# In the United States Court of Federal Claims

**OFFICE OF SPECIAL MASTERS**

**No. 16-539V**

(to be published)

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| CARLENE SCHULTZ,<br><br>Petitioner,<br><br>v.<br><br>SECRETARY OF HEALTH AND HUMAN SERVICES,<br><br>Respondent. | Chief Special Master Corcoran<br><br>Filed: January 24, 2020<br><br>Influenza vaccine; Stroke; Cerebral Vasculitis; Autoimmune Disease; Onset; Intracranial bleed |

*Andrew D. Downing*, Van Cott & Talamante, Phoenix, AZ, for Petitioner.

*Robert P. Coleman, III*, U.S. Dep't of Justice, Washington, D.C., for Respondent.

## ENTITLEMENT DECISION[1]

On May 2, 2016, Carlene Schultz filed a petition seeking compensation under the National Vaccine Injury Compensation Program ("Vaccine Program")[2] alleging that she experienced an adverse reaction to the influenza ("flu") vaccine she received on October 25, 2013, causing her to have a stroke/spontaneous intracranial bleed. Pet. at 1–5 (ECF No. 1). An entitlement hearing took place in Washington, D.C., on June 25, 2019.

Now, having reviewed the record and considered all other filings in the matter along with

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

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

the testimony at hearing, I hereby deny an entitlement award. As discussed in greater detail below, Petitioner has not carried her burden of establishing with preponderant evidence that the flu vaccine can cause stroke—or that it did so in this case to Petitioner. Nor did she establish that her symptoms were the product of an autoimmune disease process.

## I. Factual Background

### A. *Ms. Schultz's Pre-Vaccination Health*

Petitioner, a nurse practitioner, has a medical history that includes asthma, depression, fatigue/exhaustion, lumbar surgery in 2006, and hypothyroidism. Ex. 3 at 1; Ex. 8 at 70, 80; Ex. 6 at 75. She also experienced some pre-vaccination conditions and symptoms that to some degree are evident in her post-vaccine medical history (as well as the specific injury alleged).

For example, before receiving the flu vaccine in October 2013, Ms. Schultz experienced several years of temporomandibular joint/facial myofascial pain, migraines with olfactory hallucination, and left sided headaches involving the left side of her face and her left eye and obtained neurologic evaluations as a result. Ex. 8 at 9, 11. A spinal MRI performed on February 11, 2010, revealed an oval hyperintense lesion that did not enhance at the level of C1 just inferior to her left vertebral artery, although the filed medical records did not deem the lesion vascular in nature, nor was it ever linked to Petitioner's facial pain or headaches. *Id*. at 8, 14. Additional MRIs performed in 2010 and 2011 either revealed signals consistent with chronic ischemic changes and microvascular disease, or the same lesion, which was eventually termed extra-axial (i.e., outside the brain matter), and ultimately considered a benign tumor. *Id*. at 13, 22, 36, 39, 57.

A little over a week before the relevant vaccination, Ms. Schultz had a physical with her primary care provider on October 18, 2013. *Id.* at 119. At that time, she complained of persistent fatigue, cold intolerance, plus a chronic headache and constant facial pain on the left side of her face and around the left front sinuses. *Id*. She reported that she was taking Zaneflex, a muscle relaxant, for her facial symptoms. *Id*. She also was noted to have a history of depression, for which she was receiving medication. *Id.*

### B. *Vaccination and December 2013 Stroke*

On October 25, 2013, Ms. Schultz received the flu vaccine (for the first time in her life). Ex. 2 at 1; Tr. at 6, 22. At that time, she was 62 years old, and the vaccine (which she was required to receive by her employer) was administered to her in her right arm, and at her place of business. Ex. 2 at 1; Tr. at 22. There is an approximately six-week gap in the medical records, but Petitioner has alleged that during this period she was experiencing some nascent symptoms related to her subsequent more-acute event. She maintains that not long after receipt of the vaccine, she ran a low-grade fever and also felt a lack of appetite, malaise and fatigue, all of

which collectively were sufficient to cause her to call in sick from work for a few days in November 2013, and also to require that she cancel her planned attendance at a conference approximately five days post-vaccination. Ex. 1 at ¶¶ 4–5. Throughout November 2013, Petitioner recalls continuing to suffer a low-grade fever and malaise-like feeling that resulted in a lack of appetite and interfered with her ability to socialize over the Thanksgiving holiday that year. *Id.* at ¶¶ 7–8. She also took several days of leave that month. *Id.* at ¶ 9.

Five weeks later, on December 1, 2013, Ms. Schultz was brought by ambulance and admitted to Buffalo Regional Medical Center ("BRMC") in Buffalo, New York. Ex. 8 at 83. While at home, she had started to feel nauseated after lunch (which she initially attributed to food poisoning). Ex. 10 at 53; *see also* Ex. 8 at 80. Thereafter, Petitioner projectile vomited, followed by sudden onset of an intense headache. Ex. 8 at 83. She then felt extremely weak, and laid on the floor in the bathroom and could not stand up, but was able to crawl to a phone to place a call to her son and 911. *Id*. at 80. Petitioner did not at this time mention the malaise and other purportedly vaccine-related symptoms she claims to have been experiencing for the prior month, although the extremely frightening nature of her immediate symptoms may have overwhelmed her ability to think clearly. Ex. 8 at 80.

On initial exam at BRMC, Petitioner displayed slurred speech, left facial droop, left homonymous hemianopsia (loss of left side of vision within both eyes), and decreased left upper and lower extremity strength with left-sided neglect. *Id.* A CT scan performed upon Ms. Schultz's arrival revealed a right-sided insular bleed into the semicentrum ovale and right lateral ventricle of her brain. *Id.* at 80, 126. A CTA[3] head and neck scan performed at the same time was consistent, observing "mild-to-moderate subacute right cerebral hematoma with mild extension ventricles [and] mild mass effect minor brain herniations." *Id.* at 127. There was also some mid-line shift and edema as well, although coagulation and platelet studies were normal, and there was no need for ventricular drainage. *Id*. at 126–32. BRMC's neurosurgery unit thereafter followed Petitioner for several days, but saw no additional concerning developments, and she had stable serial CT scans as well over a 24-hour period. *Id*. at 78.

Ms. Schultz remained at BRMC until December 5, 2013. At discharge, she was noted to have likely experienced an intracranial bleed deemed spontaneous, due to her lack of history of hypertension or anticoagulation, plus the absence of evidence of aneurysm from the CT stroke study. *Id.* at 77. Petitioner admitted taking Motrin in the past for her back but was instructed to avoid it for several months at least. *Id*. She was deemed to warrant medical management and observation, but no neurologic interventions were proposed. *Id.*

Thereafter, Petitioner was transferred to BRMC's acute rehabilitation section, where she

[3] CTA stands for "computed tomography angiography," and involves an injection of contrast material into blood vessels, performed in conjunction with standard CT scanning to help diagnose and evaluate blood vessel disease or related conditions, such as aneurysms or blockages. *Mosby's Manual of Diagnostic and Laboratory Tests* 1090 (5th ed. 2014) (hereinafter "*Mosby's*").

remained from December 6, 2013, to February 4, 2014. *Id.* at 166–68. She improved with physical therapy, and by the time of discharge could ambulate with a cane, and also was able to perform most activities of daily living with minimal assistance. *Id*. She did, however, retain some mild cognitive deficits with impaired safety awareness, problem solving, and task execution, and also displayed mild slurred speech. *Id*. at 166–68. CT scans performed during admission showed a hematoma in evolution. Ex. 10 at 40–42.

C. *Treatment in 2014*

Petitioner subsequently received inpatient subacute rehabilitation at Greenfield Health & Rehabilitation Center in Lancaster, New York, from February 4, 2014, to May 2, 2014. Ex. 8 at 185, 192. During this time period, she informed her primary care physician in a phone message of her belief (recorded now for the first time in the medical history) that her stroke might be associated with the flu vaccine she had received, repeating the allegation to treaters at a neurosurgical clinic. *Id.* at 146, 171.[4] During this second round of rehab, Petitioner became more able to perform most daily living activities independently, although she needed a cane (plus some assistance to walk longer distances), and experienced improved left leg strength but continued left arm flaccidity. *Id*. at 193–94. By May 5, 2014, home health physical therapy was deemed appropriate. *Id.* at 179.

On July 30, 2014, an MRA[5] of Ms. Schultz's head showed minor atherosclerotic disease but was otherwise normal and non-acute. Ex. 10 at 14. It was thus deemed consistent with remote hemorrhagic stroke and probable secondary degeneration in the area. *Id*. at 17. However (as a medical record from an August 2014 follow-up visit with the neurosurgery department at Erie County Medical Center indicated), Petitioner's records were now consistently, if erroneously, suggesting that her December 1st stroke onset had occurred *one week* after receipt of the flu vaccine (when in fact—and regardless of whether it was related—onset actually occurred no sooner than five to six weeks post-vaccination). *Id.* at 1. Because the hemorrhage had completely resolved, Petitioner was instructed to follow up as needed. *Id*. at 2.

A September 2014 neurology consultation similarly indicated few lingering symptoms, beyond some mild left leg weakness and fatigue of uncertain etiology (although Petitioner expressed the view that it might be associated with a statin drug she took). Ex. 7 at 38–41. Petitioner did, however, find that the lifestyle impact of her December 2013 stroke had caused some psychological sequelae, and she was therefore referred to a psychologist on October 21, 2014. Ex. 11 at 18. Petitioner had another neurology visit in mid-December 2014, following an episode of gait imbalance earlier that month plus a brief ER visit that ruled out new stroke. Ex.

