In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 15-736V

(To be Published)

* *	Special Master Corcoran
GLADYS GUZMAN, *	
*	Filed: May 14, 2019
Petitioner, *	
*	Decision; Influenza ("flu") Vaccine; Chronic Urticaria; Urticarial Vasculitis; Cutaneous Vasculitis
v. *	
*	
SECRETARY OF HEALTH AND HUMAN SERVICES, *	
*	
Respondent. *	
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* *	

Virginia E. Anello, Douglas & London, P.C., New York, NY, for Petitioner.

Debra Filteau Begley, U.S. Dep't of Justice, Washington, DC, for Respondent.

DECISION DENYING ENTITLEMENT[1]

On July 16, 2015, Ms. Gladys Guzman filed a petition seeking compensation under the National Vaccine Injury Compensation Program ("Vaccine Program").[2] Petitioner alleges that she experienced cutaneous vasculitis ("CV") due to her receipt of the influenza ("flu") vaccine on February 18, 2014. An entitlement hearing was held on October 25, 2018, in New York, New York. For the reasons stated in more detail below, Petitioner has not demonstrated entitlement to compensation under the Vaccine Program.

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[1] This Decision has been formally designated "to be published," and will be posted on the Court of Federal Claims's website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means 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 Decision in its present form will be available. *Id*

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3758, codified as amended at 42 U.S.C. §§ 300aa-10 through 34 (2012) [hereinafter "Vaccine Act" or "the Act"]. Individual section references hereafter will be to § 300aa of the Act (but will omit that statutory prefix).

I. Factual Background – Medical Record

Although Petitioner's pre-vaccination history does not bear significantly on the outcome of this case, it does reveal that she previously experienced allergies or allergic-like symptoms that could be associated with her post-vaccination condition. For example, on May 3, 2013 (the year before the vaccination at issue), Ms. Guzman sought treatment for a reported fever, loss of appetite, sneezing, a runny nose, and eye discharge, and treaters assessed her with allergic rhinitis and poor appetite. Ex. 1 at 173, 175. A few days later, on May 8, 2013, she sought treatment for a one-day history of pain on her right side and was diagnosed with post-herpetic neuralgia. *Id*. at 185-87. Then, at a September 2013 appointment, Petitioner reported that she had developed a rash in association with a new medication (Famotidine) she had recently started taking, although the records do not indicate that this was an ongoing concern for which additional treatment was sought. *Id*. at 487. Ms. Guzman also received the flu vaccine in April 2013 (over a year before the vaccination in question) without recorded incident. *Id.* at 21-22.

On February 18, 2014, Ms. Guzman received a flu vaccine at the walk-in clinic of New York Presbyterian Hospital after seeking treatment for possible heart palpitations. Ex. 1 at 526-27, 534. There is no immediate record evidence in the subsequent time period of any reaction. *Id.* Eight days later, on February 26, 2014, she went to an urgent care clinic for treatment of an itchy rash, which she stated had begun "about 48h after flu shot (2/18/14)," with more pressing symptoms developing over the prior four days. *Id*. at 493. She also reported a similar reaction following receipt of the flu vaccine in 2013 (although as noted above the filed records from 2013 do not memorialize such a reaction). *Id.* The records from this February 2014 visit describe the rash as a "diffuse[,] fine, erythematous,[3] maculopapular[4] rash" present everywhere on her body except for her face and lower legs. *Id*. at 494.

Ms. Guzman was assessed with a "recurrence of rash 48h after flu shot without other clear exposures." Ex. 1 at 494. The treating physician noted her rash was most consistent with a "systemic allergic reaction; allergen not yet known," prescribed hydrocortisone cream (topical steroids) and an allergy medication (Loratadine[5]), and recommended she see an allergist. *Id*.

Ms. Guzman sought additional treatment at the New York Presbyterian walk-in clinic less than a week later, on March 1, 2014, for the same rash which she again identified as having begun

[3] Erythema is defined as "redness of the skin produced by congestion of the capillaries." *Dorland's Illustrated Medical Dictionary* 643 (32nd ed. 2012) (hereinafter *Dorland's*).

[4] Macules are discolored skin lesions that are not elevated above the surface of the skin. *Dorland's* at 1094. Papules are small circumscribed, superficial, solid elevations of the skin (which are no larger than one centimeter in diameter). *Id.* at 1373.

[5] Loratadine is an antihistamine used to relieve or prevent symptoms associated with allergies by mitigating the effects of histamine – a substance in the body that causes itching, sneezing, runny nose, and watery eyes. *See Antihistamine (Oral Route)*, Mayo Clinic, https://www mayoclinic.org/drugs-supplements/antihistamine-oral-route-parenteral-route-rectal-route/description/drg-20070373 (last accessed on April 16, 2019).

within two days of her receipt of the flu vaccine. Ex. 1 at 497. She was, as before, assessed with a possible allergic reaction and prescribed a short course of oral steroids. *Id*. at 499. She next sought treatment on March 24, 2014, because the rash remained (although her overall symptoms had subsided somewhat in severity). *Id*. at 501-02. The examining physician observed a "macular erythematous rash over arms and esp[ecially] trunk, blanching, improving from prior documentation." *Id*. at 502. Ms. Guzman was assessed with "allergic/drug rash" and directed to follow-up with an allergist. *Id.* The following month, on April 15, 2014, Petitioner returned to New York Presbyterian to see her internist, Dr. Amanda Westlake. *Id.* at 503-05. She informed Dr. Westlake that her "[r]ash ha[d] completely resolved," but that she was nevertheless "intermittently using steroid cream" and taking Loratadine. *Id.* at 503.

Over the next eleven months, Ms. Guzman sought medical treatment multiple times for a variety of conditions, but she did not report a rash at any such time, and no rash was ever observed on any examination. Ex. 1 at 507-52; Ex. 4 at 1. Of note, on August 29, 2014, Petitioner was treated by an ear, nose, and throat specialist, Dr. Jeffery Ahn, for allergic rhinitis and ear wax removal. Ex. 4 at 1-6. Notes from the visit indicated that Petitioner was still taking Loratadine and using hydrocortisone cream as needed (though the notes do not reveal any specific health problems related to the medication use). *Id.* at 1. No mention was made of a current rash at that time.

The following year, in March 2015, Petitioner saw an allergist, Dr. Stephen Canfield, at New York Presbyterian. Ex. 1 at 555-57. She repeated her prior assertion that she had developed a rash within two days of the February 2014 flu vaccine, but now added as well that she had also experienced a "fever, burning sensation, headaches, weak[ness], + nausea, swelling of breasts." *Id*. at 555. Significantly, however, although she complained of a number of symptoms she had purportedly experienced since that time (and which she associated with exposure to deodorant, detergents, perfumes, lipstick, and Clorox), she made no mention of a persisting rash over the intervening period, and did not display one on exam. *Id*. at 555-56. Based upon the history provided above, Dr. Canfield concluded that it was "unlikely" that Ms. Guzman had experienced an allergic reaction to the flu vaccine. *Id*. at 556. He also offered to test Petitioner's possible vaccine allergy with a challenge test to the flu vaccine next year. *Id.*

Over the next four months, Ms. Guzman sought care many times for a myriad of complaints, but she did not mention to any treaters that she had a rash. Ex. 1 at 557-67. Later that summer, in July 2015 she returned to Dr. Canfield, again reporting a one-year history of myalgias and fatigue following her February 2014 flu vaccine, but not mentioning an ongoing rash. *Id.* at 576. Her exam did, however, reveal that she had a rash on her inner elbow that was described as "erythema" or "erythematous rash with papules, not itchy." *Id.* at 576-77. Dr. Canfield assessed Ms. Guzman with "unclear etiology for diffuse myalgias and fatigue" and determined it was "unlikely for symptoms to be secondary to previous flu vaccine . . . due to [the] persistence of symptoms." *Id*. at 577. He recommended that Ms. Guzman be tested for Lyme disease and a vitamin D deficiency. *Id.* Testing thereafter revealed a negative Lyme's disease titer, as well as a normal IgE level, and normal inflammatory markers. *Id*. at 593-95.

Since the middle of 2015, the record establishes several instances in which Petitioner has sought medical care but has not complained of a persistent or concerning rash – nor do medical treaters seem to have observed one. Ex. 2 at 1-20. At most, at a visit to Dr. Canfield on April 7, 2016 (after this action had been initiated), Petitioner again complained of a history of an "erythematous rash with papules, not itchy," adding that the rash improved when she applied hydrocortisone cream or other over-the-counter lotions or ointments. *Id.* at 27. Her exam, however, did not reveal a rash, and Dr. Canfield maintained his view that Ms. Guzman's ongoing, intermittent symptoms were probably not related to her 2014 flu vaccination. *Id.* at 28. Petitioner saw Dr. Canfield the following month, at which time she again reported a history of a "erythematous rash with papules[.]" *Id.* at 42. She did not, however, display any rash on exam, and a skin test for allergens produced results termed "equivocal." *Id.* at 43. Petitioner has not filed any medical records for subsequent time periods.[6]

II. Witness Testimony

A. *Gladys Guzman*

Petitioner testified at hearing via Spanish translator and filed an affidavit in support of her claim. Tr. at 6-56; *see also* Affidavit, filed as Ex. 3 (ECF No. 20-1). Her testimony largely consisted of her own recollection of her overall health history post-vaccination, with some additional explanation of disputed issues relevant to certain medical records.

Consistent the with medical record detailed above, Ms. Guzman testified that she received the flu vaccine on February 18, 2014, at the New York Presbyterian office of her primary care treaters. Tr. at 8. She did not recall experiencing any adverse reaction or symptoms immediately following vaccine administration. *Id.* at 9.

Within forty-eight hours thereafter, however, Ms. Guzman represented, she began to experience weakness, nausea, headaches, a burning sensation, and a rash extending to the back, thighs, upper torso, and arms. Tr. at 9, 11, 37. The skin on her back appeared red and she began to put water on it in hopes it would help alleviate her symptoms. *Id.* at 10.

