecedent respiratory infection was more likely the cause of Mr. Howard's CIDP. First Vartanian Rep. at 13.

Dr. Vartanian is a board-certified neurologist. Curriculum Vitae, filed as Ex. B at 3 (ECF 33-2) ("Vartanian CV"). He is currently a professor at the Weill Cornell Medical College and an attending neurologist at New York Presbyterian Hospital. Vartanian CV at 2. He also works as the Chief Medical Advisor for the National Multiple Sclerosis Health Care Advisory Committee, Southern New York Chapter. *Id*. Dr. Vartanian attended Oakland University for his undergraduate education and the University of Chicago for his Ph.D. and medical school. *Id*. He completed an internal medicine internship at the Brigham and Women's Hospital in internal medicine, and then a neurology residency at the Massachusetts General Hospital. *Id*. at 1–2. He was also a fellow at Beth Israel Hospital in Boston and Harvard Medical School. *Id*. at 2.

Dr. Vartanian has conducted research into a number of neuroscience and pathophysiology matters. Vartanian CV at 10–11. He has previously sat as a regular member on the National Institute of Neurologic Disorders and Stroke, Cellular and Molecular Biology of Glia study section at the National Institutes of Health. *Id*. at 12. And he has published numerous peer-reviewed articles and other works specifically addressing the central nervous system, demyelination, and receptors. *Id*. at 13–20.

First Report

Dr. Vartanian reviewed Petitioner's medical records and summarized the points he deemed most pertinent. First Vartanian Rep. at 2–6. He particularly highlighted evidence of Petitioner's bronchitis diagnosis prior to vaccination, as recognized by some of the treaters who saw Mr. Howard. *Id*. at 3–4. Overall, Dr. Vartanian did not contest Petitioner's CIDP diagnosis, although he disputed the validity of Dr. Sheikh's causation theories. *Id*. at 10. Petitioner's antecedent respiratory infection was, in Dr. Vartanian's estimation, the most likely cause of his CIDP. *Id*. at 13.

As background for his opinion, Dr. Vartanian discussed peripheral neuropathies generally, contrasting CIDP with related but monophasic conditions. CIDP typically presents as a combined motor and sensory neuropathy involving the proximal and distal muscle groups. First Vartanian Rep. at 6. Its presentation distinguishes it from GBS, along with its fluctuating and

lengthier course, and the fact that sensory symptoms are predominant at onset. *Id*. In addition, a number of secondary complications (dysautonomia, respiratory failure, and cranial neuropathies) are primarily associated with GBS/ADIP. *Id.* CIDP is, however, reasonably understood to be immune-mediated, like GBS. *Id.* at 7.

CIDP may feature a relapsing or progressive course. First Vartanian Rep. at 6. But despite its chronic nature, it can *begin* acutely—and hence can initially be mistaken for GBS, before its chronicity is evident. *Id.* As a result, it can be difficult to diagnose CIDP, since it may present in different ways, with CIDP variants also existing. *Id*. at 7; A. Kimura et al., *Motor-Dominant Chronic Inflammatory Demyelinating Polyneuropathy*, 257 J. Neurol 621, 621 (2010), filed as Ex. I (ECF No. 34-7) ("Kimura); F. Rotta et al., *The Spectrum of Chronic Demyelinating Polyneuropathy*, 173 J. Neurological Scis. 129, 135–38 (2000), filed as Ex. M (ECF No. 35-1).

As research shows, CIDP often follows an upper respiratory or gastrointestinal infection, thus suggesting an infectious etiology in some cases. K. Gorson et al., *Chronic Inflammatory Demyelinating Polyneuropathy: Clinical Features and Response to Treatment in 67 Consecutive Patients with and without a Monoclonal Gammopathy*, 48 Neurology 321, 322, 324–25 (1997), filed as Ex. F (ECF No. 34-4) ("Gorson"); P. McCombe et al., *Chronic Demyelinating Polyradiculoneuropathy: A Clinical and Electrophysiological Study of 92 Cases*, 110 Brain 1617, 1617, 1622, 1626 (1987), filed as Ex. J (ECF No. 34-8) ("McCombe"). Gorson, for example, observed that 21 percent of 67 studied CIDP patients "recalled an antecedent infection in the weeks preceding the onset of symptoms," while in McCombe the share was even greater (35 percent of the 92 individuals studied). Gorson at 322, 324–25; McCombe at 1617, 1622, 1626.

CIDP has not, however, in Dr. Vartanian's understanding been persuasively linked to the Tdap vaccine. First Vartanian Rep. at 7. Dr. Vartanian could not identify any epidemiologic proof making such a connection, noting that an internet search he performed of the Pubmed database (utilizing basic search terms and word combinations like "CIDP and Tdap") produced not a single positive "hit." *Id*.

Dr. Vartanian also maintained the evidence Petitioner offered in the absence of supportive epidemiologic proof was unhelpful. He deemed only the Pollard & Selby article filed by Petitioner to be a "striking" example of potential association—and yet it was (in his reading) facially distinguishable. *Id.* Pollard & Selby was a case report of a 42-year-old man who experienced three episodes of relapsing demyelinating neuropathy (akin to CIDP although not identified as such in the article) following an injection of tetanus toxoid, administered variously between 1962 and 1976. *Id*. at 7–8; Pollard & Selby at 114. But (in addition to the fact that the report did not specifically involve the Tdap vaccine) its authors surmised the tetanus toxoid antigenic stimulation was provoking a non-specific cellular, T cell-driver myelin attack, rather than one that was antibody-driven. Pollard & Selby at 121–22; First Vartanian Rep. at 7. Thus,

the association demonstrated in Pollard & Selby did not explain *how*, or by what mechanism, a tetanus toxoid antigen could stimulate CIDP, even if *some* association had been demonstrated (and confirmed via testing) in this single patient. Pollard & Selby at 123–24.

