In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 10-578V

Filed: August 18, 2016

MORGAN A. JOHNSON,	*	**PUBLISHED**
Petitioner,	*	Special Master Hamilton-Fieldman
v.	*	Gardasil; Human Papillomavirus ("HPV") Vaccine; First Symptom or Manifestation of Onset; Systemic Lupus Erythematosus ("SLE"); Causation-in-Fact; Dismissal.
SECRETARY OF HEALTH AND HUMAN SERVICES	*	
Respondent.	*	

Franklin John Caldwell, Jr., Maglio, Christopher & Toale, Sarasota, FL, for Petitioner.
Lara Ann Englund, United States Department of Justice, Washington, DC, for Respondent.

DECISION[1]

On August 26, 2010, Morgan Johnson ("Petitioner") petitioned for compensation under the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-10 to -34 (2012) (hereinafter "Vaccine Act" or "the Act"). Pet., ECF No. 1. Petitioner alleged that she developed Systemic Lupus Erythematosus ("SLE") as a result of the administration of Human Papillomavirus ("HPV") vaccinations on November 21, 2007, and March 5, and June 3, 2008. *Id.* at 1.

Respondent recommended against compensation. Resp't's Report at 1, ECF No. 10.

[1] Because this decision contains a reasoned explanation for the undersigned's action in this case, the undersigned intends to post this decision on the website of the United States Court of Federal Claims, in accordance with the purposes espoused in the E-Government Act of 2002. *See* 44 U.S.C. § 3501 (2012). Each party has 14 days 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).

Generally, Respondent argued that Petitioner's claim was "based entirely on a '*post hoc ergo propter hoc*' line of reasoning (*i.e.*, her symptoms started after the vaccinations, therefore they were caused by the vaccinations)." *Id.* at 8.

Petitioner filed an expert report, authored by Yehuda Shoenfeld, M.D. Pet'r's Ex. 8, ECF No. 29-1. Shortly thereafter, Petitioner submitted medical literature in support of Dr. Shoenfeld's report. *See* Pet'r's Exs. 87-100.[2]

Respondent countered with an expert report from Carlos Daniel Rose, M.D. Resp't's Ex. A, ECF No. 34-1. Respondent likewise submitted medical literature buttressing her expert's report. Resp't's Exs. A.1-4, ECF Nos. 2-5.

Special Master Daria Zane scheduled a two-part entitlement hearing for October 29 and December 17, 2013, in Washington, D.C. Prehearing Order at 1, ECF No. 37. On September 9, 2013, the case was reassigned to the undersigned. Notice of Reassignment at 1, ECF No. 41. The hearing proceeded as scheduled. *See* Minute Entry (Oct. 29, 2013); Minute Entry (Nov. 13, 2013).

After considering the entire record, the undersigned concludes that Petitioner has failed to prove that the Gardasil vaccine caused her injury in a manner sufficient to satisfy the legal standard established in *Althen v. Sec'y of HHS*, 418 F.3d 1274, 1278 (Fed. Cir. 2005). Accordingly, Petitioner is not entitled to compensation under the Vaccine Act.

I. FACTUAL BACKGROUND

Petitioner was born on May 22, 1991. Pet'r's Ex. 118 at 1, ECF No. 65-1. She was a good student, *id.* at 1, and an avid soccer player, participating year-round. Tr. of Proceedings (Oct. 29, 2013) at 16, ECF No. 54 (hereinafter "Tr. A"). Petitioner even developed acne as a result of her soccer career—she tended to wipe the sweat from her face onto her jersey. *Id.* at 40. When she received an invitation to the prom in Spring 2007, she and her mother sought treatment for the acne. *Id.* at 40. She was prescribed Accutane, which she took until September of that year. *Id.* at 40-41. Her weight, at a June 19, 2007 appointment with Dr. Sadd, her pediatrician, was 141.4 pounds. Pet'r's Ex. 1 at 9, ECF No. 7-1.

On November 21, 2007, Petitioner received her first Gardasil vaccination, as well as the Influenza and Meningococcal vaccines. *Id.* at 6. At that time, she weighed 143.2 pounds. *Id.*

[2] Where the exhibits were filed via compact disc, the undersigned provides no ECF reference number.

When she received her second HPV vaccination, on March 5, 2008, Petitioner weighed 144 pounds. *Id*. at 5. On June 3, she received her third HPV vaccination, but the physician did not document her weight. *Id*. at 2.

Less than one year later, on March 18, 2009, Petitioner returned to her pediatrician, complaining of fatigue, difficulty breathing, a racing heart, athlete's foot, and a rash on her neck. *Id.* at 4. She also weighed almost six pounds less (138.2 pounds) than she did at her last documented visit. *Id.*

When she returned to Dr. Saad on April 21, her weight was down another four pounds, at only 133.8. *Id.* at 6.[3] At that visit, Dr. Saad ordered a number of lab tests. *Id.* at 3. The complete results are not documented in the records, but those documented show elevated SS-A and SS-B antibodies and an elevated C3 Complement level. *Id.* at 17.