Due to the above concerns, Ms. Guzman presented to the hospital at New York Presbyterian on February 26, 2014 (roughly one week following her receipt of the vaccine). Tr. at 11. She recalled being examined by multiple physicians. *Id.* She represented that one such treater advised her that she had experienced an adverse reaction to the flu vaccine, and prescribed Loratadine and hydrocortisone cream to treat her symptoms (two medications she had not taken prior to that date). *Id.* Ibuprofen was recommended for her headaches. *Id.* at 12. Ms. Guzman also recalled that hospital treaters advised her to schedule an appointment with an allergist, but she

[6] Exhibit 5 contains Ms. Guzman's relevant pharmacy records, and Exhibit 6 contains photos of Ms. Guzman's hands (dated July 30, 2015), which are discussed below.

maintained that the appointment could not be scheduled until March 2015 (as the attending allergist was on maternity leave). *Id.*

Ms. Guzman returned to the New York Presbyterian office of her primary care provider the next day to refill her prescriptions. Tr. at 13-14. The office was closed, however, so Ms. Guzman instead went to a local urgent care clinic. *Id.* at 14. The urgent care physician examined Ms. Guzman and prescribed Prednisone (along with refills of Loratadine and hydrocortisone cream). *Id.* The physician also advised her to return to the hospital if her symptoms did not improve. *Id.*

Ms. Guzman testified that she took Prednisone for "several days" thereafter, but could not specify for how long. Tr. at 16. She recalled returning to the office of her primary care provider thereafter because of her persistent symptoms. *Id.* Ms. Guzman continued to take Loratadine and hydrocortisone cream with some improvement, though she maintained that her rash never cleared fully (despite record evidence to the contrary). *Id.* at 17, *see* Ex. 1 at 503.[7] At times, however, Ms. Guzman recalled that she would stop taking Loratadine due to adverse side effects (i.e., sleepiness), at which time the rash would reappear on her palms, arms, legs, chest, and upper torso. Tr. at 17-18. Ms. Guzman otherwise testified that she continues to take Loratadine at present (as well as use various over-the-counter medications and lotions). *Id.* at 18, 22.[8]

Given her perception that she could not see the allergist at New York Presbyterian for several months, Ms. Guzman began to search for another specialist.[9] On August 29, 2014, she presented to Dr. Jeffrey Ahn. Tr. at 19. Upon arrival, Ms. Guzman realized that Dr. Ahn's specialty (ear, nose, and throat) meant that he did not treat patients with the condition she was experiencing, but she went through with the examination regardless. *Id.* She recalled that Dr. Ahn examined her eyes, nose, and throat, and also cleaned her ear canals. *Id.*

Thereafter, Ms. Guzman was seen by an allergist, Dr. Canfield, at Columbia University Medical Center. Tr. at 20. Ms. Guzman maintained that her rash was still present at this time (despite a normal examination), though it had improved somewhat. *Id.* at 45-46, 47. She recalled that Dr. Canfield concluded she had experienced an adverse reaction to the flu vaccine, and wanted to complete testing to confirm this. *Id.* at 43.[10] She explained that Dr. Canfield also suggested the

[7] Ex. 1 at 503, for example, indicates that Ms. Guzman told her internist, Dr. Westlake, the rash had "completely resolved" as of April 15, 2014. Tr. at 37-38, 49-50. Ms. Guzman maintained at hearing, however, that she showed Dr. Westlake the rash and was prescribed the same medications. *Id.* at 37-38.

[8] Although Ms. Guzman maintained she used hydrocortisone cream routinely in 2014, her pharmacy records suggest that between April 2014 and July 2015 the prescription was not refilled. Tr. at 39-40.

[9] As noted earlier, Petitioner maintained that she could not see the allergist at New York Presbyterian until 2015 (due to the treater's scheduled maternity leave). Tr. at 30-32. She acknowledged at hearing, however, that she did not attempt to schedule an appointment with a different allergist at the same hospital as an alternative. *Id.* at 34.

[10] On cross, Respondent pointed out that the medical record reveals that Dr. Canfield suggested that the flu vaccine likely played *no* role in Petitioner's onset of rash (or other symptoms). Tr. at 43; *see* Ex. 1 at 577 ("[u]nlikely for

vaccine had compromised her immune system and lowered her "defenses." *Id.* at 23. According to Ms. Guzman, Dr. Canfield recommended that she continue taking Loratadine and using hydrocortisone (and prescribed Tamiflu). *Id.* at 23, 40-42.[11]

At present, Ms. Guzman continues to see Dr. Canfield, but only as needed (as she has found his treatment to be unhelpful in resolving her symptoms). Tr. at 23. The Loratadine helps at times, but as she testified earlier, her rash returns when she stops taking the medication. *Id.* at 35. Ms. Guzman described her rash as "more spotty today" than when it initially began. *Id.* at 37.

On cross, Petitioner maintained that she truthfully reported her symptoms to her treaters over the course of her illness. Tr. at 28. Ms. Guzman also submitted photographs of the palms of her hands (taken in July 2015 – at the time of the filing of this action, and thus almost eighteen months post-vaccination), which in her view corroborated her claims of a vaccine reaction. *Id.* at 51-53; *see* Ex. 6 (ECF No. 21-1).[12] She otherwise maintained that she continues to suffer from a rash at present (though she described it as a "subcutaneous" problem), despite the lack of contemporaneous medical record support. Tr. at 53.

Ms. Guzman acknowledged at hearing that she had experienced certain seasonal allergies prior to receiving the vaccine at issue in this matter. Tr. at 28-29. She attributed these allergies to "certain medications" and "detergents" which caused only "watery eyes." *Id.* at 29. She also acknowledged taking medication for these allergies, though she maintained the symptoms at the heart of her petition occurred only after receipt of the flu vaccine. *Id.* at 29-30, 53-54.[13]

B. *Petitioner's Expert – Dr. David Axelrod*

Dr. Axelrod prepared two written reports for this case and testified at hearing. Tr. at 66-120; Expert Report, dated Aug. 19, 2015 (ECF No. 31-1) ("First Axelrod Rep"); Expert Report,

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symptoms to be secondary to previous flu vaccine given last year due to persistence of symptoms"). Petitioner, however, insisted that Dr. Canfield advised her that she should not receive the flu vaccine in the future. Tr. at 43.

[11] Respondent pointed out, however, that Ms. Guzman submitted no record evidencing a prescription for Tamiflu. Tr. at 45.

[12] The filed color photograph does not suggest the presence of a rash to the untrained eye. At best, the photo reveals some skin redness in the bottom corners of both palms. Otherwise, Ms. Guzman's hands appear to look normal. As discussed in greater detail below, Respondent's expert posited that this photographic evidence was not consistent with vasculitis or chronic urticarial lesions (as Petitioner's expert suggests). Tr. at 154. Dr. Levinson's first expert report characterizes the rash as showing "macular erythema on the palms" or "a totally non-specific eruption . . . not emblematic of a vasculitis process in both appearance and location." *See* Expert Report, dated Dec. 2, 2016 (ECF No. 22-1) ("First Levinson Rep.") at 9.

[13] Ms. Guzman could not recall how long she had taken at least one of the allergy medications, but was unable to deny on cross-examination that the record suggested she had filled prescriptions for the medication since 2004. Tr. at 29-30.

dated Feb. 15, 2017 (ECF No. 64-1) ("Second Axelrod Rep."). He offered the opinion that the flu vaccine Petitioner received caused her to suffer from "chronic urticaria," which he deemed a subset of cutaneous vasculitis. Tr. at 64, 69, 98, 101.[14]

Dr. Axelrod graduated from the University of Michigan Medical School in 1974 (after obtaining his bachelor's degree at Michigan as well). *See* Curriculum Vitae, filed as Ex. 40 (ECF No. 38-16) ("Axelrod CV") at 1. He completed two residencies in internal medicine, one at the University of Toronto and one at William Beaumont Hospital, followed by additional fellowships in allergy, immunology, and rheumatology at McGill University. *Id.* He then served as a fellow for the National Institutes of Health in the Clinical Immunology Laboratory. *Id.* Dr. Axelrod holds board certifications in allergy and immunology, adult rheumatology, and medical laboratory immunology. *Id.* He currently works in private practice, with the vast majority of his patients having allergies, immunologic conditions, or autoimmune rheumatic diseases. Tr. at 59-61. Dr. Axelrod testified at hearing that he has treated patients with vasculitic and urticarial conditions in his rheumatology and immunology practices. *Id.* at 64-67. He does not appear, however, to have ever conducted research or published on immunologic matters relevant to urticarial vasculitis (or vasculitic conditions generally). Axelrod CV at 2-4; Tr. at 90.

To begin, Dr. Axelrod defined vasculitis and provided a brief overview of its relevant presenting symptoms. Tr. at 63. In his view, vasculitis is best described as "inflammation of the blood vessels." *Id.* The relevant literature filed by Dr. Axelrod indicates that vasculitis causes cell destruction or narrowing of the blood vessel wall, in which blood flow is restricted, thereby resulting in organ or tissue damage. *See* N. Kluger, et al., *Cutaneous Vasculitis and Their Differential Diagnoses*, 27 Clin. Exp. Rheum. 124 (2009), filed as Ex. 9 (ECF No. 21-4) ("Kluger").

Dr. Axelrod characterized Petitioner's injury as "cutaneous," or a form of vasculitis isolated to the skin (and thus, not systemic in nature). Tr. at 64; Second Axelrod Rep. at 1. Cutaneous vasculitis is an all-defining term, given the multiple types in existence, which Dr. Axelrod asserted vary depending on the type and size of the blood vessel involved (i.e., arterial or venial, for example[15]). Tr. at 63-64. Dr. Axelrod offered cutaneous leukocytoclastic vasculitis[16] – an idiopathic inflammation in the smaller arterial blood vessels – as an example of a cutaneous

[14] Notably, Dr. Axelrod's first expert report identified Petitioner's injury as "isolated cutaneous vasculitis," not chronic urticaria. First Axelrod Rep. at 2-3, 5. His second report similarly only discusses vasculitis with an emphasis on cutaneous involvement. Second Axelrod Rep. at 1-3. The term "chronic urticaria" appears in none of his expert reports as a descriptor of Petitioner's condition.

[15] An arterial vasculitis, in Dr. Axelrod's view, would be more severe in terms of the patient's overall health course. Tr. at 103.

[16] At hearing, Dr. Axelrod acknowledged that Ms. Guzman did not have cutaneous leukocytoclastic vasculitis given the absence of any palpable purpura evidenced in her records. Tr. at 71-72. He appears to have used the condition only as an example, and he later admitted it does not bear on his opinion in this case. *Id.* at 77.

vasculitis. *Id.* at 64. It presents with "palpable purpura," or "nonblanching lesions," and typically does not respond to antihistamines. *Id.* at 64, 72-73, 94. Pathologic evidence is used to confirm a cutaneous vasculitis diagnosis. *Id.* at 99; *see* Kluger at 124 ("histology is *mandatory* to confirm the diagnosis of vasculitis") (emphasis added).

Chronic urticaria, Dr. Axelrod maintained, is also a subset of cutaneous vasculitis[17] and involves inflammation of the venules or "the other side of the capillaries." Tr. at 64, 98, 101.[18] It does not have specific diagnostic criteria apart from the presence of hives and persistence (i.e, lasting for six weeks or more). *Id.* at 95-96; *see* A. Kaplan, *Chronic Spontaneous Urticaria: Pathogenesis and Treatment Considerations*, 9 Allergy Asthma Immunol. Res. 477 (2017), filed as Ex. 27 (ECF No. 38-3) ("Kaplan"). Symptoms of chronic urticaria typically manifest as post-inflammatory hyperpigmentation lesions affecting all areas of the body (including the feet and palms), and it can be diagnosed without evidence of palpable purpura. Tr. at 96. Relying on his own treatment experience, Dr. Axelrod posited that the vast majority of patients with chronic urticaria also congruently experience vasculitis. *Id.* at 103, 111-12. Literature he filed in support, however, does not support this assertion. *Id.* at 100; *see* Kluger at 129 ("[urticarial vasculitis] is a rare . . . condition, that affects 5 to 10% of the patients with chronic urticaria").

