In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 16-808V
Filed: October 20, 2020
PUBLISHED

DOLORES SOLTERO ARIAS, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	Special Master Horner Causation in fact; Guillain Barre Syndrome (GBS); Influenza (Flu) Vaccination; Factor Unrelated; Cytomegalovirus (CMV) infection

Kelly Danielle Burdette, Burdette Law, PLLC, North Bend, WA, for petitioner.
Mallori Browne Openchowski, U.S. Department of Justice, Washington, D.C., for respondent.

RULING ON ENTITLEMENT[1]

On July 7, 2016, petitioner, Dolores Soltero Arias, filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10-34 (2012),[2] alleging that she suffered acute inflammatory demyelinating polyneuropathy ("AIDP") or Guillain Barre Syndrome ("GBS") as a result of her November 16, 2015 influenza vaccination.[3] For the reasons set forth below, I conclude that petitioner is entitled to an award of compensation for this injury.

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

[2] All references to "§ 300aa" below refer to the relevant section of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

[3] For purposes of this decision, the terms AIDP and GBS will be used interchangeably.

I. Applicable Statutory Scheme

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

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

In this case, petitioner alleges that she suffered Guillain Barre Syndrome or "GBS" following her influenza vaccination. Currently, GBS is a Table Injury for the influenza vaccination if it occurs between three and 42 days after vaccination. 42 C.F.R. § 100.3(a)(XIV). However, the petition in this case, dating back to July of 2016, was filed prior to the March 21, 2017 addition of GBS to the Vaccine Injury Table. *See* National Vaccine Injury Compensation Program: Revisions to the Vaccine Injury Table, Final Rule, 82 Fed. Reg. 6294, Jan. 19, 2017; National Vaccine Injury Compensation Program: Revisions to the Vaccine Injury Table, Delay of Effective Date, 82 Fed. Reg. 11321, Feb. 22, 2017 (delaying the effective date of the final rule until March 21, 2017). Accordingly, petitioner must bear the burden of demonstrating causation-in-fact without the benefit of a presumption of causation. § 300aa-14(c)(4) (explaining that modifications to the Vaccine Injury Table "apply only with respect to petitions for compensation under the Program which are filed after the effective date of such regulation").

The showing of "causation-in-fact" must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); *see also Althen*, 418 F.3d at 1279; *Hines*, 940 F.2d at 1525. Under that

standard, the petitioner must show that it is "more probable than not" that the vaccination was the cause of the injury. *Althen*, 418 F.3d at 1279. The petitioner need not show that the vaccination was the sole cause but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition, and was a "but for" cause. *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). Thus, the petitioner must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury[,]" with the logical sequence being supported by "reputable medical or scientific explanation, *i.e*., evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F.3d at 1278; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner may not receive a Vaccine Program award based solely on his or her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1).

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

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

Althen, 418 F.3d at 1278 (citations omitted). The *Althen* court noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279-80. The court also indicated that, in finding causation, a Program fact-finder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Id*. at 1280.

Generally, respondent bears the burden of demonstrating the presence of any alternative cause by preponderant evidence only if petitioner satisfies her *prima facie* burden. § 300aa-13(a)(1)(B); *Walther v. Sec'y of Health & Human Servs*., 485 F.3d 1146, 1150 (Fed. Cir. 2007). Respondent may also present evidence relating to an alternative cause to demonstrate the inadequacy of petitioner's evidence supporting her case in chief, but petitioner does not bear the burden of eliminating alternative causes where the other evidence on causation is sufficient to establish a *prima facie* case under *Althen*. *de Bazan v. Sec'y of Health & Human Servs*., 539 F.3d 1347, 1352-53 (Fed. Cir. 2008); *Walther*, 485 F.3d at 1150.

II. Procedural History

Based on the allegations in the petition, this case was initially assigned to the Special Processing Unit ("SPU") for potential discussions regarding settlement or proffer. (ECF No. 5.) Soon thereafter petitioner filed medical records marked as Exhibits 1 through 3 and a statement of completion. (ECF Nos. 7-14.) Additional records were later filed as Exhibits 4 through 6. (ECF Nos. 16, 21.)

Respondent confirmed in September of 2016 that he was not amenable to pursing settlement discussions in this case (ECF No. 18) and later filed his Rule 4(c) report on February 17, 2017 (ECF No. 24). In his report, respondent argued that petitioner's medical records do not provide preponderant evidence in satisfaction of petitioner's *prima facie* burden of proof because the records document a cytomegalovirus ("CMV") infection, which is an established prodrome for GBS. (ECF No. 24, p. 10.) Accompanying respondent's report, he filed an expert report by immunologist Kenneth Fife, M.D. (ECF No. 25; Exhibit A.)

Based on these filings, the case was removed from the SPU and reassigned to Special Master Millman. (ECF No. 27.) Special Master Millman held a status conference in which she explained the parties' respective burdens of proof regarding the significance of petitioner's CMV infection and urged the parties to settle the case. Respondent again declined to pursue settlement discussions and petitioner was instructed to file an expert report responding to Dr. Fife. (ECF Nos. 30, 33.)

Subsequently, petitioner filed additional medical records marked as Exhibit 7 (ECF No. 31) and an expert report by neurologist Mary Reif, M.D. (ECF No. 36 (Ex. 8).)[4] Thereafter, the parties exchanged several expert reports by Drs. Fife and Reif. (ECF No. 40 (Ex. C); ECF No. 41 (Ex. 33); ECF No. 43 (Ex. D).) In August of 2018, petitioner filed, but then moved to strike a third report by Dr. Reif due to incorrect exhibit designations. (ECF Nos. 44-46.) That report was not immediately refiled.

The case was reassigned to me on June 7, 2019. (ECF No. 49.) On January 14, 2020, I issued a Scheduling Order in which I indicated that based upon my review of the docket, respondent had not been prompted to revisit his position regarding settlement since petitioner had filed her expert reports. (ECF No. 51.) I briefly addressed the substance of the case and noted that the issues in the case appeared to be both narrow and well addressed by the expert reports. (*Id*. at 3.) I advised that if the parties did not wish to resolve this case informally, I may resolve the case on the written record. (*Id*.)

[4] Confusingly, petitioner filed her expert report at ECF No. 36 without any exhibit designation and marked the accompanying attachments (a curriculum vitae and medical literature) as Exhibits A through X. However, petitioner had previously been using Arabic numeral designations and respondent alphabetic designations. Accordingly, Special Master Millman issued an order redesignating petitioner's filings as Exhibits 8 through 32 respectively. (ECF No. 37.) Accordingly, references in this decision to Exhibit 8 refer to petitioner's expert report filed as the main document at ECF No. 36. References to Exhibits 9-32 refer respectively to the attached documents as ECF No. 36-1, et seq, which appear incorrectly on the docket as Exhibits A-X.

On June 18, 2020, respondent confirmed that he still was not amenable to settlement discussions. (ECF No. 56.)

On June 24, 2020, I advised the parties that I intend to resolve this case based on the written record pursuant to Vaccine Rule 8(d). (ECF No. 57.) I provided the parties 60 days to file simultaneous briefs supporting their respective positions and a further 30 days to file rebuttal briefs, if any. However, petitioner subsequently was permitted to refile her previously struck expert report, which was then filed on August 13, 2020 and the parties' briefing deadline was extended.[5] (ECF Nos. 58, 59 (Ex. 35).)

The parties filed their initial briefs on September 18, 2020. They were then allowed until October 19, 2020, to file rebuttal briefs, but no rebuttal briefs were filed. Based on review of the parties' briefs, as well as the record as a whole, I have concluded that the record is fully developed and that the parties have had a full and fair opportunity to present their respective cases. *Kreizenbeck v. Sec'y of Health & Human Servs.*, 945 F.3d 1362, 1366 (Fed. Cir. 2020); *see also* Vaccine Rule 8(d); Vaccine Rule 3(b)(2). Accordingly, this case is now ripe for a ruling resolving entitlement.

