In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: December 8, 2014

**********	PUBLISHED
NATALIE ROWAN, *	
*	No. 10-272V
Petitioner, *	
*	Special Master Dorsey
v. *	
*	
SECRETARY OF HEALTH *	Entitlement; Human Papillomavirus
AND HUMAN SERVICES, *	Vaccine ("HPV") or Gardasil; Headaches;
*	Migraines; Chronic Fatigue Syndrome.
Respondent. *	
*	
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Patricia Ann Finn, Piermont, NY, for petitioner.
Darryl J. Wishard, U.S. Department of Justice, Washington, DC, for respondent.

DECISION DENYING ENTITLEMENT[1]

I. Introduction

On May 3, 2010, Michael Rowan, on behalf of his daughter, Natalie Rowan[2] ("petitioner" or "Ms. Rowan"), filed a petition for compensation under the National Vaccine Injury Compensation Program ("the Program")[3] alleging that the human papillomavirus ("HPV"

[1] Because this published decision contains a reasoned explanation for the 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 E-Government Act of 2002 § 205, 44 U.S.C. § 3501 (2006). In accordance with the Vaccine Rules, each party has 14 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). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted decision. If, upon review, the undersigned agrees that the identified material fits within the requirements of that provision, such material will be deleted from public access.

[2] Michael Rowan filed a motion to Amend the Caption on December 12, 2013, as Ms. Rowan had attained the age of majority. The motion was granted the next day.

[3] The Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-10 et seq. ("the Act"). Hereafter, individual section references will be to 42 U.S.C. § 300aa.

or "Gardasil") vaccines that his daughter, Natalie Rowan, received on August 21, 2007, November 12, 2007, and July 14, 2008, caused her to develop headaches, including migraines, difficulty walking, abdominal pain, dizziness, weight loss, bronchial spasms, and an inability to leave her bed. Petition at 1-2. Respondent recommended against compensation, arguing that petitioner had not presented adequate evidence demonstrating causation. See Respondent's Report ("Resp't's Rep't"), filed October 29, 2010, at 15. The parties submitted expert reports. An entitlement hearing was held in New York, NY, on January 14, 2014, and in Washington D.C. from January 15 to 16, 2014. Michael Rowan, Natalie Rowan and the parties' respective experts testified. Petitioner filed her post-hearing brief on July 8, 2014, and respondent filed her post-hearing brief on August 29, 2014. This matter is now ripe for adjudication.

The parties agree that the issues to be decided are: (1) whether petitioner has presented preponderant evidence that she had a "medically-recognized autoimmune condition," and (2) if so, whether petitioner has presented preponderant evidence of vaccine causation of the injuries. See Jt. Sub. at 4. After a review of the entire record, see § 300aa-13(a)(1), the undersigned finds that petitioner has provided preponderant evidence of illness or injury.[4] She has failed, however, to establish by a preponderance of the evidence that the Gardasil vaccinations caused her injuries. Accordingly, petitioner is not entitled to compensation and her petition must be dismissed.

II. Standards for Adjudication

The Vaccine Act established the Program to compensate vaccine-related injuries and deaths. § 300aa-10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Human Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioner's burden of proof is a preponderance of the evidence. § 300aa-13(a)(1). The preponderance of the evidence standard, in turn, has been interpreted to mean that a fact is more likely than not. Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). A petitioner who satisfies this burden is entitled to compensation unless respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 300aa-13(a)(1)(B).

[4] While the parties stipulated that the first issue to be decided is whether petitioner had a "medically-recognized autoimmune condition," the undersigned did not limit her analysis to just autoimmune conditions, but considered whether petitioner could recover for any illness or injury. See § 300aa-11(c)(1)(C)(ii)(I).

III. Summary of Relevant Facts

Ms. Rowan was born on October 11, 1995. She had asthma, but was otherwise noted to be a well-child. Petitioner's Exhibit ("Pet. Ex.") 3 at 1. Prior to receiving her first HPV vaccination, there were two documented occasions when Ms. Rowan complained of headaches. Ms. Rowan complained of a headache on December 7, 2005, which was associated with an upper respiratory infection. Jt. Sub. at 2. On March 6, 2007, Ms. Rowan saw Dr. Joanne Fogarty, her primary care provider, for a chief complaint of a headache associated with complaints of abdominal pain and strep pharyngitis. Jt. Sub. at 2; Pet. Ex. 4 at 1.

Ms. Rowan received her first HPV vaccine on August 21, 2007. There were no documented adverse events associated with that vaccine. Petition at 1; Pet. Ex. 1 at 3. She received her second HPV vaccine on November 12, 2007. Id. On November 21, 2007, she presented to Dr. Fogarty with complaints of a headache and stomach ache. Pet. Ex. 4 at 1. Dr. Fogarty diagnosed petitioner with a "viral syndrome." Id.

Approximately six months later, on May 15, 2008, petitioner saw Dr. Fogarty and complained of "headaches since Monday." Pet. Ex. 4 at 3. Dr. Fogarty documented that petitioner started her menses in March of 2008, and noted a family history of migraines. Id. Dr. Fogarty diagnosed petitioner with headaches, prescribed Advil and Fiorcet and advised Ms. Rowan to increase her fluids. Id.

Ms. Rowan's third HPV vaccine was administered on July 14, 2008. Petition at 1; Pet. Ex. 1 at 1. On September 24, 2008, Ms. Rowan saw Dr. Fogarty with complaints of a sore throat and Dr. Fogarty noted petitioner's history of migraines. Pet. Ex. 4 at 4. Dr. Fogarty diagnosed petitioner with pharyngitis. Id.; Jt. Sub. at 2. On October 28, 2008, November 3, 2008, and November 14, 2008, Ms. Rowan saw Dr. Fogarty for ongoing complaints of headaches. Dr. Fogarty prescribed medication and physical therapy. Pet. Ex. 4 at 6-10.

On December 30, 2008, Ms. Rowan saw neurologist Dr. Karen Powers for complaints of headaches. Pet. Ex. 3 at 1. Dr. Powers noted that Ms. Rowan had been experiencing headaches since October 2008, and that she complained that the headaches were causing her to have difficulty concentrating in school and causing school absences. Id. Ms. Rowan's father provided a history to Dr. Powers of petitioner's migraines stating that the headaches began after petitioner's first menstrual cycle in March of 2008. Jt. Sub. at 2; Pet. Ex. 3 at 1. Medications, including "naproxen, hydrocodone, butalbital APAP, cyclobenzaprine, and Imitrex" were ineffective. Jt. Sub. at 2. Dr. Powers diagnosed petitioner with "chronic daily headache, with some intermittent headaches with more migraine features, as well as a strong family history of migraines." Pet. Ex. 4 at 3. Ms. Rowan was prescribed Topamax for her headaches. Jt. Sub. at 2.

Petitioner continued to see Dr. Powers and Dr. Fogarty for her headaches throughout 2009. In February and March 2009, Ms. Rowan saw Dr. Fogarty for complaints of abdominal pain. Pet. Ex. 4 at 9-11. An abdominal scan was performed and remarkable only for constipation. Jt. Sub. at 3. Also in March 2009, petitioner reported that she had no benefit from

trying a gluten-free diet. Id. On March 26, 2009, Dr. Powers's diagnosis was "primary headache syndrome consistent with a new daily persistent headache." Pet. Ex. 3 at 7.