By contrast, reliable evidence seriously undercut the conclusion that CIDP can be reliably associated with the Tdap vaccine. First Vartanian Rep. at 8–9. The IOM, for example, found "neither epidemiologic nor mechanistic evidence for a link between components of the Tdap vaccine and CIDP." Stratton at 477–78. It specifically identified five publications "in which CIDP had been reported after vaccination with tetanus toxoid containing vaccines." First Vartanian Rep. at 9; Stratton at 478–80. But two of the five "did not provide substantive evidence beyond a temporal association and were thus not considered relevant." *See, e.g.*, Pritchard et al., *Risk of Relapse of Guillain-Barré Syndrome or Chronic Demyelinating Inflammatory Polyradiculoneuropathy Following Immunisation*, 73 J. Neurology Neurosurgery Psychiatry 348, 348–49 (2002), filed as Ex. L (ECF No. 34-10); U. Quast et al., *Mono- and Polyneuritis After Tetanus Vaccination*, 43 Dev. Biology Standard 25, 25, 31 (1979), filed as Ex. T (ECF No. 38-2). The other three articles mentioned by the IOM were found to not rule out other causes or anything further than a temporal relationship (except Pollard & Selby—although the circumstances it presented were unique in displaying three instances of post-vaccine rechallenge). First Vartanian Rep. at 9; *see also* L. Reinstein et al., *Peripheral Neuropathy After Multiple Tetanus Toxoid Injections*, 63 Archives Physical Med. Rehab. 332, 332–34 (1982), filed as Ex. U (ECF No. 38-3) (individual experienced peripheral neuropathy after receipt of three tetanus toxoid injections over five-month timeframe).

Next, Dr. Vartanian summarized Dr. Sheikh's theories, acknowledging the reliable support Dr. Sheikh found from case reports like Pollard & Selby, as well as the medical/scientific evidence linking GBS/AIDP to infections. First Vartanian Rep. at 9. But Dr. Vartanian emphasized that Dr. Sheikh's theory provided insufficient support for certain integral links to its overall chain. For example, "what components within the Tdap vaccine share epitopes . . . with peripheral nerve myelin" that are sufficient to lead to a mimicking cross-reaction by antibodies generated in reaction to the vaccine. *Id*. at 11. Given the absence of credible epidemiologic evidence linking the Tdap vaccine and CIDP, Dr. Vartanian argued, a more reliable and specific mechanistic showing needed to be made in order to establish the potentiality of molecular mimicry as the applicable autoimmune mechanism. *Id.*

Dr. Vartanian considered molecular mimicry the sole proposed causal mechanism that Dr. Sheikh had attempted to substantiate with any evidence or argument (in comparison to the three other mechanisms, which Dr. Sheikh only described in cursory fashion). First Vartanian Rep. at 11. But he questioned its reliability in this case. In particular, Dr. Vartanian disputed that the Tdap vaccine's tetanus toxoid component has the capacity to instigate autoimmunity by binding "to glycolipids from the muscle it is injected into," resulting in conjugates that "are processed at

the injection site by antigen presenting cells to generate an immune response against gangliosides." *Id*. The toxoid's binding affinity was for receptors or structures on *nerve-oriented* tissues rather than muscle, making it "not rational" to propose a muscle-specific situs for cross-reaction. *Id.* And even if the toxoid were to travel beyond the injection situs in order to be picked up by some kind of receptor, "it would then do what it is known to do which is to become internalized and transported, retrograde, to the neuronal cell body thus escaping immunity." *Id.*; Weller at 1055, 1058–62. It therefore could not credibly spark an autoimmune response in the manner proposed by Dr. Sheikh.

Second Report

Dr. Vartanian's second report sought to rebut some of Dr. Sheikh's criticisms. Dr. Vartanian allowed that the absence of definite evidence in support of Petitioner's theory did not per se rule it out (although he also noted that if reliable evidence of an association between a vaccine and GBS or CIDP even existed, the vaccine would not likely be in widespread use at all). Second Vartanian Rep. at 1. But he reiterated his prior point that epidemiologic studies could provide useful insight into public health risks. *Id.* at 2. And the mere plausibility of Petitioner's causal theory did not mean it was *likely*. *Id.* at 4.

Dr. Vartanian next argued that Dr. Sheikh lacked scientific support for many of his contentions. Second Vartanian Rep. at 4, 6. He specifically revisited the issue of whether (and where) the tetanus toxoid component could bind to receptors sufficient to spark an autoimmune cross-reaction against other nerve structures. Dr. Vartanian conceded that "muscle expresses gangliosides" (via nerves found intertwined in muscle fiber), but emphasized his point was that it was *nerve* structures to which the toxoid would ultimately bind (as opposed to the muscle itself). *Id.* at 5. Regardless, Dr. Vartanian contended, the tetanus toxoid in the vaccine would not likely reach these receptors and then bind in a sufficient manner to produce an autoimmune cross-reaction. *Id*. at 5. Even if the toxoid did leak out of the muscle and bind to small nerve fiber, it would not incite cell damage or death. *Id*. Therefore "there is no mechanism for release of ganglioside bound to toxin, phagocytosis of toxin-ganglioside complexes by APCs, presentation of protein or glycolipid antigens T or B cells, and production of autoreactive antibodies." *Id.*

Dr. Vartanian concluded by questioning whether any other components of the Tdap vaccine could be causal of CIDP. Nonviral/bacterial adjuvants contained in the vaccine, for example, are present in most vaccines, and are therefore unlikely to play a role in causation, as high rates of GBS or CIDP do not inherently follow vaccination as a general matter, and without regard to the vaccine at issue. Second Vartanian Rep. at 6. In his view, Petitioner's upper respiratory, pre-vaccination infection remained the "most plausible inciting event" in this case, as the medical record consistently notes that it had occurred. *Id.* And the "fertile field" hypothesis

had not been substantiated to likely encourage CIDP's pathogenesis in the context of receipt of the Tdap vaccine. *Id.*

