In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: September 14, 2021

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JUDY ECHOLS,	*	
	*	No. 17-838V
Petitioner,	*	
v.	*	Special Master Gowen
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Influenza (Flu); Neuralgic Amyotrophy; Brachial Neuritis; Parsonage-Turner syndrome; Onset; Pre-Existing Bursitis; Causation-in-Fact; Alternative Complement Pathway; Innate Immune Response.
Respondent.	*	
* * * * * * * * * * * * *	*	

Laura Levenberg, Muller Brazil LLP, Dresher, PA, for petitioner.
Mollie D. Gorney, United States Department of Justice, Washington, D.C., for respondent.

RULING ON ENTITLEMENT[1]

On June 21, 2017, Judy Echols ("petitioner") filed a petition in the National Vaccine Injury Compensation Program.[2] Petition (ECF No. 1). Petitioner alleged that as a result of an influenza ("flu") vaccine received on November 12, 2015, she developed neuralgic amyotrophy.[3] *Id.* at

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[1] Pursuant to the E-Government Act of 2002, *see* 44 U.S.C. § 3501 note (2012), because this opinion contains a reasoned explanation for the action in this case, I am required to post it on the website of the United States Court of Federal Claims. The court's website is at http://www.uscfc.uscourts.gov/aggregator/sources/7. **This means the opinion will be available to anyone with access to the Internet.** Before the decision is posted on the court's website, each party has 14 days to file a motion requesting 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). "An objecting party must provide the court with a proposed redacted version of the decision." *Id.* **If neither party files a motion for redaction within 14 days, the decision will be posted on the court's website without any changes.** *Id.*

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 to 34 (2012) (hereinafter "Vaccine Act" or "the Act"). Hereinafter, individual section references will be to 42 U.S.C. § 300aa of the Act.

[3] Petitioner identified her injury as "brachial plexopathy." *See* Petition at Preamble. The Vaccine Injury Table creates a presumption of causation for "brachial neuritis" if onset occurs within 2 – 28 days after receipt of a vaccine containing tetanus toxoid (but no such similar presumption for seasonal flu vaccine, as implicated in this case. *See* 82 Fed. Reg. 6294 (Jan. 19, 2017); 42 C.F.R. §§ 100.3(a), (c)(6). These terms as well as Parsonage-Turner syndrome ("PTS") and neuralgic amyotrophy ("NA") are all used to describe the same set of symptoms. *See, e.g.*, *Davis v. Sec'y of Health & Human Servs.*, No. 16-276V, 2021 WL 3910609, at n.3 (Fed. Cl. Spec. Mstr. July 23, 2021). However, the most recent medical literature filed in this case indicates that neuralgic amyotrophy is "the most common term in the literature and also neutral with respect to the extent and localization of nerve involvement." Van Alfen (2016)

Preamble, ¶ 17. For the reasons discussed herein, I hereby find that petitioner has carried her burden to establish causation-in-fact and therefore, she is entitled to compensation.[4]

I. Procedural History

Petitioner timely filed her claim on June 21, 2017, *see* Petition (ECF No. 1), followed by supporting documentation, Petitioner's Exhibits ("Pet. Exs.") 1 – 12. The claim was originally assigned to the Chief Special Master's Special Processing Unit ("SPU"), which is designed to expedite the processing of claims that have historically been resolved without extensive litigation. SPU Initial Order filed June 22, 2017 (ECF No 7). An initial status conference was held on August 3, 2017. Scheduling Order (ECF No. 9).

On January 31, 2018, respondent filed his report pursuant to Vaccine Rule 4(c), in which respondent recommended that compensation be denied. Respondent's Report (Resp. Rep't) (ECF No. 15). Respondent first contended that the medical records contained conflicting notations as to the onset of petitioner's injury occurring either before or at differing times after the vaccination. *Id.* at 10, n. 2 (internal citations omitted). Respondent also noted that petitioner had the burden of establishing causation-in-fact. Resp. Rep't at 10. Respondent contended that to date, petitioner's medical records alone fell short of establishing causation-in-fact and that she had not yet provided a supportive expert report or literature. *Id.* at 10-11.

After reviewing respondent's report, the Chief Special Master determined that the claim was no longer appropriate for the SPU and reassigned it to my docket. *See* Order Reassigning Case filed February 6, 2018 (ECF No. 16).

My chambers scheduled a status conference. Shortly before the scheduled time, petitioner filed two additional affidavits. Pet. Exs. 12-13. During the status conference, respondent's counsel requested additional time to review the affidavits and confirm his position as to further proceedings. *See* Scheduling Order filed March 8, 2018 (ECF No. 22). Respondent subsequently confirmed that a fact hearing would be useful for resolving onset of petitioner's symptoms. Resp. Status Report filed March 9, 2018 (ECF No. 23).

A fact hearing was held in Birmingham, Alabama, on September 13, 2018. The witnesses were petitioner and her additional fact witness Yvonne Meads. *See* Transcript filed September 28, 2018 (ECF No. 32). At the conclusion of the hearing, I read my findings of fact into the record. I ordered that any experts retained in the case shall incorporate my findings of fact before addressing vaccine causation including my specific questions. Tr. 118-27.

[Pet. Ex. 15.4] (full citation provided *infra* at n. 25) at 1. This opinion refers most consistently to neuralgic amyotrophy.

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

Petitioner then filed the first report of neurologist Daniel DiCapua, M.D.[5] Pet. Ex. 15 filed February 15, 2019 (ECF No. 38). Respondent filed a responsive report from neurologist Brian Callaghan, M.D.[6] Resp. Ex. A filed June 21, 2019 (ECF No. 40). Respondent also filed two reports from immunologist S. Mark Tompkins, Ph.D.[7] Resp. Exs. C, D filed June 21, 2019 (ECF Nos. 41, 44).

[5] Dr. DiCapua graduated from the University of Connecticut with a Bachelor of Science degree in 2000. Pet. Ex. 15-1 at 1. He graduated from Temple University School of Medicine with a medical degree in 2005. *Id.* In 2005, he joined Yale University and New Haven Hospital in New Haven, Connecticut. *Id.* After a one-year internship in primary care, he has built an academic and clinical specialty in neurology and a subspecialty in neuromuscular disorders. *Id.* He is currently an assistant professor in neurology, the neurology clerkship director, and the neuromuscular medicine fellowship director at the Yale University School of Medicine. *Id.* He is board-certified in psychiatry and neurology with a subspecialty in neuromuscular medicine (but unlike Dr. Callaghan, is not separately board-certified in electrodiagnostic medicine). *Id.* Dr. DiCapua is also engaged in clinical research and has published articles but does not currently serve as a reviewer for any peer-reviewed journals. *Id.* at 2-9. In discussing his own qualifications, Dr. DiCapua stated that he has an active clinical practice in which he sees close to 2,000 patients per year (for over eight years) mostly related to peripheral nerve disease. Pet. Ex. 15 at 1. He has received teaching awards at Yale and more broadly, he is regularly invited to speak at interdepartmental conferences, he is the director of the weekly continuing medical education (CME) approved Neuromuscular Educational Conference series, and he has served on nationwide committees including with the American Academy of Neurology. *Id.* In consideration of his qualifications, his opinion in this case, and the lack of objection from respondent, I hereby admit Dr. DiCapua as an expert in the subjects of neurology, neuromuscular disorders, and peripheral neuropathy.

[6] Dr. Callaghan graduated from the University of Michigan with a Bachelor of Science degree in 1996. Resp. Ex. B at 1. He graduated from the University of Pennsylvania Medical Center with a medical degree in 2004. *Id.* He remained at the University of Pennsylvania Medical Center for an internship in preliminary medicine from 2004 – 2005 and a residency in neurology from 2005 – 2008. *Id.* Afterwards, Dr. Callaghan affiliated with the University of Michigan Medical School, at first to accept a fellowship in neuromuscular medicine and to enroll in a master's degree in clinical research design and statistical analysis, which he completed in 2011. *Id.* In 2009, he was hired onto the Michigan faculty, where he is currently an associate professor in neurology. *Id.* Dr. Callaghan is also a clinical neurologist and director of the ALS Clinic at the Veterans Affairs Ann Arbor Health System. *Id.* at 1-2. He is board-certified in psychiatry and neurology as well as electrodiagnostic medicine. *Id.* Dr. Callaghan stated that his primary interest is in patients with neuropathy and neuralgic amyotrophy. Resp. Ex. A at 3. While Dr. Callaghan did not state what number or proportion of his patients have these disorders, his curriculum vitae reflects that he teaches, conducts research, publishes, and serves as an editor for numerous peer-reviewed journals focusing on peripheral neuropathy. *See generally* Resp. Ex. A. Dr. Callaghan is hereby admitted as an expert in the subjects of neurology, neuromuscular disorders, and peripheral neuropathy.

[7] Dr. Tompkins graduated from the University of Illinois with a Bachelor of Science degree in 1990. Resp. Ex. D at 1. He graduated from Emory University with a Ph.D. in Immunology in 1997. *Id.* From 1997 to 2002, he held a post-doctoral research position at Northwestern University Medical School. *Id.* at 1, 3. Dr. Tompkins stated that this research focused on "immunologic mechanisms of induction of autoimmune disease, specifically interrogating antigen- and virus- induced models of experimental autoimmune encephalomyelitis [and?] models for the neurologic autoimmune disease multiple sclerosis." Resp. Ex. C at 1. From 2002 to 2005, he held a post-doctoral research position at the U.S. Food and Drug Administration (FDA) Centers for Biologics Evaluation and Research (CBER), where, Dr. Tompkins explained, his research focused on "understanding the immune response to influenza infection and vaccination." Resp. Ex. C at 1; *see also* Resp. Ex. D at 1, 3. In 2005, Dr. Tompkins affiliated with the University of Georgia College of Veterinary Medicine, where he is currently the assistant department head, curriculum coordinator, and full professor in the department of infectious diseases. Resp. Ex. D at 2. He devotes twenty percent of his time to teaching, specifically in the subjects of immunology and virology, and the remaining eighty percent to research. *Id.*; Resp. Ex. C at 1. Dr. Tompkins averred: "While aspects of my research entail zoonotic influenza viruses [those that spread from animal to human] and understanding the determinants of infection, transmission, and pathogenesis, the core of my research remains understanding the immune response to viral infection and vaccination." Resp. Ex. C at 1. His recent research has focused on novel vaccines, adjuvants, therapies, and mechanisms of vaccine- or therapeutic-associated protection and disease. *Id.*; *see also* Resp. Ex. D at 15-21. He has authored numerous articles

I then observed that Dr. Callaghan and Dr. Tompkins, in their initial reports, did not incorporate my findings of fact set forth in the transcript. They both cited to the emergency room triage notes rather than the nursing notes which I found were more persuasive as to the onset of left shoulder symptoms other than pain. I ordered that if this case proceeded on a litigation track, respondent's experts shall file supplemental reports incorporating my findings of fact. However, the parties should first explore informal resolution. Scheduling Order filed August 12, 2019 (ECF No. 46). Petitioner conveyed a demand to respondent, after which counsel advised that they had reached a tentative settlement agreement. 15-Week Stipulation Order filed September 26, 2019 (ECF No. 50). However, respondent advised that the Attorney General's authorized representative declined to grant settlement authority for the proposed tentative settlement. *See* Resp. Status Report filed October 30, 2019 (ECF No. 51); 15-Week Removal Order filed October 31, 2019 (ECF No. 52

With the case returned to a litigation track, respondent filed supplemental reports from Drs. Callaghan and Tompkins. Resp. Exs. E, F filed December 30, 2019 (ECF No. 54). During another status conference, I suggested and both parties agreed that entitlement could be resolved on the written record without need for a hearing. *See* Scheduling Order filed May 11, 2020 (ECF No. 58). Petitioner confirmed that she was alleging only causation-in-fact and not significant aggravation. Pet. Status Report filed June 9, 2020 (ECF No. 59). Petitioner then filed Dr. DiCapua's second report. Pet. Ex. 17. Respondent then filed Dr. Callaghan's third report. Resp. Ex. G.

After being granted several extensions of time, *see* ECF Nos. 62-64, petitioner filed a motion for a ruling on the record. Pet. Mot. filed November 20, 2020 (ECF No. 67).[8] Respondent filed a response. Resp. Response filed December 23, 2020 (ECF No. 69). Petitioner did not file a reply. This matter is now ripe for adjudication.

II. Legal Standard[9]

The Vaccine Act was established to compensate vaccine-related injuries and deaths. Section 10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" *Rooks v. Sec'y of Health & Human Servs.,* 35 Fed. Cl. 1, 7 (1996) (quoting H.R.

and chapters on immunology and virology. Resp. Ex. D at 27-38. He also serves as a peer reviewer or on the editorial board for numerous medical journals. *Id.* at 5. Dr. Tompkins is hereby admitted as an expert in the subject of immunology.