[4] In both cases, Petitioner incorrectly informed these treaters that her stroke occurred within one to two weeks of vaccination. Ex. 8 at 146, 171.

[5] MRA, or magnetic resonance angiography, is a noninvasive procedure that utilizes radio waves and magnetic fields to visualize blood flow and identify possible blockages in arteries. *Mosby's* at 1189.

5 at 30–31. Radiographic studies, however, were normal. Ex. 7 at 32–34.

D. *2015 and Thereafter*

Despite the generally favorable prognosis for Petitioner's post-stroke recovery, she continued to experience some sequelae in 2015 that treaters deemed likely associated with her December 2013 incident (although not all of her medical visits directly pertained to it). Thus, at a June 26, 2015 neurology follow-up, petitioner was noted to have continued fatigue and headaches that occurred during therapy for her left hand and arm. Ex. 7 at 29. An exam did revealed improvements—she now had only mild weakness at the left ankle and could raise her left arm to shoulder level—but she otherwise continued to have issues with distal arm weakness and partial fisting of the hand. *Id*. The neurology department treaters, however, elected to follow her weakness rather than directly treat it, and subsequent follow-up visits she had mainly involved Botox treatments for her hand. *Id*. at 29, 45.

Ms. Schultz went back to her primary care physician in September 2015, but she was largely complaining of chronic back pain and its impact on her ambulation, or sinus problems, rather than stroke sequelae. Ex. 4 at 9–11. At an occupational therapy appointment on October 21, 2015, Petitioner (now professionally retired) was noted to be capable of many activities of daily living (e.g., driving), but did require assistance with personal grooming and many domestic activities (e.g., cooking, laundry, etc.). Ex. 6 at 8–11. She did, however, demonstrate better movement and control of her left arm, although some issues with her left hand remained. *Id.* at 7–10. Examination by her primary care provider in December 2015 revealed continued mild weakness with flexion of the left elbow, along with her need of a cane to ambulate. Ex. 4 at 3.

Ms. Schultz's capacity for self-care continued to improve into 2016. Ex. 19 at 9. Although she saw a counselor for her mood disorder and her handling of chronic pain through May 2016, the pain was observed not to be obstructing her daily living. *Id*. at 15–22. Her neurologic issues also continued to lessen, except for ongoing problems with her left arm and hand, which were treated with Botox injections. Ex. 15 at 21–23. By February 2016, Petitioner was able to discontinue physical therapy. *Id.* at 19. She also had additional rehabilitation and neurologic follow-up visits in the summer of 2016, some of which considered alternative treatments for her December 2013 stroke, such as transcranial magnetic stimulation. *Id.* at 4, 6–7. Her persistent back pain was attributed to spinal disease, however, rather than the prior stroke. Ex. 18 at 3.

E. *Record Evidence of Vaccine Causation*

The record contains some instances in which treaters discussed with Ms. Schultz a potential association between her vaccination and subsequent stroke. However, these instances are mostly either contained in medical history recitations or reflect the *Petitioner's* comments to treaters. They largely do not reveal reasoned comment by a doctor raising the possibility of

an association, and none are contemporaneous with the time of stroke itself.

For example, the record contains a note from Petitioner's June 2, 2015 visit to her primary care physician, stating that Petitioner "believes influenza vaccine triggered stroke," and that therefore it was appropriate to submit a VAERS[6] report. Ex. 4 at 22; *see also* Ex. 24; Ex. 25. In response, such a report was thereafter completed on July 23, 2015, by Frederick Elliott, M.D., setting onset of Petitioner's stroke on December 1, 2013, as well as the fact that approximately thirty days prior (rather than the week or so that earlier records purport) Ms. Schultz had begun experiencing initial symptoms of the kind mentioned above (i.e., fatigue, malaise, decreased appetite, etc.). Ex. 3 at 1. A year later, at Petitioner's physical medicine and rehabilitation evaluation with Amrit Singh, M.D., in June 2016, the same vaccination a month prior to stroke was noted. Ex. 20 at 1–4.

## II. Hearing Testimony

### A. *Expert Witnesses*

#### 1. Dr. Yehuda Shoenfeld

Dr. Shoenfeld was the first of Petitioner's experts to testify, and he did so in association with the single expert report he filed. Tr. at 52–109; Expert Report of Dr. Yehuda Shoenfeld, filed as Ex. 37 on Nov. 3, 2017 (ECF No. 33-1) ("Shoenfeld Rep.").

Dr. Shoenfeld specializes in internal medicine, clinical immunology, and allergy. Tr. at 53. He serves as head of The Center for Autoimmune Diseases at Sheba Medical Center in Tel-Aviv, Israel, and he also acts as the Incumbent of the Laura Schwarz-Kipp Chair for Research of Autoimmune Diseases at Tel-Aviv University. Shoenfeld Rep. at 1; Curriculum Vitae of Dr. Shoenfeld, filed as Ex. 38 on Nov. 3, 2017 (ECF No. 33-2) ("Shoenfeld CV"). Dr. Shoenfeld has spent his career researching autoimmune and rheumatic diseases, and he is extensively published in these fields. Shoenfeld Rep. at 1; Shoenfeld CV at 3–4, 20–122.

Dr. Shoenfeld is admittedly not an expert in stroke or cerebrovascular injury. He nevertheless claimed that his overall experience with internal medicine had exposed him to individuals who had experienced some kind of "cerebrovascular incident" like stroke. Tr. at 56. He also maintained that literature he has authored on the connection between the flu vaccine and autoimmune disease includes some reference to this kind of injury, although he seemed to suggest that such writing has yet to be published. *Id.* at 56. He admitted, however, that he does not routinely

[6] The Vaccine Adverse Event Reporting System ("VAERS") is a national warning system designed to detect safety problems in U.S.-licensed vaccines. *See About VAERS*, https://vaers.hhs.gov/about.html (last visited Jan. 21, 2020). It is managed by both the CDC and the FDA. VAERS monitors and analyzes reports of vaccine related injuries and side effects from both healthcare professionals and individuals.

see stroke patients, and could not precisely state whether or when he had seen a patient with a cerebrovascular accident associated with brain bleeding as here. *Id.* at 75–77.

Dr. Shoenfeld's overall view was that Ms. Schultz's particular stroke manifestation, "intracerebral bleeding," was not predicted by her medical history, given the absence of any commonly-associated risk factors. Tr. at 57–58. She had no history of hypertension or diabetes, had not been a smoker, and was not taking medications that would make her prone to bleeding. *Id.* at 48. He also deemed Ms. Schultz relatively young for such an incident. *Id.* at 57.[7] By contrast, Dr. Shoenfeld believed that Petitioner likely had a genetic propensity for autoimmune disease, given the fact that she had experienced thyroid disease, and others in her family had suffered from inflammatory bowel disease. *Id.* at 59, 80, 83 ("all autoimmune diseases are genetic"). He opined that Ms. Schultz's stroke was also likely the product of an autoimmune reaction to vaccination. Shoenfeld Rep. at 7.

As a backdrop to this aspect of his opinion, Dr. Shoenfeld explained autoimmunity as a general concept. An autoimmune disease involves the immune system being "redirected" against the self, with some individuals being more prone genetically to experiencing such an aberrant immune response. Tr. at 59–60. Women are particularly likely to experience autoimmune disease, something Dr. Shoenfeld attributed to hormonal stimulation that causes the female immune response to be particularly sensitive and robust. *Id.* at 60–61. What would often trigger this response, he maintained, was some kind of environmental factor. *Id.* at 60. A person with the proper susceptibility would be subject to a large variety of possible triggers. *Id.* at 85.

The flu vaccine, Dr. Shoenfeld maintained, was just such a factor. He deemed the flu vaccine "quite notorious" in having the capacity to induce a variety of autoimmune diseases—in particular, ones associated with "nervous system involvement," such as Guillain-Barré syndrome. Tr. at 61–62. He also proposed that the wild flu virus *itself* could precipitate an autoimmune reaction, via induction of autoantibodies attacking self-cerebral/vascular constituents, and that vaccination had been shown to reduce these incidents (thus bulwarking the wild virus's association). *Id.* at 62–63. He offered some literature supporting an association between infection and ischemic stroke. *See, e.g.*, Shoenfeld Rep. at 9, referencing H. Emsley, et al., *Acute Ischaemic Stroke and Infection: Recent and Emerging Concepts*, 7 Lancet Neurology 341–53 (2008), filed as Ex. 56 (ECF No. 50-9). A vaccine, like the flu vaccine, could potentially trigger the same reaction, given that it contained wild virus molecular components, even if the chances of stroke after wild virus infection were greater. Tr. at 63.

This proposed association between the vaccine and vascular injury, Dr. Shoenfeld

[7] When asked what kind of evidence Dr. Shoenfeld would deem necessary to rule out the vaccine, he said only the *presence* of such definitive alternative explanations. Tr. at 105–06.

maintained, was bulwarked by certain items of filed literature. Tr. at 68, referencing T. Watanabe, *Vasculitis Following Influenza Vaccination: A Review of the Literature,* 13 Current Rheumatology Revs. 1–9 (2017), filed as Ex. 85 (ECF No. 53-8) ("Watanabe"). Dr. Shoenfeld characterized Watanabe as a "wonderful" review article, in addition to providing direct research support for his contentions. Tr. at 69. Watanabe considered 65 individuals (taken from 45 case reports) who reported receipt of the flu vaccine before experiencing some form of vasculitis—although the article explored a number of systemic vasculitides or forms of vasculitis different from what Petitioner is alleged to have experience, with only one identified case involving cerebral hemorrhage after ANCA-associated vasculitis (a form that is not alleged to have occurred in this case).[8] Watanabe, *supra*, at 5. Dr. Shoenfeld nevertheless found significant Watanabe's reporting of post-flu vaccine vasculitis, even though the article itself could only associate the two events temporally. Tr. at 96–98.