III. Parties' Arguments

Petitioner's Brief

Petitioner argues that the Tdap vaccine he received was a substantial factor in causing his CIDP, relying heavily on Dr. Sheikh's opinion in support. Mot. at 8. He maintains that (similar to the AIDP/GBS variant), CIDP is "mediated by humoral and cellular immunity against Schwann cell/myelin target antigens in the nerves." *Id.* at 10. Molecular mimicry triggered by vaccination can (in an inflammatory context) result in GBS—and CIDP as well. *Id.* Anti-ganglioside autoantibodies are also important to Petitioner's theory, since animal models demonstrate these may produce inflammatory nerve injuries similar to that in AIDP patients. *Id.* at 11. All of the above is reasonably asserted even if, as Dr. Sheikh acknowledges, less is known overall about CIDP. *Id.*

Petitioner focuses in particular on the two phases of his injury: the initial acute manifestations of symptoms, followed by a chronic condition. Mot. at 13. The first acute phase resulted in Petitioner being diagnosed with GBS, which Dr. Sheikh found proper at the time, but once Petitioner's symptoms did not abate, the diagnosis was reasonably amended to acute onset CIDP. *Id.* at 13–14. Overall, based on Dr. Sheikh's analysis Petitioner maintains the Tdap vaccine was "the best and most proximate triggering event." *Id.* at 14. He therefore contends he has met all three *Althen* prongs through his expert report, medical records, and clinical history. *Id.* at 15–16.

Respondent's Opposition

Respondent accepts the CIDP diagnosis, but disputes that Petitioner has preponderantly proven that CIDP can be caused by the Tdap vaccine. Opp. at 9. First, he maintains the "can cause" causation prong has not been met. Petitioner has not preponderantly shown "that CIDP shares pathogenic mechanisms with AIDP or any other type of GBS." *Id.* at 10. Indeed, Dr. Sheikh acknowledged that CIDP's pathogenesis is not well understood. *Id*. at 10–11. While Petitioner's expert relies on the similarities between CIDP and GBS to conclude they likely have the same pathogenesis, Respondent argues that they are only congruent to the extent both are immune-mediated neuropathies, with substantial differences that make it impossible to simply take what is known about the association of some infections, or vaccines for that matter, with GBS and apply it herein. *Id.* at 11–12. The same goes for molecular mimicry as a mechanism more generally, since "a possibility that a certain proposed immunological response may occur does not make it more likely than not that that response actually occurs—particularly where that

proposed response is not consistent with what is known about the microbiological processes involved." *Id.* at 13.

Respondent also maintains that Dr. Sheikh's argument about the tetanus toxoid component binding to muscle as an alternative mechanism for an autoimmune reaction was rebutted by Dr. Vartanian. Opp. at 13. Dr. Sheikh admitted that only a small number of CIDP patients even have tested positive for the purportedly disease-driving anti-ganglioside antibodies. *Id.* And case reports involving individual patients who experienced CIDP or comparable chronic conditions after receipt of a tetanus-containing vaccine are not persuasive because they only establish a temporal relationship with vaccination. *Id.* at 14.

Respondent further argues the "did cause" prong has not been met. There is, he maintains, no record evidence of any treater conclusions in favor of vaccine causation in Petitioner's case, even though they were aware of the prior vaccination. Opp. at 16. By contrast, Petitioner did have a URI prior to his injury which was more likely causal; the fact that no specific viral cause was ever identified does not make it more likely that the vaccine was causal. *Id.* at 17. At bottom, the record only establishes a temporal relationship between vaccination and illness. *Id*. at 18–19. Finally, Respondent contends that the two-week timeframe for post-vaccination onset has not been addressed or explained to be medically reasonable. Opp. at 19–20. The fact that other cases have deemed such a timeframe acceptable is not dispositive of this causation element. *Id.* at 20–21.

Petitioner's Reply

Petitioner's reply initially maintains that the "can cause" causation prong is subject to a plausibility evidentiary standard rather than preponderance, as Respondent argues. Reply at 2–3. It then reiterates his theories of causation, putting emphasis on Dr. Sheikh's extensive expertise in treating and understanding CIDP and GBS, and the fact that both experts agreed herein that CIDP is immune-mediated and can (in some cases) have an infectious etiology. *Id.* at 3. It notes that certain prior cases relied upon by Respondent, but which involved Tdap and CIDP (such as *Houston v. Sec'y of Health & Hum. Servs.*, No. 18-420V, 2021 WL 4259012 (Fed. Cl. Spec. Mstr. Aug. 19, 2021)) are distinguishable on the facts as well as differences in the expert opinions offered. *Id.* at 4. And Petitioner notes how often Tdap/CIDP cases have settled. *Id.*

Otherwise, Petitioner argues that his causation theory involving the tetanus toxoid's potentiality to bind to receptors located on "nerve fibers innervated in the muscle fibers," and thereafter instigate an autoimmune response, was well-conceived and explained, with Dr. Sheikh effectively rebutting Dr. Vartanian's contentions on this point. Reply at 5–6. Dr. Sheikh's other proposed mechanisms were also reasonably and persuasively advanced, with the "fertile field" model even taking into account a synergy between the prior URI and subsequent vaccination to

cause an autoimmune injury. *Id.* at 6–8. The IOM Report did not conclusively dispute the possibility of vaccine association with CIDP—nor could it, since no epidemiologic evidence exists rebutting the possibility. *Id.* at 7. And this is not a case where treaters affirmatively discounted vaccine causation; instead, they simply did not even consider the possibility (which thus is not evidence of it being rejected, as Respondent proposes). *Id.* at 9.

IV. Procedural History

The claim was initiated in November 2016, and Petitioner filed medical records thereafter with the statement of completion filed in December 2016. ECF No. 9. Respondent's Rule 4(c) Report was then filed on April 24, 2017. ECF No. 24. The expert reports referenced above were filed thereafter, with the process completed by October 2018. The case was eventually reassigned to me in March 2021, and after reviewing the pre-hearing briefs filed by both parties, I determined this matter could be decided via a ruling on the record. *See generally* ECF Nos. 61, 62, 65. The claim is now ripe for resolution.

V. Relevant Legal Standards

A. *Standards for Vaccine Claims*

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[11] In this case, Petitioner cannot assert a Table claim based on CIDP.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health*

[11] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Hum. Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Hum. Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Hum. Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

& Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate 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)); *Pafford v. Sec'y of Health & Hum. Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005): "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury."