On April 28, petitioner visited a rheumatologist, Dr. Morris Kokhab. Pet'r's Ex. 3 at 14, ECF No. 7-3. She reported that she had been in good health until four months before the visit, when she began to endure progressive fatigue and ultimately lost ten pounds. *Id.* About a month before the visit, she began to suffer from joint pain, swelling, and morning stiffness. *Id.* She also had a rash on her cheek,[4] and her feet showed signs of Raynaud's.[5] *Id.* An examination revealed active arthritis in her PIPs[6] and confirmed the presence of Raynaud's on her feet. *Id.* The labs taken on April 21 "showed significant findings, including leukopenia at 3.8, anemia at 11.2, elevated ESR of 30, and low C3 of 74 along with positive ANA, ds-DNA, SSA, and SSB titers." *Id.* Dr. Kokhab diagnosed Petitioner with SLE; treated her with 125 mg of SoluMedrol, administered intramuscularly; and prescribed prednisone at a dose of 20 mg per day. *Id.*

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[3] Although "133.8" is actually in the space on the form designated "HT", the undersigned presumes that it refers to her weight, as 133.8 inches would be over 11 feet tall, and 133.8 centimeters would be only four feet and seven inches tall, and medical records from 2007 suggest that she was 67 inches (or five feet and seven inches) tall. *See* Pet'r's Ex. 1 at 7.

[4] The medical records document a "malar" rash, and malar is derived from "mala," which means "cheek." Malar, *Dorland's Illustrated Medical Dictionary* (32nd ed. 2012) (hereinafter "*Dorland's*").

[5] Raynaud's (which is also known as Raynaud phenomenon or Raynaud disease) is "intermittent bilateral ischemia of the fingers, toes, and sometimes ears and nose, with severe pallor and often paresthesias and pain, usually brought on by cold or emotional stimuli and relieved by heat; it is usually due to an underlying disease or anatomical abnormality." Phenomenon, Raynaud, *Dorland's*.

[6] PIPs are proximal interphalangeal joints. Joint, PIP, *Dorland's*.

Petitioner saw Dr. Kokhab again on May 4. *Id.* at 12. She was "[m]arkedly better." Although occasionally dizzy, she had no pre-syncope or visual issues. *Id.* She was prescribed Plaquenil and CellCept. *Id.* Dr. Kokhab ultimately referred her to an ophthalmologist. *Id.* Her weight was down to 131 pounds. *Id.*

Petitioner returned to Dr. Kokhab on May 7. *Id.* at 11. Her pain was much better, but she developed a cough on the previous night. *Id.* Dr. Kokhab gave her Cipro and advised that she stop CellCept for five days. *Id.*

On May 8, Petitioner saw Kerry Gallagher, M.D., at the Ronald Reagan UCLA Medical Center for a second opinion. Pet'r's Ex. 5 at 8, ECF No. 7-5. Dr. Gallagher's narrative explains that Petitioner "developed fatigue, myalgias, and arthralgias, and weight loss over the previous 4 months when she began with progressive difficulty in participating in her soccer games," as well as joint swelling, morning stiffness, additional muscle fatigue, Raynaud's, blurred vision, and a cavity. *Id.* at 8. Petitioner also reported that she had a paternal aunt with rheumatoid arthritis. *Id.* at 9. Dr. Gallagher noted that Petitioner had "a positive ANA, double-stranded DNA, low C3, mild proteinuria, and positive Sjogren's antibodies." *Id.* at 8. A review of Petitioner's systems revealed alopecia,[7] dry eyes, a mild malar rash, and a history of vitiligo.[8] *Id.* at 9-10. Dr. Gallagher's examination notes state that Petitioner's lower extremities were "dusky and slightly cool to palpitation." *Id.* In sum, Dr. Gallagher agreed with Dr. Kokhab's evaluation: Petitioner had lupus, should begin CellCept, and should see an ophthalmologist. *Id*. at 10.

On May 19, Petitioner saw Daniel Arkfeld, M.D., at the USC Keck School of Medicine for another opinion. Pet'r's Ex. 2 at 2-4, ECF No. 7-2. Petitioner reported that "she was in good health until December or January when she started with fatigue, weight loss." *Id.* at 2. In March and April, her joint pain increased, but was especially noteworthy in her hands and wrists. *Id.* She also had facial redness (which she thought was a butterfly rash), "very cold blue feet," and vitiligo. *Id.* Dr. Arkfeld noted her visits to Drs. Kokhab and Gallagher; Petitioner attested that she felt better after the steroid injection, but still felt fatigued. *Id.* She had also been given Plaquenil, but she developed a rash and it was discontinued. *Id.* On examination, Dr. Arkfeld observed no malar rash. *Id.* at 3. He did observe "[q]uestionable thyromegaly,[9] but no nodules or masses." *Id.* Further examination revealed a hypopigmented area on the lower right side of

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[7] Alopecia refers to the "lack or loss of hair from skin areas where it normally is present." Alopecia, *Dorland's*.