Dr. Shoenfeld proposed some biologic mechanisms by which the flu vaccine could instigate an autoimmune reaction leading to cerebral vasculitis, referencing molecular mimicry, epitope spreading, and/or bystander activation (all mechanisms frequently invoked in Program cases to explain how vaccination might induce autoimmunity). Shoenfeld Rep. at 12–13. He also attempted to establish the existence of amino acid sequence homology between the wild virus components of the flu vaccine and human body constituents in the relevant location (here, vascular structures in the brain). Tr. at 64, 88–89. Through "BLAST" searches,[9] Dr. Shoenfeld identified several self-associated amino acid sequences contained in brain proteins that are homologous to sequences in the wild flu virus. Due to their function (and capacity to enable hemorrhage) if autoantibodies are generated in response to the flu wild virus, vaccine components could theoretically also mistakenly attack the self-structures. *Id.* at 65–68, 89–90; *see also* Table 2 to Shoenfeld Rep. at 29. Eventually an inflammatory process initiated by autoimmune attack would precipitate the bleeding. Tr. at 65–66, 73–74. However, and even though his overall testimony seemed to embrace an adaptive immune response as causal herein (e.g., the production of autoantibodies cross-reacting with self-tissue structures), Dr. Shoenfeld felt that Petitioner's reaction was probably also encouraged by an innate response, amplified by her prior life exposure to the wild flu virus. *Id.* at 106–07.

As Dr. Shoenfeld admitted, it could not readily be corroborated by the existing record that the mechanism of molecular mimicry, mediated by autoantibody attack, more likely than not

[8] A sub-type of vasculitis—p-ANCA vasculitis—is distinguishable from other vasculitides due to the presence of antineutrophil cytoplasmic autoantibodies believed to be associated with the condition. *Dorland's* at 2026.

[9] A "BLAST" search involves a bioinformatics algorithm that computes the level of similarity between amino acid sequences contained in viral particles and humans. Tr. at 64–66. The analysis in this case was conducted by searching an online database for homologous amino acid sequences contained in the flu vaccine administered to Petitioner and the sequences commonly associated with intracerebral stroke, vascular disease, transient ischemic attacks and/or cerebral infarction, and ruptured vessels. *See* Schoenfeld Rep. at 13, 28–32.

caused Petitioner's stroke—but he represented that the kind of proof that might substantiate that conclusion, like a brain biopsy, could not safely be performed. Tr. at 86–88. When confronted by the possibility that homologies could exist with respect to human tissue structures that were *not* disease-associated (given the lack of evidence frequently associating vaccination with such events), Dr. Shoenfeld responded that it was actually the overall genetic susceptibility that was the "x factor" in this case. *Id.* at 92.

Dr. Shoenfeld also testified as to the propriety of the timeframe of Ms. Schultz's stroke onset.[10] He deemed her onset reasonable, noting that thirty to forty days from vaccination to cerebrovascular incident was appropriate for an autoimmune reaction. Tr. at 70–71. The fact that Petitioner had likely had prior exposure to the wild flu virus also made the timeframe reasonable. *Id.* at 71 ("[n]obody can escape from the influenza"). In his opinion, Petitioner's earlier, malaise-like symptoms were evidence of her initially-strong immune response, which progressed to bleeding once the production of autoantibodies was complete. *Id.* at 73–74. He proposed that these kinds of symptoms were not uncommon after vaccination, but (unlike Ms. Shultz) would usually subside after a few days. *Id.* at 84–85. At bottom, he felt that the fact that the vaccine had been received within about a month of onset was too significant a fact to ignore. *Id.* at 92.

On cross, Dr. Shoenfeld was asked several questions about the grounds for his contention that stroke could be considered autoimmune at all, let alone an autoimmune-mediated injury. He agreed that instances of cerebral vasculitis with a single brain bleed (effectively what Petitioner experienced) were not routinely deemed to require surgical intervention (especially in the absence of evidence of a brain aneurysm) and were more often than not left untreated. Tr. at 77–78. Rather (and especially if the instance was not found to be attributable to a kind of vasculitis), the patient would be observed, and not likely treated with the kind of immunomodulating medications used in vasculitides known to be associated with certain autoantibodies. *Id.* at 78–80.

An overarching issue in Dr. Shoenfeld's testimony was the degree to which he assumed that Ms. Schultz's injury was properly viewed as a *kind* of vasculitis. Tr. at 100–01. Certain elements of his report, or filed literature like Watanabe, refer to vasculitides facially not relevant to this case—nor was Petitioner ever so diagnosed. *See generally* Watanabe, *supra*. Dr. Shoenfeld nevertheless maintained that Petitioner's injury could be considered a "cerebral vasculitis," the precise diagnosis of which would be difficult to corroborate, due to location of the bleed and the dangers associated with brain biopsies. Tr. at 100–02. Even if she had not experienced the *disease* of vasculitis, the inflammation of her blood vessels resulting in bleeding constituted a vasculitic

[10] Consistent with the opinions he has offered in other cases, however, Dr. Shoenfeld could not resist stating his overarching view (a view I have specifically criticized before, and one that has not found favor on appeal) that significantly longer onset timeframes (potentially measured in years) are reasonable for at least some injuries, despite what is more commonly "accepted" as medically reasonable in Vaccine Program cases. Tr. at 70–71, 95 (discussing possible 10-year incubation for systemic lupus erythematosus).

*mechanism*. *Id.* at 101–02. And even though other kinds of vasculitides (for example, p-ANCA vasculitis) have known associations with identified antibodies, that does not preclude the possibility of establishing that the kind of injury Petitioner experienced is also associated with an as-yet-unidentified autoantibody sometime in the future. *Id.* at 103–04.

2. Dr. Laura Boylan

Dr. Boylan, a neurologist, also testified in support of Petitioner, expanding upon the opinions set forth in her written reports. Tr. at 109–66; Expert Report of Dr. Laura Boylan, filed as Ex. 23 on Mar. 31, 2017 (ECF No. 24-1) ("Boylan Rep."); Supplemental Expert Report of Dr. Laura Boylan, filed as Ex. 31 on July 5, 2017 (ECF No. 29-1) ("Boylan Supp. Rep.").

Dr. Boylan is a board-certified neurologist, and she currently serves as an attending neurologist at Bellevue Hospital Center in New York City as well as a casual staff neurologist at St. Mary's Medical Center/Essentia Health in Duluth, Minnesota. Curriculum Vitae of Dr. Boylan, filed as Ex. 39 on Dec. 6, 2017 (ECF No. 34-1) ("Boylan CV"). She obtained a Bachelor of Arts from Barnard College, followed by a medical degree from Columbia University College of Physicians & Surgeons. *Id.* at 1. She then completed an internship at St. Vincent's Hospital and a residency in neurology at The Neurological Institute at Columbia-Presbyterian Medical Center in New York City. *Id.* at 2. Dr. Boylan has served as an instructor and professor on the subject of neurology, and she has published numerous articles on the topic. *Id.* at 8–12. Although Dr. Boylan is admittedly not a specialist in stroke, she has familiarity via her teaching responsibilities with focal cortical syndromes, which would encompass stroke. Tr. at 112. She has otherwise treated stroke patients and classified the condition as a "subspecialty within neurology." *Id.* at 114.

Dr. Boylan began her testimony with an overview of stroke. She defined stroke to be any "damage to the brain of vascular origin," although the kinds of stroke can otherwise vary. Tr. at 115. Thus, an "ischemic stroke" involves a lack of blood flow through the vessels to the brain, while a "hemorrhagic stroke" (what Ms. Schultz experienced) features vessel rupture causing a damaging "excess burst of blood" into the brain. *Id.* at 115–16, 135–36. Strokes can occur both with those vessels that carry blood out of the brain (the veins) as well as the arterial vessels bringing blood to the brain (the kind of vessels involved in Ms. Schultz's stroke). *Id.* at 116. Despite the opinion she offered in this case, Dr. Boylan allowed that a stroke could be idiopathic in origin or merely coincidental to vaccination. *Id.* at 158–59, 161.

Cerebral vasculitis, by contrast, is an uncommon inflammatory autoimmune disorder of both arteries and veins in the brain. Tr. at 116, 120–21. In it, the processes of the immune system would attack the vessels themselves, causing blockage or rupture. *Id.* at 118–19, 121. It can present not only with an ischemic stroke "but also with haemorrhage, encephalopathy and tumour-like brain lesions." P. Kempster, et al., *Ten Year Clinical Experience with Stroke and Cerebral*

*Vasculitis*, 27 J. Clinical Neurosci. 119–25 (2017), filed as Ex. 26 (ECF No. 25-2) ("Kempster"), at 119. Also referred to as "cerebral angiitis," Kempster observes that it can be difficult to diagnose but is often suspected in patients who present with multiple infarcts (vessel blockages) or evidence of arterial narrowing, or secondary to some other known systemic form of vasculitis. *Id.* at 120. It often initially presents as stroke (although, at least in the cases reviewed in Kempster, more often as ischemic rather than hemorrhagic stroke). *Id.* at 120–21, 124. Kempster's authors ultimately deemed cerebral vasculitis too uncommon to be considered or tested for as part of a differential diagnosis when screening patients who present with stroke. *Id.* at 125.