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras*, 121 Fed. Cl. at 245.

In discussing the evidentiary standard applicable to the first *Althen* prong, the Federal Circuit has consistently rejected the contention that it can be satisfied merely by establishing the proposed causal theory's scientific or medical *plausibility*. *See Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019); *see also LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) ("[h]owever, in the past we have made clear that simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof" (citing *Moberly*, 592 F.3d at 1322)). And petitioners always have the ultimate

burden of establishing their *overall* Vaccine Act claim with preponderant evidence. *W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted); *Tarsell v. United States*, 133 Fed. Cl. 782, 793 (2017) (noting that *Moberly* "addresses the petitioner's overall burden of proving causation-in-fact under the Vaccine Act" by a preponderance standard).[12]

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical 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 particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

Medical records and statements of a treating physician, however, do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Hum. Servs*., 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Veryzer v. Sec'y of Dept. of Health & Hum. Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review denied*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 F. Appx. 765 (Fed. Cir. 2012).

[12] In some prior decisions that have not yet been formally published, I have addressed at length the deficiency in arguments that *any* recent Federal Circuit determinations stand for the proposition that a "mere plausibility" standard with respect to *Althen* prong one controls this claim's disposition. This contention is based on a misreading of applicable controlling precedent from another, non-precedential Court of Federal Claims decision. I reject this reasoning herein as well, and do not give credence to Petitioner's contentions (in his briefing) that I should only evaluate *Althen* prong one from a plausibility standpoint.

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must align with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 F. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review denied* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Law Governing Analysis of Fact Evidence*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [ ] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Hum. Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (determining that it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

As noted by the Federal Circuit, "[m]edical records, in general, warrant consideration as trustworthy evidence." *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Hum. Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd*, *Rickett v. Sec'y of Health & Hum. Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). A series of linked propositions explains why such records deserve some weight: (i) sick people visit medical professionals; (ii) sick people attempt to honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Hum. Servs.*,

No. 11–685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Hum. Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Hum. Servs*., No. 03–1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are often found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Hum. Servs*., 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, the Federal Circuit has also noted that there is no formal "presumption" that records are accurate or superior on their face to other forms of evidence. *Kirby v. Sec'y of Health & Hum. Servs.,* 997 F.3d 1378, 1383 (Fed. Cir. 2021). There are certainly situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Hum. Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Hum. Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Hum. Servs*., No. 90–2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *La Londe v. Sec'y of Health & Hum. Servs*., 110 Fed. Cl. 184, 203–04 (2013), *aff'd*, 746

F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Hum. Servs*., 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594–96 (1993). *See Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). Under *Daubert*, the factors for analyzing the reliability of testimony are:

> (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community.

Terran, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

In the Vaccine Program the *Daubert* factors play a slightly different role than they do when applied in other federal judicial settings, like the district courts. Typically, *Daubert* factors are employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable or could confuse a jury. By contrast, in Vaccine Program cases these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs*., 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs*., 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion

"connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 (1997)); *see also Isaac v. Sec'y of Health & Hum. Servs*., No. 08–601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review denied*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. App'x. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. *Consideration of Medical Literature*

Both parties filed numerous items of medical and scientific literature in this case, but not every filed item factors into the outcome of this Decision. While I have reviewed all the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case—just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.,* 527 F. Appx. 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

E. *Standards for Ruling on the Record*

I am resolving Petitioner's claim on the filed record. The Vaccine Act and Rules not only contemplate but encourage special masters to decide petitions on the papers where (in the exercise of their discretion) they conclude that doing so will properly and fairly resolve the case. Section 12(d)(2)(D); Vaccine Rule 8(d). The decision to rule on the record in lieu of hearing has been affirmed on appeal. *Kreizenbeck v. Sec'y of Health & Hum. Servs*., 945 F.3d 1362, 1366 (Fed. Cir. 2020); *see also Hooker v. Sec'y of Health & Hum. Servs*., No. 02-472V, 2016 WL 3456435, at *21 n.19 (Fed. Cl. Spec. Mstr. May 19, 2016) (citing numerous cases where special masters decided case on the papers in lieu of hearing and that decision was upheld). I am simply not required to hold a hearing in every matter, no matter the preferences of the parties. *Hovey v. Sec'y of Health & Hum. Servs*., 38 Fed. Cl. 397, 402–03 (1997) (determining that special master acted within his discretion in denying evidentiary hearing); *Burns*, 3 F.3d at 417; *Murphy v. Sec'y of Health & Hum. Servs.*, No. 90-882V, 1991 WL 71500, at *2 (Fed. Cl. Spec. Mstr. Apr. 19, 1991).

I previously determined that I would decide this case on the papers, and reached that conclusion only after hearing from both sides on the question. Order at 2-3. Because my earlier Order sets forth the bases for my determination, and is consistent with the law permitting special masters (in the proper exercise of their discretion) to determine how best to resolve a matter, I do not herein reiterate my reasoning.

ANALYSIS

I. Relevant Prior Reasoned Decisions

A. *Vaccines Alleged to Cause Demyelinating Polyneuropathies Generally*

There is a large body of reasoned decisions[13] affirming the existence of an association between the flu vaccine and peripheral neuropathies *other* than CIDP—most often GBS. Indeed, GBS occurring after receipt of a flu vaccine is the basis for a Table claim. 42 C.F.R. § 100.3. [14] This means the Government agreed that sufficiently-probative and reliable science on the topic existed to justify (in effect) *conceding* causation, at least for Program purposes. *Haskins v. Secretary of Health & Hum. Servs.*, No. 18-1776, 2020 WL 1870279 (Fed. Cl. Spec. Mstr. Mar. 13, 2019). Indeed, even in cases where a Table element for a flu vaccine-GBS claim cannot be met (for example, when onset is too short or long to fit within the timeframe of 3-42 days set for the claim), any subsequent causation-in-fact analysis does not usually turn on the "can cause" first *Althen* prong. *See, e.g.*, *Welch v. Sec'y of Health & Hum. Servs.*, No. 18-494V, 2019 WL 349360 (Fed. Cl. Spec. Mstr. July 2, 2019).