III. Factual History

a. Prior to Petitioner's November 16, 2015 Flu Vaccination

Petitioner received the flu vaccination at issue in this case on November 16, 2015. (Ex. 4, p. 1.) Before November of 2014, petitioner was a relatively healthy forty-nine-year-old woman except for a history of hyperlipidemia, obesity, and an abnormal cervical cytology. (Ex. 2, p. 1.) Petitioner received the flu shot every year since 2007 except for 2009 without any adverse effects. (Ex. 1, p. 1.)

On September 3, 2014, petitioner complained about arthritis in her hands and was recommended fish oil and ibuprofen as needed. (Ex. 2, pp. 9-13.) During this visit, the physician noted that petitioner suffered from occasional right upper arm pain and pain in the right second finger, left fifth finger, and occasionally in the distal phalanx. (*Id.* at 11.) However, petitioner's pain was not severe enough to require any medication. (*Id*.)

On November 24, 2014, petitioner was seen for mild-to-moderate right shoulder pain that was described as intermittent but worsening. (*Id.* at 26.) Petitioner noted that this pain was not preceded by any injury and was aggravated by lifting. (*Id.*) Petitioner's physical examination showed tenderness of her right shoulder in the upper humerus in the lateral aspect.[6] (*Id*. at 28.) Petitioner's examination also showed that she was not suffering from any pain at the clavicle or scapula, but that she had a

[5] In completing this filing, petitioner incorrectly duplicated the previously used designation of Exhibit 33. In an order issued September 23, 2020, I redesignated this report as Exhibit 35. (ECF No. 63.)

[6] Although the physical exam compares the "left shoulder" to the "left arm," it is suspected that this was a mistake and that the physician incorrectly listed the results of petitioner's right arm exam under the comments of the "left arm" exam. (*See* Ex. 2, p. 28.)

decreased active range of motion. (*Id.*) Petitioner received a flu vaccination following her physical examination during this visit and was diagnosed with bursitis of the right shoulder. (*Id.* at 26, 29.) Petitioner was prescribed nabumetone b.i.d. and pendulum exercises. Petitioner did not seek additional consultation for her bursitis. (*Id.*)

Petitioner was next seen by her physician on April 14, 2015 for a cough lasting three weeks. (*Id.* at 30.) Petitioner was taking black cohosh and omega fatty acid at this time and was recommended guaifenesin for her cough. (*Id.* at 31.)

On July 22, 2015, petitioner was seen for complaints about new right shoulder pain that arose without injury and had lasted for around two months. (Ex. 2, p. 33.) Petitioner was told to use ice or heat, over the counter painkillers, and physical therapy to manage her pain. (*Id.)* Petitioner also complained of a burning sensation on the inside and outside of her lips, as well as swelling and dryness of her lips. Petitioner's physician believed that petitioner's lip condition was caused by her new toothpaste. (*Id.)*

Although there is no record of the clinical visit for petitioner's November 2015 flu vaccination, a patient chart summary printed on June 23, 2017 indicates that she received a flu vaccine on November 16, 2015 around 11 a.m. (Ex. 4, p. 1; Ex. 7, p. 2.)

b. After Petitioner's November 16, 2015 Flu Vaccination

Petitioner reported to the emergency room on November 29, 2015, about two weeks after she received the vaccination at issue in this case. (Ex. 3, p. 52.) She was seen for generalized body aches, numbness all over, and a subjective fever that had lasted four days. (*Id.*) Petitioner denied focal weakness, headache, coughing, sore throat, and had not measured her temperature. (*Id.*) Petitioner was found to have 1+ occult blood in her urine and negative leukocyte esterase. (*Id.* at 54.) Her absolute lymphocyte count was elevated while her white blood cell count was normal. (*Id.*) Petitioner's liver function was tested; her SGOT/AST was 402, elevated over the normal maximum of 40. (*Id.* at 55.) Her SGP/ALT was 381, also elevated over the normal maximum of 60. (*Id.*) Nursing triage noted a headache and diminished appetite. (*Id.* at 57.) Petitioner was treated with Toradol and IV fluids and anti-nausea medications. (*Id.* at 56.) Petitioner was discharged with plans to follow up with her primary care provider regarding the results of a hepatitis panel. (*Id.*) Petitioner tested negative for hepatitis A, B, and C. (*Id.* at 66.) Petitioner was diagnosed with aches and elevated liver enzymes, however there was an additional notation in this record that listed "viral syndrome" as the diagnosis. (*Id.* at 80.)

On November 30, 2015, one day after she visited the emergency room, petitioner reported to her primary care physician, Dr. Laurel, at Healthpoint Clinic. (Ex. 2, p. 38.) Petitioner reported five days of sweats and chills, numbness of the upper and lower extremities, headache, nausea, weakness, lack of appetite, posterior headache, and mouth numbness. (*Id.* at 38, 40.) Dr. Laurel suspected that petitioner's symptoms were

"probably [a] sign" of GBS, meningitis, or other acute illness. (*Id.* at 38.) Dr. Laurel referred Petitioner to the ER. (*Id.*)

Following her visit to Dr. Laurel, petitioner reported to Auburn Medical Center emergency department on November 30, 2015 for ataxia, nausea, and headache. (*Id.* at 77.) She described to the attending physician a one-week course of night sweats, fever, headache, and body aches. (*Id.*) Petitioner denied cough or runny nose, had a normal head CT scan, and normal cerebral spinal fluid levels of 29 mg/dl. (Ex. 2, pp. 80, 85.) Petitioner received a neurological consult from Dr. Ashish Trivedi on November 30, 2015 while she was at the emergency room. (Ex. 3, p. 268.) Dr. Trivedi's exam noted absent ankle jerks and that abdominal reflexes were difficult to obtain. Petitioner's toes were pointing down, her reflexes were -1 in the upper extremities and 2+ at the knees. (*Id.* at 270.) Dr. Trivedi noted complaints of saddle distribution, paresthesia in the feet and hands, and generalized weakness. (*Id.* at 269.) Dr. Trivedi suggested a potential sensory level on the trunk at T6, and some diminished vibration in the distal one third of the feet. (*Id.*) Subsequent to her neurology consult, petitioner was deemed appropriate for admission with weakness and suspected GBS. (Ex. 2, pp. 81-82.)

Petitioner was then admitted. (Ex. 3, pp. 83, 85-86.) The attending physician was concerned that that petitioner was suffering from acute inflammatory demyelinating polyradiculopathy ("AIDP"), ordered a neurology consult, and prescribed five days of gammaglobulin. (*Id*. at 96.) Dr. Lisa M. Soehren assessed petitioner with "saddle anesthesia, paresthesia of the upper and lower extremities, elevated liver enzymes, fever, and headache." (Ex. 2, p. 85.) Petitioner's fever was attributed to a "possible viral illness in the last week," and petitioner was suspected of having GBS or "other ascending neurological disorder, myopathy, or autoimmune process." (*Id.* at 85-86.) On December 1, 2015, petitioner's bloodwork revealed elevated liver function. (*Id*. at 87.) At this time, Petitioner tested negative for Epstein-Barr virus, but tested positive for cytomegalovirus ("CMV") at a level of 1100 IU/ml. (Ex. 3, p. 686-87.)

By December 3, 2015, petitioner was suffering additional cranial nerve problems including right lower facial droop, bilateral lid lag, and worsening weakness of her left upper extremities. (Ex. 2, p. 92.) Petitioner could barely open her mouth and was having hypertensive crisis with a blood pressure of 220/120. (*Id*.) Tachycardia and hyponatremia were also noted. (*Id*. at 88.) Petitioner's initial exam included MRIs of her brain and spine, performed on December 2, 2015, both of which were normal. (*Id*. at 91.) Petitioner was seen by Dr. Trivedi again on this date. (Ex. 3, p. 360.) Dr. Trivedi noted that petitioner was areflexic at the knees and that she could not get her head off of the bed, but that she had a normal shoulder shrug. (*Id.*) Dr. Trivedi started petitioner on IVIG. (*Id.* at 361.) IVIG was administered from December 3, 2015 to December 7, 2015. (*See id.* at 361, 467.) On December 4, 2015, petitioner required intubation. (*Id*. at 272.) She remained intubated until December 10, 2015. (*Id.* at 259.)