A cerebral vasculitis would typically have some kind of environmental trigger (and Dr. Boylan seemed to embrace the idea that a trigger and cause were difficult to distinguish). Tr. at 121, 156. In addition, as the result of an autoimmune process, it could present with a "prodromal phase" before the direct brain harm occurred. *Id.* Vasculitides in general did not have to always be systemic but could involve only one organ. *Id.* at 159–60. Dr. Boylan agreed that not all strokes (and specifically hemorrhagic ones akin to what Ms. Schultz experienced) are autoimmune in nature. *Id.* at 162. However, she ultimately opined that "*acute* provocations which cause a surge in the body's auto-immune response" could cause neurological injury, and such provocations would include (in rare cases) vaccines. Boylan Rep. at 2.

Like Dr. Shoenfeld, Dr. Boylan maintained that diagnosing an autoimmune-caused cerebral vasculitis was difficult in the absence of a brain biopsy, an invasive test that would rarely be performed. Tr. at 117. It also would often involve extremely small vessels likely too minute to capture in normal vascular imaging. *Id.* at 119–20; Boylan Rep. at 5. As a result, a patient's cerebral vasculitis diagnosis would more often than not be dependent upon the "whole clinical picture of the patient," rather than a specific test result. Tr. at 118.

Further echoing Dr. Shoenfeld, Dr. Boylan went on to delineate a possible association between the flu vaccine and cerebral vasculitis. First, she represented that it was beyond dispute that a wild virus flu infection could cause vasculitides generally, including cerebral vasculitis. *Id.* at 122–23. She also noted that even a minor infection could be sufficient to trigger an acute ischemic stroke, directly or even as a result of the indirect effect of inflammation caused by the infection. *Id.* at 123–25; H. Fullerton, et al., *Infection, Vaccination, and Childhood Arterial Ischemic Stroke*, 85 Neurology 1459–66 (2015), filed as Ex. 29 (ECF No. 25-5) ("Fullerton"). Indeed, although Fullerton (which was limited to evaluation of childhood cases of arterial ischemic stroke) suggested that vaccines could lower the known associated risk of vasculitic events caused by wild infections, Dr. Boylan maintained that Fullerton allowed for the possibility of an *increased* stroke risk *after* vaccination due to transient inflammation (although Fullerton in fact disavows that proposition). Tr. at 125–26; Fullerton, *supra*, at 1464 ("[v]accines could conceivably . . . transiently increase risk by causing inflammation. In our analyses, all adjusted for age, *we found*

*only a protective effect of vaccination*" (emphasis added)).[11] And she relied to some extent on the proposition that if a particular wild virus were associated with a disease or pathologic condition, then the vaccine based upon it could (in rare cases) do the same. Tr. at 156–58.

Dr. Boylan also offered case reports involving instances of stroke after receipt of flu vaccines, and she argued these articles constituted reliable evidence associating the two. Tr. at 128–29, 131–32; R. Mader, et al., *Systemic Vasculitis Following Influenza Vaccination – Report of 3 Cases and Literature Review,* 20 J. Rheumatology 1429–31 (1993), filed as Ex. 27 (ECF No. 25-3) ("Mader"); Y. Lin, et al., *Ischaemic Stroke and Influenza a H1N1 Vaccination: A Case Report*, 7 Archives Med. Sci. 2:345–48 (2011), filed as Ex. 28 (ECF No. 25-4) ("Lin"). Lin involved a single case in which an elderly male experienced posterior circulation ischemia within twelve hours after receiving the flu vaccine (thus consistent with the proposition that transient post-vaccination inflammation could be causal of a vasculitic reaction). Lin, *supra*, at 348. Such a rapid timeframe is of course not at all consistent with Petitioner's experience in this case.

Mader considered three cases of systemic vasculitis following flu vaccines and suggested the possibility that the vaccine could induce an "aberrant hypersensitivity state," potentially amplified by the culturing process by which the vaccine was created. Mader, *supra*, at 1429–30. Mader also referenced another article (not filed in this case) that in approximately nine percent of an unspecified number of studied patients, individuals experienced a flu-like malaise a few weeks after vaccination, although with no other particular identified adverse event, whether stroke, vasculitis, or otherwise. *Id.* at 1431. Dr. Boylan deemed this consistent with what Ms. Schultz experienced, which she considered to be some kind of autoimmune-derived inflammatory process occurring before her stroke. Tr. at 129–30. Dr. Boylan admitted on cross, however, that neither Mader nor Lin directly established that the flu vaccine was causally related to stroke or vasculitis, and also agreed that some of the literature she offered generally did not differentiate between ischemic and hemorrhagic stroke. Tr. at 153–55.

Besides opining on a proposed association between the flu infection/vaccine and cerebral

[11] In the course of examining Dr. Boylan about the meaning of this finding in Fullerton, Petitioner's counsel posed a question that seemed to challenge the very import of a finding that a given vaccine is not, from a statistics perspective, meaningfully associated with a particular injury (here, stroke). *See* Tr. at 127 ("[i]f a paper says that there is no statistical increased risk of stroke, does that mean it can't happen [to an individual]?"). But this question (which reflects a common sentiment among Vaccine Program claimants) betrays a mistaken conflation of the *kinds* of evidence a Petitioner may offer with the *weight* to be afforded the evidence that *is* offered.

Thus, Vaccine Act petitioners may prevail without offering sound statistical or epidemiologic evidence to support an alleged association between vaccination and a given injury. This broad standard of the kind of evidence Petitioners can marshal fairly takes into account the fact that vaccine injuries are rare, and hence a number of indirect pieces of evidence may be required to prevail. But reliable statistical studies that undermine the conclusion that a vaccine would *likely* cause a particular injury *does* reduce the effectiveness of a claimant's preponderant showing—and simply attempting to rebut such evidence with the argument "vaccine injuries are rare" is inadequate.

vasculitis generally, Dr. Boylan also discussed how either infection or vaccine could produce stroke via the same autoimmune mechanism. Tr. at 127. Vaccines contain components of the wild virus they are directed against, and thus (even taking into account the relevance of genetic susceptibility) the same homologies between amino acid sequences in the wild virus proteins and self/human structures that are at play in an autoimmune cross-reaction would also occur between the vaccine components and self-amino acid protein sequences. *Id.* at 127–28.

Dr. Boylan went on to review Ms. Schultz's medical records, testifying how they corroborated Petitioner's causation theory. Consistent with Dr. Shoenfeld, Dr. Boylan deemed significant the fact that pre-vaccination, Ms. Schultz was overall quite healthy and active, lacking the kinds of risk factors commonly associated with stroke, and also relatively young to have experienced stroke. Tr. at 134–35. The evidence from the time of Petitioner's post-stroke ER visit did not establish hypertension or any of the other kinds of risk factors that more commonly would be present in stroke patients. *Id.* at 138–40. It was unusual, in Dr. Boylan's view, for a patient to suffer the sort of intracranial bleed Petitioner experienced without hypertension or evidence of some other cause. *Id.* at 142–43. In Ms. Schultz's case, no other cause for the stroke was identified. *Id.* at 143–44. The record[12] also confirmed that Ms. Schultz had experienced a "systemic, nonspecific inflammatory prodrome" in November 2013 before her stroke event, characterized by malaise and a lack of energy that caused her to miss work. *Id.* at 135, 160–61. Dr. Boylan deemed this to corroborate the fact that the flu vaccine was responsible for the subsequent stroke, because it established that her immune system was, over time, "gearing up" to the direct injury she ultimately experienced. *Id.* at 136–37.

On cross, Dr. Boylan acknowledged that Ms. Schultz did not have a systemic form of vasculitis, that her alleged prodrome did not feature some symptoms that would be considered vasculitic, and that there was some latency before they manifested. *Id.* at 150–51. Dr. Boylan also presumed that Ms. Schultz experienced worsening symptoms between vaccination and her stroke event, although she was somewhat nonspecific about which symptoms worsened or how. *Id.* at 152–53.

In discussing the absence from the medical record of identified causes for Petitioner's stroke, Dr. Boylan questioned some alternative explanations offered by Respondent. For example, although one of the antidepressants Ms. Schultz had been taking has been associated with hypertension (which in turn could lead to stroke), no treaters had ever concluded that she in fact was hypertensive. *Id.* at 144. In addition, even if certain cholesterol-controlling statins can be linked to stroke, Petitioner was not taking such medication at the time of her event. *Id.* at 145. And

[12] Dr. Boylan admitted that she relied heavily on Petitioner's own representations about her health during November 2013 rather than any independent medical evidence, although she maintained that (as a health care provider herself), Ms. Schultz was the kind of person not likely to immediately seek medical intervention, and also that other corroborative evidence (for example, proof of her absences from work) for these allegations likely existed. Tr. at 165–66.

no record evidence (including certain post-stroke imaging) supported the possibility that she had any kind of arteriovenous malformation (nor did any treaters ever reach that conclusion based on the record). *Id.* at 146–48. All that remained was the determination that the stroke could have been cryptogenic, or idiopathic (of unknown cause)—a conclusion that, in Dr. Boylan's view, was undercut by the actual record evidence of vaccination and subsequent prodrome. *Id.* at 148–49.

Dr. Boylan acknowledged that she did not possess an opinion as to the most likely post-vaccination onset for vaccine-caused stroke generally. Tr. at 153. But to support the reasonableness of the timeframe Ms. Schultz experienced, Dr. Boylan referenced a different item of literature filed by Respondent. Tr. at 132; L. Smeeth, et al., *Risk of Myocardial Infarction and Stroke After Acute Infection or Vaccination,* 351 N. Eng. J. Med. 2611–18 (2004), filed as Ex. E (ECF No. 61-3) ("Smeeth"). Smeeth is an observational study employing the self-controlled case-series method[13] that sought to evaluate the degree to which instances of acute/abrupt inflammation (whether instigated by a wild virus infection or vaccination) could be the cause of "a short-lived increase" in the incidence of stroke or myocardial infarction. Smeeth, *supra*, at 2612.