Based on his review of the record, Dr. Axelrod opined that Ms. Guzman developed autoimmune "chronic urticaria"[19] as the result of her receipt of the flu vaccine in February 2014. Tr. at 69, 75-76, 87-88. In forming his opinion regarding her proposed diagnosis, Dr. Axelrod relied primarily on Ms. Guzman's medical records (which notably evidenced *no* treater support for such a diagnosis), his own treatment experience, and Ms. Guzman's testimony (along with the photographic evidence from July 2015) tending to suggest that her rash presented close-in-time to the vaccine and thereafter persisted for quite some time. *Id.* at 104-05, 119.

The sole medical record references Dr. Axelrod relied upon (from late February to March 2014) reveal that Ms. Guzman's initial rash was noted to be "maculopapular" or "branching." Tr.

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[17] Notably, literature filed by Petitioner in support of her claim *directly contradicts* the assertion that chronic urticaria is a form of vasculitis. *See, e.g.*, I. Jauregui, et al., *Antihistamines in the Treatment of Chronic Urticaria*, 17 J. Investig. Allergol. Clin. Immunol. 41, 43 (2007), filed as Ex. 26 (ECF No. 38-2) ("[Chronic urticaria] is characterized by a perivascular infiltrate around the venules, *without vasculitis* or immune complex deposits") (emphasis added).

[18] Throughout his hearing testimony, Dr. Axelrod equated chronic urticaria with "urticarial vasculitis." Tr. at 67 (noting both terms refer to "urticaria . . . in the skin"). At times, however, he also suggested the two differed in some respects. *Id.* at 67 (noting urticarial vasculitis can be associated with low complement levels in the blood); 101 ("urticarial vasculitis is inflammation maybe in the arterials and the venules . . . we mostly see venules with chronic urticaria"). On cross, he seemingly clarified that he merely intended to reference urticarial vasculitis as an additional example of cutaneous vasculitis, in order to underscore that palpable purpura is not required to make a chronic urticaria diagnosis. *Id.* at 91-96.

[19] Dr. Axelrod distinguished autoimmune chronic urticaria from urticaria related to allergies. Tr. at 88. In his view, urticaria related to an allergy is an acute, monophasic event. *Id.* Otherwise, if the reaction is chronic, it is deemed autoimmune. *Id.*

at 69, 77, 86; *see* Ex. 1 at 492-94, 502. That same record, however, included no treater speculation that Ms. Guzman's rash was consistent with urticarial lesions. Tr. at 91-92, 104. Dr. Axelrod nonetheless posited that a maculopapular eruption of the sort Petitioner displayed at the time is common in patients presenting with autoimmune urticaria. *Id.* at 69-70, 93, 104-06.[20] Ms. Guzman's symptoms also responded well to antihistamine treatment (as well as topical steroids), which he deemed significant. *Id.* at 70, 72-73, 103-04, 112; *see* I. Jauregui, et al., *Antihistamines in the Treatment of Chronic Urticaria*, 17 J. Investig. Allergol. Clin. Immunol. 41, 43-44 (2007), filed as Ex. 26 (ECF No. 38-2) (discussing the beneficial effects of antihistamines in treating urticarial lesions); A. Ellingsen, et al., *Treatment of Chronic Idiopathic Urticaria with Topical Steroids*, 76 Acta. Derm. Venereol. 43 (1996), filed as Ex. 42 (ECF No. 38-18) (stating the same).

Moreover, Ms. Guzman's rash persisted for more than six weeks, rendering it "chronic" in nature. Tr. at 69-70, 105. Indeed, Dr. Axelrod noted, Ms. Guzman herself claimed to have experienced the effects of her rash for months following her vaccination (despite the long gap noted in the record where Petitioner did not appear to complain of adverse symptoms, or display them on examination). *Id.* at 105. He also emphasized that Petitioner used various medications to treat her symptoms over a seventeen-month period, and those treatments may have masked her overall state. *Id.*; *see also* Second Axelrod Rep. at 2.

Dr. Axelrod could not, however, point to any other record tending to support his diagnostic findings as a whole. Tr. at 107. Rather, he posited that relevant photographic evidence submitted by Ms. Guzman confirmed his suspicion that she was still experiencing urticaria symptoms into July 2015. *Id.* at 107-08; Second Axelrod Rep. at 2. In his view, the photo of Petitioner's hands evidenced a "macular" rash, but nothing palpable or purpuric, which as noted earlier, would not in his opinion be uncommon in the typical urticaria presentation. Tr. at 107. Dr. Axelrod agreed, however, that the photograph alone was insufficient to confirm an ongoing process. *Id.* at 108.

Apart from the above, Dr. Axelrod acknowledged that the relevant medical record lacked any other evidence to support a chronic urticaria or vasculitic diagnosis. Indeed, Ms. Guzman never underwent skin biopsy testing for her condition (which relevant literature suggests is *required* for diagnostic confirmation of cutaneous vasculitis). Tr. at 73-74, 101-02; Second Axelrod Rep. at 1; Kluger at 124. But Dr. Axelrod suggested that physicians typically only perform urticarial biopsies if the patient has not responded well to antihistamines or to rule out

[20] In support of his opinion that a maculopapular rash could be a symptom associated with vasculitis (and chronic urticaria more specifically), Dr. Axelrod referenced one item of literature. Tr. at 93; *see* L. Calabrese, et al., *The American College of Rheumatology 1990 Criteria for the Classification of Hypersensitivity Vasculitis*, 33 Arthritis & Rheum. 1108 (1990), filed as Ex. 8 (ECF No. 21-3) ("Calabrese"). But Calabrese defines the diagnostic criteria for *hypersensitivity* vasculitis (a vasculitis induced due to some "over reacti[on]" to a drug, for example), which Dr. Axelrod acknowledged at hearing was not entirely relevant to his opinion in his case (as he was not suggesting Petitioner had hypersensitivity vasculitis). Tr. at 77-76. On cross, Dr. Axelrod emphasized that he offered Calabrese only to show that certain forms of vasculitis could manifest symptoms consistent with a maculopapular rash (as evidenced in Ms. Guzman's records), without purpura. *Id.* at 91-93, 94-95.

other conditions. Tr. at 73-74. Given that Ms. Guzman's symptoms were alleviated by antihistamines, Dr. Axelrod did not find it concerning that a biopsy was never conducted. *Id.* He also agreed that he could not definitively state that Ms. Guzman had any form of cutaneous vasculitis absent a biopsy. *Id.* at 102. Nonetheless, Dr. Axelrod opined that a majority of biopsied patients (who do *not* respond well to medication) typically would have evidence of some form of inflammation around the venules in any event – thus, the presence or absence of biopsy results did not weight heavily against his opinion. *Id.*

Dr. Axelrod similarly acknowledged that none of Ms. Guzman's treaters proposed chronic urticaria (or any other form of cutaneous vasculitis) as an appropriate diagnosis for Ms. Guzman's symptoms. Tr. at 105. And Dr. Axelrod agreed that there was no evidence in the record to suggest that Ms. Guzman tested positive for the relevant antibodies associated with cutaneous vasculitis (or *any* form of vasculitis for that matter). *Id.* at 105, 117-18. He nevertheless maintained that no other possible explanation (i.e., chronic liver disease, infection, pregnancy, or similar condition) existed for Ms. Guzman's post-vaccination symptoms. *Id.* at 70-71; First Axelrod Rep. at 2, 5. He thus concluded that the vaccine was the most likely cause of the condition, given its close temporal relationship to her reported onset of rash and other symptoms. Tr. at 109.

Dr. Axelrod next proposed a mechanism by which the flu vaccine could have caused Ms. Guzman's chronic urticaria: an idiotype network theory, coupled with a secondary immune response due to prior vaccine exposure. Tr. at 78-79, 80-83, 86; First Axelrod Rep. at 5-6. According to Dr. Axelrod, the formation of idiopathic networks (or "lattice[s]") occurs when the initial antibodies produced in response to a vaccine cause the body's immune cells to produce *additional* antibodies that bind with vaccine antigens – thereby producing idiotype immune complexes. Tr. at 83; First Axelrod Rep. at 5-6; Second Axelrod Rep. at 1-2; *see* N. Jerne, *Towards A Network Theory of the Immune System*, 125 Ann. Immunol. 373 (1974), filed as Ex. 14 (ECF No. 21-9). In Ms. Guzman's case, Dr. Axelrod theorized, upon receipt of the flu vaccine idiotype immune complexes were formed, transported, and "deposit[ed]" into the blood vessel wall – therein "recruit[ing]" an overproduction of lymphocytes to the area – and resulting in urticaria. Tr. at 82-83; Second Axelrod Rep. at 1-2.[21]

In support of Petitioner's proffered medical theory, Dr. Axelrod offered various scientific studies purportedly showing how idiotype immune complexes can both form and expand post-vaccination, resulting in a pathologic process capable of producing chronic urticaria. *See* C. Brozek, et al., *Crossreactivity and Inheritance of Idiotype Restricted to Human Anti-Tetanus Toxoid Antibodies*, 79 J. Clin. Invest. 1242 (1987), filed as Ex. 16 (ECF No. 21-11) ("Brozek"). Brozek, for example, suggests that tetanus toxoid antigens can bind with human IgG antibodies and produce idiotype determinants. Another article described a mouse model study in which the

[21] The same concept, Dr. Axelrod maintained, could apply to leukocytoclastic vasculitis, in which case the immune complexes would "fix complement" instead of depositing/recruiting lymphocytes. Tr. at 83-84, 86.

flu virus was found to result in a major idiotype having specificity for virus hemagglutinin.[22] *See* A. Brown, *In Situ Detection of Autoanti-Idiotype Anti-Body Forming Cells Induced by Influenza Virus Infection*, 139 Cellular Immunol. 162 (1992), filed as Ex. 41 (ECF No. 38-17) ("Brown").

Dr. Axelrod also referenced literature suggesting that vaccines can be used to treat patients with certain types of cancer or parasitic illnesses by promoting idiotype antibody/antigen formation. *See* M. Warnke, et al., *Control of the Specificity of T Cell-Mediated Anti-Idiotype Immunity by Natural Regulatory T Cells*, 60 Ctr. Immunol. Immunother. 49 (2011), filed as Ex. 25 (ECF No. 38-1); M. Bhattacharya-Chatterjee, et al., *Anti-Idiotype Antibody Vaccine Therapy for Cancer*, 2 Exp. Op. Biol. Ther. 870 (2001), filed as Ex. 18 (ECF No. 21-13) ("Bhattacharya-Chatterjee"); M. Phillips, et al., *The Regulation of Resistance to Schistosoma Mansoni by Auto-Anti-Idiotype Immunity*, 145 J. Immunol. 2272 (1990), filed as Ex. 17 (ECF No. 21-12) ("Phillips"). All in all, however, none of the above-described studies suggest that a vaccine can initiate immune complex formation in the context of a pathologic process resulting in cutaneous vasculitis.