[8] Vitiligo is "a chronic, usually progressive, type of hypomelanosis in which melanocytes are destroyed, resulting in white patches on the skin that may be surrounded by a hyperpigmented border." Vitiligo, *Dorland's.*

[9] Thyromegaly is also known as "goiter." Thyromegaly, *Dorland's*.

her abdomen, which Petitioner called vitiligo, but which Dr. Arkfeld explained might simply be a birth mark. *Id.* The notes document "significant cyanosis in both feet" and "1+ swelling in the lower extremities." *Id*. Her hand grip was "fair," but Dr. Arkfeld detected mild weakness. *Id.* In closing, Dr. Arkfeld agreed that the proper diagnosis was lupus. *Id.* He recommended that Petitioner stay on prednisone until June (of 2010) and then start tapering, that she stay on CellCept and increase her dosage up to 2000 mg, and that she see an ophthalmologist. *Id.* at 3-4.

Petitioner returned to Dr. Kokhab on June 9. Pet'r's Ex. 3 at 10. She reported that while she was feeling much better overall and her blurred vision had resolved, she still had occasional morning stiffness for 15 minutes or less. *Id*.

On July 8, 2009, Petitioner saw Dr. Kokhab for a follow-up. *Id.* at 8. She complained of having a cough, runny nose, fatigue and sore throat for one week, as well as joint pain and morning stiffness. *Id.* Dr. Kokhab gave her Cipro and told her to stop the CellCept for five days. *Id.*

Petitioner revisited Dr. Kokhab on July 28. *Id.* at 7. She had been off of CellCept because of an upper respiratory infection, but restarted it two days before the appointment and now felt less energetic. *Id.* Dr. Kokhab also noted that her hair loss had stabilized, and that she had neither morning stiffness, joint pain, nor a rash. *Id.*

On August 17, 2009, petitioner again returned to Dr. Kokhab. *Id.* at 6. She reported that she was "markedly better," with no morning stiffness, joint pain, or rashes; however, she did have some hair loss and sleep issues. *Id.*

Petitioner again saw Dr. Kokhab on September 17. Ex. 3 at 5. At that time, she noted that her lupus symptoms had flared up and she had a urinary tract infection. *Id.* at 5. She was treated with an increase in prednisone and with Cipro. *Id.* Although she was doing better and denied joint problems, she felt fatigued. *Id.*

On November 25, Petitioner saw Dr. Kokhab for a follow-up. *Id.* at 4. She reported that she had lost 13 pounds over the past 8 months and that she sometimes got a butterfly rash. *Id.* She denied alopecia or joint pain. *Id.* Five days later, a twenty-four hour urine sample was collected, which showed an elevated protein/creatinine ratio and total protein level. *Id.* at 19.

Petitioner revisited Dr. Kokhab on December 21, 2009. Ex. 3 at 3. Her weight was 128 pounds. *Id.* She reported that she had developed pharyngeal pain and swelling. *Id.* She had been given Bactrim and it quickly resolved. *Id.* She was referred to Dr. Kalunian at UCSD Medical Center for another opinion regarding treatment options. *Id.*

On January 14, 2010, Petitioner saw Dr. Kalunian. Pet'r's Ex. 6 at 6, ECF No. 7-6. At

that time, she was taking 15 mg of prednisone (alternating with 10 mg every other day) and 2 g of CellCept. *Id.* Examination was normal except for occasional purplish discoloration in her feet. *Id.* Labs were taken to determine her treatment options. *Id.*

On February 5, Petitioner returned to Dr. Kokhab for a follow-up. Pet'r's Ex. 3 at 2. She reported that she had increased joint pain and fatigue and felt a "great deal of stress" because of relationships and school work. *Id.* She denied rashes. *Id.* Her prednisone was increased to 20 mg daily. *Id.*

Petitioner returned to UCSD Medical Center on February 24, and saw Matthew Husa, a resident M.D., with review by Dr. Kalunian. Pet'r's Ex. 6 at 2. She reported for a recent two to three week period, she experienced pain in her skin when touched, but that it was now resolved. *Id.* She also denied joint pain and morning stiffness. *Id.* at 3. At that time, she was taking 20 mg daily of prednisone and reported that taking less than 20 mg resulted in flares of her lupus symptoms. *Id*. An examination revealed no abnormalities. *Id.* Her labs from January 10 had shown mild leucopenia, mild anemia and "roughly" 300 mg of protein in her 24-hour urine test. *Id.* The impression was that her symptoms seemed well-controlled on the prednisone, and the plan was to continue her on 20 mg daily of prednisone and to repeat the lab testing. *Id.* at 4-5.

On June 8, 2010 Petitioner saw Dr. Jennifer Grossman for another opinion concerning the CellCept and the need for a renal biopsy before beginning that treatment. Ex. 104 at 17-19, ECF No. 50-4. On the new patient questionnaire, Petitioner hand-wrote that her symptoms of "rapid loss of lots of hair" and "weight loss of 20 lbs," had occurred "before [she was] diagnosed." *Id.* at 35. Dr. Grossman described the "History of Present Illness" as one "whose symptoms began . . . several years ago," *id.* at 17, and noted that she was positive for "20-pound weight loss before she was diagnosed with lupus and has gained some of the weight back, hair loss before she was diagnosed which has improved," *id*. at 18. Her weight at this visit was 125 pounds. *Id*. Dr. Grossman did not recommend a kidney biopsy, but did think the CellCept was an appropriate alternative for steroid sparing. *Id*. at 18-19. Dr. Grossman also recommended that Petitioner try Plaquenil again, as a better alternative for steroid sparing. *Id.* at 19. The doctor suggested Petitioner try brand name Plaquenil rather than generic, to see if she tolerated it better. *Id.* Continued use of sunscreens was also recommended. *Id*.