Petitioner was examined by Dr. Soehren on December 4, 2015. Her examination was negative for Epstein-Barr PCR, rheumatoid factor, SSA/SSB, HIV, and

antimitochondrial antibodies. (Ex. 2, p. 94.) Dr. Soehren noted that petitioner's CMV positivity "possibly indicating cause for GBS variant." (*Id.*) Petitioner was not tested for other potential causes of GBS/AIDP including Campylobacter Jejuni, mycoplasma pneumonia, Haemophilus influenzae, Zika, hepatitis E, and HSV.

Petitioner also underwent an electrodiagnostic test performed by Dr. Trivedi on December 4, 2015. (Ex. 3, p. 189.) This test showed slowing on motor nerve conductions into 15 to 30 meters per second (M/s) compared to the normal range of 40 to 60 M/s. (*Id.*) Dr. Trivedi performed an EMG on a limited number of petitioner's muscles, showing no active denervation at that time, but noted that petitioner's results were consistent with demyelinating polyneuropathy and diagnosed petitioner with "presumed post viral, AIDP." (*Id.* at 189, 379.) Petitioner's vital signs subsequently dropped, mainly worsening respiratory reserve, and she was moved to the intensive care unit ("ICU"). (Ex. 2, p. 100-01.) At the time she was moved to the ICU, petitioner was complaining of band-like sensation around lower chest/abdomen, increased numbness of her lower extremities, and significant right-side mouth droop. (*Id.* at 100.) On December 5, 2015, day three of five of IVIG treatment, Dr. Triveldi assessed petitioner with AIDP and noted that petitioner was able to move all four extremities and had gained somewhat better strength. (Ex. 3, p. 398.)

On December 6, 2015, Dr. Rizwana Khan noted that petitioner was being treated with ceftriaxone, metronidazole, fentanyl, propofol, ranitidine, DOS, Senna, enoxaparin, and immune globulin. (Ex. 3, p. 392.) Dr. Khan noted that petitioner had an acute respiratory failure and that the weakness in petitioner's upper extremities seem stable although still areflexic. (*Id*. at 396.) Labs performed on December 8, 2015 showed normal white blood cell count, slightly reduced platelet count of 136,000, and a slightly elevated absolute lymphocyte percentage which returned to normal by December 13, 2015. (Ex. 2, p. 123.) Petitioner was discharged from the ICU on December 12, 2015, but remained in acute hospital care until December 23, 2015. (*Id.* at 109; Ex. 3, p. 246.)

Petitioner's primary diagnosis throughout her hospitalization was AIDP. (Ex. 2, pp. 108, 120, 126.) Petitioner's physicians consistently noted her elevated liver function and blood pressure. (*Id.* at 109.) Resident physician, Sowmya Paturi, DO assessed petitioner on December 15, 2015. (*Id.* at 143.) Dr. Paturi noted that petitioner was on day fifteen of her hospitalization for AIDP and that the etiology was CMV versus influenza vaccination. (*Id.*) Cecelia Dinh, DO noted on December 17, 2015 that she suspected that petitioner's "AIDP is possibly due to [her] recent flu vaccine or CMV as evident in blood studies on 12/1/15." (*Id.* at 153.) Dr. Dinh explained that she was reporting petitioner's case to the CDC so that she could "hopefully . . . be compensated for her medical care." (*Id.*; Ex. 3, p. 472-74.) Petitioner's physician filed a report with the Vaccine Adverse Event Reporting System ("VAERS") on December 20, 2015.[7] (Ex. 5; Ex. 2, p. 179.)

[7] The VAERS form filed by petitioner as Exhibit 5 is actually a photograph of a computer screen displaying a website confirmation of the VAERS submission. It is too blurry to discern the details of the report. However, Dr. Dinh separately recorded in petitioner's medical records a confirmation that the VAERS submission was completed online. (Ex. 2, p. 179.) According to Dr. Dinh's note, it was reported

By December 22, 2015, petitioner's attending physician noted that she was "stable for transfer to in-patient rehab." (Ex. 2, p. 191.) Petitioner was subsequently transferred to Good Samaritan Hospital for rehabilitation on December 23, 2015. (*Id.* at 217; Ex. 3, p. 246.) Petitioner's elevated liver enzymes gradually decreased upon sequential testing until normalizing in mid-January 2016. (Ex. 3, p. 2766.) On January 5, 2016, petitioner's physical therapist noted that she was able to drive an electric wheelchair, but that she would not require the chair at discharge. (*Id*. at 2678.) Petitioner was also using a left ankle foot orthosis during her rehab. (*Id.*) Petitioner's physical therapist indicated that she might benefit from bilateral ankle-foot orthoses. At this point, petitioner was able to walk 70 feet with a front-wheeled walker, and a moderate assist for hip alignment and balance. (*Id.*) Petitioner was discharged from the Good Samaritan rehabilitation unit on January 26, 2016. (*Id.* at 3986.) At the time she was discharged, petitioner was able to walk with a front-wheeled walker and had near-independence in many daily life activities including cooking, light cleaning, showering, and using the bathroom. (*Id.* at 3990.)

Petitioner began outpatient physical therapy with a consultation on February 18, 2016. (Ex. 6, pp. 2, 12.) Her diagnosis was GBS. (*Id*. at 12.) Petitioner complained of left upper extremity weakness, left shoulder pain, weakness in her hands, difficulties performing household chores, difficulties squatting, and that she became easily fatigued. (*Id*.) She had 2/5 manual muscles testing strength in ankle plantarflexion, 3/5 with hip abduction and extension, 4/5 ankle dorsiflexors, and 4-/5 bilateral knee flexion. (*Id.* at 42.) On that same day petitioner's left-hand grip strength was 15 to 19 pounds and 25 to 28 pounds on the right. (*Id.* at 43.) Petitioner continued her occupational therapy until at least March 1, 2016 where petitioner's physical therapist noted that most mild exercises targeting petitioner's rotator cuff caused her a great deal of pain. The physical therapist recommended evaluation by an orthopedic surgeon.

On February 29, 2016, petitioner reported continued "tingling and burning" to her primary care physician, Dr. Laurel. (Ex. 2, p. 43.) Dr. Laurel's primary diagnosis was GBS following vaccination, adhesive capsulitis of the left shoulder, and peripheral neuropathy due to inflammation which she characterized as "secondary to GBS." (*Id.*) Dr. Laurel noted that petitioner was no longer using assistive devices despite continued, but improved, tingling and numbness in her hands and feet. (*Id.*) Petitioner's gait was observed to be "slow, but steady" during this visit. (*Id.* at 47.)

Petitioner sought treatment from Dr. Laurel for her continuing left shoulder pain on March 2, 2016. (*Id.* at 49.) Dr. Laurel believed that petitioner's left frozen shoulder pain was due to the fact that her left side was most affected by her GBS. (*Id.*) Dr. Laurel observed no significant improvement in petitioner's shoulder on March 14, 2016, and referred her back for additional outpatient physical therapy. (*Id.* at 53.)

Petitioner's left shoulder pain was evaluated on March 25, 2016. (Ex. 3, p. 4365.) Dr. Patrick Nguyen noted "dramatic improvement in terms of [petitioner's GBS]

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that petitioner received a flu vaccine on November 16, 2015, and experienced "[f]atigue, weakness, and fever" that started November 25, 2015. (*Id*.)

where she is able to walk on her own and needs no assistive device." (*Id.* at 4366.) At this time, petitioner was only taking vitamins, sleep medicine, and nortriptyline for nerve pain. (*Id.*) Dr. Nguyen believed that petitioner's shoulder pain was not due to musculoskeletal injury, but was most likely due to the fact that she was "still recovering from [GBS]." (*Id.* at 4366-67).