In May 2009, Mr. Rowan filed a VAERS report on behalf of his daughter. Pet. Ex. 1 at 2. Also in May 2009, Ms. Rowan consulted with Dr. Charles Argoff regarding Botox treatment and in June she consulted with physicians at Albany Medical Center. Jt. Sub. at 2; Pet. Ex. 3 at 22. On September 29, 2009, petitioner had a low white blood count ("WBC") of 3.2 with elevated lymphocytes of 54. Pet. Ex. 2 at 1. Ms. Rowan saw Dr. Joanne Porter, a pediatric hematologist, in October 2009. Pet. Ex. 3 at 20-21. Mr. Rowan told Dr. Porter that he believed that his daughter's headaches began after her last HPV vaccine. Id. Ms. Rowan continued to seek treatment for her headaches throughout 2009. Pet. Ex. 3 at 17-18; Pet. Ex. 4 at 16.

On January 14, 2010, Dr. Powers noted that Ms. Rowan continued to experience headaches. Pet. Ex. 6 at 20. Dr. Powers's impression was that Ms. Rowan's symptoms, which began as headaches, had "evolved into multiple somatic complaints of headache, leg weakness, difficulty walking, gastrointestinal pain, and what appears to be depression." Pet. Ex. 6 at 21. Ms. Rowan underwent a diagnostic workup for her complaints of headaches. The results included a negative Lyme test, a normal sinus and CT scan, a normal MRI of the brain, a normal MR angiography and venogram of the head, a negative cervical spine x-ray, and normal lab results from a lumbar puncture. Jt. Sub. at 3. In March 2010, Ms. Rowan saw Dr. Barbara Shapiro, who examined the petitioner and performed an EMG. Tr. 41. The results of the EMG were normal although petitioner was unable to ambulate at the time and was in a wheelchair. Pet. Ex. 44 at 4. Ms. Rowan's diagnostic testing was normal; however, she had an elevated IgE level, likely due to her asthma. Tr. 465, 469-70.

Petitioner's complaints and headaches continued until June or July 2010, when her family sought advice from a lawyer, Lloyd Phillips, who was recommended by another parent who said that her daughter had been injured by the Gardasil vaccine. Mr. Rowan testified that Mr. Phillips recommended that Ms. Rowan begin a vitamin regimen which included a specific type of vitamin K. Tr. 49-52. Within several weeks of beginning a specialized diet and the vitamin regimen, Ms. Rowan's condition gradually improved. Tr. 52-62. By mid-2011, Ms. Rowan had returned to her baseline, and "was like her old self." Tr. 63.

Ms. Rowan testified at the hearing on January 14, 2014. She testified that she was attending college, and living on campus. Tr. 120. Ms. Rowan appeared healthy and well-spoken. She also testified that her condition had improved and she is feeling better now. Tr. 121.

IV. Has Petitioner Presented Preponderant Evidence of Illness or Injury?

The parties first dispute whether Ms. Rowan has presented preponderant evidence that she suffered illness or injury. See Jt. Sub. at 4, and footnote 4. The medical records, including but not limited to those facts set forth in the above summary, and the testimony of petitioner's expert, Dr. Yehuda Shoenfeld, provide relevant evidence on the issue of Ms. Rowan's diagnosis.

Petitioner's expert, Dr. Yehuda Shoenfeld, testified that Ms. Rowan was seen by approximately "13 different physicians," but because she did not "have any organic manifestation," she was never given a diagnosis. Tr. 208. Ms. Rowan was seen by neurologists, an infectious disease specialist, a physical medicine rehabilitation specialist, a pain management specialist, a hematologist and oncologist, and a Lyme disease specialist. Tr. 229. Dr. Shoenfeld testified that instead of diagnosing petitioner, the treating physicians merely "diagnosed the symptoms." Tr. 218-19, 222, 258. Ms. Rowan underwent many "examinations, quite sophisticated, and all of them were interpreted as normal." Tr. 209. He testified that petitioner's diagnosis, "post factum" was "chronic fatigue syndrome." Tr. 210, 221. Dr. Shoenfeld defined chronic fatigue syndrome ("CFS") as "chronic fatigue and [] unrefreshing sleep on waking" lasting for six months. Tr. 221; see also Pet. Ex. 15 at 3. Dr. Shoenfeld rejected any notion that Ms. Rowan's abdominal pain was a vaccine-related symptom. Tr. 223.

Based on a review of the records and expert testimony at hearing, the undersigned finds that Ms. Rowan has presented preponderant evidence that she was diagnosed and treated for headaches. There is not preponderant evidence that she has chronic fatigue syndrome.[5] See Althen v. Sec'y of Health & Human Servs., 418 F.3d 1275, 1278 (Fed. Cir. 2005).

V. Causation Analysis

The parties next dispute whether Ms. Rowan has presented preponderant evidence under Althen, 418 F.3d at 1278, that the Gardasil vaccines caused her alleged injuries. Jt. Sub. at 4-6.

A. Legal Framework

To receive compensation under the Program, petitioner must prove either: (1) that she suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that she received, or (2) that she suffered an injury that was actually caused by the HPV vaccine. See §§ 300aa-13(a)(1)(A) and 11(c)(1); Capizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1319-20 (Fed. Cir. 2006). 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, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)).

Because petitioner does not allege she suffered a Table injury, she must prove that the HPV vaccines she received caused her injuries. To do so, she must establish, by preponderant evidence: (1) a medical theory causally connecting the vaccine and her injury ("Althen Prong One"); (2) a logical sequence of cause and effect showing that the vaccine was the reason for her

[5] Petitioner also alleged that the vaccinations caused her to experience difficulty walking, abdominal pain, dizziness, weight loss, bronchial spasms, and ultimately led to her becoming bedridden. Petitioner, however, did not provide preponderant evidence that these other conditions were allegedly related to her vaccinations. Even if petitioner had proven by a preponderance of evidence that she suffered from all of the conditions that she has alleged, the undersigned's ruling as to causation would be the same.

injury ("Althen Prong Two"); and (3) a showing of a proximate temporal relationship between the vaccine and her injury ("Althen Prong Three"). Althen, 418 F.3d at 1278; § 300aa–13(a)(1).

The causation theory must relate to the injury alleged. Thus, a petitioner must provide a reputable medical or scientific explanation that pertains specifically to the vaccinee's case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioner cannot establish entitlement to compensation based solely on her assertions. Rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 300aa-13(a)(1). In determining whether petitioner is entitled to compensation, the special master shall consider all material contained in the record, § 300aa-13(b)(1), including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation . . . of the petitioner's illness." § 300aa-13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' offered experts and rule in petitioner's favor when the evidence weighs in his favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence"); Althen, 418 F.3d at 1280-81 ("close calls" are resolved in petitioner's favor).

Another important aspect of the causation-in-fact case law under the Program concerns the factors that a special master should consider in evaluating the reliability of expert testimony and other scientific evidence relating to causation issues. In Daubert v. Merrell Dow Pharmaceutical, Inc., 509 U.S. 579 (1993), the Supreme Court listed certain factors that federal trial courts should utilize in evaluating proposed expert testimony concerning scientific issues. In Terran v. Sec'y of Health & Human Servs., 195 F.3d 1302, 1316 (Fed. Cir. 1999), the Federal Circuit ruled that it is appropriate for special masters to utilize Daubert's factors as a framework for evaluating the reliability of causation-in-fact theories presented in Program cases.