II. APPLICABLE LEGAL STANDARD

To receive compensation under the Vaccine Act, Petitioner must prove either that she suffered (1) a "Table Injury," i.e., an injury falling within the Vaccine Injury Table,[10]

[10] The Vaccine Injury Table "lists the vaccines covered under the Act; describes each vaccine's compensable, adverse side effects; and indicates how soon after vaccination those side effects should first manifest themselves." *Bruesewitz v. Wyeth, LLC*, 562 U.S. 223, 228 (2011).

corresponding to one of her vaccinations, or (2) an injury that was actually caused by a vaccine. *See* 42 U.S.C. §§ 300aa-11(c)(1), 13(a)(1)(A) (2012). Petitioner must show that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly v. Sec'y of HHS*, 592 F.3d 1315, 1321-22 (Fed. Cir. 2010) (internal quotation marks omitted).

Because Petitioner does not allege a Table injury in this case, she must show that her injury was caused-in-fact by a covered vaccine. To do so, Petitioner must satisfy all prongs of the test established by the Federal Circuit in *Althen*, which requires Petitioner to set forth: "(1) a medical theory causally connecting the vaccination and the injury [("*Althen* Prong One")]; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury [("*Althen* Prong Two")]; and (3) a showing of a proximate temporal relationship between vaccination and injury [("*Althen* Prong Three")]." 418 F.3d at 1278.

To establish entitlement to compensation under the Program, Petitioner must establish each of the three prongs of Althen by a preponderance of the evidence. *Id.* The preponderance of the evidence standard has been interpreted to mean that Petitioner must show that the fact to be proven is more likely than not. *Moberly*, 592 F.3d at 1322 n. 2.

In determining whether Petitioner is entitled to compensation, the undersigned will consider all relevant material contained in the record. 42 U.S.C. § 300aa-13(b)(1). That material can include circumstantial evidence. *Capizzano v. Sec'y of HHS*, 440 F.3d 1317, 1325 (Fed. Cir. 2006). Although Petitioner is not required to present proof of causation to the level of scientific certainty, the undersigned is, as the finder of fact, "entitled—indeed, expected—to make determinations as to the reliability of the evidence presented . . . and, if appropriate, as to the credibility of the persons presenting that evidence." *Moberly v. Sec'y of HHS*, 592 F.3d 1315, 1326 (Fed. Cir. 2010).

The Supreme Court has set forth a number of factors courts should consider in evaluating the reliability of expert testimony. *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579, 592 (1993). The Federal Circuit has explained that it is appropriate for the undersigned to utilize *Daubert*'s factors as a framework for evaluating the reliability of causation-in-fact theories presented under the Vaccine Act. *Terran v. Sec'y of HHS*, 195 F.3d 1302, 1316 (Fed. Cir. 1999); *see also Coombs v. Sec'y of HHS*, No. 08-818V, 2014 WL 1677584, at *3 (Fed. Cl. Spec. Mstr. Apr. 8, 2014). *Terran* clarified that the undersigned is not required to apply all of the *Daubert* factors, but is encouraged to use the *Daubert* framework as a tool for inquiring into the reliability of the evidence. 195 F.3d at 1316.

"Claimants who show that a listed injury first manifested itself at the appropriate time are prima facie entitled to compensation." *Id.*

Accordingly, the undersigned and other special masters regularly use the following factors for analyzing the reliability of expert testimony: "(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*); *see Snyder v. Sec'y of HHS*, 88 Fed. Cl. 706, 744-45 (2009) (holding that the special master's "application of *Daubert* was in accordance with the law").

Where opinion evidence is only connected to the data upon which it purports to rely by the *ipse dixit* of the expert, that evidence may be accorded less weight. *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997) (explaining that "nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert."). The undersigned may also deem an opinion or theory unreliable where "'there is simply too great an analytical gap between the data and the opinion proffered.'" *Cedillo v. Sec'y of HHS*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (quoting *Joiner*, 522 U.S. at 146); *see also Caves v. Sec'y of HHS*, 100 Fed. Cl. 119, 136 (2011) (holding that Special Master did not err in deeming expert's theory unreliable where theory and its conclusions "were too far removed from the other evidence" in the case), *aff'd sub nom.*, 463 F. App'x 932 (Fed. Cir. 2012).

A. *Althen* Prong One

To satisfy the first prong of *Althen*, Petitioner must provide "a medical theory causally connecting the vaccination and the injury." *Althen*, 418 F.3d at 1278 (internal quotation marks omitted). Petitioner's theory must show that it is more likely than not that the vaccine she received "can" cause the type of injury Petitioner alleges the vaccine caused. *Pafford v. Sec'y of HHS*, 451 F.3d 1352, 1356 (Fed. Cir. 2006) (internal quotation marks omitted).