To account for the quick onset of Ms. Guzman's symptoms (two days following administration of the flu vaccine), Dr. Axelrod proposed that Ms. Guzman likely experienced a "secondary adaptive response" – or a reaction to a *subsequent* exposure to the same antigen – connected to her receipt of the flu vaccine the year before the vaccination at issue, which resulted in an amplified or inherently more rapid cellular response. Tr. at 79, 81-82; First Axelrod Rep. at 4-5. In contrast to a primary immune response[23] that may not peak for a period of weeks after vaccination or antigen exposure, a secondary response to an antigen to which an individual has been previously exposed can begin within two to four days thereafter. Tr. at 79-81; First Axelrod Rep. at 4. Given the similarities in strains of the two vaccines Petitioner received, Ms. Guzman's 2014 exposure to the flu vaccine (after having received a flu vaccination in 2013) likely contributed to her development of chronic urticaria thereafter, which would be consistent with a "challenge-rechallenge" response.[24] Tr. at 81; First Axelrod Rep. at 5.

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[22] Influenza viruses are divided into subtypes based on two viral proteins located on the surface of the virus: the hemagglutinin and the neuraminidase. *See Types of Influenza Viruses*, CDC, https://www.cdc.gov /flu/about/viruses/types htm (last accessed on May 6, 2019). Hemagglutinin proteins enable the flu virus to bind to surfaces cells in the host. *Dorland's* at 830.

[23] Dr. Axelrod acknowledged that Petitioner's manifestation of symptoms was too soon after vaccination to be primary. Tr. at 81.

[24] Challenge-rechallenge is "a paradigm for exploring whether one substance caused an adverse reaction. Under this model, an individual who has had an adverse reaction to the initial vaccine dose (the challenge event) suffers a worsening of symptoms after a second or third injection (the rechallenge event.)" *Viscontini v. Sec'y of Health & Human Servs.*, No. 98-619V, 2011 WL 5842577, at *22 (Fed. Cl. Spec. Mstr. Oct. 21, 2011) (quoting *Doe/70 v. Sec'y of Health & Human Servs.*, 95 Fed. Cl. 598, 603 (2010) (quotations omitted)), *mot. for review den'd*, 103 Fed. Cl. 600 (2012).

In support of his opinion, Dr. Axelrod cited to two studies exploring the concept of immunologic memory as it relates to the body's ability to respond more quickly upon re-exposure to a foreign antigen. *See* A. Abbas, Cellular and Molecular Immunology 10 (8th ed. 2015), filed as Ex. 12 (ECF No. 21-7) ("Abbas"); J. Miller, et al., *The Speed of the Second Immune Response to Tetanus Toxoid With a Review of War Reports and Observations on Simultaneous Injections of Toxoid and Antitoxin*, 3 Pediatrics 64 (1949), filed as Ex. 13 (ECF No. 21-8) ("Miller"). Neither Miller or Abbas, however, supports Dr. Axelrod's theory that a vaccine can initiate a secondary pathologic response resulting in *any* disease process (let alone vasculitis or one of its subtypes), or that a second event response would be expected to occur even in the absence of an identifiable *initial* event response (since, as noted above, Ms. Guzman's medical records do not suggest she experienced any reaction at all to her 2013 flu vaccination).

Dr. Axelrod also proposed a mechanism for the ongoing destruction or perpetuation of Petitioner's chronic urticaria that might account for the chronic nature of her alleged symptoms. Tr. at 84; First Axelrod Rep. at 5-6; Second Axelrod Rep. at 2. The antibody response to the vaccine (i.e, the formed immune complexes) could cause damage to the surrounding tissue and allow for a secondary damaging immune response to other structures of the skin. Second Axelrod Rep. at 2. This could theoretically happen through the mechanism of epitope spreading, a process in which invading agents accelerate an ongoing autoimmune process by local activation of antigens presenting as a result of the existence of immune complexes. *Id.*; *see* B. McRae et al., *Functional Evidence for Epitope Spreading in the Relapsing Pathology of Experimental Autoimmune Encephalomyelitis*, 182 J. Exp. Med. 75 (1995), filed as Ex. 22 (ECF No. 25-3); A. Vojdani, *A Potential Link between Environmental Triggers and Autoimmunity*, 2014 Autoimmune Diseases 1 (2014), filed as Ex. 15 (ECF No. 21-10).

Beyond the generalities of his causation theory, Dr. Axelrod referenced various case reports of cutaneous vasculitis with onset following flu vaccine administration – although many involved leukocytoclastic vasculitis, a condition he admitted (as noted above) did not bear upon Ms. Guzman's actual condition. Tr. at 71-72, 77, 84.[25] One case report involved urticarial

[25] *See* S. Chen, et al., *Cutaneous Leukocytoclastic Vasculitis Following Influenza Vaccination in Older Adults: Report of Bullous Purpura in an Octogenarian after Influenza Vaccine Administration*, 10 Cureus E2323 (2018), filed as Ex. 28 (ECF No. 38-4); S. Cao, et al., *Leukocytoclastic Vasculitis Following Influenza Vaccination*, BMJ Case Rep. (2017), doi:10.1136/bcr-2016-217755, filed as Ex. 29 (ECF No. 38-5); S. Ulm, et al., *Leukocytoclastic Vasculitis and Acute Renal Failure after Influenza Vaccination in an Elderly Patient with Myelodysplastic Syndrome*, 29 Onkologie 470 (2006), filed as Ex. 31 (ECF No. 38-7); S. Walker, et al., *Leukocytoclastic Vasculitis and Influenza Immunization*, 29 Clin. Exp. Derma. 91 (2004), filed as Ex. 32 (ECF No. 38-8); N. Yanai-Berar, et al., *Influenza Vaccination Induced Leukocytoclastic Vasculitis and Pauci-Immune Crescentic Glomerulonephritis*, 58 Clin. Nephrol. 220 (2002), filed as Ex. 33 (ECF No. 38-9); S. Tavadia, et al., *Leukocytoclastic Vasculitis and Influenza Vaccination*, 28 Clin. Exp. Derma. 154 (2003), filed as Ex. 34 (ECF No. 38-10); S. Monjazeb, et al., *A Case of Leukocytoclastic Vasculitis Following Influenza Vaccination*, 2 JAAD Case Rep. 340 (2016), filed as Ex. 35 (ECF No. 38-11); F. Giuseppe, et al., *Leukocytoclastic Vasculitis After Influenza Vaccination*, 12 J. Clin. Rheumatol. 48 (2006), filed as Ex. 36 (ECF No. 38-12); P. Liu, et al., *Cutaneous Vasculitis Following Influenza Vaccination*, 49 Int. Med. 2187 (2010), filed as Ex. 30 (ECF No. 38-6).

vasculitis post-vaccination (and notably involved various symptomatology distinguishable from that Petitioner experienced). *See* R. Hughes, et al., *Urticarial Vasculitis Secondary to H1N1 Vaccination*, 90 Acta. Derm. Venereol. 1 (2010), filed as Ex. 37 (ECF No. 38-13). The subject discussed in this case report was a twenty-one-year-old woman who presented with wide-spread pruritis and fixed urticarial plaques (along with purpura and peripheral pallor) six days following vaccination with the H1N1 influenza A vaccine. *Id.* at 1. A biopsy of the affected area of skin confirmed the diagnosis. *Id.* The patient was prescribed antihistamine treatment for ten days, and the urticarial rash resolved over a two-week period thereafter. *Id.*

Dr. Axelrod also spent some time at hearing analogizing Ms. Guzman's condition to drug-induced vasculitis. Tr. at 77-78, 85; First Axelrod Rep. at 2-3; Second Axelrod Rep. at 1; M. Radic, et al., *Drug-Induced Vasculitis: A Clinical and Pathological Review*, 70 J. Med. 12 (2012), filed as Ex. 10 (ECF No. 21-5) ("Radic"). Radic is a review article aimed at distinguishing drug-induced vasculitis from those originating due to idiopathic autoimmune syndromes. Radic at 12. Notably, Radic does *not* discuss vaccines in the context of drug-induced triggers, nor do the authors attempt to analogize vaccines to the various drugs considered to be causal (i.e., antibiotics, anti-tumor drugs, psychoactive agents). Dr. Axelrod posited, however, that the flu vaccine is a drug that could initiate a vasculitic process akin to one developed after taking oral medication. Tr. at 77-78. In so stating, Dr. Axelrod acknowledged that Ms. Guzman's records revealed she was taking multiple medications prior to her receipt of the flu vaccine. *Id.* at 78. He maintained, however, that when compared to the pre-existing prescription medications, the flu vaccine was newly-introduced, and thus the more likely cause of Ms. Guzman's urticaria given the temporal relationship between the two. *Id.*

Regarding onset, Dr. Axelrod posited that the timing of Ms. Guzman's injury supported his contention that her chronic urticaria was indeed vaccine-caused. Ms. Guzman received the flu vaccine and within two days experienced a secondary adaptive immune response, resulting in her physical manifestation of symptoms. Tr. at 80, 87.[26] In his view, a two to four-day onset of symptoms would be reasonable for onset of a vaccine injury based on Miller. *Id.* at 80, 87, 110; Second Axelrod Rep. at 2. As noted earlier, Miller suggests that re-exposure to a vaccine (or "booster") can amplify an immune response with subsequent injections – thereby enhancing a host's immunity to a particular infectious agent (specifically, the tetanus toxoid) in measurable titer quantities within a period of two to seven of days following reimmunization. Miller at 68-71. Dr. Axelrod admitted on cross, however, that two days would be on the "lower end" of what would be considered medically appropriate for a secondary immune response. Tr. at 110. He did not, however, offer literature supporting such a timeframe as it would relate to a vaccine-induced pathologic process (as opposed to the typical booster response).

[26] Dr. Axelrod's filed expert reports, however, placed symptom onset at four days post-vaccination. First Axelrod Rep. at 6; Second Axelrod Rep. at 1.

C. *Respondent's Expert – Dr. Arnold Levinson*

Dr. Levinson was Respondent's expert. He filed two written reports in the matter and testified at hearing. Tr. at 121-231; Expert Report, dated Nov. 28, 2016, filed as Ex. A (ECF No. 22-1) ("First Levinson Rep."); Expert Report, dated Sept. 6, 2017, filed as Ex. B (ECF No. 27-1) ("Second Levinson Rep."). Dr. Levinson opined that Ms. Guzman did not suffer from any form of cutaneous vasculitis and did not have chronic urticaria – and any inflammatory reaction that might otherwise characterize her post-vaccination symptoms was not caused by the flu vaccine. Tr. at 139-40; First Levinson Rep. at 5; Second Levison Rep. at 3-4.