B. Althen Analysis

(1) Althen Prong One: Petitioner's Medical Theory

Under Althen Prong One, petitioner must set forth a medical theory explaining how the HPV vaccine could have caused her alleged injury. Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1375 (Fed. Cir. 2009). Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1355-56 (Fed. Cir. 2006).

Petitioner's theory of causation must be informed by a "sound and reliable medical or scientific explanation." Knudsen, 35 F.3d at 548; see also Veryzer v. Sec'y of Health & Human Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 300aa-13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioner relies upon a medical opinion to support her theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira

v. Sec'y of Health & Human Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) ("An expert opinion is no better than the soundness of the reasons supporting it.") (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980)).

a. Petitioner's Expert, Dr. Yehuda Shoenfeld

Dr. Yehuda Shoenfeld graduated from the Hadassah Medical School in Israel in 1972. He was appointed lecturer in internal medicine at the Tel Aviv University Medical School in 1975 and then advanced to senior lecturer in 1980. He received a diploma *cum laude* for his studies in internal medicine at the Postgraduate Medical School of Tel Aviv University in 1978. Beginning in 1976, he served as senior resident in the Department of Internal Medicine and the Out Patient Clinic of Hematology and Immunology of Beilinson Medical Center in Israel. Dr. Shoenfeld conducted research in hematology and internal medicine there, and became head of those departments in 1985. Between 1976 and 1982, Dr. Shoenfeld also participated in clinical fellowships in hematology/oncology at City of Hope, in Duarte, California; at the Tufts New England Medical Center of Boston, Massachusetts; and at the Cornell Medical Center of New York. See Shoenfeld Curriculum Vitae (2013) - Exhibit to Witness List filed on November 19, 2013; Tr. at 151-52.

In 1984, Dr. Shoenfeld became head of the Department of Medicine at the Sheba Medical Center of Tel Aviv University, where he continued to serve at the time of his testimony in this case. He received an academic appointment as Associate Professor in 1985, then Professor of Medicine in 1990, at the Tel Aviv University Medical School, Sackler Faculty of Medicine. Concurrently, he was the head of the Hybridoma Unit and Research Laboratory for Autoimmune Diseases of the Soroku Medical Center of Ben Gurion University of the Negev. In that capacity, he founded the Center for Autoimmune Diseases, and continues to serve as its Director. See Shoenfeld Curriculum Vitae (2013) - Exhibit to Witness List filed on November 19, 2013; Tr. at 152; Pet. Ex. 12 at 1-2.

Dr. Shoenfeld's 2013 *curriculum vitae* includes more than 1750 published professional articles, 60 books, and 130 chapters in medical texts, which he authored or co-authored, many of them focusing on autoimmune diseases. He served on the editorial boards of numerous medical journals, primarily concerning autoimmunology and rheumatic diseases. He has also been an organizer of many medical conferences, and a member of numerous professional organizations, both in Israel and internationally. See Shoenfeld Curriculum Vitae (2013) - Exhibit to Witness List filed on November 19, 2013; Tr. at 151-52.

Dr. Shoenfeld's causation theory in this case is "Adjuvant Induction of Autoimmune Disease" or ASIA.[6] Tr. 187-88, 230. While Dr. Shoenfeld has previously used ASIA syndrome

[6] Also referred to as "Autoimmune/inflammatory syndrome induced by adjuvants." See Pet. Ex. 16. During the hearing, Dr. Shoenfeld testified that ASIA is not his theory in this case. Tr. at 230. However, Dr. Shoenfeld's expert reports, petitioner's pleadings and her counsel's arguments frequently cite to ASIA as petitioner's theory of causation. See Tr. at 230-35 (Dr. Shoenfeld testified that ASIA "is not the theory in this case,") but see Jt. Sub. at 4 ("ASIA as applied to the instant matter is a plausible medical [] explanation."); Tr. at 11 (Ms. Finn states

to describe illness associated with silicone implants and other conditions, he uses it here to describe "adjuvant-induced side effects of vaccines." Tr. 232-33. Although Dr. Shoenfeld posits ASIA as the applicable medical theory, he acknowledges that ASIA is not a proven theory, and that the data only "suggest the possibility of accelerated autoimmunity/inflammation following vaccination." Pet. Ex. 16 at 4-5.[7]

"An adjuvant…is an agent that may stimulate the immune system and increase the response to a vaccine, without having any specific antigenic effect in itself."[8] Adjuvants are added to vaccines to "induce protective antibodies" and enhance the immunological reaction that protects against the virus, which in this case is HPV. Tr. 175. Without the use of adjuvants, the body will not "mount an immunological reaction…namely, [production of] protecting antibodies, which …neutralize the virus if the virus is encountered by the vaccinee in the future." Id.

Aluminum is the adjuvant used in the HPV vaccine. Tr. 175-77. Dr. Shoenfeld describes aluminum as a toxin that accumulates with each administration of the HPV vaccine. Id. at 177-78. Phagocytes from the "reticuloendothelial system" rid the body of aluminum, but the process is not very efficient. Id. at 178-79. Dr. Shoenfeld testified that phagocytes take aluminum from the vaccine injection site to the brain, and, in the brain, aluminum is toxic. Tr. 179. Dr. Shoenfeld is unable to state whether the aluminum only causes injury. Tr. 180-81.

Dr. Shoenfeld explained that precisely how adjuvants cause autoimmune illness "is not always known." Pet. Ex. 11 at 3; see also Pet. Ex 13.[9] "[A]djuvants seem to modulate a common set of genes, promote antigen-presenting cell recruitment and mimic specific sets of conserved molecules…thus increasing the innate and adaptive immune responses to the injected antigen." Pet. Ex. 14 at 2. The primitive immune system, which fights infections, has "toll-like receptors" which "start the cascade of the immune system." Tr. 186. Dr. Shoenfeld posits a mechanism where aluminum stimulates the "toll-like receptor 4." Tr. 186-87. Once stimulated, these receptors induce the secretion of inflammatory cytokines. Tr. 187.

Dr. Shoenfeld opines that "the aim of an adjuvant is to chronically stimulate the immune system." Tr. 167. This "chronic stimulation of the immune system can induce chronic fatigue…[and] headache." Tr. 187. Dr. Shoenfeld compares his theory of chronic stimulation of

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"Dr. Shoenfeld will explain this, but under the ASIA theory, which is Petitioner's theory of causation…"); Petitioner's Pre-Hearing Brief ("Pet. Br.") at 5 ("the symptoms Dr. Shoenfeld asserts demonstrate ASIA syndrome 'appeared only after the vaccines were delivered'") and 8 ("The expert report from Dr. Shoenfeld stated that the symptoms [petitioner] experienced can follow from administration of the HPV vaccine based on the ASIA medical disorder and illness"); Tr. at 10 ("[o]ur theory is that Natalie is experiencing -- her injuries were caused by what's known as ASIA, and that's an Autoimmune Syndrome Induced by Adjuvants"). For purposes of this decision, ASIA, "adjuvant induced" and similar phrases will be used interchangeably; they all refer to the theory set forth by Dr. Shoenfeld.

[7] Shoenfeld Y., et al., 'ASIA – Autoimmune/inflammatory syndrome induced by adjuvants, Journal of Autoimmunity 36 (2011) 4-8.

[8] Israeili E., et al., Adjuvants and Autoimmunity, Lupus (2009); 1217-1225.