The medical theory set forth by Petitioner need only be "legally probable, not medically or scientifically certain." *Knudsen v. Sec'y of HHS*, 35 F.3d 543, 548-49 (Fed. Cir. 1994). However, the theory cannot be baseless or completely speculative; it must be informed by "sound and reliable medical or scientific explanation." *Id.* at 548; *see Veryzer v. Sec'y of HHS*, 98 Fed. Cl. 214, 223 (2011) (noting that under 42 U.S.C.A. § 300aa-13(b)(1) and Vaccine Rule 8(b)(1), special masters must consider only evidence that is both "relevant" and "reliable"). When Petitioner proffers a medical opinion to support the theory alleged, the basis for the opinion and the reliability of that basis must be considered in determining how much weight to afford the offered opinion. *Broekelschen v. Sec'y of HHS*, 618 F.3d 1339, 1347 (Fed. Cir. 2010); *see Perreira v. Sec'y of HHS*, 33 F.3d 1375, 1377 n. 6 (Fed. Cir. 1994) ("An expert opinion is no better than the soundness of the reasons supporting it.").

The Federal Circuit has issued a number of decisions discussing what constitutes a "reputable medical or scientific explanation" of a theory sufficient to satisfy the aforementioned requirement. For example, a petitioner who provides a theory that the government concedes is plausible will satisfy *Althen*'s first prong. *Jay v. Sec'y of HHS*, 998 F.2d 979, 984 (Fed. Cir. 1993). A theory that has basic indicia of reliability that is put forward by qualified experts will also satisfy the first prong of *Althen*. *Capizzano*, 440 F.3d at 1326.

By contrast, "where basic indicia of reliability do not exist, the special master may reject a petitioner's medical theory." *Paluck v. Sec'y of HHS*, 104 Fed. Cl. 457, 470 (2012). Thus, the Federal Circuit affirmed a special master's conclusion that a theory relying upon "a literature review based on two papers from the early 1950s, which in turn considered vaccine cases between 1929 and 1952," was insufficient to satisfy *Althen*'s first prong. *Broekelschen*, 618 F.3d at 1350. The Federal Circuit likewise affirmed the rejection of a theory linking a pertussis vaccine to brain damage when the theory had never been tested and was criticized by the government's expert as biologically implausible, noting that the testimony of the petitioner's expert was "contradictory and confusing," and "shockingly poor." *Moberly*, 592 F.3d at 1321, 1325.

B. *Althen* Prong Two

While the first prong of Althen focuses on general causation, that is, whether the administered vaccine can cause the particular injury from which the vaccinee suffers, the second prong focuses on specific causation, that is, whether the administered vaccine actually caused the injury. *See Pafford v. Sec'y of HHS*, 451 F.3d 1352, 1355-56 (Fed. Cir. 2006). To satisfy the second prong of *Althen,* Petitioner must establish "a logical sequence of cause and effect showing that the vaccination was the reason for the injury." *Althen*, 418 F.3d at 1278. Petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions; she is not required to offer "epidemiologic studies, rechallenge, presence of pathological markers or genetic disposition, or general acceptance in the scientific and medical communities" to establish a logical sequence of cause and effect. *Capizzano*, 440 F.3d at 1322.

C. *Althen* Prong Three

To satisfy the third prong of *Althen*, Petitioner must produce preponderant evidence of "a proximate temporal relationship between vaccination and injury." *Althen*, 418 F.3d at 1278. This prong helps to establish the connection between the causal theory of Prong One and the more fact-based cause and effect arguments of Prong Two by demonstrating "that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." *De Bazan v. Sec'y of HHS*, 539

F.3d 1347, 1352 (Fed. Cir. 2008).

III. ANALYSIS

A. Background Information

1. Gardasil Vaccine

Gardasil is a relatively new vaccine, approved for the first time in 2006. Merck & Co., Inc., *Gardasil Physician Prescribing Information* (2011), at *1, *available at* http://www.merck.com/product/usa/pi_circulars/g/gardasil/gardasil_pi.pdf. It was developed to immunize young women (although it is also given to young men) against HPV. *Id.* Gardasil is a recombinant vaccine, not a live virus vaccine. *Id.* That is, Gardasil "[i]s a non-infectious recombinant quadrivalent vaccine prepared from the purified virus-like particles (VLPs) of the major capside (L1) protein of HPV Types 6, 11, 16, and 18," which are "produced by separate fermentations in recombinant *Saccharomyces cerevisiae* and self-assembled into VLPs." *Id.* at 12. There are at least 130 genetically different HPV subtypes known to date. *See* Margaret Stanley, *Immunobiology of HPV and HPV vaccines*, 109 Gynecologic Oncology S15, at *1, (2008). Two of them, HPV 16 and HPV 18, are known to cause cervical, esophageal, and anal cancer, and two, HPV 6 and HPV 11, are known to cause genital warts and herpes. *Id.* at *1-2. These four subtypes are incorporated into the quadrivalent Gardasil vaccine. *See Prescribing Information* at 1. The Gardasil vaccine also contains an adjuvant[11] that has aluminum as a component. *Id.* at 12.