Dr. Levinson currently serves as Emeritus Professor of Medicine and Neurology at the Perelman School of Medicine at the University of Pennsylvania (in addition also being a consultant to other biotech and pharmaceutical companies). *See* Curriculum Vitae, filed as Ex. A, Tab 1 (ECF No. 22-2) ("Levinson CV") at 2-5; Tr. at 121-23. During his career with the Perelman School, Dr. Levinson held a number of positions: Chief of the Allergy and Immunology Section, Director of the Fellowship Training Program in Allergy and Immunology, and Director of the Center for Clinical Immunology. Levinson CV at 1-2; Tr. at 122-25. He received his undergraduate degree and medical degrees from the University of Maryland. Levinson CV at 1. He is also currently board certified in internal medicine and allergy and clinical immunology, and holds a medical license in the state of Pennsylvania. *Id.* at 2-3.

Over the course of his career, Dr. Levinson conducted a clinical practice where he evaluated and treated patients with immune-mediated diseases, including autoimmune, neurologic system disorders, and vasculitic conditions. Tr. at 124-25. During his tenure at the Perelman School, Dr. Levinson estimated that he spent ten percent of his time in a clinical allergy and immunology teaching role. *Id.* at 128. Seventy percent of his time was devoted to research focused on IgE-mediated hypersensitivity disorders, and immunodeficiency with an emphasis on autoimmunity. *Id.* at 129. Dr. Levinson testified that he has treated five to ten patients with urticarial vasculitis, but many more with chronic urticaria and/or leukocytoclastic vasculitis. *Id.* at 126.

Dr. Levinson has served on the editorial board of multiple journals, including the *Journal of Allergy and Clinical Immunology*. Levinson CV at 4. He has published peer-reviewed articles centering on immune-mediated diseases skin diseases (including vasculitis syndromes that impact the neurologic system), drug reactions, and anaphylaxis EAE models. *Id.* at 10-21; Tr. at 123-24, 130-32. Dr. Levinson has also published a textbook chapter on vasculitis. Tr. at 131-32. At hearing, he testified that much of his career has centered on studying "prototypic" autoimmune diseases, specifically myasthenia gravis (including the antibody/antigen mechanism for the disease). *Id.* at 133. Although, Dr. Levinson does not currently see patients, he consults on complex hypersensitivity cases or cases suggestive of immunodeficiency. *Id.* at 125-26.

Dr. Levinson began his testimony by defining vasculitis as well as the relevant subtypes offered by Petitioner in support of her claim. Tr. at 140. In his view, vasculitis refers to inflammation of the blood vessels, along with resulting destruction or injury to the vessels (and other organ systems) brought about by the inflammation. *Id.*; *see also* First Levinson Rep. at 6. He defined this inflammatory process as "fibrinoid necrosis," which involves the deposition of fiber-looking material into the vessel wall, and results in tissue ischemia, skin lesions, and/or injury to other organs in the body that are supplied by the targeted vessel. Tr. at 140; First Levinson Rep. at 6. Vasculitic disorders can be primary (i.e., with no identifiable cause) or secondary to some other disease process or microbial trigger. First Levinson Rep. at 6.[27] The subtypes vary in severity, ranging from involvement of small to large vessels (with emphasis also placed on any associated inflammatory/systemic process), and are distinguishable based on clinical and histopathological features (as well as therapeutic response). *Id.*; *see also* J. Jennette, et al., *2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides*, 65 Arth. & Rheumat. 1 (2013), filed as Ex. A, Tab 3 (ECF No. 23-2).

Although vasculitis might be immune-mediated, Dr. Levinson maintained that it is not necessarily an autoimmune disease, because in most vasculitic conditions antibodies typically attack "exogenous" antigens (i.e., drugs or microbial organisms) rather than self structures. Tr. at 176, 178 (vasculitis is not always "a product of an autoimmune response against a self-antigen"); *see also* C. Langford, *Vasculitis*, 125 J. Allergy & Clin. Immunol. 216, 216-17 (2010), filed as Ex. A, Tab 2 (ECF No. 23-1) (discussing the various antibodies associated with the vasculitic variants and their roles). A vasculitic injury occurs when antibodies produced in response to some foreign antigen bind to that antigen, forming immune complexes. Tr. at 176; First Levinson Rep. at 6. Those complexes are then deposited in the vasculature and result in damage to the vessel wall. Tr. at 176; First Levinson Rep. at 6. The type and severity of the vasculitis is determined by the location of deposit (i.e., whether in the venules, capillaries, or arterials). Tr. at 176.

Dr. Levinson next considered the purported vasculitis subtypes referenced by Dr. Axelrod on direct: leukocytoclastic vasculitis, urticarial vasculitis, and chronic urticaria. Tr. at 141-44. He described leukocytoclastic vasculitis as a "histopathological description" of a type of vasculitis largely associated with inflammation and destruction of post-capillary venules, and which results in direct infiltration of the vessel wall. *Id.* at 141. Leukocytoclastic vasculitis is neutrophil-driven – meaning neutrophils[28] undergo cell death in the vessel wall – causing necrosis or wall obstruction. *Id.* at 142-43. Symptoms can include palpable purpura (i.e., raised lesions/bruising

[27] Dr. Levinson agreed that vasculitis can be drug-induced or manifest as a result of other therapeutic agents. Tr. at 152-53. He did not, however, accept Dr. Axelrod's opinion that Ms. Guzman's symptoms were indicative of drug-induced vasculitis (or any vasculitis for that matter) for the reasons discussed herein. *Id.* at 153; *see also* Second Levinson Rep. at 1.

[28] Neutrophils are white blood cells that aid the body in fighting off infections. *See Neutropenia*, Mayo Clinic, https://www mayoclinic.org/symptoms/neutropenia/basics/definition/sym-20050854 (last accessed on May 2, 2019).

associated with accumulation of red blood cells in the dermis tissue) or petechia (i.e., smaller lesions that occur when red blood cells/other blood products are released into the skin). *Id.* at 155-56; First Levinson Rep. at 6. Dr. Levinson admitted that leukocytoclastic vasculitis is the consequence of an immune reaction, but disputed that it occurs via an autoimmune mechanism (i.e., in which an antibody attacks a self-antigen or structure in the body). Tr. at 175-76.

Urticarial vasculitis is a rare subtype of leukocytoclastic vasculitis in which patients have chronic urticaria or angioedema reflected in individual lesions and localized pain. Tr. at 143, 178-79; First Levinson Rep. at 7; Kluger at 126, 139. It is often seen in patients with serum sickness, connective-tissue disorder, infections, or physical urticarias. First Levinson Rep. at 7. Seventy percent of cases are idiopathic, and many times its onset points to the existence of some form of underlying systemic disease. Tr. at 148, 152. It is considered to be a chronic condition (i.e., lasting six weeks or more). *Id.* at 156. Symptoms are limited to urticaria and pain – thus, urticarial vasculitis patients do not present with palpable purpura or petechia. *Id.* In Dr. Levinson's view, an urticarial vasculitic condition cannot be diagnosed without a biopsy. *Id.* at 174; First Levinson Rep. at 7. It also usually does not respond well to antihistamine treatment.[29] Tr. at 143, 178-79.

Dr. Levison was firm in opining that chronic urticaria is *not* equivalent to urticarial vasculitis. Tr. at 141. Although symptoms associated with urticarial vasculitis can involve chronic urticaria, the urticarial vasculitic clinical course is more severe, and involves other distinguishable symptoms. *Id.* at 144. For example, urticarial vasculitic lesions "linger" for a period of twenty-four to forty-eight hours (i.e., they do not come and go rapidly like regular hives). *Id.* at 144, 184-85, 214; Kluger at 126. Lesions related to urticarial vasculitis are also typically accompanied by pain and pruritis (i.e., itching), unlike lesions associated with chronic urticaria (which are usually erythematous with a blanching, pale center). Tr. at 144-45, 150-52. In addition, urticarial vasculitic lesions typically involve hyperpigmentation – a process wherein red blood cells have escaped from the lesion – thereby leaving visible marks or "footprints" on the skin. *Id.* at 145, 184-85, 214; Kluger at 126. Maculopapular-type rashes (as described in Petitioner's records) are not indicative of urticarial lesions (i.e., a hive or welt), but are more likely associated with an alternate condition (such as a drug reaction or prior infection, for example). Tr. at 151-52. As noted earlier, the two are also pathologically distinguishable, as cutaneous vasculitis, histologically, is associated with

[29] On cross, Petitioner referenced literature suggesting that vasculitis could in fact be successfully treated with antihistamines. Tr. at 181-83; *see* C. Langford, *Vasculitis*, 125 J. Allergy & Clin. Immunol. 216, 223 (2010), filed as Ex. A, Tab 2 (ECF No. 23-1). Dr. Levinson, however, countered that patients who present with some form of a rash/urticaria might first try an antihistamine for a couple of weeks to see if the treatment alleviated the symptoms and/or assisted the treater determine the etiology of the rash. Tr. at 183, 213. But, by in large, the antihistamine treatment would later (in his experience) prove ineffective in successfully resolving any form of vasculitis. *Id.* at 183.

distinct patterns (typically evidenced as eosinophilia[30] or granulomas[31]). *Id.* at 146-47; *see* Kluger at 133.

Dr. Levinson asserted that the two conditions are also distinguishable based on the appropriate treatment protocol (and in fact attempts to identify the most effective treatment can aid in determining the nature of the patient's condition). Tr. at 147-49. Patients presenting with acute urticaria are typically treated initially with antihistamines but *not* corticosteroids. *Id.* at 147. Urticarial vasculitis, on the other hand, is more often associated with systemic disease in which aggressive corticoid steroids/anti-inflammatory/immunosuppressive drugs are deemed necessary. *Id.* at 148. Moreover, topical corticosteroid creams are typically not used to treat urticarial vasculitis (if the lesions are disseminated) since they could have an adverse effect on the patient if the steroid is widely absorbed. *Id.* at 148-49; *see* J. Ference, et al., *Choosing Topical Corticosteroids*, 79 Am. Family Phys. 135, 137 (2009), filed as Ex. C (ECF No. 35-1) ("Ference"). Dr. Levinson otherwise posited that patients with chronic urticaria rarely also experience vasculitis at the same time, and pointed to literature confirming that only five to ten percent of patients present with both conditions. *Id.* at 141; Kluger at 129.