Relying on data from the United Kingdom's General Practice Research Database derived from the 1987-2001 time period, Smeeth's authors considered the incidence of stroke after administration of three vaccines, including the flu vaccine, as well as after onset of a respiratory or urinary tract infection. *Id.* at 2615. For approximately 19,000 individuals who reported stroke, the incidence rate was lower than expected for anyone who experienced stroke up to 28 days post-vaccination, and for those who experienced stroke 29-91 days after vaccination was almost identical to the baseline incidence rate. Table 1 at *Id.* By comparison, the incidence rate for the same periods was across-the-board higher for individuals who first experienced an infection then stroke. *Id.* From this, Smeeth's authors concluded that "[t]he mild transient inflammation . . . induced by vaccination *does not appear to translate into a detectable increase in the risk of vascular events*." *Id.* at 2618 (emphasis added).

Despite the fact that Smeeth seems largely to undercut Petitioner's case, Dr. Boylan attempted to note methodologic deficiencies in its analysis. For example, she interpreted a chart in Smeeth to demonstrate that even if a "tighter" temporal relationship between stroke and wild infection existed (when compared to the time between stroke and vaccination), Smeeth still revealed 409 instances (among the 19,000 flu vaccination events considered, but still a "large percent" of the total) in which the relevant individual experienced a stroke within 15 to 28 days of vaccination—not much less than the five week period at issue for Ms. Schultz's stroke. Tr. at 132–

[13] A self-controlled case-series study uses subject cases as their own controls. The age at vaccination is regarded as fixed, and the random variable is the age/time at which the adverse event is experienced, conditionally on its occurrence within a predetermined observation period. Institute of Medicine, *Adverse Effects of Vaccines: Evidence and Causality* 644 (2012) (hereinafter "IOM Report").

33, *citing* Smeeth, *supra*, at 2615.[14] Additionally, Smeeth's authors did not attempt to evaluate the actual cause of stroke any of this sub-cohort (and thus could not completely preclude the possibility that a stroke was vaccine-caused). Tr. at 133.

In the end, however, Dr. Boylan placed some weight on the sheer temporal relationship between vaccine and stroke—although she maintained that her conclusions were greatly bulwarked by the November 2013 "sustained inflammatory-type prodrome illness" Petitioner had reported experiencing. Tr. at 149. She also proposed that Petitioner's overall course, which featured mild symptoms that did not immediately occur after vaccination, was nevertheless reasonable given the time she felt it would appropriately take for the immune system to "ramp up" in an autoimmune reaction. *Id.* at 151.

3. Dr. Steven Messe

Dr. Messe, a vascular neurologist, was Respondent's sole testifying expert. Tr. at 167–222; Expert Report of Dr. Steven Messe, filed as Ex. A on June 16, 2017 (ECF No. 26-1) ("Messe Rep."); Supplemental Expert Report of Dr. Messe, filed as Ex. L on Jan. 19, 2018 (ECF No. 35-1) ("Messe Supp. Rep."). He opined that the flu vaccine did not cause Petitioner's stroke. Tr. at 174.

Dr. Messe is a board-certified neurologist and is currently employed by the Department of Neurology at the Hospital of the University of Pennsylvania. Curriculum Vitae of Dr. Messe, filed as Ex. B on June 18, 2017 (ECF No. 27-1) ("Messe CV"). He graduated with a Bachelor of Arts from Yale University and thereafter obtained his medical degree from the University of Michigan School of Medicine. Messe CV at 1. Dr. Messe then completed an internship and residency in neurology at the University of Pennsylvania. *Id.* He went on to complete a fellowship at the University of Pennsylvania—focusing on stroke and neurocritical care. *Id.* In addition to his clinical practice, Dr. Messe holds several academic appointments and serves on several editorial boards. *Id.* at 1–3. He himself has performed research and authored numerous publications relating to neurology—and more specifically on vascular neurology and stroke. *Id.* at 6–14; Tr. at 169–70.

Dr. Messe's clinical practice involves the frequent treatment of stroke patients. Tr. at 171–72. He estimated that fifteen to twenty percent of all strokes reported in the U.S. are intracerebral hemorrhages, consistent with what Ms. Schultz was diagnosed with, and so he regularly sees that kind of stroke in treating patients. *Id.* at 172. He less commonly experiences patients with vasculitis, although he attributed that in part to the rare nature of that condition. *Id.* at 172–73.

Dr. Messe defined Petitioner's injury as an intracerebral hemorrhage stroke. He deemed

[14] Dr. Boylan later acknowledged in her testimony that she may have in part mistakenly assumed that Ms. Schultz's onset was within 28 days of vaccination—shorter than the records actually show. Tr. at 163–65.

stroke generally a "very heterogenous disorder," and noted that a stroke's cause could not always be identified. Tr. at 181. Regardless of whether a known risk factor (for example, hypertension—which he acknowledged was not present in Ms. Schultz's case)[15] was to blame, however, the symptoms would be the same. *Id.* at 181–82, 188. Strokes typically present acutely, and therefore do not regularly feature preceding symptoms. *Id.* at 182. An infection, including a flu wild virus infection, could increase stroke risk, and could do so in some connection with an immune response, although he deemed the support for this (specifically proposed mechanisms by which it would occur) mostly speculative in nature. *Id.* at 192–95.

Dr. Messe contrasted the above with vasculitis, which he expressed doubt Petitioner had experienced. Tr. at 176–77. He accepted Dr. Shoenfeld's overall characterization of the autoimmune nature of vasculitis as a general matter, as well as its potential causes (such as a wild virus flu infection). *Id.* at 179, 192. He also acknowledged that a vasculitis affecting the central nervous system, like cerebral vasculitis, would be a "difficult diagnosis to make," but noted that to his knowledge the condition would be characterized by diffusion in the brain, rather than a single location or occurrence, and thus would be an "unheard of" diagnostic explanation for a single episode of bleeding, as Petitioner experienced. *Id.* at 175, 177. Vasculitis would also feature a "progressive and fulminant" presentation, including a prodrome of weeks or months, with an overall subsequent poor prognosis. *Id.* at 175, 182. Vasculitis usually is not diagnosed before presentation of a stroke, although (especially if it were a cerebral vasculitis) it would be reflected by pre-stroke symptoms like headache or possibly cognitive issues. *Id.* at 215. Other findings that would corroborate a vasculitis diagnosis would include evidence of inflammation from blood vessel studies or cerebrospinal fluid analysis. *Id.* at 177.[16] This did not in his view describe what Petitioner had experienced. *Id.* at 175, 177.

The actual medical history, in Dr. Messe's view, supported the stroke diagnosis over cerebral vasculitis. Petitioner's treaters conducted a full analysis of her condition, including a variety of scans and imaging tests, but did not see the kind of evidence of inflammation that would be expected if vasculitis were present. Tr. at 180. Likewise, they did not propose giving her immunosuppressive drugs—something that would not occur if vasculitis were thought to be present, as not treating such a condition in this way would result in "progressive brain injury with swelling, blockages, and/or bleeding" (none of which Ms. Schultz has experienced). Tr. at 179.

[15] At hearing, Dr. Messe similarly accepted that Petitioner's stroke had not likely been caused by prior use of a statin (even though his expert report had mentioned this possibility). Tr. at 191–92.

[16] Dr. Messe disputed the contentions of Petitioner's experts about the dangers of brain tissue biopsies, and thus the unavailability of such testing to confirm a contemplated cerebral vasculitis diagnosis. He maintained that such testing was done "all the time," especially if vasculitis was suspected, since the treatments for vasculitis involved drugs with many debilitating side effects (thus encouraging treaters to confirm the diagnosis with a biopsy before proceeding to treatment). Tr. at 178.

As for the cause of Ms. Schultz's stroke, Dr. Messe favored an idiopathic explanation, despite her absence of common risk factors. Tr. at 207, 209, 219–20. He maintained that a stroke brought on by intracranial bleeding was a frequent occurrence in his experience, and something that often had no clear explanation. *Id.* at 221–22. He also did not deem her purported pre-stroke symptoms from November 2013 to be significant or correlated to the stroke, although he suggested that one possible explanation—a "structural cause"—could have been ruled out via angiogram, but such a test was never performed. Tr. at 207–10.[17] Dr. Messe admitted, however, that he could not say for sure that such testing would have revealed a malformation, and that overall there was no evidence in the record to establish that she did. *Id.* at 212–13. He felt that the alleged prodromal phase of a potential autoimmune condition was especially unlikely to have anything to do with a hemorrhagic stroke. *Id.* at 209–10.

Dr. Messe rejected the concept that vaccines could cause stroke generally. He denied such a conclusion found support in the medical literature, and added that given the commonplace nature of vaccination and stroke, he would expect to have heard about the association far more if it were scientifically reliable. Tr. at 174. At best, there was some case report evidence associating infection, not vaccination, with ischemic stroke. *Id.* at 208. And case reports referenced by Dr. Boylan, like Lin or Mader, that seemed to propose an association between the flu vaccine and ischemic stroke were deemed by Dr. Messe inadequate proof of association. In Lin, for example, the kind of stroke in question—a "posterior circulation stroke" experienced by a 75-year-old—was in Dr. Messe's experience "incredibly common," making it unreasonable to deem it as possibly related to a prior vaccination. *Id.* at 208.[18] Watanabe also revealed only seven cases of a CNS-oriented disease out of the total 65 post-vaccination instances considered, none of which (unlike Ms. Schultz's case) involved intracranial bleeding, and thus supported the conclusion that post-vaccination vasculitis was extremely uncommon. *Id.* at 175, 185–86. Dr. Messe otherwise noted that case reports generally did not constitute robust evidence of causation on their own, although he admitted that they at least had value in suggesting the need for reliable controlled studies into the questions they raised. *Id.* at 209, 217–19.