Other vaccines have also been found causal of GBS. *See,* e.g., *Koller v. Sec'y of Health & Hum. Servs.*, No. 16-439V, 2021 WL 5027947 (Fed. Cl. Spec. Mstr. Oct. 8, 2021) (pneumococcal vaccine caused GBS). But it cannot be said that the Program has developed a consistent view as to what the science preponderantly "says" about causation when the flu vaccine is *not* involved. Overall, it appears that the outcome in such cases is mostly a function of the evidence before the special master, with no clear trend one way or the other.

This is definitely true in the context of claims that the *Tdap vaccine* can cause GBS. Several cases decided in the past ten years found no causal association between the two. *See, e.g.*, *Winkler v. Sec'y of Health & Hum. Servs.,* No. 18-203V, 2021 WL 6276203 (Fed. Cl. Spec. Mstr.

[13] As already noted, although prior decisions from different cases do not control the outcome herein, special masters may reasonably take into account, for guidance, the logic of reasoned entitlement determinations. In fact, it is wise to do so, given how often similar causation theories or fact patterns arise in Vaccine Program cases.

[14] The fact that a flu-GBS Table claim exists is not, however, helpful to Petitioner herein, since a CIDP diagnosis "disqualifies" such a claim for Table consideration. 42 C.F.R. § 100.3(c)(15)(vi).

Dec. 10, 2021), *mot. for review docketed,* Jan. 10, 2022 (ECF No. 62); *Montgomery v. Sec'y of Health & Hum. Servs.,* No. 15-1037V, 2019 WL 2511352 (Fed. Cl. Spec. Mstr. May 21, 2019); *Tompkins v. Sec'y of Health & Hum. Servs.,* No. 10-261V, 2013 WL 3498652 (Fed. Cl. Spec. Mstr. Jue 21, 2013), *mot. for review den'd,* 117 Fed. Cl. 713 (2014); *see also Isaac v. Sec'y of Health & Hum. Servs.,* 108 Fed Cl. 743 (2013) (affirming special master denial of claim alleging tetanus vaccine was causal of GBS), *mot. for review den'd,* 540 Fed. App'x 999 (Fed. Cir. 2013).

In *Winkler,* for example, the petitioner offered molecular mimicry as his causal theory, noting also that certain known causes of GBS, like a *Campylobacter* infection, are understood to have molecular mimicry as their mechanism. *Winkler,* 2021 WL 6276203, at *23. But the special master determined that the claim turned not on the petitioner's first prong success, but rather on the fact that he had a demonstrated gastrointestinal infection, and that this infection was more likely causal (making it impossible to find that the vaccine "did cause" GBS). *Id.* at *23–25. Thus, evidence of a petitioner's intercurrent illness was dispositive, regardless of the persuasiveness of the causal theory. The *Tompkins* special master denied entitlement in a case alleging that a number of vaccines received at the same time, including the Tdap vaccine, caused a petitioner's GBS, but the causal theory put forward attempted to assert that the vaccines could also *individually* trigger the disease. *Tompkins,* 2013 WL 3498652, at *15. The petitioner's expert, however, relied heavily on VAERS passive surveillance data,[15] and otherwise invoked a number of theories (molecular mimicry, or endotoxin in tetanus-containing vaccines) that were only cursorily discussed. *Id.* at *19–23.

At the same time, several cases go the other way. *See, e.g.*, *Mohamad v. Sec'y of Health & Hum. Servs.,* No. 16-1075V, 2022 WL 711604, at *18 n.17 (Fed. Cl. Spec. Mstr. Jan. 27, 2022) (ruling in the petitioner's favor in a Tdap-GBS case, but almost wholly based on determination that the Government had conceded the first *Althen* prong, plus evidence of prior post-vaccination demyelination, suggesting proof of "rechallenge"); *Swaiss v. Sec'y of Health & Hum. Servs.,* No. 15-286V, 2019 WL 6520791, at *23-27 (Fed. Cl. Spec. Mstr. Nov. 4, 2019) (small fiber neuropathy (characterized in *Swaiss* as "a variant" of GBS) could be caused by the Tdap vaccine via the mechanism of molecular mimicry, but acknowledging that the evidence offered to associate GBS and Tdap *generally* was somewhat lacking). Thus, it certainly cannot be said that claims relying on the Tdap vaccine are categorically ruled out—even if it is also clear, at the

[15] The Vaccine Adverse Event Reporting System ("VAERS") is a national warning system designed to detect safety problems in U.S.-licensed vaccines. *See About VAERS*, VAERS, https://vaers hhs.gov/about.html (last visited Apr. 5, 2022). It is managed by both the CDC and the FDA. VAERS monitors and analyzes reports of vaccine related injuries and side effects from both healthcare professionals and individuals. But it has been observed in the Program that VAERS data is not particularly probative of causation unless supplemented with other reliable evidence—since a VAERS report only establishes a temporal, post-vaccination occurrence, and thus shines no light on the possibility of causation itself. *See also Vig v. Sec'y of Health & Human Servs.*, No. 01–198V, 2013 WL 6596683, at *17 (Fed. Cl. Spec. Mstr. Nov. 14, 2013) ("VAERS is a stocked pond, containing only reports of adverse events after vaccinations but no data about the number of vaccines administered or the occurrence of the same adverse event in individuals who have not been vaccinated").

threshold, that there is a meaningful decline in the amount of reliable scientific evidence associating that vaccine to this kind of nerve injury, when compared to what is known about GBS and the flu vaccine.

B. *Tdap and CIDP*

There are even fewer reasoned decisions specifically involving the Tdap vaccine and CIDP. At most, an association has often been *assumed*, based on the supposition that CIDP is merely "long GBS." *See Strong v. Sec'y of Health & Hum. Servs.*, No. 15-1108V, 2018 WL 1125666 (Fed. Cl. Spec. Mstr. Jan. 12, 2018). That association may not be all that well-reasoned or substantiated, but it has been deemed enough for success in the Program, in the past at least.