[8] Petitioner also filed a copy of the fact hearing transcript as her exhibit 19 on November 13, 2020 (ECF No. 65). Her motion for a ruling on the record cites to this filing. However, the transcript is already in the record. For clarity, all citations will be to the existing transcript ("Tr.").

[9] Decisions of special masters and the U.S. Court of Federal Claims (some of which are referenced in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Human 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 & Human Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd*, 104 F. App'x 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Human Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

No. 908 at 3, *reprinted in* 1986 U.S.C.C.A.N. at 6287, 6344).

A petitioner bears the burden of establishing his or her entitlement to compensation from the Vaccine Program. The burden of proof is by a preponderance of the evidence. Section 13(a)(1).

A. Findings of Fact

A special master must consider, but is not bound by, any diagnosis, conclusion, judgment, test result, report, or summary concerning the nature, causation, and aggravation of petitioner's injury or illness that is contained in a medical record. Section 13(b)(1). "Medical records, in general, warrant consideration as trustworthy evidence. The records contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium. These records are also generally contemporaneous to the medical events." *Curcuras v. Sec'y of Health & Human Servs*., 993 F.2d 1525, 1528 (Fed. Cir. 1993).

Accordingly, where medical records are clear, consistent, and complete, they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Human Servs*., No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). However, this rule does not always apply. In *Lowrie*, the special master wrote that "written records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent." *Lowrie*, at *19.

The United States Court of Federal Claims has recognized that "medical records may be incomplete or inaccurate." *Camery v. Sec'y of Health & Human Servs*., 42 Fed. Cl. 381, 391 (1998). The Court later outlined 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 & Human Servs*., 110 Fed. Cl. 184, 203-04 (2013), *aff'd*, 746 F.3d 1335 (Fed. Cir. 2014).

The Court has also said that medical records may be outweighed by testimony that is given later in time that is "consistent, clear, cogent, and compelling." *Camery*, 42 Fed. Cl. at 391 (citing *Blutstein v. Sec'y of Health & Human Servs*., No. 90-2808, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998). The credibility of the individual offering such testimony must also be determined. *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1379 (Fed. Cir. 2009); *Bradley v. Sec'y of Health & Human Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

The special master is obligated to fully consider and compare the medical records, testimony, and all other "relevant and reliable evidence contained in the record." *La Londe*, 110 Fed. Cl. at 204 (citing Section 12(d)(3); Vaccine Rule 8); *see also Burns v. Sec'y of Health & Human Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (holding that it is within the special master's discretion to determine whether to afford greater weight to medical records or to other evidence,

such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is rational).

B. Nature of Injury

Special masters are generally not tasked with diagnosing injuries. In *Lombardi*, the Federal Circuit explained: "The function of a special master is not to 'diagnose' vaccine-related injuries, but instead to determine 'based on the record evidence as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the petitioner's injury.'" *Lombardi*, 656 F.3d at 1343, *citing Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1382 (Fed. Cir. 2009).

However, the Federal Circuit has determined that in certain instances, "if there is a dispute as to the nature of a petitioner's injury, the special master may opine on the nature of the petitioner's injury." *Contreras v. Sec'y of Health & Human Servs.*, 844 F.3d 1363, 1368 (Fed. Cir. 2017), *citing Hibbard v. Sec'y of Health & Human Servs.*, 698 F.3d 1355 (Fed. Cir. 2012); *see also Locane v. Sec'y of Health & Human Servs.*, 686 F.3d 1375 (Fed. Cir. 2012); *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339 (Fed. Cir. 2010)).

C. Causation

A petitioner may prevail by proving either that (1) the vaccinee suffered an injury listed on the Vaccine Injury Table with onset beginning within a corresponding time period following receipt of a corresponding vaccine (a "Table Injury"), for which causation is presumed or that (2) the vaccinee suffered an injury that was actually caused by a vaccine. Under either method, however, the petitioner must also show that the vaccinee "suffered the residual effects or complications of the illness, disability, injury, or condition for more than six months after the administration of the vaccine." Section 11(c)(1)(D)(i).

In the present case, petitioner does not and cannot allege a Table injury. Thus, she bears the burden of establishing actual causation. To do so, she must "show by preponderant evidence that the vaccination brought about the injury by providing 1) a medical theory connecting the vaccination and 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." *Althen v. Sec'y of Health & Human Servs.,* 418 F. 3d 1274, 1278 (Fed. Cir. 2005). There must be preponderant evidence for each *Althen* prong. *Caves v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 119, 132 (2011), *aff. per curiam*, 463 Fed. Appx. 932 (Fed. Cir. 2012).

Under *Althen* prong one, the causation theory must relate to the injury alleged. Thus, a petitioner must provide a "reputable" medical or scientific explanation that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355-56. The theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen*, 35 F.3d at 548. It must only be "legally probable, not medically or scientifically certain." *Id.* at 549. However, the theory still must be based on a "sound and reliable medical or scientific explanation." *Id.* at 548. The Federal Circuit explained in *Althen* that "while [that petitioner's claim] involves the possible link between [tetanus toxoid] vaccination and central nervous system injury, *a sequence hitherto unproven in*

medicine, the purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field *bereft of complete and direct proof of how vaccines affect the human body." Althen,* 418 F.3d at 1280 (emphasis added).

Under *Althen* prong two, petitioner must prove "a logical sequence of cause and effect showing that the vaccination was the reason for [her] injury." *Althen,* 418 F.3d at 1278. This prong is sometimes referred to as the "did it cause" test; i.e. in this particular case, did the vaccine(s) cause the alleged injury. *Broekelschen,* 618 F. 3d at 1345 ("Because causation is relative to the injury, a petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case"). Temporal association alone is not evidence of causation. *See Grant v. Sec'y of Health & Human Servs.*, 9556 F.2d 1144, 1148 (Fed. Cir. 1992). This sequence of cause and effect is usually supported by facts derived from petitioner's medical records. *Althen,* 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326; *Grant*, 956 F.2d at 1148.

Althen prong three requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen* at 1281. That term has equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is medically acceptable timeframe must align with the theory of how the relevant vaccine can cause an injury (*Althen* prong one). *Id.* at 1352.

The preponderance of the evidence standard requires the petitioner to demonstrate that it is "more likely than not" that the vaccine caused the injury. *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). A petitioner must demonstrate that the vaccine was "not only [a] 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 & Human Servs.*, 135 F.3d 1344, 1352-53 (Fed. Cir. 1999); *Pafford v. Sec'y of Health and Human Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006). Causation is determined on a case-by-case basis, with "no hard and fast *per se* scientific or medical rules." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). A fact-finder may rely upon "circumstantial evidence" which is consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Althen,* 418 F. 3d at 1280.

The petitioner often presents expert testimony in support of his or her claim. *Lampe v. Sec'y of Health & Human Servs.,* 219 F.3d 1357, 1361 (Fed. Cir. 2000). Expert testimony in the Vaccine Program is usually evaluated according to the factors set forth in *Daubert v. Merrell Dow Pharm., Inc.,* 509 U.S. 579, 594-96 (1993); *see also Cedillo,* 617 F.3d at 1339 (citing *Terran v. Sec'y of Health & Human Servs.,* 195 F.3d 1302, 1316 (Fed. Cir. 1999). A special master may use the *Daubert* framework to evaluate the reliability of expert testimony, but expert testimony need not meet each *Daubert* factor to be reliable. *Boatmon v. Sec'y of Health & Human Servs.,* 941 F.3d 1351 (Fed. Cir. 2019). The *Daubert* factors are "meant to be helpful, not definitive," and all factors "'do not…necessarily apply even in every instance in which the reliability of scientific

testimony is challenged.'" *Boatmon*, 941 F. 3d at 1359 (citing *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 151, 119 S. Ct. 1167, 143 L.Ed.2d 238 (1999). Thus, for Vaccine Act claims, a "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly* at 1324. 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 & Human Servs.*, 219 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe,* 219 F.3d 1357 at 1362).

If the petitioner makes a *prima facie* case supporting vaccine causation-in-fact, the burden shifts to respondent to show by a preponderance of the evidence that the injury is instead due to factors unrelated to the administration of the vaccine. *Deribeaux v. Sec'y of Health & Human Servs.*, 717 F.3d 1363, 1367 (Fed. Cir. 2013) (citing Section 13(a)(1)(B)). Respondent has the burden of demonstrating that: "[A] factor unrelated to the vaccination is the more likely or principal cause of injury alleged. Such a showing establishes that the factor unrelated, not the vaccination, was 'principally responsible' for the injury. If the evidence or alternative cause is seen in equipoise, then the government has failed in its burden of persuasion and compensation must be awarded." *Knudsen,* 35 F.3d at 551.

III. Summary of Relevant Facts

A. Medical Records

Petitioner was born in 1945. She filed primary care and neurology records starting in 2010 and orthopedic records starting in 2012, which reflect established diagnoses of asthma, migraines, hypertension, osteopenia, osteoarthritis, and Addison's disease.[10] *See generally* Pet. Exs. 2, 3, 11.

On April 10, 2013, petitioner presented to Chandra Gehi, M.D., at Anniston Neurology Anniston, Alabama with a new complaint of bilateral hand numbness in a median nerve distribution, which was accompanied by abductor pollicis brevis muscle[11] weakness and a positive Tinel's sign[12] at the wrist and elbow. Pet. Ex. 2 at 38, 40. Dr. Gehi diagnosed petitioner with bilateral carpal tunnel syndrome.[13] *Id.* Petitioner followed with this neurology practice on a regular basis, but she did not have any worsening symptoms or new complaints pertaining to her left arm. *Id.* at 15-20, 28-39.

[10] Addison's disease is defined as: "A chronic type of adrenocortical insufficiency characterized by hypotension, weight loss, anorexia, weakness, and a bronze-like hyperpigmentation of the skin. It is due to tuberculosis- or autoimmune-induced destruction of the adrenal cortex…" *See Dorland's Medical Dictionary Online*, at https://www.dorlandsonline.com (hereinafter "*Dorland's*").

[11] The abductor pollicis brevis ("ABP") muscle abducts the thumb. It is innervated by the median nerve. *Dorland's*.

[12] Tinel's sign is "a tingling sensation in the distal end of a limb when percussion is made over the site of a divided nerve [which] indicates a partial lesion or the beginning of regeneration of the nerve." *Dorland's*.

[13] Carpal tunnel syndrome is as "an entrapment neuropathy characterized by pain and burning or tingling paresthesias in the finger or hand, sometimes extending to the elbow. Symptoms result from compression of the median nerve in the carpal tunnel." *Dorland's*.

On November 28, 2013, petitioner presented to the emergency room ("ER") at Northeast Alabama Regional Medical Center ("NEARC") with left forearm pain after a fall, which was diagnosed as a left radius fracture. Pet. Ex. 5 at 360, 363, 365.

There are no pertinent medical records for another two years, until October 28, 2015, when petitioner presented to orthopedist John R. Payne, M.D. at Anniston Orthopedic Associates. Pet. Ex. 11 at 14-16. Petitioner reported a painful left shoulder not related to any specific injury. *Id.* at 14. Dr. Payne recorded the following objective evaluation:

> Pain on abduction and forward flexion typical of impingement[14] and bursitis.[15] No particular warmth, redness, or swelling. X-rays were carried out, 3 views of the shoulder. On the internal rotation view, no pathological lesion, no fractures and no major degenerative changes. On the external rotation view, there is superior subluxation[16] of the humeral head not touching the acromion but definitely some superior subluxation. There is small degree of spurring off the humeral head.

Pet. Ex. 11 at 15. Dr. Payne diagnosed petitioner with left shoulder impingement and bursitis. *Id.* He injected Depo-Medrol 40mg into the left shoulder, as well as a separate injection of Toradol 60 mg.[17] He also prescribed Tramadol 50mg tablets for pain. *Id.* at 16.

On November 5, 2015, petitioner saw her primary care provider Dr. Hanna at the Anniston Medical Clinic for a complaint of left shoulder pain. Pet. Ex. 3 at 35-43. Dr. Hanna recorded under history of present illness that the onset was five weeks ago and sudden following no specific incident. *Id.* at 35. The pain was persistent and gradually worsening. *Id.* The pain was characterized as a sharp stabbing; it was aggravated by physical activity, any movement, sports activities, work duties, overhead activity, lifting, and throwing. *Id.* "There [was] no relief and nothing [was] working." *Id.* Dr. Hanna recorded under review of systems: "severe recurring pain in right [sic, left] shoulder. Still has good mobility. Followed by Dr. Payne and recently injected with 3 days of relief." *Id.* at 40. Under physical exam, Dr. Hanna did not record any neurological deficits such as loss of sensation or strength. *Id.* at 41. He also recorded: "Musculoskeletal global assessment: Joints – move freely. Range of motion - active and passive intact." *Id.* However, Dr.