On May 10, 2016, petitioner returned to Dr. Nguyen for a follow up exam on her shoulder. (*Id.* at 4378.) Petitioner reported that she still experienced occasional eye and mouth symptoms and limitation in the range of motion of her left shoulder. (*Id.* at 4378.) Dr. Nguyen recommended that petitioner continue her exercises and did not recommend taking a flu shot. (Ex. 3, p. 4379-80.) Petitioner averred as of the time she filed her petition that she continued to suffer from the ill effects of GBS. (Ex. 1, ¶ 6.) Subsequent records show that peripheral neuropathy secondary to GBS remained on petitioner's active problems list as of June 2017 and that she continued to take nortriptyline at that time. (Ex. 7.)

IV. Expert Opinions

In this case, respondent presented the first expert opinion along with his Rule 4 report. Respondent filed a report by Dr. Kenneth H. Fife, M.D. Ph.D to support his contention that petitioner's GBS was likely caused by a CMV infection and not her November 16, 2015 flu vaccination. Dr. Fife is board certified in internal medicine and board eligible in infectious diseases.[8] (Ex. A, p. 1.) In response, petitioner presented an opinion by neurologist Dr. Mary Reif to support the claim that her GBS was caused by her November 16, 2015 flu vaccination.[9] (Ex. 8.)

a. Dr. Fife's Initial Report

Dr. Fife notes that when petitioner was initially hospitalized for her AIDP, she presented with elevated liver enzymes, a finding he suggests is not usually associated with AIDP. (Ex. A, p. 3.) Based on her elevated liver function, petitioner was tested and found positive for CMV. (*Id.*) Dr. Fife points out that CMV infections often involve the liver and that half of GBS patients associated with CMV present with elevated liver enzymes. (*Id.*) Dr. Fife concludes, based on these facts, that petitioner's elevated liver enzymes strongly suggest an ongoing CMV infection. (*Id.*) Dr. Fife explains that after petitioner's positive PCR assay for CMV, her attending physicians began to note a potential link between her GBS and November 16th flu vaccination relative to the

[8] Dr. Fife is currently Professor of Medicine in the Division of Infectious Diseases and holds appointments in the Departments of Microbiology & Immunology and Pathology at the Indiana University School of Medicine. (Ex. A, p. 1.) Dr. Fife is a fellow of the American College of Physicians and a Fellow of the Infectious Diseases Society of America. (*Id.*) His bibliography includes 144 peer-reviewed publications, 8 of which relate to vaccine development and testing. (*Id.*)

[9] Dr. Reif received her medical degree in 1978 from the University of Iowa. (Ex. 9, p. 1.) She is licensed by the National Board of Medical Examiners and the State of Washington. (*Id.*) She has researched neurological conditions, with an emphasis on multiple sclerosis, since 1995. (*Id.* at 2.) Currently, Dr. Reif serves as a neurologist for Swedish Medical Group in Seattle. (*Id.* at 1.)

potential for compensation. (*Id.*) Dr. Fife does not suggest any impropriety based on these notes but concludes that "there is certainly no medical justification for narrowing the petitioner's diagnostic possibilities down to a single entity." (*Id.*)

Dr. Fife concludes that petitioner's GBS was most likely caused by her CMV infection and not by the flu vaccine. (*Id.*) According to Dr. Fife, GBS has been linked to influenza vaccines, however, "the vast majority" of those cases were linked to the A/New Jersey vaccination administered in the United States from 1976-77. (Ex. A, p. 3.) Dr. Fife states that since that time, GBS cases following flu vaccines are rare and may be purely coincidental. (*Id.*) Dr. Fife contrasts these statistics with the fact that CMV is associated with 10-15% of GBS cases. (*Id.*) Based on the potentially coincidental nature of vaccine-induced GBS, and the rate of CMV-associated GBS cases, Dr. Fife concludes that it is over 100 times more likely that petitioner's GBS was the result of a CMV infection than an adverse reaction to the flu vaccine. (*Id.*)

b. Dr. Reif's Initial Report

Dr. Reif notes that petitioner's GBS began on approximately November 25, 2015, about ten days after her flu vaccination. (Ex. 8, p. 6.) According to Dr. Reif, a "stimulus," either infectious or immune stimulating, is found prior to onset in two-thirds of GBS cases. (*Id.*) Dr. Reif indicates that although the antecedent stimulus is self-limiting in GBS cases, it creates a "cascade of immune events" which cannot be stopped once started that ultimately lead to GBS. (*Id.* (citing Emily J. Woo, Scott K. Winiecki, & Alan C. Ou, *Motor Palsies of Cranial Nerves (Excluding VII) After Vaccination. Reports to US Vaccine Adverse Event Reporting System*, 10 HUMAN VACCINES AND IMMUNOTHERAPEUTICS 301-05 (2014) (Ex. 20).).) This cascade phenomenon is believed to be caused by molecular mimicry and other unknown immunological factors, including the host's genetic markers. (Ex. 8, p. 6.) Additionally, Dr. Reif explains that petitioner's onset of weakness was 1-2 weeks post immunization, consistent with the standard onset following an antecedent event in all cases of GBS regardless of etiology. (*Id.*)

Dr. Reif explains that CMV is nearly as ubiquitous as Herpes Type 1, meaning there is a high likelihood that Petitioner had contracted the virus at some point prior to her vaccination. (*Id.*) CMV is a virus that remains dormant once the host is infected. (*Id.* at 7.) Dr. Reif notes that because an IgG antibody test for CMV was never performed, it is impossible to determine precisely whether petitioner's CMV was a chronic or primary infection. (*Id.*) Dr. Reif notes that while petitioner was positive for CMV, she never presented with a sore throat, the most common presentation of a primary CMV infection and was not caring for grandchildren nor any other infants which Dr. Reif explains is the "main vector" in primary CMV infections in late adulthood. (*Id.* (citing Awad Al-Omani et al., *Cytomegalovirus Infection in Immunocompetent Critically Ill Adults: Literature Review*, 6 ANNALS OF INTENSIVE CARE 110 (2016) (Ex. 15.)).) Dr. Reif believes that petitioner's positive CMV assay was the result of a reactivation of a chronic infection and not a primary infection. (*Id.*) In support of that position, Dr. Reif cites a study finding that 36% of ICU patients have reactivated CMV infections due to extreme physiologic stress. (Ex. 8, p. 7; Al-Omani et al., *supra*, at Ex. 15.) Dr. Reif

notes that although petitioner was CMV positive prior to being admitted to the ICU, she had been extremely ill and was therefore under levels of stress comparable to the ICU patients in the study. (*Id.*)

Although CMV infection can be accompanied by disturbed liver function, Dr. Reif explains that GBS can also be accompanied by disturbed liver function when no etiologic agent is defined. (*Id.*) Dr. Reif cites a study finding 38 out of 100 GBS patients had abnormal liver function tests, but only 10 out of that 100 were CMV positive. (*Id.* (citing Peter G. Oomes et al., *Liver Function Disturbances in Guillain-Barre Syndrome: A Prospective Longitudinal Study in 100 Patients*, 46 NEUROLOGY 96 (1996) (Ex. 16.)).)