Based on his review of the literature coupled with relevant medical records, Dr. Levinson concluded that Ms. Guzman did not likely have any form of vasculitis *or* chronic urticaria. Tr. at 153, 164-65, 199. He acknowledged that Petitioner presented to treaters in late February 2014 with a blanching, maculopapular rash on exam roughly two weeks post-vaccination, and that the rash persisted until late March or mid-April 2014. *Id.* at 155-56, 161-62, 163-64, 196-97; *see* Ex. 1 at 502-03 (4/15/2014 visit note indicating rash had completely resolved). But in Dr. Levinson's understanding, blanching, maculopapular lesions (absent palpable purpura or petechia) are not indicative of either vasculitis or chronic urticaria. Tr. at 155. Those same records also did not suggest that Ms. Guzman was experiencing chronic hives (or any hives at all for that matter) at the time of those visits. *Id.* at 156. Dr. Levinson acknowledged that visit notes from August 2014 did suggest that Ms. Guzman was still using Loratadine and hydrocortisone cream (even though no rash was seen on exam). *Id.* at 201-02. Even so, the fact that Ms. Guzman may have been successfully treating her symptoms in this manner further supported his opinion – given that vasculitic conditions would not likely respond well to antihistamine treatment. *Id.* at 162-63, 198.

Petitioner's visit with Dr. Canfield thereafter in March 2015 revealed no rash on exam. Tr. at 204-05. Dr. Levinson admitted that this record made some reference to a vaccine reaction (or allergy to the flu vaccine), but he proposed it was unclear who authored the note, which could

[30] Eosinophilia is a higher than normal level of eosinophils (or disease-fighting white blood cells). The condition is most often associated with a parasitic infection, allergic reaction, or cancer. *See Eosinophilia*, Mayo Clinic, https://www mayoclinic.org/symptoms/eosinophilia/basics/definition/sym-20050752 (last accessed on May 2, 2019).

[31] Granuloma annulare is a skin condition that causes raised reddish or skin-colored lesions (or bumps) in a ring pattern on the skin. *See Granuloma Annulare*, Mayo Clinic, https://www mayoclinic.org/diseases-conditions/granuloma-annulare/symptoms-causes/syc-20351319 (last accessed on May 2, 2019). It typically presents on the hands or feet. *Id.*

merely reflect the history recounted by Petitioner. *Id.* at 206-07. Dr. Canfield did continue to prescribe Loratadine and hydrocortisone cream, but Dr. Levinson attributed those medications as needed to treat other allergies. *Id.* at 208. Dr. Levinson also acknowledged that a subsequent visit record from July 2015 indicated that Ms. Guzman had some erythema (or "red patch of skin") on the inner elbow. *Id.* at 208-09; *see* Ex. 1 at 576-77. He agreed that his could be evidence of an active skin rash, but asserted that such a rash was likely different from the maculopapular rash described in February 2014. Tr. at 210-12.[32] Overall, however, Dr. Levinson maintained that no treater ever diagnosed Ms. Guzman with chronic urticaria/hives or vasculitis, and he found no evidence in the medical record of such lesions on exam over the course of her treatment. *Id.* at 157, 186-87.

The July 2015 photo submitted by Ms. Guzman similarly did not alter Dr. Levinson's opinion. Tr. at 154. In his view, it revealed no evidence of vasculitis *or* chronic urticaria. *Id.* Moreover, based on his review of the medical literature, lesions associated with either condition almost never appear on the palms (as the photograph purports to show) or soles of feet. *Id.* at 151. He thus found this evidence more supportive of his opinion that Petitioner did not suffer from either condition.

Dr. Levinson next discussed the biologic mechanism offered by Dr. Axelrod in support of Petitioner's causation theory. Tr. at 165-66. In his view, Dr. Axelrod accurately explained the workings of an idiotype/anti-idiotype network, a process that regulates the adaptive immune system in responding to certain foreign stimulants like infection. *Id.* at 166-67; Second Levinson Rep. at 2. Petitioner was also arguing, accurately, that the initial antibodies produced in an adaptive immune response caused additional T cells/B cells to produce additional antibodies (specific to the original antigen/antibody response) – which thereafter bind to the insulting antigen and form an "idiotype" or mosaic complex. Tr. at 167-68.

But Dr. Levinson did not, however, find Dr. Axelrod's application of the theory in this case to be credible – because the mechanism had not been shown to be pathogenic in nature. Tr. at 169, 170; First Levinson Rep. at 9-10. Rather, Dr. Axelrod was describing a "physiologic" response that (even if vaccine-triggered) has never been demonstrated to be capable of producing immune complexes resulting in pathology akin to what Petitioner had allegedly experienced. Tr. at 169-70. Dr. Levinson posited that the literature offered by Dr. Axelrod on this point suggested that *no* animal (or human) experimental models have indicated that these complexes can *actually* (as opposed to theoretically) form from the above-described antibody interaction. *Id.* at 169. And in any event, none of the literature cited by Petitioner (i.e., Jerne, Phillips, Bhattacharya-Chatterjee,

[32] Dr. Levinson also found it significant that Dr. Canfield did not choose to biopsy the rash noted on exam at this visit. In his view, Dr. Canfield is a well-credentialed and experienced allergist would request a biopsy be performed if he felt Ms. Guzman had any form of vasculitis. Tr. at 146-47. Since there was no record evidence of a biopsy, Dr. Levinson felt this weighed against concluding Petitioner's condition included vascular involvement in any way.

Brown, Brozek) suggested that these complexes could be vaccine-induced, or result in vasculitis or chronic urticaria. First Levinson Rep. at 10; Second Levinson Rep. at 2.

Dr. Levinson further critiqued Dr. Axelrod's theory that the concept of epitope spreading could accurately account for how the alleged initial vaccine-induced response could produce a chronic condition. Tr. at 170. In his view, that theory could only be credibly linked to autoimmune diseases already *known* to be mediated by autoreactive T cells or B cells (or autoantibodies). *Id.*; *see also* First Levinson Rep. at 10. In the context of the present case, however, Dr. Levinson posited, there is no evidence of an autoimmune reaction in the proffered medical records – thereby rendering the concept inapplicable, given that epitope spreading depends on initial tissue damage due to a primary autoimmune reaction that then in turn causes secondary expression of other autoantibodies to "spread" damage. Tr. at 170-71; First Levinson Rep. at 10; Second Levison Rep. at 2-3; *see* C. Vanderlugt, et al., *Epitope Spreading in Immune-Mediated Disease: Implications for Immunotherapy*, 2 Immunol. 85, 86-91 (2002), filed as Ex. A, Tab 9 (ECF No. 23-8). Vasculitis, by contrast, is simply "autoreactive" from the outset – and thus would not present in this manner. Tr. at 171.

Ultimately, Dr. Levinson maintained that vaccines cannot cause urticarial vasculitis or chronic urticaria. Tr. at 215. At best, some formulations of the flu vaccine (specifically those containing the allergen ovalbumin) could theoretically cause an individual with an egg allergy to develop urticarial lesions immediately post-vaccination, but such a reaction would only lead to acute urticaria, not a chronic form. *Id.* at 215-26. Dr. Levinson did allow for the hypothetical possibility that chronic hives could manifest post-vaccination, but he doubted that a plausible biologic scientific or medical mechanism exists to explain such a reaction. *Id.* at 216-17. He also seemingly conceded that Ms. Guzman's initial maculopapular rash could have been associated with the flu vaccine (given that she complained of other symptoms commonly associated with vaccination, like nausea, headache, etc.). *Id.* at 219. But despite the above, Dr. Levinson maintained that facts of this case and the testimony offered (both by Petitioner and Dr. Axelrod) in support could not credibly establish that Petitioner's own symptoms could be so explained. *Id.* at 217-19.

Instead of vaccination, Dr. Levinson suggested that Ms. Guzman's symptoms could be more reliably attributed to various chemical hypersensitivities (for example, cleaning detergents, perfumes, lipstick, etc.). Tr. at 218; First Levinson Rep. at 8. He referenced medical records suggesting that Ms. Guzman had reported experiencing allergies and/or skin reactions following exposure to these agents (as well as documented diagnosis of allergic rhinitis). Tr. at 218; *see, e.g.*, Ex. 1 at 173, 175. In his view, these agents could not be ruled out as potential causes for her symptoms – although he admitted that no treater had conducted an allergic evaluation to determine if her skin rash symptoms could be attributed to these sensitivities. First Levinson Rep. at 8.

III. Procedural History

Ms. Guzman filed her Petition on July 16, 2015. Pet. at 1. Following the filing of pertinent medical records, Respondent filed the Rule 4(c) Report on April 11, 2016 (ECF No. 15), contesting Ms. Guzman's right to an entitlement award. Updated medical records were filed thereafter. *See* ECF No. 17.

Due to the issues identified in the Rule 4(c) Report, I ordered the parties to file expert reports in support of their respective positions. Petitioner filed an initial report for Dr. Axelrod on September 9, 2016 (ECF No. 21-2). Respondent's initial report from Dr. Levinson was filed thereafter on December 2, 2016 (ECF No. 22-1). Supplemental expert reports were filed on May 10, 2017 (ECF No. 25-1) and September 8, 2017 (ECF No. 27), respectively.

I set the matter for hearing on October 25, 2018 (ECF No. 29). The hearing took place as scheduled, and included testimony from the experts identified above (along with testimony from Petitioner). Following the hearing's conclusion, the parties did not submit post-hearing briefs. The matter is ripe for adjudication.

IV. Applicable Law

A. *Petitioner's Overall Burden in Vaccine Program Cases*

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury" – i.e., an injury falling within the Vaccine Injury Table – corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & 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) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs*., 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (*quoting Shyface v. Sec'y of Health & 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, 1278 (Fed. Cir. 2005): "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury." *Althen*, 418 F.3d at 1278.

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received can cause the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & 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.

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. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Human Servs.*, 121 Fed. Cl. 230, 245 (2015) ("[p]lausibility . . . in many cases may be enough to satisfy *Althen* prong one" (emphasis in original)), *vacated on other grounds*, 844 F.3d 1363 (Fed. Cir. 2017). But this does not negate or reduce a 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).

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'") (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); *Caves v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 119, 136 (2011), *aff'd*, 463 F. App'x 932 (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 (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) (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.")).

However, there are 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). "The *Daubert* 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).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial for a (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, 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 his 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 v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the ipse dixit of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (*quoting Gen. Elec. Co. v. Joiner*, 522 U.S. 146 91997)); *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 Fed. App'x 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325-26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & 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 every filed item factors into the outcome of this decision. While I have reviewed all of 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*., 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Human Servs*., 527 F. App'x 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. Overview of Relevant Medical Terms and Prior Relevant Decisions

As noted above, Respondent argues that the diagnoses proffered by Petitioner (whether cutaneous vasculitis *or* chronic urticaria) are unsupported by the medical record in light of

scientific/medical understanding of these conditions. Because Petitioner's causation theory turns on the determination that Dr. Axelrod properly characterized her condition, I will briefly discuss what the expert testimony and filed literature says about the two most relevant proposed diagnoses.