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[14] Impingement is the "advancement of one thing out of its expected place to where it may collide with something else." *Dorland's*. Impingement syndrome is "a type of overuse injury with progressive pathologic changes resulting from mechanical impingement by the acromion, coracoacromial ligament, coracoid process, or acromioclavicular joint against the rotator cuff; changes may include reversible edema and hemorrhage, fibrosis, tendinitis, pain, bone spur formation, and tendon rupture." *Id*.

[15] A bursa is "a sac or saclike cavity filling with a viscid fluid and situated at places in the tissues at which friction would otherwise develop." *Dorland's*. Bursitis is "inflammation of a bursa usually accompanied by a calcific deposit in the underlying tendon; the most common site is the subdeltoid bursa." *Id*. The subdeltoid bursa is between the deltoid and the glenohumeral (shoulder) joint capsule. *Id*.

[16] Subluxation is defined as "an incomplete or partial dislocation." In this specific anatomical site, "slippage or subluxation of the humeral head out of the glenoid fossa" is also termed "glenohumeral instability." *Dorland's*.

[17] While it is not stated in the medical records, petitioner testified that the Toradol injection was into the south side on one of her hips, probably her right hip. Tr. 69.

Hanna did not state that these findings were in any particular extremities such as the affected left shoulder. Such findings in the left shoulder would conflict with the history of present illness that left shoulder pain was aggravated by movement, *see id.* at 35. Dr. Hanna diagnosed petitioner with bursitis, for which he planned another Toradol injection as well as Mobic 7.5mg once daily with food. *Id.* at 42.

On Thursday, November 12, 2015 at 11:33 a.m., petitioner presented to her pulmonologist Dr. Beaty at Pulmonary Associates of the Southeast, P.C. for regular follow-up of her asthma. Pet. Ex. 4 at 99-102. Dr. Beaty recorded that petitioner was having "a difficult time with multiple issues," including "pain from arthritis." *Id.* at 99. The pulmonologist recorded under the review of systems that petitioner "denie[d] tingling or numbness [or] muscular weakness." *Id.* at 101. The neurological exam was non-focal with "no muscle weakness, no sensory loss." *Id.* Dr. Beaty ordered a split inactivated high-dose flu vaccine to be administered via the intramuscular route to "RD." Pet. Ex. 1 at 1, 5. The practice submitted a claim for Q2037 and G0008, which are the administration charge claims for such a vaccine (brand name Fluvirin). Pet. Ex. 1 at 5, Pet. Ex. 4 at 98.

That same day, Thursday, November 12, 2015, at 4:11 p.m., petitioner presented to the NEARMC ER, where a nurse practitioner handled intake. Pet. Ex. 5 at 248. Petitioner reported left arm pain rated at 5/10, but her chief complaint was "left arm weakness." *Id.* at 249. The nurse practitioner made conflicting notations as to onset: she wrote "left arm weakness since 11/6/2015" but then, on the same page, that petitioner's "symptoms have been occurring for four days," which would date back to November 8, 2015. *Id.* The nurse practitioner also recorded an incorrect date for petitioner's prior encounter with Dr. Payne. *Id.*

Afterwards, a registered nurse conducted a focused assessment and recorded that petitioner's "numb arms" and "weakness" had started on "Thursday, November 12, 2015" (that same day). Pet. Ex. 5 at 266-67, 69.

A CT scan of the cervical spine visualized C5-C6 disc extrusion appearing to cause mild disc compression. Pet. Ex. 5 at 263-64.

Approximately three hours after presenting to the hospital, at 7:13 p.m., petitioner was discharged with a tentative diagnosis of cervical disc disorder and radiculopathy and instructions to follow up with her orthopedist. *Id.* At discharge, she was noted to have continuing left arm weakness. *Id.* She was not given or prescribed any pain medication. *Id.* She was also given pamphlets on how to recognize signs of a stroke. *Id.* at 294.

On Monday, November 16, 2015, petitioner returned to her orthopedist Dr. Payne, who recorded that: "[Petitioner] woke up last Thursday morning with numbness and unable to use the left arm. She went to the emergency room where they did a CT scan of the head and neck and told her that it did not appear that she had a stroke…" Pet. Ex. 11 at 9. Dr. Payne also recorded that petitioner "saw Dr. Hannah [sic] who sent her to physical therapy and physical therapy came down and asked if we could evaluate her," *id.*, but there are no records of these encounters. Dr. Payne observed on exam: "She has no biceps function at all in the left arm. She has a little bit of triceps, just a twinge of triceps. She has no ability to lift her wrist. The radial nerve is totally out. She

cannot lift her fingers. She has associated decreased sensation in her arm." *Id.* at 10. Dr. Payne added that the CT scan showing disc bulging or extrusion with mild cord compression at C5-6 "does not explain the multiple nerve roots involved on the left side." *Id.* Dr. Payne referred petitioner for a neurological consult. *Id.* at 11.

On November 19, 2015, petitioner presented to Anthony Esposito, M.D. at the Anniston Neurology practice, who recorded a seven-day history of left arm paralysis and numbness associated with neck pain. Pet. Ex. 2 at 12. The physical exam revealed diminished sensation to pain and temperature in the left hand. *Id.* at 13. Deep tendon reflexes at the biceps were 0+. *Id.* Motor function at the left biceps, wrist extension, and hand grip were 1/5. *Id.* Dr. Esposito's differential diagnosis was a left C5 or C6 radiculopathy versus plexopathy. *Id.* at 14. He planned an MRI of the cervical spine as well as nerve conduction velocity ("NCV") and electromyography ("EMG") studies. *Id.*

On November 23, 2015, petitioner underwent an MRI of the cervical spine that revealed only mild degenerative changes at the levels of C4 – C7, which tended to rule out the differential diagnosis of cervical radiculopathy. Pet. Ex. 2 at 1, 11.

On December 8, 2015, petitioner underwent the electrodiagnostic studies to evaluate for the continued numbness and weakness in her left arm and hand. Pet. Ex. 2 at 25-27. The NCV study, which was limited to the left median nerve, revealed evidence of a mild left carpal tunnel syndrome and mild cubital tunnel syndrome. *Id.* at 25, 26. The EMG study was of eight muscles in the left upper extremity with various nerve roots from C5-6 to C8-T1 (which was unremarkable on the cervical spine MRI). *Id.* at 26. The median-nerve supplied ABP muscle was normal. *Id.* The other seven muscles tested - the dorsal interosseous, flexor carpi radialis, biceps, triceps, deltoid, flexor carpi ulnaris, and brachioradialis muscles – all showed evidence of denervation specifically positive short waves, increased amplitude, increased duration, increased potential, and a reduced recruitment pattern. *Id.* Dr. Esposito recorded that the EMG revealed evidence of a "severe acute brachial plexopathy on the left affecting multiple branches but predominantly the upper cord." *Id.* at 25.

At a January 8, 2016, follow-up appointment, Dr. Esposito recorded that petitioner still had left arm paralysis and numbness associated with neck pain. Pet. Ex. 2 at 9. On physical exam, she still had diminished sensation to pain and temperature in the left hand and 0+ deep tendon reflexes at the biceps. *Id.* at 10. However, motor function in the biceps, wrist extension, and hand grip were improved at 3/5. *Id.* Dr. Esposito diagnosed "left brachial plexopathy possibly due to the flu vaccine," which was "improving, progressing as expected." *Id.* at 11.

On January 11, 2016, Dr. Hanna saw petitioner for recheck of left shoulder pain which had begun "after flu shot 2mo ago," was "gradually improving," and was currently "mild to moderate" and "a dull aching." Pet. Ex. 3 at 21. Petitioner was wearing a sling on the left arm. *Id.* The review of systems included "severe neuropathy left arm" and the physical exam findings included "left arm immobilized in sling, hand swollen." *Id.* at 26, 28; s*ee also id.* at 12-20 (further records from Dr. Hanna).

On March 17, 2016, petitioner started physical therapy ("PT") for her left arm and hand. Pet. Ex. 5 at 95. She wrote on an intake form that these symptoms started "4 months ago" following "flu shot." *Id.* at 120. A physical therapist conducted an initial evaluation, then informed Dr. Esposito that occupational therapy ("OT") would provide more tailored treatment and better address activities of daily living ("ADLs") relating to the hand. *Id.* at 116.

On May 31, 2016, Dr. Esposito recorded that petitioner was no longer experiencing pain, but she had continued left hand weakness. Pet. Ex. 2 at 2. She was unable to do simple ADLs such as making the bed and household cleaning. *Id.* On physical exam, she still had diminished sensation in the left hand and 0+ deep tendon reflexes at the biceps. *Id.* at 4. Strength at the deltoid was 4+/5, but 3+/5 in the triceps and 2/5 in the biceps. *Id.* Dr. Esposito recorded that the left brachial plexopathy was "unchanged" and he planned repeat electrodiagnostic studies to help evaluate the prognosis. *Id.* at 5.

On June 28, 2016, petitioner was discharged from OT because she was reaching her therapy cap for the year and she wanted to repeat the electrodiagnostic studies to determine future care. Pet. Ex. 5 at 168. Upon discharge, she still had burning and tingling in a left radial nerve distribution, from her elbow down to her hand and fingers. *Id.* at 166. Sensation was 1/5 in the left thumb, 2/5 in the forearm as 2/5, and 5/5 in all other areas of her LUE. *Id.* at 167. She still had problems performing household chores. *Id.* at 166. She was discharged with a radial nerve splint and a home exercise program. *Id.* at 168.

On July 19, 2016, Dr. Esposito conducted the repeat electrodiagnostic studies. Pet. Ex. 2 at 22-24. His NCV study included the left median nerve, but he did not comment on the results. *Id.* at 23. The EMG study addressed the same eight left arm muscles. *Id.* Dr. Esposito recorded that the findings supported a "severe chronic brachial plexopathy [neuritis] on the left with improvement noted especially in proximal arm muscles when compared to the prior study in 12/2015." *Id.* at 22.

B. Later Recollections

At the fact hearing in September 2018, petitioner recalled that in 2013, she was diagnosed with bilateral carpal tunnel syndrome at her neurology practice. Tr. 6. Afterwards, she began wearing wrist braces, primarily at night, which "resolved that problem." Tr. 6-8. Petitioner also recalled that on November 28, 2013, which was Thanksgiving, she was lifting a ten-pound ham out of the oven and she fell, sustaining burns and a fracture to her left forearm. Tr. 8-9. Petitioner recalled that her fracture healed within approximately six weeks and that afterwards, she returned to her normal activities including playing golf and working out on exercise machines and with weights. Tr. 10; *see also id.* at 17.

Petitioner recalled that on October 28, 2015, she presented to her orthopedist Dr. Payne with pain. She recalled that this pain began about six weeks prior. Pet. Ex. 14 at ¶ 2. She attributed this pain to overuse, as she and her husband worked out about three days per week and played golf about two days per week. Tr. 10-11. She recalled that this pain was at one single point in her left shoulder and did not extend above or below. Tr. 12. The pain did not go up towards her neck. Tr. 12. She described the degree of pain as a "pinprick." Tr. 42. Petitioner recalled that at the time

of her diagnosis with bursitis, it was somewhat painful to play golf, but she was able to complete activities of daily living such as buttoning her blouse, cooking, and driving. Tr. 13-15; *see also* Pet. Ex. 14 at ¶ 2. Petitioner recalled that Dr. Payne diagnosed this pain as bursitis and administered a steroid injection "right in the bursa," at the very top of her left arm where it goes into the shoulder. Tr. 11-13; *see also* Tr. 68-70.

Petitioner did not have any specific recollections of the November 5, 2015, appointment with her primary care provider Dr. Hanna. Tr. 72-75.

Petitioner recalled that on November 12, 2015, in the morning, she did not experience any numbness in her left arm or hand, or any pain in her left arm. She was able to get dressed and drink coffee using her left hand. Tr. 21, 85; *see also* Pet. Ex. 14 at ¶ 4.

Petitioner did not have any specific recollections of the November 12, 2015, appointment with her pulmonologist Dr. Beatty for follow-up of her asthma. She did not think that she told Dr. Beatty about her diagnosis of left shoulder bursitis. Tr. 75. She did recall that during this encounter at the pulmonology practice, a nurse administered the flu vaccine into her left arm. Tr. 76-77. Petitioner testified that she always gets vaccines in her left arm because she is right-handed. Tr. 21-22, 77. Within hours, her arm began to tingle and feel numb. Tr. 22, 78-79; *see also* Pet. Ex. 14 at ¶ 5. She became concerned that these symptoms were indicative of a stroke, particularly because her father, when he was fifty-eight (58) years old, had a stroke which brought on a massive heart attack which led to his sudden death. Tr. 22-23, 79; *see also* Pet. Ex. 14 at ¶ 5. Therefore, petitioner went to the emergency room. Tr. 23. Petitioner recalled that in the emergency room, her father and his sudden death were "first on [her] mind." Tr. 27; *see also id.* at 80. She did not recall telling someone in the emergency room that her left arm symptoms had been occurring for four days. Tr. 81.