Finally, Dr. Reif also proposes that the presence of CMV will improve the immune response to influenza. This means that petitioner's reactivated CMV could add to her increased immune response to the flu vaccine and increase the likelihood of a cascading immune response leading to GBS. She explained that numerous viral reactivations and neurological conditions can occur after flu vaccinations including HSV-1, HSV-2, Herpes Zoster, transverse myelitis, and cranial nerve palsies. (*Id.*) She also proposes that even seasonal flu shots can generate not only the seasonal antibodies that they are intended to generate, but also polyclonal varied neutralizing antibodies that can cross react with prior vaccinations such as H1N1 or H5N1, which can be more pathological for the molecular mimicry associated with GBS. (Ex. 8, p. 8 (citing Davide Corti et al., *Heterosubtypic Neutralizing Antibodies are Produced by Individuals Immunized with a Seasonal Influenza Vaccine*, 120 J. OF CLINICAL INVESTIGATION 1663 (2010) (EX. 14.)).) Based on these findings, Dr. Reif concludes that it is possible for the flu vaccine to reactivate CMV. (Ex. 8, p. 8.)

c. Dr. Fife's First Supplemental Report

In his second report, Dr. Fife notes that while it took at least ten days from admission for ICU patients with reactivating CMV to reach a viral load of 1000 in the ICU study cited by Dr. Reif, petitioner reached that viral load in a matter of days after being admitted to the ICU. (Ex. C, pp. 1-2.) Dr. Fife suggests that petitioner's rapid viral load increase is more indicative of a primary CMV infection. (*Id.* at 2.) He further indicates that "[i]t is not possible to determine when the petitioner was first infected with CMV, so it remains plausible that she had a primary CMV infection at the time of the neurological illness. In addition, although most studies that associate CMV with AIDP/GBS focus on primary CMV infection, it is not known whether reactivated CMV infection can trigger AIDP/GBS. Many of the studies of CMV and AIDP/GBS were done before the advent of sensitive molecular techniques that can detect CMV reactivation." (*Id*.at 1.) Dr. Fife also asserts that while elevated liver function can occur without a primary CMV infection, the alternative explanations offered by petitioner are less likely than a primary CMV infection to have caused her elevated liver enzymes. (*Id.*) Although some cases have linked the flu vaccine to reactivation of herpesviruses, these studies fail to establish a causal relationship. (*Id.*)

d. Dr. Reif's First Supplemental Report

In her second report, Dr. Reif notes that there is no data available to support the idea that reactivated CMV can cause GBS. (Ex. 34, p. 1.) Further, Dr. Reif states that if it were true that reactivated CMV caused GBS, there would be a noticeable trend in the ICU and neurological communities. Because there has been no such trend, Dr. Reif is confident concluding that reactivated CMV cannot trigger GBS. (*Id*.)

Dr. Reif disagrees with Dr. Fife's suggestion that petitioner's CMV titer levels were too high too quickly in comparison to the subjects of the ICU study cited in her prior report. (Ex. 34, p. 1.) In the ICU study, viral loads of reactivated CMV in ICU patients took at least ten days to exceed 1000 titers. (Al-Omani et al., *supra*, at Ex. 15.) Dr. Reif stresses, however, that the study did not correlate titer levels with severity of illness. (*Id*.) Dr. Reif further explains that petitioner's viral load was ultimately within the boundaries of typical reactivation cases regardless of the rate at which she developed that viral load. (*Id*. at 1-2.) Dr. Reif concludes that the rapid increase in petitioner's viral load does not eliminate the possibility that petitioner's CMV was the result of reactivation. (*Id*. at 2.)

e. Dr. Fife's Final Supplemental Report

Dr. Fife's final supplemental report agrees that petitioner was at high risk of contracting CMV early in her life, but notes that there is still a small chance that this was her first CMV infection. (Ex. D, p. 1.) Dr. Fife cites several reports which found that reactivated CMV caused GBS in organ transplant patients to counter Dr. Reif's argument that there is no evidence that reactivated CMV can cause GBS. (*Id.*) Dr. Fife restates his argument regarding petitioner's CMV viral load, stating that "the fact that the petitioner had levels above 1000 on her second hospital day suggests that the CMV [reactivation] . . . occurred before hospitalization and the acute neurological illness, again consistent with CMV as a cause of the neurologic illness." (*Id.* at 1-2.)

Dr. Fife notes that while Dr. Reif has provided a variety of explanations beside CMV for petitioner's elevated liver function, elevated liver function is nonetheless strongly associated with CMV. (*Id.* at 2.) Dr. Fife explains that petitioner's liver enzyme elevation was 8.3 times the upper limit of normal which is common with CMV infection but much less common in AIDP. (*Id.*) Based on these facts, Dr. Fife concludes that CMV remains the most likely cause of petitioner's elevated liver function. (*Id.* at 2.)

Dr. Fife concludes his report stating that "it is plausible that the petitioner had a CMV reactivation rather than a primary CMV infection at the time of her hospitalization." But because reactivated CMV has been shown to cause AIDP, he opines that CMV infection remains "the most probable cause" of petitioner's GBS. (*Id*. at 2.)

f. Dr. Reif's Final Supplemental Report

Dr. Reif's final report addresses Dr. Fife's later assertion that CMV reactivation can trigger GBS. Dr. Reif notes that the first study he cited focuses on organ transplant patients who are clearly immunodeficient, a cohort that petitioner is not in. (Ex. 35, p. 1.) The second study focuses on organ transplant patients and HIV positive patients, who are also clearly immunocompromised. Dr. Reif concludes that because there is no evidence that petitioner was immunocompromised, neither of these studies are relevant to petitioner's case. (*Id.*)

V. Analysis of Petitioner's *Prima Facie* Showing Under *Althen*

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

a. *Althen* Prong One

Petitioner's burden under the first *Althen* prong is to provide, by preponderant evidence, "a medical theory causally connecting the vaccination and the injury." *Id*. at 1278. Such a theory must only be "legally probable, not medically or scientifically certain." *Knudsen v. Sec'y of Human & Health Servs.*, 35 F.3d 543, 549 (Fed. Cir. 1994). Here I find that petitioner has presented preponderant evidence pursuant to *Althen* prong one that the influenza vaccine can cause GBS.

Dr. Reif persuasively opined that the influenza vaccine can cause GBS.[10] (Ex. 8, pp. 7-8.) This is based on several factors. First, Dr. Reif explains that it is generally accepted that GBS constitutes a post-infectious or post-inflammatory autoimmune reaction affecting the peripheral nerves. It is also generally accepted that this autoimmune process likely results from molecular mimicry. (*Id*. at 6.) Moreover, studies have confirmed that certain formulations of the influenza vaccination, most notably the 1975-76 swine flu and 2009 H1N1 vaccines, have been clearly associated with increased incidents of GBS. Additionally, although the strongest evidence has related to pandemic formulations, seasonal influenza vaccinations have also been shown to

[10] Notably, Dr. Reif's opinion is also consistent with prior Program cases. Even before inclusion of GBS on the Vaccine Injury Table, prior decisions had concluded that the association between influenza vaccination and GBS satisfies *Althen* prong one's "can cause" requirement. *See, e.g., Stitt v. Sec'y of Health & Human Servs.,* No. 09–653V, 2013 WL 3356791 (Fed. Cl. Spec. Mstr. May 31, 2013); *Stewart v. Sec'y of Health & Human Servs.*, No. 06–777V, 2011 WL 3241585, at *16 (Fed. Cl. Spec. Mstr. July 8, 2011); *see also Barone v. Sec'y of Health & Human Servs.,* No. 11–707V, 2014 WL 6834557 (Fed. Cl. Spec. Mstr. Nov. 12, 2014).

demonstrate some increase in incidences of GBS. (*See e.g.*, L.H. Martin Arias et al., *Guillain-Barre Syndrome and Influenza Vaccines: A Meta-Analysis*, 33 VACCINE 3773 (2015) (Ex. 12); Woo, Winiecki & Ou., *supra*, at EX. 20.)