I recently have denied entitlement in two cases where the petitioner alleged that CIDP was caused by the Tdap vaccine. *Sanchez v. Sec'y of Health & Hum. Servs.*, No. 18-1012V, 2022 WL 1013264 (Fed. Cl. Spec. Mstr. Mar. 11, 2022); *Houston v. Sec'y of Health & Hum. Servs.,* No. 18-420V, 2021 WL 4259012 (Fed. Cl. Spec. Mstr. Aug. 19, 2021). Although some facts of both cases are readily distinguishable, these determinations still provide some useful guidance herein. *Sanchez,* 2022 WL 1013264, at *23; *Houston,* 2021 WL 4259012, at *17–18.

In *Sanchez,* the petitioner received the Tdap vaccine approximately one month before giving birth, and she alleged she began experiencing neuropathic-like symptoms around the time of birth. *Sanchez,* 2022 WL 1013264, at *1-2. Although the evidence supported the CIDP diagnosis, I did not find that the *Althen* prongs had been met. *Id.* at *21-24. To meet the first prong, the petitioner's expert relied too much on case reports, or science applicable to GBS, while pointing to evidence of a T-cell driven attack that was inconsistent with what *was* known about CIDP's pathogenesis (which involves an antibody-driven attack). *Id.* at *21-22. Petitioner also had failed to show that her symptoms did not pre-date vaccination—or that her pregnancy could not have played a predominant causal role in her disease development. *Id* at *22.

In *Houston,* another pregnant petitioner (with a history of neuropathic symptoms likely associated with diabetes) received a Tdap vaccine two to three weeks before onset of symptoms arguably associated with CIDP (although she was not diagnosed with it until about two months after vaccination). *Houston,* 2021 WL 4259012, at *1-2. Admittedly (and as Petitioner in this case has pointed out in briefing the present ruling on the record), some of the evidentiary balancing that led to my determination was the product of a different mix of evidence distinguishable from the present matter. For example, the *Houston* petitioner's demonstrated history of prior neuropathic symptoms seemed likely related to her post-vaccination CIDP symptoms. *Id*. at *18-19. In addition, the experts were *less* evenly-matched than here, with the *Houston* petitioner relying on a knowledgeable treatment specialist who nevertheless lacked specialized expertise in neuropathies or immunology, rather than an individual like Dr. Sheikh, who clearly possesses deep understanding of demyelinating diseases. *Id.* at *17. And literature offered therein (but not in this

case) suggested CIDP was less likely caused by infection than AIDP—whereas in this case both experts not only embrace infection as potentially causal, but Dr. Vartanian has actively referenced Petitioner's pre-vaccination URI as *likely* causal.

Even though the circumstances of these two cases can be reasonably distinguished in many regards from the present matter, *Sanchez* and *Houston* do stand for at least one important conclusion that is relevant herein: for purposes of Program determinations, it is improper to think of GBS and CIDP as "two sides of the same coin," despite their overlap. Not only do different autoantibodies likely drive each respective neuropathic process, but their underlying pathogenic beginnings (which further result in distinguishable course lengths, treatments, and some symptoms) are attributable to cross-reactive attacks at different nerve situses. *Houston,* 2021 WL 4259012, at *10. These differences matter for purposes of determining causation—especially since far less is known about CIDP generally. Petitioners cannot just "borrow" what is known about GBS and vaccination generally as a template for proving causation in the context of a CIDP injury.

II. Relevance of Prior Settled Cases to Entitlement Decisions

In briefing the ruling on the record, Petitioner has pointed to seven settled cases involving the Tdap vaccine and CIDP from the past two years. *See generally* Reply at 4, and Addendum (ECF No. 65-1) at 2. Although Petitioner maintains that this list is intended to provide an explanation for why so few reasoned Tdap-CIDP decisions exist, it is reasonable to infer that Petitioner *also* wanted to suggest that Respondent "knows" that the causation theory advanced in this case has scientific/medical reliability (since if it did not, it is unlikely Respondent would so readily agree to settle comparable cases). *See* Opposition to Motion to Strike (ECF No. 68) at 1 ("Respondent is settling a significant number of these claims . . . thereby avoiding reasoned decisions in favor of causation").

Of course (and as I pointed out earlier in the case)[16], settled cases provide *no* reliable precedential value. *K.O. v. Sec'y of Health & Hum. Servs.*, No. 13-472V, 2016 WL 7634491, at *15 (Fed. Cl. Spec. Mstr. July 7, 2016). At most, the existence of a kind of case that has been consistently been settled suggests to petitioners (and more specifically counsel who reasonably pay attention to developments in the Vaccine Program) that a matter might be one Respondent would be *amenable* to settle. But settlements are adopted for a myriad number of reasons, some of which may have little to do with a claim's substance, and therefore the decision by Respondent to settle a case says nothing about whether the *Althen* prongs have been satisfied—or could easily be satisfied if the matter were tried.

[16] In January 2022, Respondent moved to strike the list of settled cases appended to the Reply from the record, arguing that they did not have precedential value and otherwise did not bear on any of the disputed fact or legal issues. ECF No. 67. I denied the motion, but recognized the legal accuracy of Respondent's contentions, and thus indicated that I would not give these cases weight in my determination. Order, dated January 18, 2022 (ECF No. 69).

I do not contest the logic behind Petitioner's view that settled cases might reflect some tacit admission by Respondent. If Respondent settles a claim multiple times, is he *not* implicitly conceding that some science might support the claim at issue? And if the disease in question is also demyelinating and autoimmune-mediated, comparable to GBS (where, as noted above, reliable science supports causation), why would it not be concluded that the settled claim was *also* understood to be viable if taken to trial?

This reasoning is seductive, especially to the special masters (who can avoid unnecessary work by encouraging parties to attempt settlement in cases that seem comparable to a type commonly resulting in settlement). But it is properly resisted—both because of the limited probative value of settlements, as well as the aforementioned distinctions between cases alleging CIDP as the injury and other peripheral neuropathy cases involving demyelination.[17] I therefore give no weight at all herein to the fact that prior Tdap-CIDP cases have settled.