Petitioner had difficulty providing specific recollections about the next day which was Friday, November 13, 2015. Tr. 25-27. However, she recalled that on Saturday, November 14, 2015, in the morning, she got up and her left arm was numb. Tr. 23; *see also* Pet. Ex. 14 at ¶ 6. When she touched her left arm (presumably with her other hand), it felt like touching "through a glove" or touching "a dead person." Tr. 23; *see also* Pet. Ex. 14 at ¶ 6. Petitioner recalled that she also had trouble getting dressed that morning: she had difficulty pulling up her jeans and fastening the button at her waist. Tr. at 32-33. Then, she could not fasten her button-up shirt, so her husband helped put a pull-over shirt over her left arm and then over her head. Tr. 32, 34. Then, when petitioner and her husband went out to breakfast, which was their "standing date" each Saturday morning for "years and years," she could not hold a coffee cup or anything else with her left hand. Tr. 23-24; *see also* Pet. Ex. 14 at ¶ 6. Petitioner explained that although she was right-handed, she habitually used her left hand to drink beverages. Tr. 29. This habit arose when she was a child, because her father was left-handed and she sat to his left, so she also began to drink left-handed to avoid accidents. *Id.*

Petitioner also recalled that on Sunday, November 15, 2015, she went to church, where she taught Sunday School class. She could not move her left arm or use the left hand to hold her Bible. Her supervisor brought her a chair and a podium to complete the lesson. Afterwards, petitioner

was so exhausted that she couldn't stay for worship and instead went home. Tr. 34-35; *see also* Pet. Ex. 14 at ¶ 7.

Petitioner recalled that this new condition also involved pain. While she described the pre-vaccination condition diagnosed as bursitis as a "pinprick", this new condition was like "a nail being driven in… very, very painful." Tr. 42. The new pain was worst in her forearm and extended down to her hand. Tr. 46-47; *see also* Pet. Ex. 14 at ¶ 13.

Petitioner disputed the accuracy of the Monday, November 16, 2015, medical record, which provides that she told Dr. Payne that her new symptoms began last Thursday morning upon waking up; rather, she recalled telling Dr. Payne that her new symptoms began after the flu shot, which was Thursday in the late morning. Tr. 47-48; *see also id.* at 84-85.

Petitioner recalled that during an encounter on January 5, 2016, her endocrinologist Dr. Rosenthal at Kirklin Endocrinology said that her new left arm injury was caused by the flu vaccine. Tr. 44, 96-98.[18] Petitioner recalled that later in the same week, her neurologist Dr. Esposito agreed that the vaccine was the cause. Tr. 98.[19] Petitioner recalled that an unspecified nurse told her about the Vaccine Injury Compensation Program. Tr. 99.

At the hearing, petitioner demonstrated that she could raise her right arm to an angle of 180 degrees; in contrast, she could only raise her left arm to about 90 degrees. Tr. 39-40. She could actively extend her left fingers to approximately 90 degrees, compared to almost full extension with passive manipulation with her other hand. Tr. 41. She also appeared to have significant atrophy in the left arm, particularly in the forearms, compared to the right side. Tr. 41-42. She testified that she still cannot use her left arm to button blouses, grasp objects, or cut food. Tr. 64-66. She had stopped driving for a period of time but resumed with some modifications in approximately September 2017. Tr. 87-89. She stopped teaching at her church, which she had been doing twice a week, in part because of her left arm injury and in part due to her husband's health problems. Tr. 89-91; *see also* Pet. Ex. 14 at ¶ 15. Overall, petitioner provided credible testimony that after the November 12, 2015 vaccination, she experienced a significant change in her condition which led to limitations in daily functioning that have persisted for well over six months.

Eleanor Yvonne Meads also offered fact testimony. Ms. Meads has known petitioner since they were together in fourth grade. Ms. Meads repeatedly related her memories of the events in question to when she and petitioner were planning their fiftieth (50^{th}) high school reunion, which caused them to talk on the phone frequently. *See generally* Tr. 100-16; Pet. Ex. 13 at ¶ 4. Ms. Meads recalled that they graduated from high school in late May 1963 and she got married shortly

[18] In the medical records of the January 5, 2016, encounter, Dr. Rosenthal did not record any belief that a vaccine caused petitioner's shoulder condition. Pet. Ex. 8 at 25-29. His only reference to the left upper extremity is: "She has bursitis in left shoulder and in a sling and has had some numbness in arm that is being managed." *Id.* at 25. There is no indication that he performed a physical exam involving the left arm and he did not address the left arm in the active problems list or his diagnostic impressions.

[19] In the medical records of the January 8, 2016, encounter, Dr. Esposito recorded the diagnosis as: "Left brachial [plexopathy]. Possibly due to flu vaccine." Pet. Ex. 2 at 11. However, he did not record the date of the flu vaccine or note petitioner's pre-vaccination left shoulder pain for which she treated with her orthopedist.

afterwards. She believed that the high school reunion was in either 2012 or 2013. Tr. 102-05, 116. She recalled that petitioner was very active leading up to the reunion. Tr. 106, 109, 116-17. Ms. Meads did not have particular recollections of petitioner's condition in 2015 prior to the vaccination. At that time, they still talked on the phone regularly, but they did not see each other in person often. Tr. 105, 112-13. Ms. Meads estimated that she had not seen petitioner in person for a month or two months before the vaccination. Tr. 116. Ms. Meads was not aware that petitioner had symptoms involving the left upper arm, was diagnosed with bursitis, and received a steroid injection before the vaccination. Tr. 105-06. 113. She did recall that petitioner saying on the telephone that her arm was numb and she had received a vaccination the day before. Tr. 101, 105-06, 113-14; *see also* Pet. Ex 13 at ¶ 5. Ms. Meads also recalled bringing petitioner to doctors' appointments after the vaccination. Tr. 107-08, 110-11, 114; *see also* Pet. Ex 13 at ¶¶ 6-7.

C. Findings of Fact

In general, the medical records summarized above are consistent and not disputed. However, respondent observed that the medical records contained conflicting notations which put into question whether "the onset of petitioner's NA [neuralgic amyotrophy] occurred after her receipt of the flu vaccine on November 12, 2015." Resp. Rep't at 10. The parties agreed that it would be helpful to convene a fact hearing to obtain testimony on this issue. At the conclusion of the hearing, I made relevant findings of fact, *see* Tr. 118-24, which are memorialized as follows.

Specifically, I found that before the vaccination, petitioner had pain which was specific to the left shoulder area at the point that the shoulder joined the top of her arm; the pain did not extend above to her neck or down to her arm or back to her neck. Tr. 118-19. She also did not have any numbness or tingling in her neck, shoulder, or arm. Tr. 120. While it was not expressly stated in the bench ruling, I find that this pain began on or about October 1, 2015. This is based on the first contemporaneous medical record which specifies the history of pain. Pet. Ex. 3 at 35; *see also* Pet. Ex. 14 at 1 (petitioner's affidavit).

I also found that on October 28, 2015, Dr. Payne diagnosed petitioner's left shoulder pain as bursitis. Tr. 118. Importantly, this is not a factual finding that petitioner indeed had bursitis at that time or any other time. As discussed in the analysis below, the parties' experts disputed whether shoulder pain initially diagnosed as bursitis can be – and whether it was, in petitioner's case – the first symptom of neuralgic amyotrophy, which begins with pain that later, usually fairly rapidly, gives rise to weakness and sometimes sensory loss.

It is undisputed that petitioner presented for the pulmonology appointment during which she received the flu vaccine on November 12, 2015, at 11:33 a.m. Pet. Ex. 4 at 99.

Respondent averred that the pulmonology practice's records do not include a vaccine administration record confirming that petitioner actually received the vaccine. Resp. Rep't at 3; Resp. Response at 3 and n. 1. Based on the pulmonologist's order for the vaccine, the practice's submitted bill to Medicare for the vaccine, the subsequent medical records, petitioner's credible testimony, and the lack of competing evidence, there is easily preponderant evidence that petitioner actually received the flu vaccine during this encounter.

Respondent also averred that no record indicates the site of vaccination. Resp. Rep't at 3; Resp. Response at 3. Based on the absence of a contemporaneous administration record, the subsequent medical records, and petitioner's later credible testimony including that she always gets vaccines in her left arm because she is right-handed, I find that there is preponderant evidence that petitioner received the subject vaccine in her left arm.

I found that after the vaccination, that afternoon, petitioner had "new symptoms of numbness and tingling in her left arm" which prompted her presentation to the emergency room. Tr. 119. Petitioner "went to the emergency room for these issues because she recalled that her father had a stroke at age 58 that led to his death and that she was concerned that she was having a stroke." *Id.* She presented to the emergency room at 4:11 p.m. Pet. Ex. 5 at 249.

I found that these new symptoms began after vaccination. In so finding, I noted that within the emergency room records, the nurse practitioner's notations suggesting that petitioner had the onset of left arm weakness, numbness, and tingling before the vaccination contradicted with another provider's record which provides that onset was on the date of vaccination, November 12, 2015. Tr. 120-21 (referring to Pet. Ex. 5 at 249, 266).

I also noted that on November 16, 2015, petitioner returned to Dr. Payne who recorded that petitioner first experienced numbness and an inability to use her left arm *upon waking up on the morning* of November 12, 2015. Based on a complete review of the record, it is more likely than not that either petitioner or Dr. Payne were mistaken in identifying the onset of numbness and inability to use her left arm as occurring before vaccination. Tr. 121-22 (referring to Pet. Ex. 11 at 9). Several other medical records reflect that petitioner's onset of left arm weakness, numbness, and tingling was *after* the vaccination on November 12, 2015. *See, e.g.*, Pet. Ex. 2 at 12; *id.* at 11; Pet. Ex. 3 at 21; *id.* at 95. In addition, petitioner offered later testimony on these events which was consistent, clear, cogent, and compelling.

I found that although petitioner *presented* for the pulmonology appointment at 11:33 a.m. and she *presented* to the emergency room at 4:11 p.m., the time between the vaccination and the onset of numbness and tingling was shorter, more likely than not three to four hours. Tr. 124.

I also found that by November 14, 2015, petitioner's condition progressed further. Namely, her left arm hung limp and could not move. She could not use the left arm to hold her coffee cup, button her blouse, or drive a car. Afterwards, petitioner's condition progressed further to the point that she could not use the left arm to perform housework or cut food. Petitioner's new functional limitations persisted to the time of the fact hearing in September 2018. She had severely limited use of the left arm. She had atrophy in the left arm, particularly in the forearm. She could not actively extend her fingers on her left hand. She could readily raise her right arm to 180 degrees, but the left arm to only about 90 degrees. *See* Tr. 119-20.

While not disputed by the parties, I expressly find that petitioner is eligible to *pursue* compensation from the Vaccine Program because there is preponderant evidence that she suffered the residual effects of neuralgic amyotrophy for more than six months after the administration of the November 12, 2015, flu vaccination. Section 11(c)(1)(D). This evidence includes petitioner's discharge from physical therapy with a radial nerve splint and a home exercise program on June

28, 2016; the repeat EMG study supporting an improved but "severe" and "chronic" nerve injury on July 19, 2016; and petitioner's credible testimony and her demonstration of some continued limitations during the fact hearing in 2018.

IV. Entitlement

A. Nature of Petitioner's Condition Before and After Vaccination[20]

1. Introduction

Here, there is no dispute that petitioner sustained left-sided neuralgic amyotrophy. That diagnosis is reflected in the medical records beginning in November 2015. See, e.g., Pet. Ex. 11 at 9-11; Pet. Ex. 2 at 9-11, 12-14. Most importantly, the December 8, 2015 EMG found denervation in seven muscles – the dorsal interosseous, flexor carpi radialis, biceps, triceps, deltoid, flexor carpi ulnaris, and brachioradialis – which are supplied by varying nerves and cervical cords. This evidenced a "severe" and "acute" injury affecting multiple branches of the brachial plexus, but predominantly the upper cord. See Pet. Ex. 2 at 25-26.

The parties dispute when petitioner sustained that injury. Petitioner contended that her left shoulder pain beginning on or about October 1, 2015, was correctly diagnosed as bursitis. She contended that after receiving the flu vaccine on November 12, 2015, she developed new numbness and tingling within 3 – 4 hours, followed within two days by weakness and loss of function in the left arm. Pet. Brief at 12. Respondent countered that the shoulder pain in October was misdiagnosed as shoulder bursitis but in fact represented the first manifestation of neuralgic amyotrophy. Resp. Brief at 18-19.