Much of Dr. Fife's opinion stresses that there is a stronger association between CMV infection and GBS than between influenza vaccination and GBS. (Ex. A). This does not refute petitioner's demonstration of a medical theory connecting the influenza vaccine to GBS under *Althen* prong one. Since GBS is generally accepted to be associated with multiple different antecedent events, the fact that an unrelated trigger potentially explains a greater number of cases does not in itself necessarily diminish the evidence favoring a connection between GBS and vaccination. *Accord Knudsen*, 35 F.3d at 550 (observing in a different context that "[t]he bare statistical fact that there are more reported cases of viral encephalopathies than there are reported cases of DTP encephalopathies is not evidence that in a particular case an encephalopathy following a DTP vaccination was in fact caused by a viral infection present in the child and not caused by the DTP vaccine.").

b. *Althen* Prong Two

The second *Althen* prong requires proof of a logical sequence of cause and effect usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). However, medical records and/or statements of a treating physician 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. *See* 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 & Human 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").

In this case, petitioner's correct diagnosis is undisputed. Petitioner's treating physicians and both experts all agree that petitioner suffered GBS. With regard to the cause of that condition, however, onset of petitioner's GBS occurred approximately ten days after her flu vaccination, but also in the course of an apparent viral illness. During her hospitalization she later tested positive for the CMV virus on PCR assay. (Ex. 3, p. 686.) Petitioner's treating physicians were unwilling to rule out *either* her influenza vaccination *or* a CMV infection as the cause of her GBS. Although petitioner's physicians initially suspected a post-viral etiology, they also later completed a VAERS report (Ex. 5) and included a diagnosis of vaccine-caused GBS in her assessment (Ex. 2, p. 153).[11] Ultimately, when petitioner was released to rehabilitation her diagnosis

[11] Dr. Fife stresses notations in petitioner's medical records indicating that her treating physicians were aware that petitioner may be entitled to compensation if her injury was caused by her vaccination. (Ex. A, p. 3.) Although he is careful to note he is not suggesting impropriety, he nonetheless intimates that the notations linking petitioner's GBS to her influenza vaccine may not have been motivated purely by medical judgment. (*Id.*) Respondent also implicitly argues that the earlier impression of a post-viral etiology should be more persuasive because "[t]here was no subsequent testing or medical explanation

was AIDP "possibly due to recent flu vaccine or CMV as evidenced in blood studies." (Ex. 2, p. 187.)

For her part, Dr. Reif similarly explained that the onset and course of petitioner's GBS is "very standard" and consistent with an antecedent event occurring one to two weeks prior, regardless of whether that event was viral, bacterial, or otherwise immune stimulated (i.e. by vaccination). (Ex. 8, p. 6.) Dr. Reif indicated that petitioner's lab results are inadequate to "forensically" determine the cause of her GBS. (*Id*. at 6.) She did, however, indicate that petitioner's presentation with a viral illness lacked any indication of a sore throat, which she characterized as a hallmark of an active CMV infection. (*Id*. at 7.) In contrast, Dr. Fife suggested that petitioner's own clinical course, with severe sensory deficits, respiratory involvement, and prolonged recovery period, is consistent with the same subgroup of GBS that is typically associated with CMV. (Ex. C, p. 3.) This was also considered by the treating neurologist. (Ex. 2, p. 95.)

While Dr. Fife's observation regarding petitioner's clinical presentation potentially provides some evidence supportive of CMV as a possible cause of petitioner's injury, it does not establish CMV as a *more likely* cause. Although Dr. Fife suggests that CMV-caused GBS has a tendency toward a certain clinical presentation, he has not asserted, let alone substantiated, that this presentation represents any contrast to the expected presentation for a vaccine-caused GBS.[12] In that regard, the same literature Dr. Fife cites for the concept of a CMV-infection subtype cautions that "none of the associations is perfect." (Frans Van Der Meche et al., *Diagnostic and Classification Criteria for the Guillain-Barre Syndrome*, 45 EUR. NEUROLOGY 133 (2001) (Ex. C, Tab 7, p. 2).) That article includes a Venn diagram showing that the subtypes of GBS overlap. (*Id.* at Fig. 1.) And, despite having specifically considered whether petitioner's clinical picture best

for the changes in her diagnosis after petitioner's discharge from the hospital." (ECF No. 62, p. 15 (citing petitioner's primary care record at Ex. 2, p. 43).) Upon my own review, I do not believe that the medical records support this skepticism of the treating physicians for several reasons. First, Dr. Fife's suspicion is prompted in part by his own apparent confidence in CMV as the more likely cause of petitioner's GBS, but this is not a confidence shared by petitioner's treating physicians. The records stress that petitioner's physicians felt her GBS was only "presumed" to be post-viral or that a post-viral etiology was "possibly" indicated and never expressed full confidence in CMV infection as the cause of her GBS. (Ex. 3, p. 379; Ex. 2, p. 153.) Additionally, and to respondent's related point, the records are clear that post-vaccination GBS was part of petitioner's assessment *during* her hospitalization and not merely after the fact. Second, the specific notations at issue are explicit in expressing that an adverse vaccine event report would be submitted only in good faith. Specifically, Dr. Dinh recorded that "[s]uspect that pt's AIDP is possibly due to recent flu vaccine or CMV as evident in blood studies on 12/1/15*. If this is the case*, will report pt's case to CDC and pt may be able to be compensated for her medical management." (Ex. 3, p. 474 (emphasis added).) Third, petitioner's hospital discharge records show that her physicians maintained CMV as a possible cause of petitioner's GBS even after discussing that an adverse vaccine event may be reported. (Ex. 2, p. 187.) For these reasons, I see no basis for suggesting that petitioner's potential for compensation influenced her physicians' clinical impressions, changed their diagnostic assessments, or that their consideration of vaccine causation otherwise constituted an unexplained afterthought.

[12] For example, the Qualifications and Aids to Interpretation for the Vaccine Injury Table identifies GBS as a spectrum of four subtypes any one of which may be entitled to a causal presumption as a Table Injury. *See* 42 C.F.R. § 100.3(c)(15).

fit post-CMV GBS, the treating physicians still remained unwilling to rule out petitioner's vaccination as the cause. (Ex. 2, p. 153.) "[T]reating 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.'" *Capizzano*, 440 F.3d at 1326 (quoting *Althen*, 418 F.3d at 1280).) In any event, Dr. Fife also agreed that there is no "definitive proof" regarding the etiology of petitioner's GBS. (Ex. A, p. 3.) Further, in discussing the evolution of petitioner's diagnosis and certain notations that leaned more heavily in favor of petitioner's vaccination as the cause of her GBS, Dr. Fife stressed that "[t]here is certainly no medical justification for narrowing the petitioner's diagnostic possibilities down to a single entity."[13] (*Id.*)

Without more, this would suggest that petitioner has met her initial burden, as she has presented both treating physician and expert opinion directly linking her vaccination to her injury as one of two medically reasonable causes that cannot be distinguished. Because petitioner's clinical history presents a logical sequence of cause and effect consistent with vaccine causation, she need not eliminate CMV infection as an alternative cause. *Walther*, 485 F.3d at 1151 (stating that "the petitioner generally has the burden on causation, but where there are multiple independent potential causes, the government has the burden to prove that the covered vaccine did not cause the harm."). Even if the viral illness and flu vaccine operated in conjunction to cause petitioner's GBS, petitioner would still be able to meet her burden of proof.[14] *Shyface*, 165 F.3d at 1353 (explaining that although the Shyfaces did not prove that the DPT vaccine was the only or predominant cause of his death, the requirements of the Vaccine Act are met *prima facie* upon proof of the substantial factor criterion.). However, in addition to discussing her clinical presentation as a whole, Dr. Fife did also raise two discrete points regarding petitioner's own clinical presentation which he felt evidenced CMV as the more likely cause of petitioner's GBS in preference to vaccination. These issues warrant further discussion; nevertheless, Dr. Reif's opinion supporting vaccine causation satisfactorily accounts for both points.