At the same time, Dr. Messe contended that it was well understood (as reflected in the larger studies) that vaccination was more likely *protective* against stroke. Tr. at 176. He invoked Smeeth in support, observing that it both demonstrated a higher association between stroke and wild infection as well as the protective function of vaccination against infection. *Id.* at 183–84; Smeeth, *supra*, at 2615. He also observed that the study's large scale rendered it reliable in terms

[17] Dr. Messe disputed that the MRI imaging that was performed on Ms. Schultz was adequate to reveal a possible malformation. Tr. at 212–13. He thus did not concede that the MRA Petitioner later received could have provided the missing information, since it "essentially" employed MRI imaging techniques. *Id.* at 213.

[18] In similar fashion, when asked about the fact that most literature exploring a potential association between vaccination and vasculitis involved the flu vaccine, Dr. Messe maintained that this was the natural result of the fact that the flu vaccine was the most widely-administered vaccine. Tr. at 216.

of "power and precision," and that the allegedly large number of persons (409) who experienced a stroke in the fifteen to twenty-eight days after the flu vaccine had to be considered in light of the fact that the incidence of stroke for these individuals was twelve percent lower than the baseline rate (i.e., the expected incidence of stroke in those who did not receive the flu vaccine), and that this determination was deemed by Smeeth's authors to be statistically reliable. Tr. at 184–85.[19] He was not comfortable, however, opining as to whether evidence regarding a wild virus's capacity to cause stroke could be applied equally to vaccines. *Id.* at 195–96.

With respect to timing issues, Dr. Messe acknowledged (consistent with the testimony of Petitioner's experts) that a "post-vaccination autoimmune disorder" might manifest overall in a period of two to six weeks, thus allowing for onset in thirty-six days. Tr. at 189–90. He also agreed that the kinds of post-vaccination symptoms Petitioner testified to experiencing could establish the existence of some kind of systemic inflammatory response (which could also raise the possibility for a later vascular event such as stroke)—although he ultimately was not confident as to the significance of her purported symptoms. *Id.* at 199–201, 214.

B. *Fact Witnesses*

1. Ms. Carlene Schultz

Ms. Schultz's testimony at trial was consistent with the medical records. *See generally* Tr. at 5–39. She thus confirmed the date of vaccination, noting that she felt what she deemed "normal soreness" at the injection site, but that this was followed within a few days by malaise—a low-grade fever, low appetite, and fatigue. Tr. at 6, 8–9. To support her allegation that she missed work for a period of time in November 2013, she offered a calendar (only filed a few days before the hearing) that she purported established this fact. *Id.* at 10–11; Ex. 91 (ECF No. 65-1).[20] She admitted, however, that she never sought medical treatment for this malaise feeling, and that she had complained of tiredness prior to the vaccination at her October 2013 exam with her primary

[19] On cross examination, Petitioner attempted to limit Smeeth's significance, observing through questioning that (a) its authors did not evaluate what the possible causes were of the instances of post-flu vaccine stroke, or (b) the article's authors employed unreliable controls in terms of comparing vaccine recipients to baseline individuals. Tr. at 201–07. Dr. Messe maintained in response that the use of a patient as a "self-control" (meaning the study compared periods when a particular individual did receive a vaccination and experience the studied injury versus when they did not get vaccinated) was in fact a particularly strong and reliable control methodology. Tr. at 205–06. He otherwise opined that Smeeth's findings of the protective, rather than pathologic, role vaccines would play with respect to stroke were still scientifically valid. *Id.* at 206.

[20] It is not apparent why these calendar excerpts could not have been filed earlier, since (as Respondent's cross-examination pointed out) Petitioner purported that she ordinarily kept such a calendar for a period of time, before switching to an electronic version on her phone. Tr. at 30–31. The calendar also referenced an ambiguous trip around November 7, 2013, to "NYC"—a trip that (had she taken it) would undercut her present representations that she had been experiencing malaise in this time period sufficient to cause her to miss work. Petitioner claimed, however, the notation was to record her daughter's visit to Buffalo and then subsequent return, and she denied travelling at all that month. *Id.* at 37–38.

care provider. Tr. at 24–25.

Ms. Schultz also provided details about the medical incident she experienced December 1, 2013. The day before, she claimed that she had decided to attempt to engage in some activities of daily living despite the malaise she had been experiencing. Tr. at 13–14. She therefore went to the grocery store, although she purports to have begun feeling nauseated while shopping. *Id.* at 13. She made a salad to eat when she got home, but then within 15 minutes felt the urge to vomit. *Id.* This was followed by intense pain in her head, followed by a sensation of left side weakness that caused her to lay on the floor. *Id.* at 14. She was nevertheless able to crawl to a phone and call 911, which led EMS to find her and take her to BRMC. *Id*.

Petitioner acknowledged that around the time of the stroke, she came to believe the vaccine could have caused it based on her own Internet research, as well as her assessment that she lacked the necessary risk factors. Tr. at 26, 28. She also admitted that she may have first told treaters after being brought to BRMC that she had experienced some kind of "GI problem" rather than attributing the vaccine (although she added that her level of consciousness in the first days of treatment was variable, and she therefore could not precisely recall what she may have said or thought at the time). *Id.* at 30.

At hearing, Petitioner recounted the treatment she received, consistent to the records review discussed above. *See generally* Tr. at 15–17. She noted that the stroke she experienced had made it difficult to use her left hand, which in turn impacted her ability to perform a variety of daily living tasks. *Id.* at 17. It has also impacted her cognitive abilities, forcing her to cease working and pursuing educational goals, while requiring the assistance of in-home care. *Id.* at 17–19.

2. Ms. Zena Hyman

Ms. Hyman—a nurse practitioner like Petitioner—also offered factual testimony. Tr. at 40–52. Ms. Hyman is a work colleague, but more of a personal acquaintance of Ms. Schultz, having known her since the 1990s, when Ms. Hyman taught the Petitioner in a graduate school medical program. *Id.* at 42, 44.

Ms. Hyman testified about the time period of Petitioner's stroke, representing that Petitioner had not felt well after receiving the flu vaccine. Tr. at 43, 47. She could not affirmatively state, however, whether she had any contact with Ms. Schultz in the approximately five-week period between her receipt of the flu vaccine and onset of stroke symptoms. *Id.* at 48. She thus most likely learned about the pre-stroke symptoms that Ms. Schultz alleges to have experienced that November after Ms. Schultz's stroke, when the two spoke by phone while Ms. Schultz was hospitalized, or when Ms. Hyman visited Petitioner in person. *Id.* at 48–49. Ms. Hyman indicated she probably had these interactions with Petitioner between December 2013 and January 2014. *Id.* at 50. She also noted that to her understanding, Ms. Schultz's pre-vaccination symptoms were

likely distinguishable from her stroke symptoms, although she could not specify when she might have discussed such matters with the Petitioner. *Id.* at 51–52.

## III. Procedural History

After the filing of the Petition in May 2016, Ms. Schultz filed records relevant to her claim, completing the process by October of that year. Respondent's Rule 4(c) Report contesting Petitioner's entitlement to a damages award was subsequently filed in December 2016. ECF No. 20. Thereafter, the parties took turns filing expert reports prepared by the individuals mentioned above, and then in February 2018 I issued a scheduling order setting the hearing for April 2019. ECF. No. 40. That date, however, was reset at the parties' request to June 2019. ECF No. 46. The hearing occurred as scheduled, and the parties did not file post-hearing briefs.

## IV. Applicable Law

### A. *Standards for Vaccine Claims*

To receive compensation in the Vaccine Program, a petitioner must prove that: (1) they suffered an injury falling within the Vaccine Injury Table (i.e., a "Table Injury"); or (2) they suffered an injury actually caused by a vaccine (i.e., a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006). In this case, Petitioner does not assert a Table claim.

For both Table and Non–Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (explaining that mere conjecture or speculation is insufficient under a preponderance standard). On one hand, proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). But on the other hand, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Human Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

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

Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549. This standard was recently clarified by the Federal Circuit. *See Boatmon v. Sec'y of Health & Human Servs.*, 941 F.3d 1351, 1359–60 (Fed. Cir. 2019) (stating that the correct standard for *Althen* prong one is "reputable," and "sound and reliable" not a "lower reasonable standard" (internal quotations omitted)).

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. This is consistent with the petitioner's ultimate burden to establish his overall entitlement to damages by preponderant evidence. *W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted).[21]

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'")

[21] Although there has been some confusion in the past as to the evidentiary standard applicable to the first *Althen* prong, ample controlling authority stands for the more straightforward proposition that it is subject to a preponderance standard. *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1350 (Fed. Cir. 2010).

(quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs*., 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Veryzer v. Sec'y of Health & Human Servs.*, No. 06–522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356–57 (2011), *aff'd without opinion*, 475 F. App'x. 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 2013 WL 1896173 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11–355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Law Governing Analysis of Fact Evidence*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [ ] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are

contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Human Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (determining that it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

Medical records that are created contemporaneously with the events they describe are presumed to be accurate and "complete" (i.e., presenting all relevant information on a patient's health problems). *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Human Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd*, *Rickett v. Sec'y of Health & Human Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). This presumption is based on the linked propositions that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Human Servs.*, No. 11–685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Human Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms.").