2. Bursitis

Bursitis is a swelling or inflammation of a bursa, which is a synovium-lined, sac-like structure found throughout the body near bony prominences and between bones, muscles, tendons, and ligaments. Resp. Ex. G-1.[21] There are over 150 known bursae in the human body, and their function is to facilitate movement in the musculoskeletal system, creating a cushion between tissues that move against one another. *Id.* Bursitis describes when the bursa enlarges with fluid. *Id.* As a result, any movement or direct pressure on the bursa will cause pain, which can result in decreased active and/or passive range of motion. *Id.*

[20] The parties briefed this issue under *Althen* prong two. I find it appropriate to resolve it first, because it informs the theory presented under *Althen* prong one, below. To preview, pre-existing biomechanical factors such as shoulder bursitis can increase the likelihood that an immune response beginning in the periphery can access the brachial plexus and result in neuralgic amyotrophy.

[21] Williams et al., *Bursitis*, StatPearls – NCBI Bookshelf (National Library of Medicine, National Institutes of Health), available at https://www ncbi.nlm.nih.gov/books/NBK513340/ (last accessed September 14, 2021). Dr. Callaghan cited this webpage in his discussion of bursitis, *see* Resp. Ex. G at 1. Respondent did not file a PDF of the webpage. For ease of citation, it is heretofore cited as Resp. Ex. G-1.

The most common site for bursitis is the subdeltoid bursa, which is between the deltoid and the glenohumeral (shoulder) joint capsule. *See Dorland's* (definition for bursitis). The pain will be "localized in the deltoid area and lateral upper arm, and movement restrictions during abduction and anteflexion of the arm will be antalgic[22] and present on both active and passive motion due to the joint pathology." Pet. Ex. 15.4.[23]

Bursitis affects people of all ages, but elderly people are often afflicted by osteoarthritis and other chronic diseases which can increase the risk of bursitis. Resp. Ex. G-1. There are many causes of bursitis including overuse injury, infectious disease, trauma, and inflammatory disorders. *Id.* While not all bursitis is associated with an overt inflammatory process, in patients with shoulder bursitis, there have been findings of increased inflammatory mediators such as tumor necrosis factor-alpha, cyclooxygenases, and specific interleukins. *Id.*

For the vast majority of patients, bursitis will heal on its own "in a few weeks," but symptoms can be improved with rest, ice, compression, elevation, and NSAIDs and/or acetaminophen. Resp. Ex. G-1. Corticosteroid injections can also provide symptomatic relief for the deeper bursa. *Id.* Physical therapy and range of motion exercises are also important because immobilization may result in atrophy, retraction, and adhesive capsulitis ("frozen shoulder"). *Id.*

3. Neuralgic Amyotrophy

Both parties' experts agreed that compared to bursitis, neuralgic amyotrophy is a much less common condition. They both cited to peer-reviewed literature by Nens van Alfen, M.D., Ph.D., who is a recognized authority on this topic.[24] In an invited review in the prominent electrodiagnostics journal Muscle and Nerve, van Alfen wrote that this condition is referred to as idiopathic brachial plexus neuropathy and Parsonage-Turner syndrome. Pet. Ex. 15.4 at 1. However, van Alfen's preferred term and also the most common term in the literature, is neuralgic amyoytophy ("NA") which is "neutral with respect to the extent and localization of nerve involvement." *Id.* The condition typically involves pain, sensory symptoms, and weakness which are "not in the same nerve territory distribution." *Id.*

While neuralgic amyotrophy is "not rare, with an incidence of 1 per 1,000 individuals, it is still often missed." Pet. Ex. 15.4 at 1. Primary care providers often diagnose glenohumeral bursitis and emergency physicians often diagnose "muscle strain." There is often a delay before a patient receives the correct diagnosis. *Id.* X-rays of the shoulder and cervical spine are "of little value"; the diagnosis instead relies on a thorough clinical evaluation. A significant number of cases

[22] Antalgic is "counteracting or avoiding pain, as a posture or gait assumed so as to lessen pain." *Dorland's*.

[23] The full citation to this article is *infra* at n. 25.

[24] *See* van Alfen et al., *The Clinical Spectrum of Neuralgic Amyotrophy in 246 Cases*, 129 Brain 438 (2006) [Resp. Ex. A-1]; van Alfen et al., *Review: Treatment for Idiopathic and Hereditary Neuralgic Amyotrophy (Brachial Neuritis)*, 3 Cochrane Database of Systematic Reviews Art. No. CD006976 (2009) [Resp. Ex. C-18]; van Alfen et al. *Neuralgic Amyotrophy and Hepatitis E Virus Infection*, 82 Neurology 498 (2014) [Resp. Ex. C-13]; van Alfen et al., *Invited Review: Neuralgic Amyotrophy: An Update on Diagnosis, Pathophysiology, and Treatment*, 53 Muscle and Nerve 337 (2016) [Pet. Ex. 15.3, also filed as Resp. Ex. C-3].

include injury to the long thoracic nerve, which innervates the serratus anterior muscle, which rotates the scapula. Such an injury causes the hallmark finding of scapular winging, *see* Pet. Ex. 15.4 at 10, although that may not be detected if the patient is not examined properly, *see Davis v. Sec'y of Health & Human Servs.*, No. 16-276V, 2021 WL 3910609, at *20 (Fed. Cl. Spec. Mstr. July 23, 2021) (summarizing two expert neurologists' debate as to whether local providers would have recognized the petitioner's scapular winging). In addition, EMG testing can yield objective evidence of denervation which would not be expected with for example, bursitis. Pet. Ex. 15.4 at 7-8.

Van Alfen wrote that neuralgic amyotrophy "has several phenotypic variations." Pet. Ex. 15.4 at 1. The classic form, seen in about 70% of patients, begins with "new-onset pain in the shoulder or upper arm." *Id.* at 4. The pain "is often in the region of the trapezius muscle and acromion, movement restriction is usually just or mainly present during active attempts at motion (i.e., due to paresis), and scapular movement is often dis-coordinated." *Id.* at 6. The pain generally becomes unbearable… within a few hours." *Id.* at 1. Van Alfen wrote in her 2006 article describing the largest case series to date of neuralgic amyotrophy, the pain was "very severe, relentless, [and] neuropathic." Resp. Ex. A-1 at 4. The pain was worse at night in 88.6% of patients and caused sleep disturbances in 93.5%. *Id.* There was evidence of increased mechanical sensitivity (e.g., pain elicited by movement of or pressure on the affected limb, a 'Lasegue sign of the arm') in 80% of male patients and in 97.4% of female patients. *Id.* This initial severe neuropathic pain does not respond to the usual analgesic treatment such as acetaminophen or NSAIDS. *Id.* at 1, 9. The best option was a combination of a long acting opioid with an NSAID, which relieved pain in 60% of patients. *Id.* Early treatment with oral or intramuscular corticosteroids may reduce pain in some patients and possibly speed up recovery in a smaller proportion of patients, although not very robust studies have been conducted. Resp. Ex. C-18 at 7-8; *see also* Resp. Ex. A-1 at 10; Pet. Ex. 15.2[25] at 3.

In van Alfen's cohort, the initial severe neuropathic pain lasted on average 27.5 days (median 19.5 days), although interestingly it lasted longer in males (average 45.3 days, median 21 days) than in females (average 23.3 days, median 17 days). Resp. Ex. A-1 at 4.

Although a minority (10%) of patients reported initial pain lasting for more than 60 days, van Alfen suggested that the outliers were unable to distinguish the initial pain from the subsequent "pain phases." *Id.* The second phase is "severe neuropathic stabbing or shooting pains usually elicited by movement, lying on, or prolonged posturing of the affected limb." *Id.* at 4. This is also described as "increased mechanical sensitivity of the damaged nerves." *Id.* at 11. The third pain phase is characterized by "a persisting musculoskeletal-type pain in both the affected and compensating muscles, especially at the site of their origin and insertion." *Id.* at 11.

Dr. Callaghan emphasized van Alfen's additional finding that 23% of males and 37.5% of females "suffered from neuropathic pains even at the final follow-up." Resp. Ex. A-1 at 4. However, this finding does not clearly pertain to the initial very severe neuropathic pain versus the second phase of stabbing pain which occurs with movement or pressure.

[25] Shaikh et al., *Acute Brachial Neuritis Following Influenza Vaccination*, BMJ Case Rep., PMID 23192585 (2012) [Pet. Ex. 15.2, also filed as Resp. Ex. C-2]

Van Alfen reported that: "In the attacks characterized by initial pain, the first signs of weakness appeared within 24 hours in 33.5% of the patients, after 1-7 days in 39.3%, and 1-2 weeks in 14.1%. In 27.2% of all cases, paresis did not manifest itself until > 2 weeks later. The mean time to the onset of weakness was 13.6 days in the male and 8 days in the female patients, but the difference was not statistically significant (P = 0.18) An increment of the paresis occurred in 30.2% of cases with severity progressing over a period of days (8.6%), weeks (16%), or months (5.6%)." Resp. Ex. A-1 at 5.

Sensory symptoms during an attack were reported by 69.2% of patients and were found by subsequent clinical examination in 78.4% of patients. *Id.* Van Alfen does not clearly state whether the sensory symptoms also tend to arise at the onset, although she wrote that pain and paresis tend to "dominate" the clinical picture, *see id.* at 10. She has also written that a patient with the classic "predominant intense pain" "may not even notice or mention" weakness and tingling. Pet. Ex. 15.4 at 1.

Van Alfen discussed that the "classic" neuralgic amyotrophy phenotype is found in about two-thirds of patients, but importantly, the condition includes significant "phenotypic variability," which "has led to the concept of a syndrome that encompasses all these acute-onset, painful mono- or multi-focal neuropathies with a monophasic course. Interestingly, there are also patients (about 4% in a large case series) with identical symptoms and a disease course that does not have pain at onset." *Id.*

In some patients, weakness of the rotator cuff muscles or decreased glenohumeral excursions can cause painful glenohumeral joint pathology, which can be visualized. Resp. Ex. A-1 at 4. In van Alfen's cohort, 17% of patients developed true frozen shoulder (glenohumeral adhesive capsulitis) and 8.4% of patients developed glenohumeral subluxation or luxation. *Id.*

4. Application

In this case, Dr. DiCapua opined that beginning on or around October 1, 2015, before the vaccination, petitioner had "shoulder pain coupled with normal active and passive ranges of motion," which would be consistent with bursitis. Pet. Ex. 17 at 2. Dr. DiCapua opined that normal active and passive range of motion would be "exceedingly unlikely" if petitioner in fact had neuralgic amyotrophy at this time, based on van Alfen's case series, in which 80% of males and 97.4% of females with neuralgic amyotrophy had that increased mechanical sensitivity. *Id.*

Dr. Callaghan agreed that the majority of patients with neuralgic amyotrophy have increased mechanical sensitivity. Resp. Ex. G at 1. But he opined that petitioner's medical records from both before and after vaccination do not address the presence or absence of mechanical sensitivity. Resp. Ex. G at 1 (citing Pet. Ex. 2 at 4, 7, 10, 13 (primary care records); Pet. Ex. 3 at 10, 19, 27, 41(orthopedic records)). This is inaccurate. At petitioner's first presentation for her shoulder on October 28, 2015, the orthopedist Dr. Payne in fact recorded left shoulder "pain on abduction and forward flexion," although he did not record her range of motion. Pet. Ex. 11 at 14. On November 5, 2015, the primary care provider Dr. Hanna recorded that petitioner "still had good mobility" and that active and passive range of motion were intact, but that is contradicted by the

history specifically pertaining to her left shoulder pain, which was aggravated by movement and reaching overhead. Pet. Ex. 3 at 35, 41. I find that there is preponderant evidence that petitioner indeed had mechanical sensitivity beginning on or around October 1, 2015. But importantly, Dr. Callaghan opined that is also a common physical exam finding with shoulder bursitis. Resp. Ex. G at 1 (citing Resp. Ex. G-1 (providing that with bursitis, specifically in the shoulder, movement will cause pain which will cause secondary restrictions in range of motion)). This finding in petitioner's case does not clarify whether she had bursitis versus neuralgic amyotrophy before vaccination. However, I will note, as did Dr. DiCapua, that in the hours and days after vaccination, petitioner experienced dramatically worse and different symptoms, which support the finding of a new injury.

Dr. DiCapua also emphasized that petitioner had "3 days of relief" upon receiving a steroid injection, which is indicated for the treatment of bursitis. Pet. Ex. 17 at 3 (citing Pet. Ex. 3 at 40). Dr. Callaghan did not opine, but the literature supports, that steroids can also alleviate neuralgic amyotrophy pain. *See* Resp. Ex. C-18 at 7-8; Resp. Ex. A-1 at 10; Pet. Ex. 15.2 at 3. This fact does not provide strong support for one diagnosis over another.