First, Dr. Fife stressed the fact of the positive CMV finding itself. He noted that "a serum PCR assay for cytomegalovirus (CMV) (a test that detects the presence of viral genetic material in the blood) was sent and it was positive, documenting the presence of virus in the bloodstream." (Ex. A, p. 3.) Dr. Reif persuasively explained, however, that CMV infection is prevalent among the adult population, especially among Hispanic women, and that once infected a person retains the virus in latency throughout life. (Ex. 8, pp. 6-7.) Although petitioner's PCR assay showed that she had the virus circulating

[13] To be clear, Dr. Fife's statement was intended to convey in response to notations regarding vaccination as a possible cause that CMV infection could not reasonably be ruled out as a cause of the GBS. Nonetheless, this statement is also operates as an explicit ratification of the treating physicians' inclusion of both the CMV and flu vaccine as potential causes.

[14] Dr. Reif suggested not only that petitioner's influenza vaccination could have reactivated her latent CMV infection, but also that her CMV positivity could have been an enhancing factor that contributed to her risk of developing GBS as a response to her influenza vaccination. (Ex. 8, p. 8.) For all the reasons discussed herein I did not find it necessary to reach that question.

in her bloodstream, physiological stress from illness or trauma has been shown to reactivate the virus. (*Id*.) For example, Dr. Reif cited a study showing positive PCR assays among ICU patients. (*Id*. at 7.) Accordingly, Dr. Reif opined that petitioner's positive PCR assay is more likely a further consequence of her post-vaccination condition than a separate cause of her GBS.[15] (*Id*. at 8.)

Although he continued to maintain that reactivated CMV could still be a cause of petitioner's GBS (discussed separately in Section VI below), Dr. Fife ultimately agreed that petitioner's PCR assay was more likely to be explained by reactivation and that there is only a "small chance" that she was experiencing a primary CMV infection at the time of her PCR assay. (Ex. D, p. 1.) Dr. Fife did not dispute Dr. Reif's opinion that the physiological stress of acute illness can cause viral reactivation, but he did question the timing in this case. (Ex. C, pp. 1-2.) He indicated that based on the study cited by Dr. Reif, it takes at least ten days of acute illness for patients to develop a CMV load comparable to what was measured in petitioner. (*Id*.) However, the evidence does not support Dr. Fife's suggestion of any identifiable threshold interval for the presence of a significant viral load. Petitioner's PCR assay was collected on December 1, two weeks following her influenza vaccination and about one week following onset of both her possible viral illness and GBS. (Ex. 3, p. 686.) This remains consistent with Dr. Reif's opinion that reactivation followed vaccination and illness.[16]

[15] Notably, if petitioner's positive finding for CMV was only a downstream consequence of her post-vaccination condition, that leaves the etiology of her presumed viral syndrome unclear. That would refute several points raised by Dr. Fife but would not preclude the presumed viral illness from being a possible cause of petitioner's GBS even if it were not CMV. Significant to that point, as noted above, Dr. Reif opined that petitioner's presentation is consistent with a prior antecedent event whether bacterial, viral, or otherwise immune. (Ex. 8, p. 6.) This would still be consistent with the idea that petitioner suffered GBS the etiology of which cannot be distinguished as between vaccination and unspecified viral illness, which, as explained above, is consistent with petitioner's burden of proof.

[16] Specifically, Dr. Fife derives the ten-day period from a chart he highlighted from a review article. (Ex. C, p. 2 (Ajit P. Limaye & Michael Boeckh, *Cytomegalovirus (CMV) in Critically-Ill Patients: Pathogen or Bystander?*, 20 REV. MED. Virol 372 (2010) (Ex. C, Tab 2).) This chart is based on a single study not otherwise a part of the record and speaks only to the probability that a CMV load will be detected in a patient and does not purport to create a threshold of what is physiologically possible. Moreover, Dr. Reif contends that the study findings do not correlate titer levels to severity of illness, making it impossible for Dr. Fife to suggest that high titer levels necessarily indicate a primary infection. (Ex. 34, pp. 1-2.) The review paper itself otherwise notes that time to detectable levels of CMV can be as little as three days. (Limaye and Boeckh, *supra*, at Ex. C, Tab 2, p. 3 (Table 4).) However, separate figures are not provided for the higher loads Dr. Fife referenced. (*Id*.) In any event, the authors of the review paper caution that prior studies have suffered significant limitations, including small population size and variations in findings based on the sensitivity of the method of detection. (Limaye and Boeckh, *supra*, at Ex. C, Tab 2, p. 2.) A separate review paper, which examined the same study among others, suggested that CMV disease occurs at any time "within the first 2 weeks of critical illness" and further explained that PCR detection is the most sensitive diagnostic test for CMV. (Al-Omani et al., *supra*, at Ex. 15, p. 10.) Dr. Fife's point is well taken to the extent that these studies tend to show that it generally appears likely that it takes longer to reach a higher viral load, but these studies are inadequate to assert that any specific timeframe is necessary to reach such viral loads.

Second, Dr. Fife indicated that "CMV infection often involves the liver, and over half of patients with Guillian-Barre syndrome (or AIDP) associated with CMV infection present with elevated liver enzymes. The fact that the patient presented with elevated liver enzymes and continued to have liver enzyme elevations until Jan 13 in the absence of any other apparent cause strongly suggests that she had ongoing CMV infection." (*Id*.) In that regard, Dr. Reif explained that while liver dysfunction can be associated with CMV infection, it is also present among GBS patients even in the absence of any known cause. (Ex. 8, p. 7.) Dr. Reif cited a study of 100 GBS patients. (*Id*. (citing Peter G. Oomes et al., *Liver Function Disturbances in Guillain-Barre Syndrome: A Prospective Longitudinal Study in 100 Patients*, 46 NEUROLOGY 96 (1996) (Ex. 16.)).) Thirty-eight subjects had evidence of liver dysfunction while only 10 of those subjects were positive for CMV infection. The remaining 28 were negative for other known causes of liver damage. (Oomes et al., *supra*, at Ex. 16, p. 1.) The study also found that treatment with IVIG "significantly increased" liver function disturbances. (*Id*. at 6.) The authors concluded "that in GBS some [liver function disturbances] may be transiently present without obvious cause and that treatment with [IVIG] may increase these abnormalities."[17] (*Id*.)

Dr. Fife responded by noting that petitioner's own enzyme elevations were 8.3 times the upper limit for normal whereas most of the study subjects had enzyme findings of no more than four times the upper limit. (Ex. C, p. 2.) While Dr. Fife is correct that this would place petitioner with a minority of the test subjects, he also acknowledged that eight study subjects had enzyme findings in excess of four times the normal limit and only half of those subjects in this higher category were CMV-infected. (*Id*.) Accordingly, Dr. Fife confirms that petitioner's degree of elevation still potentially fits the study's findings even in the absence of CMV-caused GBS.

Nonetheless, Dr. Fife contends that the fact that half of the relevant subset of study subjects had CMV infection represents a "strong association." (Ex. D, p. 2.) This is unpersuasive in the context of the study. It is not disputed that CMV infection can be associated with liver function disturbances. Yet this study demonstrates that, regardless of how often liver dysfunction follows CMV infection, CMV infection does not conversely explain liver function disturbances among a majority share of GBS patients who exhibit such disturbance, even including some with significantly elevated enzymes. Dr. Fife also noted that one possible explanation for the study findings was under-reporting of CMV infections. (Ex. D, p. 2.) However, the authors also posited a direct immune-mediated explanation for the liver dysfunction and ultimately concluded that the

[17] Among the group of patients receiving IVIG, the study saw a significant increase in the number of patients experiencing liver function disturbances, from 35% at admission to 69% after IVIG treatment. The increase in incidences of liver function disturbances dropped significantly by four weeks post treatment, but did not fall to below the rate seen among the control group until fourteen weeks post-treatment. (Oomes et al., *supra*, at Ex. 16, p. 3.) Overall, liver function disturbances peaked at either two weeks post-admission or one-week post-IVIG. (Id. at 6.) In this case, petitioner was found to have elevated liver enzymes upon admission which decreased during the course of her hospitalization. (Ex. 2, p. 88.) They had returned to normal range by January 13, 2016, approximately six weeks after her initial hospitalization. (Ex. 3, p. 2766.) Potentially consistent with this study, an autoimmune process affecting the liver was suspected. (Ex. 2, p. 88.)

liver dysfunction is present "without obvious causes." (Oomes et al., *supra*, at Ex. 16, p. 6.)