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

There are, however, situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Human Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("'[w]ritten records which are, themselves, inconsistent, should be accorded less deference than

those which are internally consistent'") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Human Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Human Servs*., No. 90–2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *La Londe v. Sec'y of Health & Human Servs*., 110 Fed. Cl. 184, 203–04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. *Analysis of Expert Testimony*

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

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

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

In the Vaccine Program, however, the *Daubert* factors play a slightly different role than they do when applied in other federal judicial settings—e.g., the district courts. Typically, *Daubert* factors are employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable or could confuse a jury. By contrast, in Vaccine Program cases

these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Human Servs*., 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts of her own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen*, 618 F.3d at 1347 (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 (1997)); *see also Isaac v. Sec'y of Health & Human Servs*., No. 08–601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review den'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. Appx. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Human Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. *Consideration of Medical Literature*

Both parties filed medical and scientific literature in this case, but not all such items factor into the outcome of this decision. While I have reviewed all the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case—just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Human Servs.*, No. 15–5072V, 2016 WL 1358616, at *5 (Fed. Cir. Apr. 6, 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Human Servs.,* 527 F. Appx. 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

## ANALYSIS

### I. Petitioner has Not Established that She Suffered from Cerebral Vasculitis

Petitioner's causation theory depends heavily on the finding that she did not simply experience a hemorrhagic stroke, but that her intracranial bleed was symptomatic of a cerebral vasculitis that had an autoimmune origin. Only then can she relate the flu vaccine to her alleged injury, since her experts depended on the causal explanation that the vaccine (in some combination of innate-response inflammation and antibody-driven cross reaction attributable to the adaptive response) propagated an autoimmune attack on brain vessels sufficient to cause a rupture and bleed. The experts did *not* propose in this case that stroke generally is autoimmune in etiology, and acknowledged that there are other, well-understood stroke causes that are not autoimmune, such as hypertension (although they took pains to point out that Petitioner did not have this risk factor or others). This is therefore just the sort of case where determination of injury is critical to evaluating a petitioner's overall success. *Broekelschen,* 618 F.3d at 1346 (when the injury suffered is disputed, it is appropriate for the special master to first determine which injury is best supported by the evidence before applying the *Althen* test to determine causation of the relevant injury).

Although a vasculitic condition might in some circumstances present as stroke, stroke is not per se evidence of vasculitis. As both parties' experts agreed, and as bulwarked by the filed medical literature, stroke can be attributable to an ischemic event involving vessel blockage or hemorrhage. Vasculitides, by contrast, while unquestionably involving the blood vessels and occasionally occuring in the brain, are categorically different in their overall course and progression. There are numerous kinds of vasculitides, most of which do not involve the brain, and those that do impact it often only do so secondarily. R. Hajj-Ali, et al., *Primary Angiitis of the Central Nervous System in Adults,* https://www.uptodate.com/contents/primaryangiitisofthecentralnervoussysteminadults 1–19 (2017), filed as Ex. H (ECF 61-6) ("Hajj-Ali"); Watanabe, *supra*, at 2–6. Cerebral vasculitis in particular is not only rare, but more often than not involves recurrent stroke along with other neurologic or cognitive impairments. Hajj-Ali, *supra*, at 2. In addition, much if not most of the literature relied upon by Petitioner involved ischemic stroke, but Petitioner did not explain why hemorrhagic stroke was just as likely to be evidence of vasculitis, especially in the absence of other diagnostic factors. And as Kempster observed, the rarity of cerebral vasculitis overall counsels treaters not to consider it as a potential diagnosis when encountering stroke, in the absence of other related factors. Kempster, *supra*, at 125.

Here, the medical record preponderates in favor of a diagnosis of idiopathic stroke due to intracranial bleeding, over Petitioner's preferred diagnosis of cerebral vasculitis, for several

reasons. First, and compellingly, no treater ever diagnosed Ms. Schultz's stroke as attributable to vasculitis of any kind, even after a fairly robust work-up at the time of her ER presentation, which included CT and CTA imaging. While (as Dr. Messe conceded) such testing did not conclusively rule out vasculitis, it nevertheless had some merit in suggesting that vasculitis was unlikely under the circumstances. Her subsequent medical history also does not corroborate the presence of vasculitis. Second, Petitioner displayed no symptoms that she was experiencing an autoimmune-in-origin vasculitis *other* than the stroke itself, and her sequelae following the stroke, while unquestionably debilitating, are most likely attributable to the harm caused by the stroke. Testing also revealed no autoantibodies that might arguably be associated with an autoimmune kind of vasculitis, and she was never treated with immune-modulating therapies (which might indirectly confirm the autoimmune nature of her injury). Additionally, there is limited to no evidence Petitioner experienced an ongoing inflammatory process that could have impacted the blood vessels in her brain before or after her stroke.

Petitioner's experts point to Ms. Schultz's pre-vaccination symptoms as proof she was experiencing a prodromal phase of her autoimmune cerebral vasculitis, during which time (presumably) her immune system was aberrantly responding to the vaccination, generating the antibodies that would subsequently harm the blood vessels in her brain. Respondent did not rebut Petitioner's contentions that she in fact experienced this malaise-like feeling before her stroke. In addition, the literature does suggest that a person suffering from cerebral vasculitis would experience some kind of prodromal phase. *See, e.g.*, Hajj-Ali, *supra*, at 1.

However, the symptoms Ms. Schultz reported from November 2013 did not last the length of time that would be considered sufficient to suspect an untreated vasculitis, but instead were followed by an acute event, nor did they include some of the symptoms commonly associated with vasculitis, like persistent headache or cognitive impairment.[22] *Id.* at 2. And again, Petitioner's post-stroke history reveals no evidence that she was experiencing a progressive condition attributable to chronic autoimmune activity, but instead suggests she had the misfortune of a one-time debilitating event.

Other than conclusory statements by her experts, Petitioner offered little in the way of reliable scientific evidence that would bulwark her conclusion that her November 2013 symptoms were most likely cerebral vasculitis precursors. The reference in Mader to a post-vaccination malaise comes from literature that was not filed in the case, and otherwise stands only for

[22] In addition, the symptoms experienced during this timeframe should be considered in light of Petitioner's overall medical history, which (pre-vaccination) reflected depression, concern for neurologic issues in her brain, fatigue, and chronic facial pain/headache/migraine. Ex. 8 at 9, 11, 119. Although Respondent may not have preponderantly demonstrated some alternative explanation for Petitioner's stroke by linking these pre and post-vaccination symptoms, the significance of her November 2013 malaise must be evaluated in light of her overall history. That history (which includes pre-vaccination symptoms *also* associated with cerebral vasculitis) was not effectively addressed or explained by Petitioner.

generalized conjecture about the impact of vaccination—*not* that vaccine-caused cerebral vasculitis manifesting with hemorrhagic stroke will first involve nonspecific malaise-like symptoms. Dr. Messe was persuasive in concluding from the record that Petitioner's overall presentation was consistent with the kind of idiopathic hemorrhagic stroke he sees frequently.

Here, as in many Program cases, Petitioner emphasizes the rarity of vaccine injury as a reason to find that *her* alleged condition—also a rare event—was the injury. But this employs false syllogistic reasoning (i.e., "vaccine injuries are rare; cerebral vasculitis is rare; Petitioner was injured after vaccination; therefore, Petitioner likely experienced cerebral vasculitis"). Common or rare, there are factors that can be considered when evaluating the presence of any alleged vaccine injury, to assess whether it is preponderantly supported by the evidence. In this case, the record does not preponderantly support the finding that Petitioner suffered from cerebral vasculitis.

## II. Petitioner Has Not Met her Preponderant Burden under the *Althen* Test

Even if I had found that Petitioner suffered from a cerebral vasculitis as alleged, I would not also be able to find that she carried her burden of proof by a preponderance under the *Althen* test.[23]

### A. *Althen* prong one

The expert testimony and other scientific evidence offered to support Petitioner's contention that cerebral vasculitis can be vaccine-caused was ultimately not (taken as a whole) sufficiently reliable to satisfy the first *Althen* prong.

At most, Petitioner established that certain vasculitides can be autoimmune in nature, and that vaccines have been associated with *other* kinds of autoimmune conditions, vasculitic or not. But as for a direct link between the flu vaccine and something arguably close to what Petitioner experienced, she relied on case reports (or mentions of discrete instances of merely an observed temporal association, in items of literature like Watanabe)—a form of evidence well understood in the Program to be of limited probative value. *See D.G. v. Sec'y of Health & Human Servs.*, No. 11-577V, 2019 WL 2511769, at *193 (Fed. Cl. Spec. Mstr. May 24, 2019) (two case reports filed by the petitioner were insufficient proof to establish a causative relationship between vaccines and rhabdomyolysis); *Crutchfield v. Sec'y of Health & Human Servs.*, No. 09-0039V, 2014 WL

[23] I do not include herein a discussion of the third *Althen* prong, since my determination hinges on the first two prongs. I do note that the timeframe in which Petitioner's purported autoimmune cerebral vasculitis actually began—five to six weeks post-vaccination—was consistent with her expert's views, and also was conceded as reasonable by Dr. Messe. However, the reasonableness of timeframe for onset of injury in any vaccine case depends on the claimant's success in establishing by a preponderance a causation theory—and here Petitioner failed in that effort. Since she did not successfully demonstrate that the flu vaccine *could cause* a cerebral vasculitis (or that this diagnosis best described her injury), it does not matter that Petitioner succeeded in establishing that an autoimmune disease might begin in the approximate timeframe at issue herein.