The literature filed in the present matter unquestionably defines vasculitis as inflammation of the blood vessels. Kluger at 125. The various vasculitic subtypes differ according to a spectrum of severity (generally dependent upon the type of blood vessel affected and the underlying inflammatory/systemic effect on the body), and are further distinguishable based on the clinical and histopathologic features (as well as the extent of the damage caused to the body's organ systems). As noted earlier, cutaneous vasculitis is isolated to the skin. It displays a wide variety of elementary lesions including urticaria, purpura, infiltrated erythema, hemorrhagic vesicles, ulcers, nodules, livedo, infarcts, and digital gangrene. Kluger at 125. The urticaria associated with vasculitis, however, is considered "atypical" with "distinct features from common urticaria." *Id.* at 126. Typically, urticarial lesions associated with vasculitis linger for a period longer than twenty-four hours, and are routinely accompanied by purpura, postinflammtatory pigmentation, and symptoms of burning. *Id.* Palpable purpura is by far the most frequent manifestation. *Id.* at 125. A skin biopsy is required to confirm the diagnosis and subtype, and treatment typically includes anti-inflammatory agents and/or stronger immunosuppressive drugs (depending on the severity of disease course). *Id.* at 128, 137.

Chronic urticaria is defined as "urticaria that is present for greater than [six] weeks." Kaplan at 477. Histologically, it is characterized by a "perivascular infiltrate around the venules, *without* vasculitis or immune complex deposits." Jauregui at 43 (emphasis added). Triggering events include identifiable agents like an allergic reaction to a food/drug or a viral illness. Kaplan at 477. There are two subtypes associated with chronic urticaria: inducible urticaria and spontaneous urticaria. *Id.* Inducible urticarial lesions appear as often as the host interacts with an identified stimulus, and typically last for more than an hour – but less than twenty-four to thirty-six hours, thereby distinguishing chronic urticaria from urticarial-related vasculitis. Jauregui at 42; Kaplan at 477. Spontaneous urticarial lesions are unpredictable, but appear in similar fashion – though they can present for multiple days at a time. Kaplan at 477. Antihistamines and corticosteroids can be used to treat both types (though antihistamine is considered the treatment option of choice). *Id.*; *see also* Jauregui at 41. Chronic urticaria usually does not involve systemic manifestations. Jauregui at 43.

Urticarial vasculitis is a rare, chronic, subtype of cutaneous vasculitis that affects five to ten percent of patients with chronic urticaria. Kluger at 129. In most cases, the disease is idiopathic in nature. *Id.* Two subtypes have been identified: hypocomplementemic (HUV) and nonhypocomplementemic (NUV). HUV can be associated with certain illnesses (including connective tissue disease, systemic lupus, cryoglobulinemia, hepatitis C infection, drugs, and viral infections. *Id.* Pathologically, HUV is also associated with elevated anti-C1q antibodies or antinuclear antibodies. *Id.* It is also typically accompanied by an elevated ESR. *Id.* NUV is usually

idiopathic, limited to the skin, and self-resolving (but can be associated with elevated eosinophil levels). *Id.* As with vasculitis generally, a biopsy is required to confirm the diagnosis. *Id.* at 137.

Cutaneous vasculitis has been deemed a compensable injury in the Program in other cases. *See, e.g.*, *McElroy v. Sec'y of Health & Human Servs.*, No. 11-679, 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). Chronic urticaria has also been alleged as an injury, but with varying degrees of success. *Waterman v. Sec'y of Health & Human Servs.*, No. 13-44V, 2016 WL 761173, at *8 (Fed. Cl. Spec. Mstr. Feb. 5, 2016) (physician-diagnosed chronic urticaria with two-week onset found to be caused by HPV vaccine); *but compare Warfle v. Sec'y of Health & Human Servs.*, No. 05-1399V, 2010 WL 2671504, at *32 (Fed. Cl. Spec. Mstr. June 15, 2010) (DTap vaccine not causal of chronic urticaria, where Petitioner failed to preponderantly establish the injury alleged and ultimately the first *Althen* prong – due primarily to the lack of evidence establishing the ability of the vaccine to cause persistent, month-long symptoms).

II. Petitioner Has Not Satisfied the *Althen* Prongs.

I am addressing the *Althen* prongs in order of their significance to my determination, rather than consistent with their sequential presentation in the underlying Federal Circuit decision.

A. *Althen Prong Two*

1. Petitioner Did Not Have Vasculitis or Chronic Urticaria

Assuming for sake of argument that Petitioner could establish that the flu vaccine can cause cutaneous vasculitis and/or chronic urticaria, I would still be unable to conclude (based on the records filed in this case) that it likely caused Ms. Guzman's symptoms – because it does not appear she suffered from *either* condition. The failure to establish a claimed injury can be fatal to a petitioner's claim. *See, e.g.*, *Lombardi v. Sec'y of Health & Human Servs.*, 656 F.3d 1343, 1353 (Fed. Cir. 2011). This is especially true in this case, as Petitioner's causation theory largely depended on my finding that Petitioner suffered some kind of vasculitis, with her rash-like symptoms being the condition's primary manifestation.

Nowhere in the record is there clear evidence that Ms. Guzman was ever diagnosed with vasculitis *or* chronic urticaria. *See* Ex. 1 at 494, 497-99, 501-02, 503-05, 555-57. 576-77; Ex. 2 at 27, 42-43. No treater documented urticarial lesions on exam, and the record is otherwise void of any concern for a vasculitic condition. No test results (i.e., a biopsy) of any kind can be credibly pointed to in this case that could suggest Petitioner experienced some vasculitic injury (or urticarial lesions).

Moreover, the record otherwise does not contain sufficient evidence from which it could be concluded that Petitioner more likely than not *did* have vasculitis or urticarial lesions, regardless of whether she was so diagnosed. The treaters most competent to weigh in on the topic of such a condition, such as Dr. Canfield, never reached any conclusions about her complaints that could be deemed consistent with vasculitis or urticaria in a meaningful sense. At best, the records close-in-time to her receipt of the vaccine in February 2014 reveal that Ms. Guzman was assessed with a maculopapular or erythematous rash consistent with a possible allergic reaction that mostly resolved within two months thereafter (or by mid-April 2014). Ex. 1 at 493, 497-99, 501-03.

Ms. Guzman's testimony at hearing similarly did not reliably establish that she experienced any *additional* adverse symptoms (that could arguably be associated with vasculitis) other than the initial rash documented in the record between February 2014 and mid-April of that year (and the inner elbow rash noted on exam in July 2015). Her statements at hearing were generally consistent with the medical records, apart from her assertion that she experienced the documented rash on and off consistently since late February 2014 (and even at the time of hearing – in October 2018). Tr. at 23, 40-42, 37, 53. Indeed, the records filed in the case reference multiple visits where no rash was found on exam following mid-April 2014. *See, e.g.*, Ex. 1 at 503-05, 508-52, 555-56; Ex. 4 at 1-6; Ex. 2 at 27, 43. To the extent Petitioner attempted to vary what the record stated, she failed to establish grounds for so doing. *See, e.g.*, *Cucuras*, 993 F.2d at 1528.

Petitioner also points to the fact that she was continuously taking, or being prescribed, certain medications that were successfully treating her condition (and thus presumably tempering her overall presentation, and thereby allowing the inference that her condition was more than regular hives). Yet, as discussed above, literature filed by both parties indicates that true vasculitis does *not* respond to antihistamine treatment – and topical creams would be used with simple urticaria rather than a vasculitis (for which, Dr. Levinson stated, such a treatment would in fact be contraindicated). *See, e.g.*, Ference; Tr. at 72-74, 148-49. Accordingly, the effectiveness of these treatments is equally supportive of the conclusion that Petitioner's condition was not an immune-mediated vasculitis, but instead something more benign.[33]

Dr. Axelrod acknowledged all of the above, but maintained that Petitioner's records were consistent with a vasculitic condition, with symptoms manifesting as chronic urticaria. In so opining, however, he relied primarily on Ms. Guzman's testimony and the photographic evidence submitted in support (which, as Dr. Levinson credibly established, was not particularly probative). Since he could not point to a contemporaneous record documenting concerns for a vasculitic condition (or urticarial lesions), Dr. Axelrod insisted that notations in the record revealing the presence of a maculopapular rash were consistent with an urticarial presentation. Tr. at 69-70, 93,

[33] The literature does suggest that antihistamines can be beneficial in treating chronic urticaria (*see, e.g.*, Jauregui; Ellingsen), but (for the reasons discussed herein) the record does not support such a diagnosis – and Petitioner's overall causation theory relies on the determination that her condition was vasculitic.

104-06. To support this assertion, Dr. Axelrod cited to Calabrese – a study he acknowledged at hearing discussed a form of vasculitis *distinguishable* from the one proffered in the present case (hypersensitivity vasculitis). Calabrese at 1110. Calabrese does include maculopapular rash as one criteria relevant to the urticarial vasculitis diagnosis, but adds that the diagnosis requires satisfaction of *three out of five* criteria (including: age at onset > 16 years, medication use at onset, palpable purpura on exam, and/or biopsy evidence consistence with that typical for a vasculitis injury) for confirmation. *Id.* I thus could not conclude from the above that Ms. Guzman's rash was by itself suggestive of a vasculitic condition without evidence of additional criteria, which in this case (beyond Petitioner's age) are absent. Otherwise, *none* of the scientific literature referenced in connection with chronic urticaria indicates that a maculopapular rash is a presenting symptom. *See, e.g.*, Kaplan; Kluger.

Dr. Levinson by contrast, offered scientific literature discussing the relevant symptomatology course associated with both vasculitis and chronic urticaria, and persuasively distinguished the conditions from the maculopapular rash revealed occasionally in Ms. Guzman's medical record. Relying on Kluger, Dr. Levinson posited that urticarial lesions associated with cutaneous vasculitis would present in a lingering form (i.e., lasting twenty-four to forty-eight hours) and would be accompanied by pain, itching, and hyperpigmentation of the skin (non-blanching). Tr. at 144, 184-85, 214; Kluger at 126. A biopsy would also be required to confirm the diagnosis (although one was never performed in this case). Tr. at 146-49; Kluger at 133. Lesions associated with chronic urticaria, by contrast, would typically manifest as an acute, erythematous, blanching, lesion with a pale center – and require standard antihistamine treatment. Tr. at 144-45, 150-52. No such lesions were noted in the medical record at any time.

Also harming Petitioner's showing on this front were limitations in Dr. Axelrod's expertise to testify on the injury in question. Although it is not uncommon in the Program for testifying experts to propose a diagnosis that no contemporaneous treater has considered or embraced, experts are only persuasive in doing so when their opinion arises from time-tested experience treating or studying the injury in question. Despite his immunologic qualifications, and although he may have some treatment familiarity with the proposed injuries, Dr. Axelrod did not demonstrate personal expertise in the study or treatment of vasculitis-oriented conditions, and certainly was less qualified to opine on such matters than Dr. Levinson (even taking into account that the latter does not regularly treat patients anymore). Petitioner therefore could not obtain from Dr. Axelrod's testimony what the record and the filed medical and scientific literature did not provide to her in support of the proposed diagnoses.