[9] Israeili E., et al., Adjuvants and Autoimmunity, Lupus (2009); 1217-1225.

the immune system caused by vaccines to the process by which infection leads to atherosclerosis, as discussed by Espinola-Klein.[10] But that comparison is inapt because the study looked at viral and bacterial infectious pathogens and not adjuvants; the authors never discussed the notion of chronic stimulation of the immune system by adjuvants. In the study, patients were tested for antibodies to determine whether they had experienced prior infection with one or more of eight different viruses and bacteria (the HPV virus was not studied). The authors found "an association between the extent of atherosclerosis" and exposure to an increased number of infectious pathogens. Id. at 17. Based on the results of the study, the authors hypothesize that there is a relationship between "the number of infectious pathogens to which an individual has been exposed and the extent of atherosclerosis." Id. at 19. Dr. Shoenfeld attempts to draw an analogy between the burden of infections and the burden of adjuvants, suggesting that both lead to disease, but this article does not provide support for petitioner's argument that the adjuvant in the HPV vaccine causes disease.

Because ASIA syndrome is characterized by chronic stimulation, Dr. Shoenfeld opines that the condition is progressive, taking months or even years to cause disease. Pet. Ex. 12 at 7. Usually, the syndrome begins with an "immediate allergic reaction to the vaccine." Id. at 6. But there may be illness after the second or third vaccine (the "boost effect"). Id. at 7. Regardless of how the syndrome begins, there is a "slow progression of the disease from few clinical manifestations . . .to a full-blown disease." Id. Dr. Shoenfeld opines that the "full blown diseases" caused by ASIA include systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and multiple sclerosis (MS). Id.

In support of his opinion that adjuvants may cause disease, Dr. Shoenfeld relies on studies performed by Reeves et al.,[11] where mice were injected with an adjuvant, which led to the production of cytokines and autoantibodies. The mice eventually developed autoimmune diseases like SLE and RA. Tr. 187-88; see also Pet. Exs. 12, 24, 29, 81. Dr. Shoenfeld conceded, however, that the adjuvant used in the studies was pristane,[12] not aluminum. Tr. 264-65. Dr. Shoenfeld also acknowledged that while the mice developed lupus-like disease or RA, tr. 265, and petitioner did not have either of these conditions. Tr. 266.

Dr. Shoenfeld also relies upon a condition known as macrophagic myofasciitis syndrome ("MMF") to support his medical theory based on adjuvants. See Pet. Ex. 16 at 4. MMF was

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[10] Espinola-Klein, C., et al., Impact of Infectious Burden of Extent and Long-Term Prognosis of Atherosclerosis. Circulation (2002); 105: 15-21. Petitioner inadvertently failed to file this exhibit; it is filed as Court Exhibit A.

[11] Satoh M., et al., Induction of Lupus-Associated Autoantibodies in BALB/c Mice by Intraperitoneal Injection of Pristane, J. Exp. Med. Dec. 1, 1994; 180(6); 2341-46.

[12] Pristane is a hydrocarbon oil which "induces chronic inflammation when introduced into the peritoneal cavity…causing a "lupus-like disease in mice." Pet. Ex. 24 at 2. "In humans, inadvertent cutaneous injection of it causes an "intense inflammatory reaction, often with skin necrosis, permanent loss of hand function, or the need for amputation of affected digits." Id; Reeves et al., Induction of autoimmunity by pristane and other naturally-occurring hydrocarbons. Trends Immunol. Sept. 2009; 30(9); 455-64.

identified and described by Gherardi,[13] et al. in 1993, as an "emerging condition of unknown cause, detected in patients with diffuse arthromyalgias and fatigue, characterized by muscle infiltration by …macrophages" based on deltoid muscle biopsy. Resp't's Ex. O, Tab 13, at 1. An MMF lesion may be seen in patients who have had an "intramuscular injection of aluminum hydroxide-containing vaccines." Id. All of the patients studied by Gherardi had received vaccines containing aluminum hydroxide adjuvants (although none received HPV vaccines). In addition to positive muscle biopsy findings, MMF patients may have abnormal diagnostic tests, including abnormal electromyogram, elevated creatine kinase, and abnormal Gallium scintigraphy studies. Id. at 9. Gherardi and his colleagues did not conclude that MMF lesions cause systemic symptoms, but recommended further study of MMF patients. Id. at 9.

Regarding the issue of whether the HPV vaccine can cause headaches, Dr. Shoenfeld testified that he reviewed VAERS reports which show that patients receiving the Gardasil vaccine were twice as likely to have migraine headaches as compared to those receiving the Menactra vaccine.[14] Tr. 215. But in a study done by Klein, et al.,[15] a Kaiser Permanente study of 346,972 doses of HPV administered to 189,629 females, the authors did not report an association between HPV and headaches or the other illnesses alleged by petitioner. The study did not reveal safety concerns other than "same day syncope and skin infections." Resp't's Ex. M at 5.

Fundamental to Dr. Shoenfeld's theory of causation is that there must be a genetic predisposition for one to develop an "autoimmune disease or chronic fatigue." Tr. 266; Pet. Ex. 14 at 2. Thus, he believes there was a "concert action" of genetics and environmental factors at play in Ms. Rowan's case. Tr. 195.

b. Respondent's Expert, Dr. James L. Whitton

Dr. James Lindsay Whitton was born in Scotland and obtained his medical training from the University of Glasgow in Scotland in 1979. Five years later, he obtained a Ph.D. after studying herpes virus transcription. In 1989, he joined the Scripps Research Institute in La Jolla, California. At that institution, he taught neuropharmacology and immunology. Dr. Whitton has acted as the editor of Virology since January 2006. He has written more than 160 articles published in peer-reviewed journals. See Resp't's Ex. G at 2–13; Tr. 295–302. He is an expert in the areas of virology and immunology. Tr. 302-05.

Dr. Whitton was called by respondent to testify about petitioner's medical theory, i.e., Althen Prong One. When asked whether the adjuvant in the vaccines Ms. Rowan received

[13] Gherardi, R.K., et al., Macrophagic myofasciitis lesions assess long-term persistence of vaccine-derived aluminum hydroxide in muscle. Brain (2001); 124: 1821-31.

[14] Dr. Shoenfeld testified that he selected the Menactra vaccine as a comparison because that particular vaccine is given to the same age group as the Gardasil vaccine.

[15] Klein, N., et al., Safety of Quadrivalent Human Papillomavirus Vaccine Administered Routinely to Females, Arch. Pediatr. Adolesc. Med. October 1, 2012; published online: 10.001/archpediatrics.2012.1451.

caused her injury, Dr. Whitton opined that there is "no biologically plausible pathway by which the aluminum adjuvant could have done so." Tr. 345.

As background information, Dr. Whitton, like Dr. Shoenfeld, explained the purpose of using adjuvants in vaccines. "Adjuvants are substances added to vaccines to enhance and direct the immune response." Resp't's Ex. K Tab 9 at 1. Adjuvants induce the "innate part of the immune system" to "produce cytokines…which are soluble proteins." Tr. 310-11. These proteins communicate with the "adaptive immune system and instruct the cells to divide and multiply… . [to] generate a very strong, vaccine-specific, antigen-specific response." Tr. 311. It is this response which protects the body against the pathogen (here HPV) if the body encounters it in the future. Tr. 311. The aluminum adjuvant also serves a "depot function." Tr. 334. The adjuvant "holds the antigen and prevents it from dispersing, allowing the induction of a stronger [] immune response…. " Tr. 334; see also Resp't's Ex. K-Tab 9 at 1 and 4. While Dr. Whitton agreed with Dr. Shoenfeld that the purpose of adjuvants in vaccines is to "increase the antigen-specific immune response," Dr. Whitton disagreed that aluminum adjuvants are harmful or that they cause injury. Tr. 306, 315, 357-58.