2. Systemic Lupus Erythematosus

SLE is a "chronic, inflammatory, often febrile multisystemic disorder of connective tissue that proceeds through remissions and relapses; it may be either acute or insidious in onset and is characterized principally by involvement of the skin, . . . joints, kidneys and serosal membranes." Lupus, Systemic Erythematosus, *Dorland's*. Although the etiology is technically unknown, "it may be a failure of regulatory mechanisms of the autoimmune system." *Id*.

B. Qualifications of the Parties' Experts

1. Dr. Yehuda Shoenfeld

[11] The aluminum adjuvant, when combined "with soluble antigen forms a precipitate," and "slow release of the antigen from the precipitate on infection causes prolonged, strong antibody response." Adjuvant, Aluminum, *Dorland's*.

Dr. Shoenfeld is a 1972 graduate of the Hadassa Medical School at Hebrew University in Jerusalem. Pet'r's Ex. 9, ECF No. 29-2. He is a specialist in internal medicine, specifically immunology and allergy, and especially autoimmunity. Transcript of Proceedings (Dec. 17, 2013) at 100, ECF No. 60 (hereinafter "Tr. B"). He served in a number of medical positions until he was appointed Head of Department of Medicine "B" Sheba Medical Center in 1989, a position he held until 2011, when he founded and became the Head of the the Zabludowicz Center for Autoimmune Diseases. Pet'r's Ex. 9. at 2. He has published well over a thousand papers, and is an editor for a number of journals, with a research focus on autoimmune diseases. Tr. B at 100-107. He was admitted as an expert in clinical immunology. *Id*. at 117.

2. Dr. Carlos Daniel Rose

Dr. Rose is a graduate of the University of Buenos Aires Medical School. Tr. B at 248. He has been the head of the Pediatric Rheumatology Division of the Department of Pediatrics at Thomas Jefferson University in Philadelphia since 1994. *Id*. at 248-49. He has a clinical and teaching practice, and has conducted research in the areas of Lyme disease and Blau syndrome. *Id.* at 249-50. He has served on many boards and commissions, and is extensively published. *See generally* Resp't's Ex. B, ECF No. 34-6. Dr. Rose was admitted as an expert in pediatric rheumatology. Tr. B at 251-52.

C. The Parties' Arguments

After the hearing, both parties filed briefs summarizing their positions. *See* Pet'r's Post Hr'g Br., ECF No. 73; Resp't's Post Hr'g Br., ECF No. 75. Petitioner argued that she was entitled to an award, explaining that (1) the adjuvants in the Gardasil vaccine could have caused her injury by "mimic[king] specific sets of evolutionarily conserved molecules," triggering an overactive response by the immune system; (2) Petitioner's healthy medical history prior to the vaccine, the lack of alternative potential causes, and the temporal proximity between the vaccine and the first symptom of SLE all suggested that the Gardasil vaccine indeed caused Petitioner to develop SLE; and (3) the onset of the first symptom of Petitioner's SLE was temporally consistent with a finding that the vaccine caused her SLE. Pet'r's Post Hr'g Br. at 10-11. To the contrary, Respondent contended, Petitioner had not presented a prima facie case entitling her to compensation because (1) Dr. Shoenfeld's theory of causation is unpersuasive because it posits that "all adjuvants are the same, that all autoimmune diseases are the same, and that any adjuvant is capable of causing any autoimmune disease"; (2) the evidence, including that of the development of the disease, was consistent with typical idiopathic childhood-onset SLE, none of her treating physicians opined in favor of causation, and that potential environmental factors went unconsidered by Dr. Shoenfeld, all rebuffed the conclusion that the Gardasil vaccine caused Petitioner to develop SLE; and (3) the six-month period between the vaccination and the first symptom of her SLE suggested no causal relationship between the two. Resp't's Post Hr'g Br. at

1-7.

D. The Undersigned's Decision

After thorough consideration of the parties arguments and review of the extensive record in this case, the undersigned concludes that Petitioner is not entitled to compensation under the Vaccine Act. While the undersigned's discussion focuses most extensively on *Althen*'s first prong, the undersigned is careful to note that she does not believe that Petitioner has met her burden under any of *Althen*'s prongs.

1. *Althen* Prong One

The fundamental problem with Petitioner's theory of causation is that the theory is overbroad, generalized, and vague, to the point that it could apply to virtually everyone in the world who has received a vaccine containing an adjuvant and then at some time in their lives developed an autoimmune disease. This makes the theory completely unhelpful for proving causation of a specific injury resulting from a specific vaccine or series of vaccines within a specific time frame.