III. Petitioner Has Not Carried His Burden of Proof[18]

A. *Althen Prong One*

As noted above, there is a foundational weakness in Petitioner's causation theory, and that is the extent to which it relies on medical science applicable to GBS to propose a comparable theory for CIDP's pathogenesis. The fact that GBS and CIDP overlap in significant ways does not compel the wholesale application of what is causally "known" about GBS to CIDP, for purposes of the legal determination I am tasked with making.

Despite Dr. Sheikh's arguments, CIDP and GBS are *not* distinguishable solely in terms of their timeframe. Rather, the autoimmune attack that propagates GBS's characteristic demyelination appears to involve different aspects/locations of the nerve—and this likely explains why GBS tends to be monophasic while CIDP is chronic. *Mason v. Sec'y of Health & Hum. Servs.*, No. 17-1383V, 2022 WL 600415 at *21 (Fed. Cl. Spec. Mstr. Feb. 4, 2022). In addition, different kinds of antibodies are likely implicated in each. Much more is also known about the autoantibodies that drive GBS—and in turn, more is known about *how* those antibodies cross-react with self structures, as well as possible instigating factors that cause them to come

[17] It is likely that Tdap-CIDP cases have settled simply on the basis of the presumption that the injury is not all that distinguishable from a case alleging post-vaccination GBS. But as already noted, it should not be assumed that the fact that GBS and CIDP are both peripheral neuropathies means they are identical for purposes of determining causation.

[18] I only discuss herein the *Althen* prongs directly relevant to my determination – since the failure to meet any one prong is fatal to the entire claim. But I do note that the timeframe for Petitioner's development of CIDP in this case (which is applicable to the third prong) is largely consistent with his causation theory; Mr. Howard's CIDP began within about three weeks of vaccination, and that is consistent with the timeframe that Dr. Sheikh's theory would propose for vaccine-induced CIDP.

into being. Even the treatments for the two diverge, since steroids are ineffective with GBS but help ameliorate CIDP. *Blackburn v. Sec'y of Health and Hum. Servs.*, No. 10-410V, 2015 WL 425935, at *22 (Fed. Cl. Spec. Mstr. Jan. 9, 2015). As a result, evidence *specific* to CIDP is reasonably called for in a case alleging that a vaccine could be causal of it.

Petitioner attempted to provide that kind of evidence, but succeeded only partially. Dr. Sheikh did offer reliable evidence showing that a few autoantibodies have been identified in the context of CIDP. *See* Lewis and Ilyas. But not enough is known about CIDP's pathogenesis to ascertain whether these autoantibodies drive the *initial* disease (as they would need to if produced in response to a vaccine), or if they appear incidentally, in the course of disease progression. Whereas a great deal is known about certain autoantibodies as driving GBS—not just that the autoantibody *initiates* disease, but how it can be produced, and its antigenic target—far less is understood in the context of CIDP, with no recent literature offered to provide clarification.

Dr. Sheikh similarly offered several case reports, with one (Pollard & Selby) more persuasively establishing a pattern of a demyelinating reaction to a tetanus-containing vaccine, based on repeated, documented instances of illness post-vaccination. However (and ignoring the generally-recognized fact in the Program that case reports are a weaker form of evidence in establishing causation),[19] Pollard & Selby (a) is a dated article, with no more recent updates to explore its implications, and (b) has not been demonstrated to involve the same kind of vaccine components at issue in the modern version of Tdap. Beyond that (and though Petitioner is correct that the IOM report does not *exclude* a finding that the Tdap vaccine could be causal), little to no other affirmative evidence was offered linking the vaccine to CIDP.

The mechanisms proposed in this case for *how* the vaccine would cause CIDP were also incompletely established, and ultimately did not add up to reliable and preponderant evidence, no matter how "plausible" it is that *any* vaccine might cause an autoimmune injury like CIDP is.[20] Of course, petitioners are never required to establish mechanism—but they often attempt to do so, and therefore it is reasonable to evaluate their success in the effort. *Samuels v. Sec'y of Health & Hum. Servs.*, No. 17-071V, 2020 WL 2954953, at *20. And (as Dr. Vartanian observed) in the context of a claim in which little direct evidence associates the given vaccine with the

[19] *Campbell v. Sec'y of Health & Hum. Servs.*, 97 Fed. Cl. at 668 ("[c]ase reports do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value ... [but] the fact that case reports can by their nature only present indicia of causation does not deprive them of all evidentiary weight.").

[20] This illustrates another sound reason for why mere plausibility cannot be the evidentiary standard for the first *Althen* prong. Vaccines are intended to cause an immune reaction, and many (if not most) of the illnesses complained of in the Vaccine Program are autoimmune-mediated. If it is true that it need only be shown that a vaccine *plausibly* could cause injury, then ***no post-vaccination autoimmune injury claim would fail to establish the "can cause" prong***. This would in turn collapse Table and causation-in-fact claims into one mass, rather than treating them with the distinction that that Act itself requires.

injury at issue, it can be vital to substantiating causation to make a persuasive showing on mechanism.

Here, Dr. Sheikh invested most of his time in attempting to establish molecular mimicry as likely causing components of the Tdap vaccine to promote the autoimmune attack believed to mediate the CIDP disease process. Again, some of his contentions were based on reliable science. In particular, he persuasively established that nerve receptors (found generally in the periphery but also in muscle nerves)[21] might have the capacity to receive the tetanus toxoid, in the process of reacting to the vaccine, even if the toxoid mostly is absorbed away after its initial introduction (and the immune system reaction to it—which would occur closer to the situs of administration). But details necessary to flesh out this aspect of his theory were missing (probably in part due to Dr. Sheikh's overreliance on science pertaining to GBS and its association with the flu vaccine). Thus (and to name only one of several missing elements), nothing was offered to show a connection between the toxoid and any specific antibody arguably relevant to CIDP in any sense, nor was reliable science offered to establish that a cross reaction *likely* occurs via mimicry (beyond the general plausibility of that occurring). Similarly, mimicry between the toxoid and self ganglioside structures was never shown, such that antibodies specific to the toxoid would in turn cross-react against nerve gangliosides; rather, it was *assumed* this would occur, based on all the other evidence relevant to GBS. In the absence of other evidence credibly linking the Tdap vaccine to CIDP, these omissions are evidentiarily significant.