Dr. Whitton bases his opinion that aluminum used as an adjuvant does not cause injury on the following. First, aluminum is a commonly used adjuvant that has been rigorously tested and found to be safe when used as an adjuvant in vaccines. Tr. 307; see also Resp't's Ex. N at 9. In his report, Dr. Whitton cites to the World Health Organization ("WHO") Global Advisory Committee on Vaccine Safety (GACVS) which states "[a]t present there is no evidence of a health risk from aluminum-containing vaccines." Resp't's Ex. N at 11. Moreover, Dr. Whitton is not aware of any medical literature or studies that suggest that aluminum, when used as an adjuvant in vaccines, causes any injury. Tr. 357-58.

As described above, Dr. Shoenfeld relied on the Reeves studies where pristane was injected in mice, inducing autoimmune diseases (SLE and RA). Dr. Whitton did not agree that the results from those studies supported Dr. Shoenfeld's theory. Tr. 308. Dr. Whitton explained that pristane is a hydrocarbon and a "relatively toxic compound," and there is no evidence to suggest that aluminum causes SLE or arthritis. Tr. 308.

Dr. Whitton also disagreed with Dr. Shoenfeld's argument that MMF provides evidence of a systemic disease caused by aluminum adjuvant in vaccines. Tr. 316. Dr. Whitton explained that MMF is simply a histological finding, i.e., a lesion that is located at the site of vaccination in the arm. Tr. 316, 336. There is no proof that an MMF lesion causes systemic disease. Tr. 317. Dr. Whitton testified that follow-up animal studies were done by Verdier et al., to investigate whether MMF lesions cause disease. Tr. 318; Resp't's Ex. O. The studies found that MMF lesions decreased over time, suggesting that the lesion ultimately cleared without causing systemic disease.[16] Tr. 318-19; see also Resp't's Ex. O, Tab 14 ("no correlation between histological findings of macrophagic myofasciitis in biopsies and the clinical symptoms");

[16] Verdier F., et al., Aluminum assay and evaluation of the local reaction at several time points after intramuscular administration of aluminum containing vaccines in the Cynomolgus monkey, Vaccine 23 (2005) 1359-67.

Resp't's Ex. O, Tab 21, 22. And importantly, as it relates to this case, Dr. Whitton emphasized there is no allegation or evidence that petitioner ever had an MMF lesion. Tr. 316.

In another paper related to MMF, by Guis et al.,[17] ten patients with diagnosed muscular diseases were found to have an MMF lesion after vaccination. These patients were also found to have genetic abnormalities associated with autoimmune diseases. Tr. 319-21. Dr. Whitton testified that Dr. Shoenfeld used the Guis study to suggest that MMF was associated with autoimmune systemic disease. Id.; Resp't's Ex. N at 7. But Dr. Whitton believes the Guis study is "flawed" because the participants of the study already had autoimmune diseases and as such were "preselected…in favor of having a genetic predisposition." Tr. 355-56. (Dr. Whitton notes that Dr. Shoenfeld ultimately agrees with Dr. Whitton's statement that there was not an appropriate control group in the Guis study). See Resp't's Ex. N at 8.

Dr. Whitton also disagreed that adjuvants induce chronic stimulation of the immune system. Tr. 332. Dr. Whitton explained that Dr. Shoenfeld could easily demonstrate this premise with a study, but no such study has been performed. Tr. 350-51. Dr. Whitton further explained that if Dr. Shoenfeld's statement were true, then second and third doses of vaccines, i.e., boosters, would not be needed. Tr. 332. Moreover, any symptoms of adjuvant activation of the immune system are usually of short duration (i.e., "achy, sore arm") and not chronic. Tr. 332-33.

Dr. Whitton agreed with Dr. Shoenfeld that there is a "very clear genetic predisposition" for some autoimmune diseases. Tr. 353. Both experts agree that a number of autoimmune conditions are related to human leukocyte antigen (HLA) genes. Id. Autoimmune diseases known to be associated with a genetic predisposition include ankylosing spondylitis, Reiter's syndrome, and SLE. Tr. 313. But Dr. Whitton is not aware of any overlap between genetic predisposition, autoimmune disorders, and adjuvants, akin to what Dr. Shoenfeld posits here. Tr. 354.

Lastly, Dr. Whitton testified that ASIA is not a generally accepted medical theory, diagnosis or syndrome, within the medical community. Tr. 306. Dr. Whitton characterized it as "a hypothesis…rather than an established syndrome." Tr. 313. As an example of the fact that ASIA is not an accepted theory, Dr. Whitton cited a 2013 comprehensive review article covering adjuvants, authored by Reed, a "world expert" on adjuvants.[18] See Tr. 341. There is no reference to ASIA or the ASIA syndrome in the review article. Tr. 341; Resp't's Ex. R.

c. Respondent's Expert, Dr. Edward W. Cetaruk

Dr. Edward Cetaruk is an emergency medicine physician and a medical toxicologist at Porter Hospital in Denver, Colorado. Tr. at 368. Dr. Cetaruk teaches at the University of Colorado Medical Center in the Medical Toxicology Fellowship Program. He graduated from

[17] Guis S., et al., HLA-DRB1*01 and macrophagic myofasciitis, Arthritis & Rheumatism, Vol. 46, No. 9, September 2002, pp. 2535-37.
[18] Reed S.G., et al., Key Roles of adjuvants in modern vaccines. Nature Medicine, Vol. 19, No. 12, December 2013, pp1597-1608.

the School of Medicine at New York University in 1991. Dr. Cetaruk received advanced training in emergency medicine. In 1996, he completed a fellowship in medical toxicology. The American Board of Emergency Medicine recognized him as having special qualifications in medical toxicology in 2000. He became a fellow in the American College of Medical Toxicology in 2009. Resp't's Ex. S at 1-2.

Like Dr. Whitton, Dr. Cetaruk was offered as an expert as to Althen Prong One, to address petitioner's medical theory regarding aluminum adjuvants. Dr. Cetaruk also provided background information about aluminum and aluminum adjuvants. Tr. 377.

Dr. Ceturak testified that aluminum has been used as an adjuvant in vaccines for over 70 years and has a safe record with a "low incidence of reported adverse events." Resp't's Ex. K-Tab 5 at 1. Dr. Ceturak is not aware of any other evidence which suggests that aluminum used as an adjuvant in vaccines causes systemic illness or disease. Tr. 399-400. The adjuvant used in the HPV vaccine, he observed, is 225 µg (nanograms) of aluminum hydroxy sulfate, an aluminum salt. Tr. 379-80. Dr. Cetaruk explained that all humans are exposed to aluminum even before birth with the primary route of exposure being ingestion, through food and water. Tr. 380-83; see also Resp't's Ex. K, Tab 9 at 8. Other sources of aluminum include medications such as aspirin and antacids. Tr. 381. Another route of exposure of aluminum is by inhalation. Welders are exposed to inhaled aluminum by virtue of their work environment. Tr. 381. Transdermal exposure is limited but occurs from use of antiperspirants. Tr. 381–82. The daily average intake of aluminum is between 7 to 10 milligrams ("mg") per day. Tr. 383.