To illustrate: Petitioner's burden in this case was to prove by a preponderance of the evidence that a series of three Gardasil vaccines, which contain an aluminum-based adjuvant, can, within a time period appropriate to the theory, cause the autoimmune disease in question, SLE. Dr. Shoenfeld's expert opinion, however, is that all adjuvants are basically the same, that they are designed to "increase the effect of the immune system," and that in so doing they cause autoimmune disease. Tr. B at 176-77. He testified that "for me, all autoimmune diseases are the same." *Id*. at 103. And, he testified that the only timing that is relevant is "that the disease came after the vaccine and not before the vaccine." *Id.* at 138-39.

In both his reports and his testimony, Dr. Shoenfeld gave numerous examples of studies that he asserts put "a nail in the coffin of indicating that adjuvant and vaccine can cause autoimmune disease." Tr. B at 150; *see* Tr. B at 145-46 (discussing H1N1 vaccine and narcolepsy); Pet'r's Ex. 26 (discussing Hepatitis B vaccine and chronic fatigue syndrome); *see generally* Pet'r's Ex. 109, ECF No. 63-2 (discussing Hepatitis B and demyelinating diseases such as GBS, transverse myelitis, and ADEM). Dr. Shoenfeld argued that these studies all demonstrate that if an adjuvant can cause *an* autoimmune disease, it can cause *any* autoimmune disease,[12] and likewise, if an autoimmune disease has been shown to have been caused by *an*

[12] Notably, the only evidence Dr. Shoenfeld put forth specifically concerning Gardsail and SLE came in the form of case reports, *see* Tr. B at 193-94, most of which involved patients with preexisting SLE or other autoimmune diseases, which made their persuasiveness on causation

adjuvant, it can be caused by *any* adjuvant. And, theoretically, the development of the autoimmune disease can happen at any time after the introduction of the adjuvant. Tr. B at 221. As he wrote in his response to Dr. Cetaruk, "**autoimmune diseases stem from a hyperactive and deranged immune system activity. Adjuvants are stimulators of hyperactive immune responses (whether it be Th1 or Th2). Hence immune adjuvants have all the necessary biochemical properties to induce autoimmune diseases.**" Pet'r's Ex. 109 at 1-2 (emphasis in original). Dr. Shoenfeld put it this way at hearing: if you have "somebody who has an hyper-stimulated immune system and you add something else, *whatever*, being aluminum, being oil, being virosome, being the new adjuvant, which will increase the immune system stimulation, will cause the eruption *eventually* of *an autoimmune disease* in somebody who is genetically prone to it." Tr. B at 176-77 (emphasis added).

The undersigned simply does not find this expansive theory logically persuasive. There is no way to measure its validity; with vaccines containing adjuvants being administered to hundreds of millions of individuals from birth (HepB) throughout childhood and into adulthood, and with no time limit placed on when the autoimmune reaction to those adjuvants can occur, there is no control group, no possible manageable way to track those millions of doses and their alleged causation of dozens, possibly a hundred or more, autoimmune diseases. By the time an individual such as Petitioner reaches the age that she was when she developed her autoimmune disease, she may have received multiple vaccines containing adjuvants and have been exposed to myriad other environmental factors for which a causative connection between the factor and autoimmunity have been shown. How, if at all, is one to determine which of those causative factors was responsible for the development of that individual's autoimmune disease? If this theory is valid, is the first adjuvant-containing vaccine administered, or environmental factor encountered, always causative? If not, why not? And if this theory is a reliable explanation for the development of any autoimmune disease in the vaccinated population, what does that do to the validity of the many studies, including those cited by Dr. Shoenfeld himself, that do show a particular connection between a particular vaccine and a particular autoimmune disease? These analytical gaps are numerous, they are large, and they are not resolved by the evidence adduced at hearing or in the record. By attempting to explain everything autoimmune-related in adjuvant

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dubious, at best, *see, e.g.,* Pet'r's Ex. 99 at 3. Dr. Shoenfeld admitted at hearing that no epidemiological link between HPV and SLE has been shown to exist. Tr. B. at 191. He also admitted that there are no published studies showing a causative link between aluminum adjuvant and SLE, and that the review article he published in 2013 concerning the effects of adjuvants on animal models did not include any studies showing that aluminum-based adjuvants caused SLE in animals. *Id.* at 175. In fact, in a study of genetically altered SLE-prone mice administered four adjuvants, including aluminum, only one of those adjuvants, not the aluminum, "accelerated the onset of proteinuria," an SLE marker symptom, in any of the mice. *See generally* Pet'r's Ex. 112, ECF No. 63-5.

terms, Dr. Shoenfeld has, at least to the undersigned, explained nothing. As a result, Petitioner has not met her burden of proof under *Althen*'s first prong.

2. *Althen* Prongs Two and Three

While Petitioner's failure to satisfy the first prong of *Althen* renders an analysis of the remaining *Althen* prongs unnecessary, the undersigned will nevertheless proceed with a brief analysis of those prongs. Because *Althen* prongs two and three have a closely overlapping analysis, and in this case, closely overlapping factual evidence and rulings,[13] they will both be discussed within this section.