When examined in detail, the expert presentations in this case underscore why petitioner's treating physicians were unable to definitively identify her GBS as either CMV-caused or vaccine-caused. Ultimately, Dr. Fife was correct to suggest that "[t]here is certainly no medical justification for narrowing the petitioner's diagnostic possibilities down to a single entity." (Ex. A, p. 3.) Although Dr. Fife highlights some points potentially supportive of CMV as a cause of petitioner's GBS, for the reasons discussed above, none of these points are able to outweigh Dr. Reif's competing opinion that petitioner's clinical course was nonetheless also consistent with vaccine-causation.

In light of all of the above, I find that petitioner has presented preponderant evidence of a logical sequence of cause and effect, based on her own clinical history, demonstrating that her influenza vaccination did cause or substantially contribute to her GBS. Accordingly, she has satisfied her burden of proof under *Althen* prong two.

c. *Althen* Prong Three

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* Here, the timing in this case is not controversial and I find that there is preponderant evidence of a proximate temporal relationship between petitioner's influenza vaccination and her GBS. Dr. Reif explained that the onset of petitioner's GBS, which occurred between one to two weeks following her vaccination, is consistent with current understanding of GBS onset following an antecedent event.[18] (Ex. 8, pp. 6, 8.) Although Dr. Fife preferred CMV as the cause of petitioner's GBS based on petitioner's clinical picture, he did not raise any question as to a medically acceptable temporal relationship in this case between the vaccination and onset of petitioner's GBS. (*See* Exs. A, C, and D generally.)

VI. Analysis of Respondent's Presentation of Factors Unrelated to Vaccination

Based on the analysis above, petitioner has presented a *prima facie* case that her GBS was, in fact, caused by her influenza vaccination by demonstrating each of the three *Althen* prongs by preponderant evidence. Once petitioner has satisfied her own

[18] This is also consistent with prior cases which have generally identified a relevant medically reasonable period of onset for GBS. *Daily v. Sec'y of Health & Human Servs.*, No. 07-173V, 2011 WL 2174535, at *9 (Fed. Cl. Spec. Mstr. May 11, 2011) (accepting two weeks as an appropriate latency for post-vaccination GBS); *Barone v. Sec'y of Health & Human Servs.*, No. 11-707V, 2014 WL 6834557, at *13 (Fed. Cl. Spec. Mstr. Nov. 12, 2014) (accepting a latency for GBS of up to six to seven weeks post-vaccination); *Accord Aguayo v. Sec'y of Health & Human Servs.*, No. 12-563V, 2013 WL 441013, at *3 (Fed. Cl. Spec. Mstr. Jan. 15, 2013) (rejecting a latency of three- and one-half months for GBS); *Corder v. Sec'y of Health &Human Servs.*, No. 08-228V, 2011 WL 2469736, at *27-29 (Fed. Cl. Spec. Mstr. May 31, 2011) (rejecting a four-month onset for GBS).

burden pursuant to the *Althen* test, the burden shifts to respondent to demonstrate that her injury was caused by factors unrelated to vaccination. § 300aa-13(a)(1)(B); *Deribeaux v. Sec'y of Health & Human Servs.*, 717 F.3d 1363, 1367 (Fed. Cir. 2013).

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

In this case, respondent cannot meet this burden based on his contention that petitioner's CMV infection caused her GBS. As explained above, petitioner's physicians were unwilling to conclude that petitioner's GBS was CMV-caused rather than vaccine-caused. (Ex. 2, p. 187.) In fact, Dr. Fife likewise explicitly opined that "[t]here is certainly no medical justification for narrowing the petitioner's diagnostic possibilities down to a single entity." (Ex. A, p. 3.) Nonetheless, he initially opined that "[a]lthough there is no definitive proof, the probability is over a hundred times higher that the petitioner's neurologic condition was a result of the CMV infection than the influenza immunization." (*Id*.) Significantly though, Dr. Fife subsequently acknowledged that it is not possible to know when petitioner was first infected with CMV and further that there is only a small chance that this was her first CMV infection. (Ex. C, p. 1; Ex. D, p. 1.) He agreed that it was more likely a reactivation of a latent infection. (Ex. D, p. 1.) He also conceded, at least initially, that it is unknown whether reactivated CMV infection can trigger GBS. (Ex. C, p. 1.)

Subsequently, however, Dr. Fife did suggest that reactivated CMV can cause GBS, citing for example a paper describing five case reports of CMV-positive transplant patients who developed AIDP. (Ex. D, p. 1.) He contended that this is evidence that CMV reactivation, and not only primary infection, can be associated with GBS. Significantly though, case reports are not strong evidence. Moreover, Dr. Reif reasonably questioned whether the context of organ transplant recipients was sufficiently analogous to petitioner (otherwise previously healthy and not known to be immune compromised) to be illuminating. (Ex. 35, p. 1.) Indeed, Dr. Reif's skepticism is supported by another paper cited by Dr. Fife, Steininger et al. That paper cautioned that organ transplant patients may be uniquely or unusually susceptible to CMV viremia. (Christoph Steininger et al., *Primary Cytomegalovirus Infection in Patients with Guillain-Barre Syndrome*, 183 J. OF NEUROIMMUNOLOGY 214 (2007) (Ex. A, Tab 4, p. 2).) The paper studied 46 GBS patients and found that almost 25% of those patients were

suffering a primary CMV infection, while 59% had detectable levels of CMV-DNA attributable to either primary infections, reactivation, or reinfection. Although the study confirms an association between CMV and GBS, it focuses principally on primary infection and does not definitively conclude that reactivated CMV infections are significantly associated with GBS. Instead, Steininger et al, cast doubt on whether the mechanism by which CMV is believed to cause GBS can be said to apply equally to cases of CMV reactivation. Specifically, the authors explained that "[m]olecular mimicry, which was proposed to be a relevant mechanism in the pathogenesis of GBS, and cross-reactivity of CMV-specific antibodies with neuronal structures would be expected to be more likely in primary CMV infection than in the course of virus reactivation because of the lower antibody-specificity and -affinity early after infection."[19] (Steininger et al., *supra*, at Ex. A, Tab 4, p. 2.)

Accordingly, Dr. Fife's repeated assertion that CMV is a far more likely cause is not persuasive given the evidence of record in this case. These assertions rely on the much stronger evidence regarding primary CMV infection, but Dr. Fife ultimately acknowledged that this is not likely what petitioner experienced in this case. Moreover, Dr. Fife has acknowledged that there is no medical justification for narrowing the cause of petitioner's GBS to a single entity and, for all the reasons discussed above, petitioner has presented a *prima facie* case, inclusive of both expert and treating physician opinions, otherwise supporting influenza vaccination as a cause of her injury. Thus, although CMV remains one *possible* factor explaining petitioner's injury, respondent has not met his burden of providing preponderant evidence that CMV infection was the sole cause of petitioner's injury to the exclusion of her vaccination.

VII. Conclusion

For all the reasons discussed above, I find that petitioner is entitled to compensation for her vaccine caused GBS. Specifically, I find that petitioner has established by preponderant evidence that her GBS was caused-in-fact by her November 16, 2015 influenza vaccination and further that respondent has not presented preponderant evidence that her injury was due to factors unrelated to her vaccination. A separate damages order will be issued.

IT IS SO ORDERED.

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

[19] Notably, Dr. Reif has also suggested that vaccination itself can cause reactivation of latent viral infection, suggesting petitioner would again point back to the influenza vaccine as at least one substantial contributing factor among others in causing petitioner's GBS, even if reactivation of the CMV infection was the immediately preceding cause. (Ex. 8, p. 8.) However, for all the reasons discussed herein, I do not reach that question.