Dr. Cetaruk testified that most of the aluminum we ingest is not absorbed into the body, but is instead excreted by the kidneys. Tr. 384–85; Resp't's Ex. K, Tab 9 at 8. More than 90% of the aluminum that is absorbed in the systemic circulation is bound to a protein called transferrin, or other smaller proteins, and distributed throughout the tissues of the body. Tr. 385-86. More than half is distributed to bone, with the balance distributed to other organs such as the spleen, liver, brain and muscle. Tr. 386. Citing the study by Priest,[19] Cetaruk testified that 54% of aluminum is in bones, 13% in skin tissues, and 14% in muscle. Resp't's Ex. K, Tab 17, at 9; Tr. at 387-88. Only 1% is found in the central nervous system. Id. In the brain, aluminum is incorporated into extracellular fluid where it can remain for a period of time. Tr. 388-89. Aluminum continuously comes into and out of the brain. Tr. 389-90.

When a vaccine containing an aluminum adjuvant is injected, the surrounding tissue responds and interacts with the immune system (as described above by Dr. Whitton). Tr. 391. Macrophages respond by engulfing and "eat[ing] the adjuvant." Tr. 391. Then, the "macrophage[s] migrate away from the immunization site… go[] out to lymph nodes and [] out to the circulation." Tr. 392. Eventually, the macrophage undergoes cell death, and aluminum is released from the cell. That "aluminum goes back into circulation…." Tr. 392. It then gets "handled the same way as aluminum that would have been ingested orally or inhaled or ingested

[19] Priest N.D., The biological behavior and bioavailability of aluminum in man, with special reference to studies employing aluminum-26 as a tracer: review and study updated, J. Environ. Monit., 2004, 6, 375-403.

through [the] skin." Tr. 393. Once aluminum is picked up by macrophages and carried out to the tissues, it no longer has an adjuvant effect. Tr. 398.

The HPV vaccine in this case, contains approximately 225 µg (nanograms) of aluminum adjuvant. Tr. 399. A person normally absorbs between 200-500 µg of aluminum daily through ingestion.[20] Tr. 398. Normal serum levels of aluminum are in the range of 5 to 6 micrograms per liter) ("mcg/L"). Tr. 428-29. Aluminum toxicity may occur when aluminum levels reach twenty or more times higher than normal. Tr. 428–29. But Dr. Ceturak testified that he has not seen chronic fatigue syndrome associated with elevated levels of aluminum. Tr. 430. Likewise, Dr. Ceturak has not seen elevated levels of aluminum cause headaches unless levels are very high. Tr. 430–31.

Dr. Cetaruk testified that dialysis patients are prone to aluminum toxicity because their kidney function is impaired and unable to rid the body of excess aluminum. Also, the fluid used in the dialysis procedure (dialysate) contains a significant amount of aluminum. Tr. 393–94. Signs and symptoms of aluminum toxicity include anemia, abnormal bone development, and sometimes encephalopathy.[21] Tr. 395-96. Blood, serum, or plasma may be tested to diagnose aluminum toxicity. Tr. 396–97.

d. Petitioner's Treating Physicians

Ms. Rowan's primary care physician, Dr. Fogarty, treated petitioner for ongoing headaches beginning in 2007. Dr. Fogarty conducted tests and prescribed medications which resulted only in minimal relief. On February 9, 2009, Ms. Rowan followed up with Dr. Fogarty for headaches and it was noted at that visit that petitioner's parents were concerned about a link to the HPV vaccines. Dr. Fogarty did not conclude, however, that the vaccines caused or contributed to Ms. Rowan's symptoms.

In late December 2008, Ms. Rowan began seeing Dr. Powers, a neurologist, for headaches. After reviewing her medical history, Dr. Powers diagnosed Ms. Rowan with chronic daily headaches and prescribed Topamax. Ms. Rowan continued to follow up with Dr. Powers from March 2009 to January 2010. The records do not note that Dr. Powers drew any association between the HPV vaccines and Ms. Rowan's symptoms.

Ms. Rowan began seeing Dr. Porter, a pediatric hematologist, in October 2009. Pet. Ex. 3 at 20-21. Although Dr. Porter was advised by Ms. Rowan's father that he believed Ms. Rowan's headache symptoms all dated back to her last HPV vaccine, Dr. Porter did not attribute Ms. Rowan's symptoms to the vaccine.

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[20] Dr. Cetaruk testified that the average person takes in 7-10 mg. of aluminum per day, but absorbs 200-500 mcg per day via their gastrointestinal tract.

[21] Dr. Cetaruk defines encephalopathy as "abnormal brain function . . . deterioration of cognitive function, and as it gets more severe, more basic functions manifesting as altered mental status, delirium, confusion . . . . [and] poor functioning of the brain." Tr. 435.

During the hearing, Mr. Rowan described Dr. Shapiro's involvement with his daughter's diagnosis and treatment. Mr. Rowan testified that in March 2010, he brought petitioner to see Dr. Shapiro, who examined her and conducted an EMG. Tr. 41. The EMG showed that there were no abnormalities, although at the time Ms. Rowan was not walking and was using a wheelchair. Pet. Ex. 44 at 2. Mr. Rowan testified that Dr. Shapiro thought that Ms. Rowan would be able to walk again but would need physical therapy in order to do so. Tr. 43. There is no evidence in the record indicating that Dr. Shapiro associated Ms. Rowan's condition with her HPV vaccines.

During the hearing, Mr. Rowan testified that none of Ms. Rowan's treating physicians attributed her condition to the HPV vaccines. Tr. 44.

e. Evaluation of the Evidence

Althen Prong One requires a petitioner to set forth a medical theory explaining how the received vaccine could have caused the alleged injury. Dr. Shoenfeld failed to provide persuasive or reliable evidence to support his theory that the adjuvant aluminum in the HPV vaccine chronically stimulates the immune system in a person with a genetic predisposition, causing ongoing headache.

Dr. Shoenfeld concedes that ASIA is not a proven theory and that the mechanism whereby adjuvants cause autoimmune illness is not known. He is unable to state whether the aluminum adjuvant, or the virus-like particles in the vaccine, or both, cause injury. Petitioner also failed to provide an evidentiary foundation or factual support for the premise that an aluminum adjuvant causes chronic stimulation of the immune system that in turn causes headaches or the other illnesses alleged.

Moreover, Dr. Shoenfeld relied on studies involving the adjuvant pristane, a toxic hydrocarbon which is not comparable to aluminum. Thus, the adjuvant studies he cited are not relevant to the facts and circumstances of this case. Dr. Shoenfeld argued that MMF is evidence of adjuvant-induced injury but the authors of the relevant studies did not reach that conclusion. Further, since petitioner did not have MMF, the argument based on those studies is not relevant to the facts here. Most importantly, Dr. Shoenfeld provided no evidence that the doses of aluminum used in the vaccinations at issue were toxic or caused the illnesses alleged by petitioner. Likewise, he provided no evidence of any genetic disorder that would predispose one to an immune disorder given the set of facts and circumstances relevant to this case.

Lastly, none of petitioner's treating physicians opined that HPV vaccines can cause headaches or any other condition experienced by petitioner. In summary, petitioner failed to provide preponderant evidence to support Prong One of Althen.