Dr. DiCapua opined that the October 28, 2015, x-ray finding of glenohumeral subluxation in petitioner's left shoulder was consistent with bursitis. Pet. Ex. 15 at 3 (citing Pet. Ex. 11 at 15. Dr. Callaghan countered with van Alfen's finding that it was not uncommon for patients with neuralgic amyotrophy to develop pain related to glenohumeral joint pathology and that 8.4% developed glenohumeral subluxation or luxation. Resp. Ex. E at 2 (citing Resp. Ex. A-1 at 4). However, the sequence of events is important in understanding this finding. Van Alfen actually posited that in neuralgic amyotrophy, paresis (weakness) of the rotator cuff muscles and secondary decreased glenohumeral excursions causes the joint pathology. Resp. Ex. A-1 at 4. As another article[26] sets forth plainly, in the setting of neuralgic amyotrophy: "If deltoid muscle is profoundly weak, recommend a sling to avoid subluxation of the humerus." Pet. Ex. 15.2 at 2. Here, petitioner underwent an x-ray examination of the shoulder and was found to have glenohumeral joint subluxation *before* she developed acute weakness and numbness. If anything, it appears, consistent with Dr. DiCapua's opinion, that her glenohumeral joint subluxation was more likely associated with her earlier bursitis rather than secondary to neuralgic amyotrophy, which did not occur until well after the x-ray.

Dr. DiCapua also opined that if petitioner experienced the onset of pain beginning on October 1, 2014, which persisted for over six weeks, that would be atypical for neuralgic amyotrophy, based on van Alfen's findings. Pet. Ex. 17 at 2-3. Dr. Callaghan countered that van Alfen actually found that the initial neuropathic pain lasts a median of 27.5 days; that a subset of patients, particularly women, reported lasting neuropathic pain; and that 61.5% of all patients reported persistent musculoskeletal-type pain. Resp. Ex. E at 2 and Resp. Ex. G at 1-2 (citing Resp. Ex. A-1].

[26] Miller et al., *Brachial Plexus Neuritis: An Uncommon Cause of Shoulder Pain*, 62 Am. Fam. Physician 2067 (2000) [Pet. Ex. 15.2].

Interestingly, the expert neurologists did not compare the "classic" onset, seen in about 70% of patients with neuralgic amyotrophy, of "very severe, relentless, neuropathic" pain that becomes "unbearable" within a few hours to petitioner's case. But the evidence reflects that petitioner never experienced pain of that severity. Before vaccination, beginning on or about October 1, 2015, she experienced the onset of "gradual" left shoulder pain which was aggravated by movement. However, she did not seek any medical attention for nearly a month, at which point she made an appointment with her orthopedist rather than seeking urgent care. She did not receive a steroid injection for another week, that is, five weeks into the course of pain. In addition, while the medical records reflect that petitioner had pain which increased with movement, she testified credibly that the pain was limited to the top of the shoulder. Petitioner also continued to play golf and complete activities of daily living such as buttoning her blouse, cooking, and driving. These activities do not seem consistent with the "classic" neuralgic amyotrophy onset of very severe pain, occurring before vaccination.

When petitioner presented to the emergency room approximately four hours after vaccination, she was concerned that she may be having a stroke. She reported moderate pain, rated as 5/10, but she also emphasized numbness and tingling in the left arm. *see* Pet. Ex. 5 at 249. She was not given any pain medication in the emergency room or at appointments with the orthopedist and the neurologist the following week. The medical records, as well as petitioner's credible testimony, establish that upon presenting for emergency medical attention, she was primarily concerned about the new acute weakness and sensory symptoms.

With regard to petitioner's onset of weakness six weeks after the onset of pain and within hours after vaccination, Dr. Callaghan emphasized van Alfen's findings that in a minority of cases (27.2%), weakness did not manifest until equal or greater than two weeks after the onset of pain. Resp. Ex. E at 2 (citing Resp. Ex. A-1 at 5). Also, in a minority of cases, the weakness progressed over a period of days, weeks, or months. Resp. Ex. A-1 at 5. Dr. Callaghan also opined that non-neurologists often do not detect weakness and that could have occurred in petitioner's case (which would be contrary to my bench ruling finding of fact). Resp. Ex. E at 2; Resp. Ex. G at 2. However, van Alfen found that in the majority of cases, weakness and sensory symptoms begin at the very beginning or the initial course of neuralgic amyotrophy. Resp. Ex. A-1 at 5-6. Van Alfen also observed that when the onset includes severe pain, that can dominate the clinical pain and obscure both the patient's and the treating physicians' observations of weakness, as well as sensory symptoms. However, the pain, weakness, and sensory symptoms are understood to all begin around the same time. *Id.* at 10; Pet. Ex. 15.4 at 1. Given that petitioner's pre-vaccination shoulder pain was not so severe, and she continued with her usual activities, it is improbable that she was also developing progressive weakness and sensory symptoms, that she and her treating physicians failed to notice, during that same time.

To reiterate the above findings of fact, within four hours after the November 12, 2015, vaccine, petitioner experienced moderate pain as well as new acute weakness, numbness, and tingling affecting not only her left shoulder, but her left arm and hand, which symptoms progressed further over the subsequent days.

There is not preponderant evidence to connect these symptoms with the earlier pain, which was more likely than not correctly assessed as bursitis. It is more likely that within four hours after vaccination, petitioner experienced the acute onset of neuralgic amyotrophy.

B. *Althen* Prong One

1. Petitioner's Expert Dr. DiCapua

Dr. DiCapua opined that neuralgic amyotrophy's etiology is "often unknown." Pet. Ex. 15 at 3. The low annual recorded incidence (1 – 3 /100,000 subjects), misdiagnosis, and delayed diagnosis hinders reporting and research. *Id.*

However, Dr. DiCapua opined that neuralgic amyotrophy is most likely autoimmune and can be precipitated by infections and vaccines, including inactivated flu vaccine. Pet. Ex. 15 at 3. This opinion has support in the literature. In one of the first descriptions of the condition, in 1948, Parsonage and Turner[27] reported the "remarkable fact" that a majority of their 136 subjects had "some precipitating factor" such as a surgical operation, trauma, or infection (typically viral). Pet. Ex. 15.8 at 1. Parsonage and Turner wrote that a mechanical cause alone did not explain the condition "for there was always a clear interval between [a surgical operation] and the first symptom of the shoulder-girdle syndrome – pain." *Id.* Parsonage and Turner also considered that vaccines could serve as a precipitating factor. While "careful inquiry into recent vaccination and inoculations were made in only 67 cases of the series[,] [o]f those 67 patients, 11 had had inoculations during the four weeks preceding the onset of their shoulder-girdle symptoms; in 6 cases the inoculation had been within the previous fortnight." *Id.* at 2. This signal persists throughout the literature. Tsairis[28] found that in a cohort of 99 subjects that developed neuralgic amyotrophy, at least 14 had received an antecedent vaccine or other injection, four of which had specifically received flu vaccine. Resp. Ex. A-3 at 3. Beghi[29] reported on a large case series, in which 3 subjects had preceding flu-like illness and 2 subjects had preceding tetanus toxoid immunizations. Resp. Ex. C-14 at 3. In the largest case series to date, published in 2006, van Alfen found that 43.5% of subjects had antecedent infections[30] and 4.3% had antecedent vaccines. Resp. Ex. A-1 at 6. In addition, there have been at least three case reports of flu vaccines followed by neuralgic amyotrophy.[31]

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[27] Parsonage and Turner, *Neuralgic Amyotrophy: The Shoulder-Girdle Syndrome*, Lancet (1948) [Pet. Ex. 15.7, also filed as Resp. Ex. A-2].

[28] Tsairis, Dyck, et al., *Natural History of Brachial Plexus Neuropathy: Report on 99 Patients*, 27 Arch. Neurol. (1972) [Resp. Ex. A-3].

[29] Beghi et al., *Brachial Plexus Neuropathy in the Population of Rochester, Minnesota, 1970 – 1981*, 18 Ann. Neurol. 320 (1985) [Resp. Ex. C-14].

[30] *See also* van Alfen (2014) [Resp. Ex. C-13] (reporting that a significant proportion of patients in the United Kingdom and the Netherlands had recent infection with Hepatitis E virus).

[31] Miller et al., *Acute Brachial Plexus Neuritis: An Uncommon Cause of Shoulder Pain*, 62 Am. Fam. Physician 2067 (2000) [Pet. Ex. 15.1, also filed as Resp. Ex. C-1]; Shaikh et al., *Acute Brachial Neuritis Following Influenza Vaccination*, BMJ Case Rep., PMID 23192585 (2012) [Pet. Ex. 15.2, also filed as Resp. Ex. C-2]; Taras et al., *Radial Nerve Motor Palsy Following Seasonal Influenza Vaccination (Case Report)*, 23 J. Surg. Orthop. Adv. 42 (2014) [Pet. Ex. 15.12, also filed as Resp. Ex. C-11].

In 2009, van Alfen wrote: "The current hypothesis is that NA [neuralgic amyotrophy] is caused by an underlying predisposition and a susceptibility to mechanical injury of the brachial plexus; the episodes are then caused by an immune-mediated response to the brachial plexus… NA [neuralgic amyotrophy] can best be defined as a disorder with a complex pathophysiological mechanism in which autoimmune, genetic and external factors all seem to play an interwoven role." Resp. Ex. C-18 at 3. Seven years later, van Alfen repeated:

> Although still speculative, we hypothesize that the predilection of NA [neuralgic amyotrophy] for the brachial plexus (especially the most mobile part, i.e., the upper trunk) is caused by mechanical stretching and compression of the nerves that follows from the wide range of motion of shoulder joints. This every day 'wear and tear' may induce focal loosening of the blood-nerve barrier. A less tight blood-nerve barrier, on the one hand, allows for development of autoantibodies, as the immune system is suddenly able to 'see' peripheral nerve components and, on the other hand, allows circulating autoantibodies or cells access to the brachial plexus… Thus, biomechanical factors may contribute to nerve inflammation by causing wear-and-tear stress to the blood-nerve barrier[.]

Pet. Ex. 15.4 at 4.

Van Alfen provided two helpful examples for this multifactorial process. The first was a cohort of employees at a knitting factory in Czechoslovakia. All employees encountered the same biomechanical stressor of "bend[ing] and stretch[ing] their right arms 8 hours/ day." Pet. Ex. 15.4 at 4. All employees encountered the same immune trigger: the local water supply which was contaminated by Coxsackie A2 virus. *Id.* However, not all employees developed neuralgic amyotrophy, which pointed to some unknown individual genetic susceptibility. *Id.*

The second example involved surfers at a specific beach. Pet. Ex. 15.4 at 4. All surfers used their arm to paddle on their surfboards and all were exposed to the ocean water which was contaminated with hepatitis E virus, but again, only two of the surfers developed neuralgic amyotrophy. *Id.*

Van Alfen did not address which specific immune cells access the brachial plexus and cause the nerve damage. Van Alfen did cite to a 1991 study in which Sierra[32] sampled blood from six subjects between 2 to 8 weeks after the onset of neuralgic amyotrophy pain. Pet. Ex. 15.8 at 1. Their blood contained cytotoxic lymphocytes, which demonstrated increased mitogenic activity when brought into contact with brachial plexus tissue, but not tissue from other parts of the body, which indicated that this is an organ-specific injury. *Id.*

[32] Sierra et al., *Blood Lymphocytes are Sensitized to Brachial Plexus Nerves in Patients with Neuralgic Amyotrophy*, Acta Neurol Scand., PMID: 2031452 (1991) [Pet. Ex. 15.8, also filed as Resp. Ex. C-8].

Van Alfen also cited a 1993 study in which Vriesendorp[33] found that three subjects' serum contained antibodies against peripheral nerve myelin as well as complement activation products during the acute phase of neuralgic amyotrophy, but those were decreased several months later during clinical recovery. Resp. Ex. C-4 at 2. Vriesendorp hypothesized that "complement-dependent antibody-mediated demyelination may [either] participate in initial peripheral nerve damage or augment an ongoing process" that causes neuralgic amyotrophy. *Id.* at 3.[34]

Dr. DiCapua likewise opined that neuralgic amyotrophy may involve both the innate and adaptive immune systems, and in particular, the innate immune system's complement component, as theorized by Vriesendorp. Pet. Ex. 15 at 4. Dr. DiCapua opined that the alternative complement pathway can rapidly activate and attack a foreign pathogen such as flu vaccine. *Id.* "While the complement pathway is normally tightly regulated, once activated can amplification loop can be set into motion which if not controlled, can cause a multitude of autoimmune diseases." *Id.* "Specifically, the alternative pathway of complement activation serves as a major mechanism of recognition and elimination of foreign or dangerous pathogens, unfortunately, it appears that it has the same capacity to destroy self-tissue." *Id.*[35]

It is important to understand that complement is a "complex innate immune surveillance system" which "serves as a first line of defense against foreign and altered host cells." Resp. Ex. C-19 at 1.[36] Complement can be initiated depending on the context by three distinct pathways – classical, lectin, and alternative. *Id.* In a healthy individual, the alternative pathway is continuously engaged in a through a process called tick-over, which converts a low level of C3 to C3b which quickly binds to any adjacent surface containing hydroxyl groups. *Id.* at 2. Host cells have "an army of membrane-expressed or fluid phase-recruited complement regulators" which rapidly inactivate C3b. *Id.* In contrast, foreign pathogens cannot inactivate C3b. *Id.* "The permanent activity of the alternative pathway allows it to *immediately* identify pathogens that are not specifically protected against complement." *Id.* at 3 – Figure 2 (emphasis added). Dr. DiCapua cited another study by Zewde[37] that demonstrated that the alternative complement pathway can recognize a foreign pathogen and initiate the innate immune response within minutes to hours.