1665227, at *19 (Fed. Cl. Spec. Mstr. Apr. 7, 2014) ("single case reports of Disease X occurring after Factor Y…do not offer strong evidence that the *temporal* relationship is a *causal* one—the temporal relationship could be pure random chance" (emphasis in original)), *aff'd*, 125 Fed. Cl. 251 (2014). In addition, Petitioner's experts too often relied on literature that conflated ischemic with hemorrhagic strokes, or other types of vasculitis, without showing that the specific kind at issue in this case could reliably be associated with the flu vaccine. She also assumed that an autoimmune-in-origin vasculitis would invariably be characterized by a pre-acute prodromal phase, without showing *why* such a phase would likely precede the acute event presenting as stroke. As noted above, no persuasive authority—literature or expert testimony—was offered to establish this, leaving Petitioner to rely on the general contention that *any* autoimmune injury would inherently include such a prodromal phase.[24]

At the same time, Respondent's expert, Dr. Messe, more persuasively established that the vast majority of strokes are *not* autoimmune in nature, and that cerebral vasculitis would be characterized by a large number of symptoms not present in this case as well as different overall course. Messe Rep. at 3. Respondent also offered reliable literature undercutting Petitioner's contention of an association between the flu vaccine and cerebral vasculitis or stroke, and that in fact vaccination was *more* likely to be preventative of stroke, due to the protections vaccines afford against viral infection (which carry a greater stroke risk).[25] Smeeth was particularly harmful to Petitioner's case, since it squarely considered—but rejected—a primary supposition of Petitioner's theory about the vaccine-vasculitis/stroke association. Smeeth, *supra*, at 2615.[26]

Petitioner's efforts to diminish Smeeth's evidentiary weight were unpersuasive. It is true, as Petitioner argues, that Smeeth does not prove with certainty that *all* flu vaccine recipients will

[24] The fact that Petitioner may have shown some sequential homology between viral components of the flu vaccine and amino acid sequences found in the proteins forming cranial blood vessels also does not appreciably assist her overall *Althen* one showing. As has been observed in other cases, there is ample such demonstrable homology when comparing antigens to human structures, raising the question in some expert's minds as to why harmful autoimmune cross-reactions of the kind proposed herein do not more *frequently* occur. *See Day v. Sec'y of Health & Human Servs.*, No. 12-630V, 2015 WL 8028393, at *14 (Fed. Cl. Spec. Mstr. Nov. 13, 2015) (discussing an expert witness's testimony that "if frequently occurring short sequence homologies were sufficient to induce an autoimmune reaction, then there would be a high incidence of autoimmune disorders in the general population"). Thus, to preponderantly establish a causal theory that relies on molecular mimicry occurring between a vaccine component and self-tissue due to purported homology, the claimant must do more—she must show that the cross reaction proposed has been associated with the injury in question, that the antigenic target is the homologous structure, that the vaccine or wild virus counterpart has been demonstrated to be involved in the proposed injury, etc. Mere demonstration of theoretical homology alone, based on computer-driven searches involving databases of amino acid sequences, does not carry the day.

[25] Indeed, even items of literature offered by Petitioner, like Fullerton, placed far greater weight on the protective value of vaccination over its theoretical possible capacity to induce vasculitis. Fullerton, *supra*, at 1464.

[26] Other reliable literature filed by Respondent bulwarked the contention that the flu vaccine more likely reduces, rather than heightens, stroke risk. *See, e.g.*, A. Grau, et al., *Influenza Vaccination is Associated with a Reduced Risk of Stroke*, 36 Stroke 1501–06 (2005), filed as Ex. C (ECF No. 61-1).

not experience a stroke. It is also correct that this kind of epidemiologic evidence can be overcome, for purposes of proving a Vaccine Act claim, with other categories of evidence sufficient to preponderantly establish an association between vaccination and stroke for a particular individual. But Smeeth was a credible and reliable item of evidence that was not effectively rebutted by Petitioner's attacks on its methodology.[27] I have repeatedly observed that epidemiologic evidence cannot be *required* of a petitioner—but I am not obligated to ignore it when it exists and offered into evidence, and especially not when it is plainly reliable, as here. *D'Tiole v. Sec'y of Health & Human Servs.*, 726 Fed. Appx. 809, 811–12 (2018) (proper for special master to consider epidemiologic evidence in finding that petitioner did not carry his *Althen* burden).

I acknowledge that the theory that a vaccine could cause a specific type of vasculitis focusing on the brain and presenting as stroke is hardly far-fetched. Similar theories have been proposed in prior Vaccine Act cases, albeit to different injuries, and have been inconsistently successful. A few cases in which stroke was alleged to be vaccine-caused involved the DPT vaccine, and neither were successful. *See Francis v. Sec'y of Health & Human Servs.*, No. 99-286V, 2000 WL 1517676 (Fed. Cl. Spec. Mstr. Aug. 31, 2000); *Wilson v. Sec'y of Health & human Servs.*, No. 90-795V, 1992 WL 118955 (Cl. Ct. May 15, 1992). But other forms of vasculitis not involving an intracranial bleed as here have been found to be vaccine-associated—and specifically attributable to the flu vaccine. *See*, *e.g.*, *Contino v. Sec'y of Health & Human Servs.*, No. 15-773V, 2019 WL 4941087, at *20 (Fed. Cl. Spec. Mstr. Sept. 5, 2019) (awarding entitlement where the petitioner developed urticarial vasculitis five days after receiving the flu vaccine); *McElroy v. Sec'y of Health & Human Servs*., No. 11-679V, 2012 WL 1739873, at *4 (Fed. Cl. Spec. Mstr. Apr. 13, 2012) (awarding entitlement where biopsy-confirmed urticarial vasculitis presented within a "few" days following the flu vaccine). The above suggests that a case where stronger and more reliable scientific/medical evidence was offered might result in a different outcome. But the evidence offered in support of Petitioner's theory *in this case* was simply not preponderant.

B. *Althen* prong two

In addition to the deficiencies in her causation theory, Petitioner did not ultimately offer preponderant evidentiary support for the contention that the flu vaccine "did cause" her hemorrhagic stroke. No treater ever proposed that her stroke was so associated (although she raised the possibility with a number of them). As noted above, the record does not suggest that Petitioner

[27] Arguments Petitioner advanced about deficiencies in the study's use of controls to establish incidence were especially unpersuasive. The self-controlled case series methodology is commonly used in vaccine design, efficacy, and safety research. *See* IOM Report, *supra*, at 112, 121–24, 145–46, 539–40 (discussing numerous studies in which the self-controlled case-series methodology has been used to study vaccines). The Food and Drug Administration has proposed this methodology as a reliable means of expediting development procedures for vaccines. *See* Cooperative Agreement to Support Innovation in Vaccine Clinical Trial Design and Collaboration in Pharmacovigilance to Advance Global Access to Safe and Effective Vaccines, 77 Fed. Reg. 28,883 (May 16, 2012). And in any event, Smeeth was not the only literature filed in this case standing for the proposition that vaccination might make stroke less likely. *See, e.g.*, Fullerton, *supra*, at 1464.

was experiencing any kind of disease process, autoimmune or not, post-vaccination leading to stroke. The symptoms she experienced in the month prior to the stroke were too nonspecific (and equally explainable as associated with Petitioner's other, demonstrated pre-vaccination conditions and symptoms), and no persuasive explanation was offered for why her November 2013 symptoms would inexorably result in an autoimmune-caused stroke, other than that they arguably could be seen in a person who did suffer from a cerebral vasculitis that was autoimmune in origin—a weak contention given the facts, as well as in light of my conclusion that her stroke was not likely associated with any form of vasculitis. I cannot conclude on the basis of the medical record that her hemorrhagic stroke was likely caused by the flu vaccine.

Petitioner and her experts placed great weight on the fact that she did not have certain risk factors, like hypertension, associated with stroke, thereby concluding that this left only the vaccine as possibly causal. But elimination of alternative possible causes is not enough of a basis for a favorable entitlement determination. *See Welch v. Sec'y of Health & Human Servs.*, No. 18-494V, 2019 WL 3494360, at *13 (Fed. Cl. Spec. Mstr. July 2, 2019) (citing *Thomas v. Sec'y of Health & Human Servs.*, No. 01-645V, 2007 WL 470410, at *25 (Fed. Cl. Spec. Mstr. Jan. 23, 2007). Rather, a claimant must *affirmatively* show that the vaccine she received was *itself* the likely cause. Otherwise, in any case in which no other explanation for an injury existed, or known explanations were eliminated, claimants would invariably prevail (at least on the second *Althen* prong) simply by demonstrating a temporal relationship between vaccination and injury, adding the "filler" of a scientific explanation to join the two. This is not the proper legal basis for application of the "did cause" prong, which requires preponderant evidence supporting the vaccine as specifically causal in the instance at issue. That standard has not been met in this case.

## Conclusion

Ms. Schultz was an engaging witness, and she plainly brought this case in the good-faith belief that the flu vaccine might be associated with her stroke event. She is to be commended for her perseverance in the face of a debilitating medical experience that would lead others into despair. But her personal qualities and character are independent to the causation inquiry that I am empowered by statute to conduct. That inquiry requires me to evaluate whether the petitioner has established by a preponderance that a particular vaccine could, and did, cause the injury at issue. Here, Petitioner did not successfully establish that her injury was autoimmune, that the flu vaccine can cause stroke brought on via intracranial bleeding, or that her own symptoms were vaccine-caused. As a result, she has not established an entitlement to damages in this case.

In the absence of a timely-filed motion for review (see Appendix B to the Rules of the Court), the Clerk shall enter judgment in accord with this decision.[28]

[28] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by filing a joint notice renouncing their right to seek review.

**IT IS SO ORDERED.**

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