(2) Althen Prong Two: Logical Sequence of Cause and Effect

Under Althen Prong Two, a petitioner must prove that there is a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." Capizzano, 440 F.3d at 1324 (citing Althen, 418 F.3d at 1278). "Petitioner must show that the vaccine was the

'but for' cause of the harm … or in other words, that the vaccine was the 'reason for the injury.'" Pafford, 451 F.3d at 1356 (citations omitted).

a. Petitioner's Expert, Dr. Shoenfeld

Dr. Shoenfeld testified that the aluminum adjuvant in the HPV vaccine induced petitioner's chronic fatigue and headaches via the ASIA mechanism. Dr. Shoenfeld argued that petitioner's symptoms are like those seen with MMF. Pet. Ex. 12 at 5-6. He explained the process as follows: "The aluminum is deposited in the muscles and can induce muscle fiber necrosis and hence the severe fatigue … (and) nanoparticles of the aluminum are diffused to the brain to induce … headaches." Id. at 6. But petitioner's medical records do not document that Ms. Rowan had MMF or muscle fiber necrosis. Further, Dr. Shoenfeld does not provide any facts from the petitioner's medical records or any other evidentiary foundation to support his conclusion that petitioner's headaches were caused by nanoparticles of aluminum in her brain.

Organ or tissue biopsies can be performed to verify the diagnosis of MMF, tr. 242-43, but no such biopsies were ordered by any of petitioner's treating physicians, and there is no evidence in the record to suggest that petitioner had MMF. Dr. Shoenfeld agreed that the results of the following studies were normal: X-rays and MRI studies performed on petitioner's brain and lumber spine, MR venogram studies, CT scans of her head and sinuses, and EMG studies. All of these diagnostic studies were normal. Tr. 223-28. Petitioner's ANA test was also normal. Tr. 225. Dr. Shoenfeld agreed that petitioner's CSF was normal. Tr. 227. Dr. Shoenfeld conceded that there are no antibodies specific for aluminum in any of petitioner's test results. Tr. 244. He testified that there is a blood test for aluminum but the petitioner was never tested. Tr. 286-87. Petitioner went "through a lot of examinations, quite sophisticated, [] all of them were interpreted as normal." Tr. 209.

Petitioner's only abnormal lab work was a low white blood count of 3.2, with elevated lymphocytes of 54, drawn on September 29, 2009. Pet. Ex. 2 at 1. Dr. Shoenfeld testified that the high lymphocyte level was evidence of stimulation of the immune system. Tr. 206.

One of the basic principles of Dr. Shoenfeld's medical theory is that one must be genetically predisposed to develop an autoimmune illness. Tr. 194- 95; 266. Dr. Shoenfeld conceded, however, that there was no evidence to suggest that the petitioner had any abnormal genetic predisposition, and, in fact, none of her physicians ever ordered that she undergo genetic testing. Tr. 266. Moreover, pursuant to Dr. Shoenfeld's theory of adjuvant-induced autoimmune disease, initial symptoms progress to "full-blown disease" such as SLE, RA, MS, or another similar disease. See Pet. Ex. 12 at 7. Here, petitioner never developed one of these chronic illnesses, but instead, after a diet and vitamin regimen, she recovered and returned to her baseline health.

b. Respondent's Expert, Dr. Stephen J. McGeady

Dr. Stephen McGeady is a retired board certified immunologist who practiced at the Nemours Foundation/Alfred I. duPont Hospital for Children in Wilmington, Delaware. Tr. 448; Resp't's Ex. B. Although he has retired from his position as an attending physician in the

Department of Allergy and Immunology in the Department of Pediatrics at the Nemours Foundation, Dr.McGeady remains a professor of pediatrics at Thomas Jefferson University in Philadelphia, Pennsylvania. Tr. 440. He graduated from the Creighton University School of Medicine in 1967. He received specialized training in pediatrics and allergy and is board-certified in pediatrics, allergy and immunology, and diagnostic laboratory immunology. Tr. 441. He served as the Chief of the Division of Allergy and Immunology in the Department of Pediatrics at duPont Hospital from 1989 until 2007. Dr. McGeady has published over 60 articles in peer-reviewed journals. See Resp't's Ex. B.

Dr. McGeady opined that petitioner's HPV vaccine did not cause her to suffer from any autoimmune or auto-inflammatory condition or disease. Tr. 450. He did not believe that petitioner's complaints of headache, fatigue, paralysis, abdominal pain, or weight loss were related to the HPV vaccines. Tr. 472. As for petitioner's headaches, Dr. McGeady testified that those symptoms experienced pre-vaccination were associated with "recurrent viral or bacterial infection[s]…[including] strep throat on one occasion." Tr. 451; 488. Petitioner's headaches in March 2008 were associated with the onset of petitioner's menses. Tr. 452. As for daily headaches, those did not occur until October 2008, based upon the testimony of petitioner's father. Pet. Ex. 1; Tr. 452. Dr. McGeady testified that petitioner's headaches at that time were "very classic for migraine headaches" in that she had sensitivity to light and sound, although another feature of petitioner's headaches, the sensation of "something pushing down on her head," was not typical for migraines. Tr. 468.

Dr. McGeady also testified that petitioner's diagnostic tests were normal and did not show evidence of any autoimmune disease process. Tr. 454. The MRIs performed in 2009 were normal, as were the results from the CT, EMG, and Lyme testing. Tr. 454-55. Cerebrospinal fluid was normal. Tr. 456. Nonspecific testing for the presence of autoantibodies, such as ANA, that often occur in autoimmune illnesses was normal. Tr. 457. Likewise, testing for C-reactive protein was normal. Tr. 457. Petitioner had an abnormal white blood cell count in September 2009, but Dr. McGeady testified that petitioner had a cough and sore throat, and did not feel well, indicating that petitioner had a viral infection. Tr. 487-488. Dr. McGeady attributed the minor abnormality in petitioner's white blood counts to her viral infection and not to any adverse reaction to vaccination. Id.

By March of 2010, petitioner's condition had worsened and she was unable to walk. Tr. 469. Diagnostic testing during the March 4, 2010 admission was normal, including but not limited to tests for celiac disease, cortisol levels, Lyme's disease, cryptococcal disease, and CSF fungal disease. Tr. 465. EMG studies were also normal. Tr. 469-70. Petitioner did have an elevated IgE, which Dr. McGeady attributed to petitioner's history of asthma. Tr. 465. Petitioner's discharge diagnoses from that admission were: "Head pain of uncertain etiology; flaccid paralysis of lower extremities without organic or neurological markers, uncertain etiology; and possible conversion disorder." Tr. 466; Pet. Ex. 8. Dr. McGeady testified that petitioner may have had a functional illness, or an illness that was psychologically based. Tr. 473.

Numerous medications, including steroids, were administered to petitioner for her headaches, without success, and Dr. McGeady testified that the fact that the medications did not work supported his opinion that petitioner did not have an organic condition. Tr. 467.

As for petitioner's allegation that she suffered from CFS due to her vaccines, Dr. McGeady testified that he did not see any support for this diagnosis in petitioner's medical record. Tr. 471.

c. Evaluation of the Evidence

The basic problem with petitioner's argument as to Althen Prong Two is that there is no evidence to support a finding that petitioner had an adjuvant-induced illness. Petitioner did not have any symptoms of aluminum toxicity, and none of her treating physicians suspected or diagnosed her with that condition. Petitioner underwent extensive testing, but there was no evidence of chronic stimulation of petitioner's immune system. Petitioner did not have an immediate allergic reaction to the vaccine. Her condition did not progress to a chronic illness as described by Dr. Shoenfeld to occur with ASIA such as SLE or RA. There is no evidence that petitioner had MMF and no evidence of a genetic predisposition.