The other proposed mechanisms were (as argued by Dr. Vartanian) only cursorily mentioned, with far less substantiation. And many of them (for example, bystander activation) would only occur in the presence of a *primary* inflammatory milieu not shown to be applicable in the context of vaccination (as opposed to occurring in the wake of a wild infectious process, in which the virus or bacterium does damage to self tissues *first*, independent of secondary damage caused by an aberrant immune response). Ironically, only the "fertile field" hypothesis was bulwarked by other evidence—and this is due to the fact (as initially denied by Dr. Sheikh, based on his admittedly incomplete review of relevant records at the time of his first expert report) that Petitioner's pre-vaccination bronchitis could be consistent with establishing the baseline conditions for an autoimmune reaction. But von Herrath says nothing about vaccines being capable of sparking this secondary autoimmune response in the presence of a prior infection, and no other evidence offered by Petitioner filled this hole.[22]

[21] I find that the back-and-forth between Drs. Sheikh and Vartanian on whether the tetanus toxoid would present to the muscle itself to have been a sideshow not bearing on the outcome of this case.

[22] This is also not a *Shyface* circumstance, in which vaccination or infection are deemed equally causal – preventing the identification of one as causal over the other, but nevertheless allowing a determination that the vaccine still played a substantial role in the subsequent illness. *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999); Respondent did not concede that the Tdap vaccine can cause CIDP, and I do not find it to be likely either.

My determination does not arise from a finding that distinctions in expert competence or credentials rendered one opinion superior to the other. Both experts were well-qualified to offer the opinions they did—indeed, on the specific injury in question, Dr. Sheikh had the *greater* demonstrated expertise (although this did not mean that his causation opinion, which involved questions of human immunology separate from his disease-specific expertise, was more persuasive). Dr. Shaikh supported many aspects of his opinion with reliable science—for example, he identified *some* autoantibodies that might contribute to CIDP's pathogenesis, independent from simply borrowing science more specific to GBS. And not all of Dr. Vartanian's points (many of which reflected efforts at "settling the score" between the experts on various smaller matters) appreciably advanced Respondent's defenses either. I do not find, for example, that an absence of Pubmed search "hits" on causation is enough to defeat an otherwise-reliable causation theory (although this does underscore the overall lack of direct associative evidence, which does bear on preponderance at least indirectly). Each expert "scored" some points while failing to substantiate others.

Nevertheless, the petitioner in a Vaccine Act claim always bears the initial burden of proof—and this means in turn that his expert opinion must establish, by preponderant evidence, a reliable medical/scientific causation theory. This did not occur in this case, despite Dr. Sheikh's demonstrated qualifications and knowledge of the relevant category of injury. The deficiency in his report primarily was evidenced by the fact that he could not offer enough proof specific to CIDP to preponderantly establish that the Tdap vaccine likely can cause even arguably CIPD-related autoantibodies to generate—or that these are initially/primarily causal, as opposed to antibodies that come into being in the midst of the disease process (which, if so, would make it more difficult to attribute vaccination to the disease's start).

B. *Althen Prong Two*

The record evidence does not preponderate in favor of the determination that the Tdap vaccine "did cause" Mr. Howard's CIDP. There is no evidence of any immediate reaction to vaccination, or transient symptoms that could suggest an aberrant immune response was beginning to manifest. No testing results established the existence of any of the autoantibodies proposed by Dr. Sheikh to be associated with CIDP. And none of Petitioner's treaters ever speculated on any association between his illness and prior vaccination. Although Petitioner reasonably observes that this may reflect the fact that they did not *consider* the possibility (as opposed to rejecting it after reasoned evaluation), it is more commonly the case that Program petitioners point to evidence that the vaccine *was* considered by treaters as possibly causal to support entitlement—and where such evidence exists, it can be persuasive. Even though treater views are never sacrosanct, the fact that treaters consider causation a possibility is a factor in a claimant's favor—and thus the *absence* of such consideration, despite awareness of the vaccination, cannot aid Petitioner. Ex. 1 at 1

In addition, the existence of Petitioner's pre-vaccination bronchitis infection cannot be disregarded, and provides further reason to doubt the "did cause" element has been met. Ex. 59 at 5, 8. Admittedly, no infectious origin was *specifically* identified, and I do not purport (in performing my more limited role as special master) to find otherwise. But it is not uncommon in my experience for patients to test negative for a specific infection—and yet have a medical history establishing they were ill pre-vaccination, likely due to some infectious cause. This only supports the conclusion that the claimant suffered from an idiopathic-in-origin illness. Also, the *fact* of the preexisting illness is undisputed—and (unlike in prior cases, where experts disclaimed the potentiality for an infectious cause for CIDP), Respondent's expert herein *embraced* the possibility.[23] All of the above clouds Petitioner's showing on this prong, undermining it preponderantly—even if, in the end, it cannot be said that his CIDP was "more likely than not" due to his pre-vaccination bout with bronchitis. I need not reach that conclusion to find that it is not more likely than not that the vaccine was causal.

CONCLUSION

A Program entitlement award is only appropriate for claims supported by preponderant evidence. Here, Petitioner has not made such a showing. Petitioner is therefore not entitled to compensation.

In the absence of a motion for review filed pursuant to RCFC Appendix B, the Clerk of the Court **SHALL ENTER JUDGMENT** in accordance with the terms of this Decision.[24]

IT IS SO ORDERED.

/s/ Brian H. Corcoran
Brian H. Corcoran
Chief Special Master

[23] At most, GBS is *more likely* to have an infectious etiology, since more is known about it generally. First Sheikh Report at 6; Lewis at 2. But Dr. Vartanian affirmatively maintained that CIDP could *also* be initiated by infection, even if that was less commonly demonstrated (something that in part could be attributed to the difficulties in identifying the initiating cause of a chronic, often-insidious condition like CIDP, where diagnosis may only occur a long time after symptoms have existed and progressed).

[24] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment if (jointly or separately) they file notices renouncing their right to seek review.