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[33] Vriesendorp et al., *Anti-Peripheral Nerve Myelin Antibodies and Terminal Activation Products of Complement in Serum of Patients with Acute Brachial Plexus Neuropathy*, 50 Arch Neurol. 1301 (1993) [Pet. Ex. 15.4; also filed as Resp. Ex. C-4].

[34] *See also* Suarez et al., *Immune Brachial Plexus Neuropathy: Suggestive Evidence for an Inflammatory-Immune Pathogenesis*, 46 Neurology 559 (1996) [Pet. Ex. 15.5, also filed as Resp. Ex. C-6 and Resp. Ex. F-10]; Moriguchi et al., *Four Cases of Anti-Ganglioside Antibody-Positive Neuralgic Amyotrophy with Good Response to Intravenous Immunoglobulin Infusion Therapy*, 238 J. Neuroimmunol. 107 (2011) [Pet. Ex. 15.6, also filed as Resp. Ex. C-7]; Loh et al, *Brachial Plexopathy Associated with Interleukin-2 Therapy*, 42 Neurology 462 (1992) [Pet. Ex. 15.10, also filed as Resp. Ex. C-9].

[35] Citing Thurman et al., *The Central Role of the Alternative Complement Pathway in Human Disease*, 176 J. Immunol. 1305 (2006) [Pet. Ex. 15.9].

[36] Merle et al., *Complement System Part I – Molecular Mechanisms of Activation and Regulation*, 6 Front. Immunol. 262 (2015) [Resp. Ex. C-19].

[37] Zewde et al., *Quantitative Modeling of the Alternative Pathway of the Complement System*, PLoS One, PMID: 27031863 (2016) [Pet. Ex. 15.11]

The alternative pathway's binding to the foreign pathogen leads to classical and lectin pathway activation, C3 convertase, C4b2a generation, and C3 cleavage. Resp. Ex. C-19 at 3. The alternative pathway continues in an "amplification loop" which augments the effect of all pathways and is the heart of the complement cascade. *Id.* Complement activation also leads to pathogen lysis, opsonization, phagocytosis, activation of host immune and non-immune cells, inflammation, stimulation of an adaptive immune response, and antibody generation. *Id.* Resp. Ex. C-19 at 3-4. Thus, the alternative complement pathway both rapidly initiates and also furthers the attack on a foreign pathogen.

The alternative complement pathway requires continuous active control, which can be overwhelmed thereby resulting in autoimmune conditions. *See generally* Pet. Ex. 15.9. Inhibition of the alternative complement pathway is associated with amelioration of those conditions. It may be that some "initial insult induces deficiencies of regulatory proteins in necrotic cells or regions of injury, setting the stage for amplification of injury by the alternative pathway." *Id.* at 6. Another potential explanation is that "infiltrating cells such as neutrophils bring in C3 and properdin that increase activation specifically at that site by providing additional substrate for the alternative pathway." *Id.*

2. Respondent's Experts' Discussion of the Theory

Respondent's expert immunologist Dr. Tompkins disputed that neuralgic amyotrophy has an immune etiology. He opined that the proposed immune etiologies are "primarily based upon associations in case reports and do not provide evidence of causation." Resp. Ex. C at 2. He opined that the Vriesendorp, Suarez, Moriguchi, and Loh studies "suggest[ed] immune involvement with neuropathy, but [did] not provide evidence of causation" as there was "no data in the literature demonstrating [that] the observed inflammation, immune cell infiltrates, or antibody responses… preceded or caused" neuralgic amyotrophy. *Id.* at 7-8. Here, Dr. Tompkins seemed to require data on healthy subjects prior to their development of neuralgic amyotrophy which is of course impractical because the onset of neuralgic amyotrophy is unforeseeable.

Similarly, respondent's expert neurologist Dr. Callaghan argued that there are "no case control or cohort studies to look at the association of any vaccine with [NA.]" Resp. Ex. A at 2. On this question, the "best data available" are the large case series such as by Parsonage and Turner, Tsairis, and van Alfen. *Id.* But Dr. Callaghan opined that these case series "only support a proximal temporal relationship" and that "[i]mportantly, a proximate temporal relationship alone is insufficient to prove causation." *Id.* Dr. Callaghan also opined that there have been "numerous" cases of neuralgic amyotrophy after tetanus toxoid vaccine but "only 3 published case reports" about flu vaccine. *Id.* While this appears to be true, the lack of studies involving a specific vaccine and a rare condition such as neuralgic amyotrophy does not rule out vaccine causation. Moreover, the leading researchers on this condition have endorsed an immune etiology, which lends support to the proposed theory.

Dr. Tompkins also opined that while the literature has implicated infections and to "a much lesser extent" vaccines, "exercise and repeated strenuous activity are… a more common antecedent event" for neuralgic amyotrophy. Resp. Ex. C at 8-9. He opined that if an immune etiology is entertained, bursitis and ongoing shoulder inflammation is a more likely inciting event. However,

in making this assertion, Dr. Tompkins cited to literature by the leading researcher Dr. Nens van Alfen, who actually reasoned that *multiple* factors *converge* to cause the injury. An individual first has some underlying susceptibility, then encounters a biomechanical stressor, which then renders the shoulder more vulnerable to a subsequent immune trigger. *See* Resp. Ex. C-18 at 2; Pet. Ex. 15.4 at 4-5.

Dr. Tompkins raised several objections to the invocation of the alternative complement pathway. First, he opined that "whole" flu virus can activate the alternative complement pathway and be neutralized, but only after antibodies have bound to the virus. Resp. Ex. C at 9.[38] Both studies cited by Dr. Tompkins concern only H1N1 flu virus and not other subtypes of influenza A or any subtypes of influenza B that are covered by seasonal flu vaccines such as in this case.[39] Additionally, Dr. Tompkins filed another study by Kim[40] (discussed further below) that stated the reverse: that C3 complement is "critical" in inducing antibodies. Resp. Ex. C-24 at 1. The latter seems more consistent with the current understanding that the complement alternative pathway initiates the rest of the innate and adaptive immune response to a foreign pathogen.

Dr. Tompkins also opined that in the process of producing inactivated flu vaccine ("IIV"), the "whole" flu virus is inactivated, detergent-split, and purified: "The virion is completely disrupted, raising the possibility that split IIVs may not effectively interact with C3b proteins and initiate the AP." Resp. Ex. C at 9.[41] Dr. Tompkins's sources do describe this vaccine production strategy but do not address complement at all.

Dr. Tompkins also opined that: "There is limited information on the use of IIVs in complement deficiencies, however, the IIV is not contraindicated for complement-deficient persons." Resp. Ex. C at 9. He then cited a 2018 study by Kim, which found that complement-deficient mice demonstrated an "adequate" immune response to flu vaccine, to argue that complement plays no more than a "modest role in the immune response to vaccination." Resp. Ex. C at 9, citing Resp. Ex. C-24. But upon review, Kim found that the mice showed several significant deficits and he concluded that complement "has a critical role in inducing humoral and cellular immune responses to vaccination and in conferring protection by immunization." Resp. Ex. C-24 at 10. There is also no indication that the petitioner in this case was complement-deficient, or that

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[38] Citing Deebe et al., *Neutralization of Influenza Virus by Normal Human Sera: Mechanisms Involving Antibody and Complement*, 130 J. Immunol. 1317 (1983) [Resp. Ex. C-20]; *see also* Rattan et al., *Synergy between the Classical and Alternative Pathways of Complement is Essential for Conferring Effective Protection against the Pandemic Influenza A(H1N1) 2009 Virus Infection.* PLOS Pathogens, doi:10/1371, e1006248 (2017) [Resp. Ex. C-21]

[39] *See* Centers for Disease Control and Prevention, *Types of Influenza Virus*, available at https://www.cdc.gov/flu/about/viruses/types htm (last accessed July 13, 2021); *see also* Sanofi Pasteur, *Package Insert - Fluzone High-Dose*. 2019 [Resp. Ex. C-23, refiled as Resp. Ex. F-13] at 11 (providing that the vaccine contained H1N1, H3N2, and B-Victoria strains).

[40] Citing Kim et al., *Complement C3 Plays a Key Role in Inducing Humoral and Cellular Immune Responses to Influenza Virus Strain-Specific Hemagglutinin-Based or Cross-Protective M2 Extracellular Domain-Based Vaccination*, 92 J. Virol. e00969-18 (2018) [Resp. Ex. C-24].

[41] Citing Soema et al. *Current and Next Generation Influenza Vaccines: Formulation and Production Strategies*, 94 Eur. J. Pharm. Biopharm. 251 (2015) [Resp. Ex. C-22]; *Package Insert - Fluzone* [Resp. Ex. C-23].

the mouse study refutes the theory that complement in normal individuals may play a significant role in recognizing a foreign pathogen and stimulating the activation of the immune system including its own role in attacking the foreign pathogen and potentially the self.

3. Conclusion on *Althen* Prong One

Petitioner's expert Dr. DiCapua opined that introduction of flu vaccine can activate the alternative complement pathway, which if not tightly regulated, does not return to homeostasis and can cause the immune response to turn against the self, specifically against the nerves in the brachial plexus.

Respondent contended that Dr. DiCapua, whose specialty is neurology, was less qualified than Dr. Tompkins to opine on these topics. *See* Resp. Response at 15-16 and n. 12 (citing Dr. Tompkins's curriculum vitae at Resp. Ex. D at 27-38). However, I am not accepting Dr. DiCapua's statements alone. The literature provides support for his theory. The literature over the course of many decades has reported that certain cases of neuralgic amyotrophy are preceded by viral infections or vaccines, sometimes specifically flu vaccines. Therefore, various immune-mediated etiologies have been proposed.

Van Alfen provides perhaps the most persuasive explanation of neuralgic amyotrophy: Some unknown trait renders an individual susceptible, after which the individual encounters a biomechanical stressor which results in "nerve inflammation" and a "focal loosening of the blood-nerve barrier," which then allows "circulating autoantibodies or cells access to the brachial plexus," where they attack the nerves. Pet. Ex. 15.4 at 4. Importantly, van Alfen acknowledged other authors' invocation of antibodies against peripheral nerve myelin, but she herself is more agnostic as to the specific immune cells involved, writing: "autoantibodies *or cells*." *Id.* (emphasis added).

Dr. DiCapua's invocation of the alternative complement pathway also fits with the literature. Despite Dr. Tompkins's objections, it does seem more likely than not that inactivated flu vaccine does activate the alternative complement pathway in order to summon the rest of the innate and adaptive immune responses against the vaccine and to build lasting immunity. The literature supports that some initial insult can cause tissue injury and also "overwhelm" the regulation of the alternative complement pathway, keeping it in the "amplification loop" which summons an ongoing immune response, which then turns against the self.

It is thus accepted that in the context of a preexisting individual susceptibility and a biomechanical stressor affecting the shoulder, an inactivated but high-dose flu vaccine administered at or around the same shoulder, can act as an immune trigger, activating the alternative complement pathway, which can then fail to return to homeostasis, remain in a continued amplification loop, and cause injury to the nerves in the brachial plexus. The vaccine can be a necessary and substantial factor in causing the injury. Petitioner has established *Althen* prong one.[42]

[42] The vaccine was likewise a necessary and substantial factor in causing the injury in Petitioner's specific case, as addressed further under *Althen* prong two.

C. *Althen* Prong Three

As in many cases, the theory of injury invites discussion of the medically acceptable timeframe for that injury. Here, as set forth above, petitioner's vaccination was followed within three to four hours by the onset of neuralgic amyotrophy symptoms, specifically numbness and tingling in her left arm. Within approximately forty-eight (48) hours, petitioner's injury had progressed further, to the point that her left arm hung limp and she could not hold her coffee cup, button her blouse, or drive a car.