Dr. Shoenfeld's opinion that petitioner had an adjuvant-induced illness in spite of the fact that she had no abnormal diagnostic studies is in stark contrast with a patient he describes in a medical article.[22] The patient described in the article had a silicone breast implant, and developed CFS following an injury to the breast that resulted in a silicone leak. Confounding the picture was the fact that the patient's illness also followed the second dose of hepatitis B vaccine. Dr. Shoenfeld and co-author Agmon-Levin concluded that "co-exposure to vaccine and silicone created an augmented adjuvant effect, leading to CFS." Pet. Ex. 15 at 3. But unlike petitioner, that patient had an abnormal physical examination (Raynaud symptoms and lymphadenopathy) and numerous abnormal tests (polyclonal gammopathy, elevated anti-adrenal hormone, anti-striated and anti-smooth muscle antibodies, elevated rheumatoid factor titers and abnormal immune complex blood work). The patient's brain MRI was also abnormal and revealed "multiple scattered T2 signal hyper intensities in the frontal and parietal occipital deep while matter and sub-cortical while matter." Pet. Ex. 15 at 3. The patient's CSF showed elevated IgA and albumin. Id.

In contrast to the patient described above, Ms. Rowan had no abnormal physical findings and no abnormal blood work to evidence an immune disorder. The only abnormality referenced by Dr. Shoenfeld is an abnormal WBC count of 3.2, with elevated lymphocytes reported in September 2009, over one year after the administration of Ms. Rowan's last HPV vaccine. According to Dr. Shoenfeld, this abnormal finding indicated stimulation of petitioner's immune system. Tr. 206. But Dr. Shoenfeld offered no medical literature or other support for his argument that this sole abnormality is sufficient evidence to support his theory that the HPV vaccinations caused a chronic dysfunction of petitioner's immune system leading to headaches

[22] Agmon-Levin N., Chronic fatigue syndrome with autoantibodies- The result of an augmented adjuvant effect of hepatitis-B vaccine and silicone implant. Autoimmunity Reviews 8 (2008) (52-55) (Pet. Ex. 15).

and CFS. Dr. McGeady's explanation that petitioner's isolated WBC results were due to a viral infection and not to any adverse reaction to vaccination is much more credible, given the lack of any other supportive evidence to the contrary.

In summary, petitioner has not provided any foundational support to show that she suffered an adjuvant- induced illness, and therefore the undersigned finds that petitioner has failed to provide preponderant evidence of a logical sequence of cause and effect showing that the HPV vaccines were the reason for petitioner's alleged injuries.

(3) Althen Prong Three: Proximate Temporal Relationship

Under Althen Prong Three, petitioner must provide "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." De Bazan v. Sec'y of Health & Human Servs., 539 F.3d 1347, 1352 (citing Pafford, 451 F.3d at 1358). The acceptable temporal association will vary according to the particular medical theory advanced in the case. See Pafford, 451 F.3d at 1358.

a. Petitioner's Expert, Dr. Shoenfeld

Dr. Shoenfeld testified that petitioner received multiple vaccines, including the HPV vaccines that contained the adjuvant aluminum. Tr. 234. In his opinion, the accumulation of aluminum after the third HPV vaccine led to her condition. Tr. 234. Petitioner received her first HPV vaccine on August 21, 2007, and her second HPV vaccine on November 12, 2007. Pet. Ex. 1 at 3. "There were no reported adverse reactions from either of these HPV vaccines." Pet. Ex. 12 at 2. Petitioner's third HPV vaccine was given on July 14, 2008. More than three months later, on October 20, 2008, petitioner complained of fatigue, sore throat and nasal congestion. P. Ex. 4 at 5. On October 28, 2008, petitioner returned to her primary care physician, Dr. Fogarty, complaining of ongoing headache and fatigue. Pet. Ex. 4 at 5; see also Pet. Ex. 12 at 2. Dr. Shoenfeld testified that petitioner therefore developed ASIA syndrome "two months after the third Gardasil injection." Tr. 245. Dr. Shoenfeld opined that the temporal relationship between the third vaccine administered on July 14, 2008 and the petitioner's onset of symptoms (ongoing headache and fatigue) in October 2008 was appropriate. Pet. Ex. 11 at 2.

Dr. Shoenfeld testified that ASIA syndrome is characterized by a "high incidence of immediate allergic reaction to the vaccine, followed by "chronic and persistent stimulation of the immune system by the adjuvant." Pet. Ex. 11 at 3. In some patients the adverse reaction does not appear for days, weeks, months, or years. Id. at 4; Tr. 245, 251.

Dr. Shoenfeld relied upon papers by Hernan and Mikaeloff[23] published in the Journal of Neurology "which show that multiple sclerosis can appear after two and a half to three years in

[23] Hernan M. et al., Recombinant Hepatitis B Vaccine and the Risk of Multiple Sclerosis: A Prospective Study. Neurology 2004; 63: 838-42; Mikaeloff, Y. et al., Hepatitis B vaccine and risk of CNS inflammatory demyelination in childhood. Neurology 2009; 72: 873-80.

patients with HPV vaccine." Tr. 246-47, 249. Dr. Shoenfeld conceded that these articles deal with demyelinating illnesses, and that petitioner did not have a demyelinating illness. Tr. 249-50.

b. Respondent's Expert, Dr. McGeady

Dr. McGeady testified that the timeframe of petitioner's onset of injuries, particularly those occurring October 2008 and later, and which occurred three months or more after petitioner's last HPV vaccination, was not persuasive evidence of an association with the vaccinations. Tr. 473.

c. Evaluation of the Evidence

Petitioner's expert failed to provide a medically appropriate timeframe for onset given his proposed theory. According to Dr. Shoenfeld, any timeframe appears to be acceptable, from days to weeks to years. However, Dr. Shoenfeld did not offer any facts or basis to support his opinion that the timeframe from vaccine to onset should be so variable. And he offered no explanation for why the timeframe from petitioner's third HPV vaccine to the onset of symptoms in October 2008, nearly three months later, was appropriate.

Moreover, Dr. Shoenfeld did not explain the inconsistency between a significant tenet of his proposed theory and Ms. Rowan's clinical course. Dr. Shoenfeld testified that a high incidence of patients with an adjuvant-induced injury have an immediate allergic reaction to the vaccine, but that did not occur in petitioner's course. Petitioner had no adverse reactions to her first and second HPV vaccines, and no reaction to the third dose until October 2008, based on Dr. Shoenfeld's testimony and expert reports. Dr. Shoenfeld also gave no explanation to support his opinion that the onset of ASIA is so variable.

Even assuming that the petitioner had provided evidence that would meet her burden under Althen Prong Three, petitioner has failed to establish by a preponderance of the evidence Althen Prongs One and Two, and she is therefore not entitled to compensation.

VI. Conclusion

For the reasons discussed above, the undersigned finds that petitioner has not established entitlement to compensation and her petition must be dismissed. In the absence of a timely filed motion for review filed pursuant to Vaccine Rule 23, the clerk is directed to enter judgment consistent with this decision.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master