2. The Record Does Not Suggest the Flu Vaccine Injured the Petitioner

Petitioner's obligation under the second *Althen* prong is to demonstrate a logical sequence of cause and effect connecting the particular facts of her case to his medical theory. *Sturdivant v. Sec'y of Health & Human Servs.*, No. 07-788V, 2016 WL 552529, at *18 (Fed. Cl. Spec. Mstr. Jan. 21, 2016) (discussing *Althen* prong two). But even if my focus is limited to those post-

vaccination symptoms and reactions that *are* reflected in the medical record, preponderant evidence has not been offered establishing that the flu vaccine is likely responsible for Petitioner's symptoms.

The medical record in this case does not establish that Ms. Guzman was experiencing *any* kind of chronic vaccine-caused injury in the months after vaccination. Rather – and contrary to testimony at hearing regarding the "chronic" nature of her symptoms – that record suggests that her rash largely resolved within a two- to three-month period post-vaccination (apart from the one notation of erythema in July 2015 well after).[34] The photographic evidence offered in support (also dated over one year from onset) similarly does not represent clear evidence that her rash persisted beyond that timeframe (and in fact is not particularly persuasive evidence of anything other than some nonspecific redness on the palms that cannot be credibly linked to Petitioner's alleged symptoms course). *See* Tr. at 154; First Levinson Rep. at 9. And qualified specialist treaters like Dr. Canfield, who did in July 2015 report observing some rash, directly disputed any causal connection between the flu vaccine and Petitioner's complained-of symptoms. *See* Ex. 1 at 577.

Moreover, there is no evidence in the record that suggests the existence of an undercurrent of autoimmunity of the kind often seen in other Program cases, such as ongoing inflammation or some other subclinical, pathologic process. Dr. Axelrod proposed that Ms. Guzman responded well to antihistamine and topical steroid treatment – which allegedly prompted her treaters to forego any biopsy testing that would have confirmed the nature of her injury. *See* Tr. at 73-74. But the medical record reveals that relevant testing for the typical inflammatory marks (including IgE and CRP) returned normal results. *See* Ex. 1 at 593-98. I give such facts greater weight than Petitioner's explanations for why certain testing evidence might be absent from the record (which can just as credibly be attributed to the fact that Ms. Guzman's existing treaters saw no reason, based upon her presentation, even to suspect that vasculitis might explain her symptoms).

I also take note of the fact that Respondent's expert identified an alternative explanation for Petitioner's symptoms that was inadequately countered by Petitioner. Dr. Levinson pointed to evidence in the record suggesting that Petitioner's symptoms could be attributable to various pre-existing hypersensitivities (i.e., cleaning detergents, perfumes, and lipsticks) or allergic rhinitis. Tr. at 218. Petitioner herself acknowledged that she complained of problems associated with these allergic agents. *Id.* at 28-29. Program case law recognizes that clearly-identified alternative diagnoses *can* call into question a petitioner's allegations that a vaccine caused their onset of adverse symptoms thereafter. *See, e.g., Pafford v. Sec'y of Health & Human Servs.*, 64 Fed. Cl.

[34] For this reason, even if it were conceded that Petitioner *had* experienced an initial allergic reaction to the flu vaccine, manifesting in the form of a rash (as evidenced by the maculopapular rash and related symptoms noted in the record from late February 2014), that reaction was transient, resolving well before the six-month period required under the Vaccine Act's severity requirement. 42 U.S.C. § 300aa-11(c)(1)(D)(i); *see e.g., Hinnefeld v. Sec'y of Health & Human Servs.*, No. 11-328V, 2012 WL 1608839, at *4-5 (Fed. Cl. Spec. Mstr. Mar. 30, 2012) (dismissing case where medical history revealed that petitioner's injury resolved less than two months after onset). And regardless, this is not the theory presented by Petitioner herein.

19, 31 (2005) ("the Special Master may look to other facts apparent in the record, including potential alternative causes that may undermine the petitioner's case . . . ."), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2006). The proposal that allergies caused Ms. Guzman's symptoms (while plausible) was certainly not established by Respondent with preponderant evidence, but it further served to undercut the overall sufficiency of Petitioner's showing on the "did cause" *Althen* prong.

B. *Althen Prong One*

Petitioner has not offered sufficient reliable scientific or medical evidence to meet her burden of establishing a reliable theory for how the flu vaccine could cause vasculitis or urticarial lesions. As described herein, Dr. Axelrod proposed that the flu vaccine can induce the production of immune complexes, thereby causing inflammation sufficient to create a favorable environment for the development of cutaneous vasculitis or chronic urticaria. But this theory has several deficiencies.

First, a significant component of Petitioner's theory unsuccessfully attempts to leverage what is known about the proper functioning of the immune system (and specifically what causes the creation of immune complexes) into proof that these anticipated processes can also be pathogenic. Petitioner has referenced reliable literature establishing that certain immune complexes can form in reaction to infection with a wild virus (s*ee, e.g.*, Brown; Brozek), and that these same complexes may play a role in various disease processes. But the theory lacks similar support for its connecting proposition – that immune complex formation *leads* to or causes vasculitis or urticarial lesions (even if those conditions involve such complexes) – as well as the linchpin concept that vaccination can instigate such an entire disease process. It is not enough to note that immune complexes have been measured in the context of certain injuries or illnesses (or are involved in the body's reaction to those illnesses). Dr. Axelrod otherwise does not have enough demonstrated expertise studying these unsupported elements of the theory to give them ballast, and no persuasive or reliable literature was offered on such points. There remain too many unsupported, but vital, planks in Petitioner's causation theory to deem it to have been preponderantly established.

Another mechanism proposed by Dr. Axelrod – that Ms. Guzman's subsequent re-exposure to antigens in the flu vaccine (administered *over* a year prior) resulted in an amplified and inherently more rapid cellular response, resulting in her alleged vasculitis – fails for similar reasons. As the record indicates, Petitioner's complained-of symptoms presented within two days following her receipt of the vaccine. Ex. 1 at 493. And, Dr. Axelrod acknowledged at hearing that he could not rely solely on a primary adaptive response to explain Petitioner's onset of symptoms. Tr. at 79-81. He therefore attempted to establish the February 2014 vaccination as a secondary response attributable to priming that Petitioner's immune system received from a vaccination administered a year earlier (and with no documented evidence of a reaction to the initial vaccination). To support this argument, Dr. Axelrod offered literature describing the concept of a vaccine booster response intended to assist the body in developing immunologic memory to certain

vaccine antigens. *See, e.g.*, Abbas; Miller. Neither Abbas nor Miller, however, provide any evidence that a cumulative effect or response to a prior vaccine can produce an adverse pathologic process (let alone one that results in vasculitis or urticarial lesions). The facts of this case otherwise do not fit the paradigm of "challenge-rechallenge," whereby a demonstrated initial reaction to a prior vaccine is followed up with a demonstrably more robust reaction (thereby implicating the vaccine). *See, e.g., Viscontini v. Sec'y of Health & Human Servs.*, No. 98-619V, 2011 WL 5842577, at *22-24 (Fed. Cl. Spec. Mstr. Oct. 21, 2011), *mot. for review den'd*, 103 Fed. Cl. 600 (2012). The mere fact Petitioner received a flu vaccine before, without apparent incident, cannot be transmuted into an explanation for a purported reaction to a second flu vaccination.

Petitioner's invocation of epitope spreading to explain the seventeen month-long, chronic character of her rash and related alleged symptoms following her receipt of the vaccine in February 2014 is also generally inconsistent with what is known about autoimmune disease processes (given the facts of Petitioner's case). As Dr. Levinson posited, epitope spreading can only occur secondary to an *initial* autoimmune process – in which case tissue damage could occur and spread *after* the initial process has already been triggered. The concept of epitope spreading (as it applies to this set of facts) is thus not applicable, given Petitioner's inability to establish a reliable theory providing an explanation for her primary alleged vaccine reaction.

Petitioner otherwise heavily relied on case reports associating forms of the flu vaccine with different types of vasculitis. *See, e.g.*, Hughes; Chen; Liu. It is well recognized in the Program that case reports are deserving of *some* evidentiary weight. *Paluck v. Sec'y of Health & Human Servs.*, 104 Fed. Cl. 457, 475 (2012) (noting that although "case reports 'do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value' . . . 'the fact that case reports can by their nature only present indicia of causation does not deprive them of all evidentiary weight'") (quoting *Campbell v. Sec'y of Health & Human Servs.*, 97 Fed. Cl. 650, 668 (2011)). However, case reports are not robust evidence favoring causation (even under the Program's comparatively lenient preponderance evidentiary standard). *W.C. v. Sec'y of Health & Human Servs.*, No. 07-456V, 2011 WL 4537887, at *13 (Fed. Cl. Spec. Mstr. Feb. 22, 2011) ("case reports are generally weak evidence of causation because case reports cannot distinguish a temporal relationship from a causal relationship"), *mot. for review den'd*, 100 Fed. Cl. 440 (2011), *aff'd*, 704 F.3d 1352 (Fed. Cir. 2013). Moreover, the case reports offered either involved vasculitic conditions that (as I note above) the record does not establish Petitioner had, or involved drug-induced disease distinguishable from vaccination (*see, e.g.*, Radic).

At bottom, Petitioner's theory (by Dr. Axelrod's admission) places great emphasis on the injury's close temporal association to vaccination (*see, e.g.*, Tr. at 74, 88, 115-17) – a factual connection well understood to be insufficient to meet a claimant's burden. *See, e.g., LaLonde v. Sec'y of Health & Human Servs.*, 746 F.3d 1334, 1341 (Fed. Cir. 2014) ("a temporal correlation alone is not enough to demonstrate causation"). She otherwise has not fleshed the theory out with reliable and persuasive literature establishing that the flu vaccine could instigate vasculitis. And

Dr. Axelrod's expertise, while somewhat sufficient to explain aspects of the theory, was not enough to fill in its many gaps. Petitioner has not met the Program's preponderant evidentiary standard with respect to the first *Althen* prong.

C. *Althen Prong Three*

The record in this case, as interpreted by Dr. Axelrod, does support the conclusion that Petitioner's injury (assuming that it *was* vasculitis and/or chronic urticaria *and* that the flu vaccine could indeed produce such a reaction) occurred in a medically acceptable timeframe consistent with her theory. As noted above, Petitioner asserts that her symptoms began two days after her receipt of the flu vaccine, and she offered reliable evidence supporting the contention that the immune response to a vaccine would still be underway at that time. *See, e.g.*, Abbas; Miller. Notably, however, as discussed above, Petitioner's causation theory in this case is not sufficiently supported with preponderant evidence. Accordingly, the consistency of the onset timing in this case with Petitioner's theory does not aid Petitioner, when that same theory has been found to lack reliability.

CONCLUSION

The evidentiary record does not support Petitioner's contention that the flu vaccine she received in February 2014 caused her to develop cutaneous vasculitis and/or chronic urticaria, or that it could have done so. Petitioner has not established entitlement to a damages award, and therefore I must DISMISS her claim.

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 accordance with this decision.

IT IS SO ORDERED.

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