The first major issue under *Althen*'s second and third prongs is that Petitioner's depiction of an injury that developed after the first dose of vaccine and increased in severity and number of symptoms after each successive dose (basically a challenge/rechallenge model), *see* Tr. B at 153, is inconsistent with the facts and medical records. While Petitioner's counsel tried mightily to construe it otherwise, the testimony of Petitioner and her parents concerning the onset of Petitioner's SLE symptoms showed a marked lack of recall and specificity. Neither parent had an independent recollection of the alleged hair loss. Petitioner's memory was also admittedly poor, *see* Tr. A at 14, but to the extent she did remember, the "scary" hair loss occurred during her senior year (2008-2009), several months after the third and final vaccination in June 2008, Tr. A at 28-29. Both Petitioner and her mother remembered that the Raynaud's was first noticeable during winter church camp. Petitioner's mother remembered that shortly after that she took Petitioner to Dr. Saad, with what turned out to be SLE. Tr. A at 48-50. The winter school break of 2008-2009 is the timing that fits with the medical records, which place that symptom, along with all the others, about four months before her first visit to Dr. Saad, in March of 2009, with what turned out to be SLE symptoms. Pet'r's Ex. 1 at 4. The fatigue, along with the slowing down at soccer practice and games, was noticed by the coach of Petitioner's club team, with whom she played when she was not playing soccer for school. Since she had no apparent problems playing on her school team during the spring of her junior year (2008), this again places the symptom after the last of the three HPV vaccines in June 2008. Finally, as to the weight loss: Petitioner reached her maximum recorded weight of 144 pounds on March 5, 2008, which was the date of her second Gardasil vaccination. She still weighed 138.2 pounds when she saw Dr. Saad on March 18, 2009, *see id.* at 4; it was not until over a year later, when she saw Dr. Grossman for the first time, that she was down nearly 20 pounds, Pet'r's Ex. 104 at 18. These records just do not support a 20 pound weight loss before diagnosis.

Taking all of the evidence together, therefore, the undersigned finds that the onset of Petitioner's SLE symptoms dates from approximately December of 2008. The timing of onset is

[13] The Federal Circuit has held that there is no "reason why evidence used to satisfy one of the *Althen* . . . prongs cannot overlap to satisfy another prong." *Capizzano*, 440 F.3d at 1326.

therefore not compatible with Dr. Shoenfeld's primary argument concerning causation, which was heavily dependent on the symptoms appearing sequentially, along with the sequential administration of the vaccines. *See* Tr. B at 153, 200-01.

Although Petitioner attempts to point to Dr. Shoenfeld's argument that the timing does not matter so long as it occurred after the vaccine, the undersigned has already dismissed that argument under Althen prong one. Indeed, accepting this argument would force the undersigned to render *Althen*'s third prong toothless, and it is therefore invalid on its face. *See Hennessy v. Sec'y of HHS*, 91 Fed. Cl. 126, 142 (2010) (rejecting the petitioner's attempt, via Dr. Shoenfeld, "to satisfy *Althen*'s third prong by defining it away, positing that any time frame is appropriate").

Finally, while it is not incumbent upon petitioners to eliminate all, or even most, potential alternative causes for their injuries, *Althen*, 418 F.3d at 1281, it is not untoward to expect that Petitioner explain an alternative cause raised by her own expert. Dr. Shoenfeld testified, both on direct and cross examination, Tr. B at 128-29, 188-89, that "sun exposure can induce" and "exacerbate" SLE. Tr. B at 188-89. For example, he noted, "in my country [Israel], SLE will be much more severe in expression than in patients with SLE from Scandinavia" because of their relative proximity to the equator. Tr. B at 129. Petitioner lived in southern California from at least 2006-2009, Pet'r's Ex. 118 at 1. Upland, where she lived, is only about three degrees further north from the equator than is Jerusalem (34 degrees versus 31 degrees). Throughout high school, until she got sick, Petitioner played soccer. She was on her high school team and a club team; she "pretty much played year-round." Tr. A at 16. Petitioner was in the peak age group for SLE, Tr. B at 306-07; she was post-pubertal and subject to the effects of estrogen, which both experts testified is related to the development of SLE, Tr. B at 103, 307-08. According to both experts, Petitioner had a genetic predisposition to the disease. Tr. B at 180, 258. On this issue, the undersigned agrees with Dr. Rose: there is no reason to believe that a temporally remote vaccination is more likely to have caused Petitioner's SLE than a well-known physical trigger (sun exposure) to which Petitioner was repeatedly exposed. Tr. B at 282-83. For this and the reasons previously discussed, the undersigned holds that Petitioner has not met her burden under either *Althen*'s second or third prongs.

IV. CONCLUSION

The undersigned sympathizes with the fact that Petitioner suffers from a painful, chronic disease. However, because Petitioner has failed to meet her burden of proof under the three prongs of *Althen*, her petition must be, and is hereby, **DISMISSED**. In the absence of a motion for review filed pursuant to RCFC Appendix B, the Clerk of the Court is directed to enter judgment herewith.[14]

[14] Pursuant to Vaccine Rule 11(a), the parties can expedite entry of judgment by filing a notice renouncing the right to seek review by a United States Court of Federal Claims judge.

/s/ Lisa D. Hamilton-Fieldman
Lisa D. Hamilton-Fieldman
Special Master