Dr. DiCapua opined that this rapid onset and further evolution of symptoms over several was consistent with an immune response, specifically activated by the innate immune system's alternative complement pathway, against the flu vaccine. Pet. Ex. 15 at 4. Dr. DiCapua opined that the alternative complement pathway would rapidly recognize flu vaccine and activate an immune response beginning within the timeframe seen here. *Id.* Compared to the classical and lectin pathways which bind to specific targets, the alternative pathway is non-specific, capable of autoactivation, and therefore more rapid. *Id.*; *see also* Thurman (2006) [Pet. Ex. 15.10] at 2. Dr. DiCapua cited a study which "demonstrate[d] "the robustness of the alternative pathway on the surface of pathogens in which complement components were able to saturate the entire region in about 54 minutes"). Zewde (2016) [Pet. Ex. 15.12]. As noted above, the alternative pathway initiates lysis of foreign pathogens, the other components of complement, the rest of the innate immune response, and the adaptive immune response. Dysregulated ongoing activation of the alternative pathway can likewise cause an ongoing immune response, and if complement becomes attached to self while dysregulated, may initiate the process of destruction of the nerve cells such as those in the brachial plexus.

Dr. DiCapua noted a case report of an individual who received a flu vaccine in his left arm and then developed the onset of left arm weakness within 12 – 16 hours thereafter, which led to the assessment of neuralgic amyotrophy. Pet. Ex. 15 at 4 (citing Taras (2014) [Pet. Ex. 15.12]).[43] The case report did not address why this timing would be acceptable but recounted that the condition has been considered a "post-vaccination neuropathy. Pet. Ex. 15.12 at 1.

Dr. DiCapua also opined that the alternative pathway and the rest of the immune response may be more rapid in the case of a foreign pathogen that has been seen before, such as here, where petitioner had received prior flu vaccines. Pet. Ex. 15 at 4.

Dr. Tompkins argued that the timing seen in this case is not acceptable because inactivated flu vaccine works specifically by priming T cell and B cell responses, for which the "first significant differences" have been measured to occur at the earliest at 15 hours post-vaccination. Resp. Ex. F at 2.[44] Dr. Tompkins allowed that it is "possible" that a vaccine or other immunologic

[43] The case report noted that "precise causation of the palsy as either [NA] or direct nerve injury is unclear because common features of both are seen." Pet. Ex. 15.12 at 3.

[44] Citing Obermoser et al., *Systems Scale Interactive Exploration Reveals Quantitative and Qualitative Differences in Response to Influenza and Pneumococcal Vaccines.* 38 Immunity 831 (2013) [Resp. Ex. F-1]; *see also* Bucasas, K.L., et al., *Early Patterns of Gene Expression Correlate with the Humoral Immune Response to Influenza Vaccination in Humans (Major Article),* 203 J. Infect. Dis. 921 (2011) [Resp. Ex. F-2]; Henn et al., *High-Resolution Temporal*

encounter can generate a more rapid response, termed a hypersensitivity (a/k/a allergic) reaction, but that is immunologically distinct and does not fit the facts seen here. Resp. Ex. F at 2-3. In addition, Dr. Tompkins opined that the immune markers observed in the condition, such as pro-inflammatory cytokines and T cells, would not be generated within the time frame seen here. Resp. Ex. F at 3-4. While it is true that the development of immune memory that is intended by the process of vaccination is *ultimately* dependent on the adaptive immune system, Dr. Tompkins's explanation appears to overlook the role of complement and other elements of the innate immune system, the activation of which occur much more rapidly and are necessary for the stimulation of the adaptive system.

Dr. Tompkins acknowledged that petitioner had "ongoing inflammatory events related to the bursitis in the left shoulder" prior to vaccination. Resp. Ex. C at 2. He opined that if an immune etiology for neuralgic amyotrophy is entertained, the "ongoing shoulder inflammation provides a chronic source of inflammatory cytokine production that could precipitate the immune response proposed by Dr. DiCapua." *Id.* at 9. This admission dovetails with van Alfen's explanation that this kind of biomechanical stressor in the shoulder would loosen the blood-nerve barrier and allow peripheral immune cells activated by the vaccine access to the brachial plexus.

Additionally, Dr. Tompkins does not discuss the timing of the alternative complement pathway. He does not dispute that it is continuously active and capable of "*immediately"* recognizing foreign pathogens, in service of activating the rest of complement, innate and adaptive immune responses. *See* Merle (2015) [Resp. Ex. C-19] at 3 and fig. 2. He does not dispute the Thurman article which stated that a variety of independent factors can cause dysregulation of the alternative pathway resulting in autoimmune disease.

In short, Dr. Tompkins acknowledged and the literature supported that bursitis could cause ongoing inflammation as well as a less tight blood-nerve barrier which would allow a peripheral immune response access to the brachial plexus. I have accepted that the flu vaccine would be recognized by the alternative complement pathway, which is undisputedly non-specific, rapid, and responsible for generating the rest of the immune response, including a "pro-inflammatory milieu," *see* Merle et al. (2015) [Resp. Ex. C-19] at 3. I find it acceptable that this inflammation would access the vulnerable brachial plexus and cause the onset, as well as the progression over several days, of neuralgic amyotrophy as seen here. Petitioner has established *Althen* prong three.

D. *Althen* Prong Two[45]

Respondent contended that the treating providers did not strongly endorse an association between petitioner's vaccine and neuralgic amyotrophy. *See* Resp. Response at 17 and n. 13. First, the neurologist Dr. Esposito did not mention it at the first encounter seven days post-vaccination. Pet. Ex. 2 at 12-13. Then two months post-vaccination, at a follow-up, Dr. Esposito diagnosed "left brachial plexopathy [neuritis] possibly due to the flu vaccine." Pet. Ex. 2 at 11. Respondent

Response Patterns to Influenza Vaccine Reveal a Distinct Human Plasma Cell Gene Signature, 3 Scientific Reports doi:10.1038/srep02327 (2013) [Resp. Ex. F-3].

[45] Respondent contended that petitioner has not established *Althen* prong two because she had neuralgic amyotrophy predating the vaccine. Resp. Response at 17-19. That dispute is resolved, in petitioner's favor, above.

averred that this is not probative because "[t]he records do not reflect that [Dr. Esposito] knew the timeline of the onset of her [NA]," *see* Resp. Response at n. 13, which is not persuasive because I have resolved that onset was shortly after the vaccination, which is in petitioner's favor. Respondent also averred that Dr. Esposito "seemed to base his comment about a potential causal relationship based on what petitioner told him." Resp. Response at n. 13. This is not clear from the record. Dr. Esposito may have been aware of the literature about neuralgic amyotrophy occurring after vaccines and other immune triggers. But either possibility involves speculation about his thought process. This record offers some degree, if only small, of probative evidence supporting *Althen* prong two.

An association between the flu vaccine and neuralgic amyotrophy was also recorded by the primary care provider Dr. Hanna three months afterwards and by a physical therapist four months afterwards. *See* Pet. Ex. 3 at 12, 21; Pet. Ex. 5 at 95. These records are more attenuated and therefore more likely to reflect petitioner's reported belief about causation rather than the providers' informed assessments.

Respondent also averred that: "The medical and scientific basis underlying any attribution of causation must be thoroughly examined, because a physician's conclusions 'are only as good as the reasons and evidence that support them.'" Resp. Response at 17-18 (quoting *Davis v. Sec'y of Health & Human Servs.*, 20 Cl. Ct. 168, 173 (1990)). In *Davis*, the Court of Federal Claims held that even if rotavirus infection causes significant mortality in the United States, the respondent's expert did not establish "that rotavirus infection caused [the specific child in that case] to become septic and die." 20 Cl. Ct. at 173. The Court also found that the parties' experts met on essentially "equal footing" because "neither expert was [the child's] treating physician; the conclusions each expert has drawn as to the cause of death were derived from the histories and records compiled by other doctors." *Id.* This is distinguished from the inquiry, where treating providers did record the potential of vaccine causation – even if that was largely based on petitioner's own belief.[46]

It can be useful to review treating physicians' hands-on evaluations and knowledge of the petitioner's specific medical history, including potential alternative causes for the injury (which were not identified in this case). Regardless, treating physicians' opinions are often not determinative when well-qualified experts are retained. In this case, Dr. DiCapua's opinion, as supported by his cited medical literature, was much more important to reaching my conclusions. He opined that "a direct injection injury" would have manifested "almost immediately." Pet. Ex. 15 at 4. In contrast, petitioner's onset of symptoms within several hours and further progression over the following few days was consistent with an immune-mediated process. *Id.* He specifically addressed the importance of her preexisting bursitis as well as why the timing was medically acceptable for activation of the alternative complement pathway (both addressed further below).

[46] Respondent also objected that: "Significantly, none of [petitioner's] providers put forth a theory causally connecting petitioner's flu vaccine to the [neuralgic amyotrophy]." Resp. Response at 17. However, petitioner has retained an expert to present a theory, which is addressed under *Althen* prong one. It is not at all evident that treating physicians are required to present a theory to support a finding under *Althen* prong two.

It is also helpful to compare van Alfen's explanation of neuralgic amyotrophy to the sequence of events in this case. First, the individual must have some underlying susceptibility. Van Alfen (2015) [Pet. Ex. 15.4] at 3-5. The experts did not address petitioner's medical history, but it may be relevant that she had a preexisting diagnosis of Addison's disease,[47] suggesting a possible susceptibility to autoimmunity.

Second, the individual must experience some biomechanical stressor involving "mechanical stretching and compression of the nerves that follows from the wide range of motion of shoulder joints." Pet. Ex. 15.4 at 4. "This everyday 'wear and tear' may induce focal loosening of the blood-nerve barrier." *Id.* Van Alfen gave examples of factory workers and surfers who engaged in repetitive arm movements prior to developing neuralgic amyotrophy. Here, petitioner recalled exercising about three days per week and playing golf twice a week. These activities do not seem as strenuous as in van Alfen's examples, but petitioner was diagnosed with bursitis in the left shoulder which was attributed to overuse and she was seventy nine (79) years old at the time of onset.

The experts also agreed that bursitis would be accompanied by increased inflammation. Resp. Ex. C at 2, 9-10; Pet. Ex. 16 at 1-2. Based on the available information, petitioner's shoulder bursitis more likely than not fits van Alfen's requirement for a biomechanical stressor which would render the brachial plexus susceptible to an autoimmune response resulting in neuralgic amyotrophy.

Dr. Tompkins opined that petitioner's bursitis and accompanying inflammation represented a "possible" mechanism for her development of neuralgic amyotrophy without any involvement by her vaccine. Resp. Ex. C at 10.

Dr. DiCapua agreed that petitioner's bursitis was "likely accompanied by increased levels of multiple inflammatory mediators," but he disputed that the bursitis could be "a chronic source of inflammatory cytokine production." Pet. Ex. 16 at 2. Dr. DiCapua reasoned that the October 28, 2015, intra-articular injection of 40 milligrams of methylprednisolone, would be systemically absorbed for about 7 days and then take a further 28 days (representing 5 half-lives) to clear from the body. *Id.* During that time, the methylprednisolone would "effectively eliminat[e]" all inflammatory mediators triggered by the bursitis from the shoulder. *Id.*

Based on that proposition, respondent's expert Dr. Tompkins asserted that petitioner's methylprednisolone injection would have "also exert[ed] its immunosuppressive effects during the initial immune response," to the flu vaccine, including "suppress[ing] the C3 cleavage and later events in the complement cascade." Resp. Ex. F at 5-6. Dr. Tompkins cited an article published in 1982[48] which indeed reached this finding, but only by introducing "very high concentrations" of methylprednisolone to human serum *in vitro*. Resp. Ex. F-26 at 2. The authors noted that such high concentrations are probably not achieved *in vivo*." *Id.* The findings indeed seem relevant for

[47] Addison's disease is defined as an "*autoimmune-induced* desctruction of the adrenal cortex." *Dorland's* (emphasis added).

[48] Citing Weiler and Packard, *Methylprednisolone Inhibits the Alternative and Amplification Pathways of Complement*, 38 Infection and Immunity 122 (1982) [Resp. Ex. F-26].

the purpose of that study, which was to explain "the efficacy of high-dose methylprednisolone therapy early in the treatment of patients with septic shock," *id.*, but seem less relevant to the current inquiry about whether one injection of just 40 milligrams of methylprednisolone, fifteen (15) days before the flu vaccine, would prevent recognition and activation of the alternative complement pathway.

After considering both experts' opinions and their literature, I find more likely than not that in petitioner's case, despite the administration of one single dose of methylprednisolone, her bursitis was associated with some degree of inflammation which loosened the blood nerve barrier, which rendered the brachial plexus more vulnerable to a subsequent peripheral immune response including complement and other innate immune mediators generated by a foreign substance such as flu vaccine.

I also find that despite the earlier methylprednisolone injection, the introduction of the flu vaccine activated the alternative complement pathway, thereby acting as the requisite immune trigger to cause the onset of neuralgic amyotrophy in this petitioner. Therefore, she has established *Althen* prong two.

V. Conclusion

For the foregoing reasons, petitioner is entitled to compensation for neuralgic amyotrophy caused by the November 12, 2015, flu vaccine. A separate damages order will be issued.

IT IS SO ORDERED.

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