In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 13-799V
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PUBLISHED

J. F., Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	Special Master Horner Tetanus diphtheria acellular pertussis ("Tdap") vaccine; Autoimmune/inflammatory syndrome induced by adjuvants ("ASIA")

Renee J. Gentry, Vaccine Injury Clinic, George Washington University Law School Washington, DC, for petitioner.
Jennifer Leigh Reynaud, U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

On October 15, 2013, petitioner filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10-34 (2012), [2] alleging that she suffered anaphylaxis caused by an adverse reaction to her June 18, 2011, Tetanus diphtheria acellular pertussis ("Tdap") vaccination. (ECF No. 1.) Petitioner amended her petition on February 21, 2014, changing the alleged injury from anaphylaxis to "autoimmune/inflammatory syndrome induced by adjuvants ('ASIA') with associated symptoms." (ECF No. 12.) For the reasons set forth below I conclude that petitioner is not entitled to compensation.

[1] When this decision was originally filed the undersigned advised his intent to post it on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). In accordance with Vaccine Rule 18(b), petitioner filed a timely motion to redact certain information. This decision is being reissued with redactions, namely reduction of petitioner and family names to initials and removal of the name of petitioner's gymnastics coach. Except for those changes and this footnote, no other substantive changes have been made. This decision will be posted on the court's website with no further opportunity to move for redaction.

[2] All references to "§ 300aa" below refer to the relevant section of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

I. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations, including showing that an individual received a vaccination covered by the statute; received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury. In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period also specified in the Table. If so, causation is presumed and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300 aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B).

In many cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table. In these cases, the presumptions available under the Vaccine Injury Table are inoperative. Instead, the petitioner bears the burden of showing by preponderant evidence that the vaccine recipient's injury was actually caused by the alleged vaccination, often referred to as "causation-in-fact". § 300aa-13(a)(1)(B); § 300aa-11(c)(1)(C)(ii); *see also Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines v. Sec'y of Health & Human Servs.*, 940 F.2d 1518, 1525 (Fed. Cir. 1991).

Under the preponderant evidence standard, the petitioner must show that it is "more probable than not" that the alleged vaccination was the cause of the alleged injury. *Althen*, 418 F.3d at 1279. The petitioner need not show that the vaccination was the sole cause of the injury, but must establish that the vaccination was at least a "substantial factor" and "but for" cause of the condition. *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). A petitioner may not receive a Vaccine Program award based solely on his or her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1). The petitioner must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury;" and this proof must be supported by "reputable medical or scientific explanation, *i.e*., evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F.3d at 1278; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992).

In what has become the predominant framing of this burden of proof, the *Althen* court described the causation-in-fact standard, as follows:

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury. If Althen satisfies this burden, she is "entitled to recover unless the [government] shows, also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine."

Althen, 418 F.3d at 1278 (citations omitted). The *Althen* court noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279-80. The court also indicated that, in finding causation, a Program fact-finder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Id*. at 1280.

Generally, respondent bears the burden of demonstrating the presence of any alternative cause by preponderant evidence only if petitioner satisfies her *prima facie* burden. § 300aa-13(a)(1)(B); *Walther v. Sec'y of Health & Human Servs*., 485 F.3d 1146, 1150 (Fed. Cir. 2007). Respondent may also present evidence relating to an alternative cause to demonstrate the inadequacy of petitioner's evidence supporting her case in chief, but petitioner does not bear the burden of eliminating alternative causes where the other evidence on causation is sufficient to establish a *prima facie* case under *Althen*. *de Bazan v. Sec'y of Health & Human Servs*., 539 F.3d 1347, 1352-53 (Fed. Cir. 2008); *Walther*, 485 F.3d at 1150.

In this case, petitioner has alleged that her Tdap vaccine caused her to suffer ASIA, a condition that is not listed on the Vaccine Injury Table relative to the Tdap vaccine. (ECF No. 12.) Thus, petitioner must satisfy the above-described *Althen* test in order to show that she is entitled to a payment from the Vaccine Injury Compensation Program.

II. Procedural History

Petitioner's parents filed a petition for compensation on October 15, 2013 alleging that she suffered anaphylaxis as a result of her June 18, 2011 Tdap vaccination. (ECF No. 1.) Thereafter, this case was assigned to Special Master Millman. (ECF No. 2.) The parents filed various medical and school records marked as Exhibits 1-25 along with an "affidavit"[3] by Mr. and Mrs. F. marked as Exhibit 26 and two additional statements, one by petitioner and one by her brother, marked collectively as Exhibit 27. (ECF No. 4.)

[3] Actually an unsworn narrative signed and dated by both parents, but designated as an affidavit on filing.

On February 21, 2014, the petition was amended, changing the alleged injury from anaphylaxis to ASIA.[4] (ECF No. 12.) Along with the amended petition, petitioner's parents filed a letter from her treating physician, pediatric rheumatologist Dr. Deborah McCurdy, marked as Exhibit 28 and several medical articles filed collectively as Exhibit 29. (ECF Nos. 12-13.) An expert report from Dr. McCurdy was subsequently filed on March 25, 2014, as Exhibit 30. (ECF No. 15.) (Dr. McCurdy's expert submissions were later struck as discussed below.) Additional medical records marked as Exhibits 31-33 were then filed on June 11 and June 27, 2014. (ECF Nos. 17, 20.)

Respondent filed two expert reports on September 10, 2014, one from toxicologist Dr. Edward W. Cetaruk, and another from immunologist Dr. Lindsay Whitton. (ECF No. 23; Exs. A-D.) On September 17, 2014, respondent filed an additional expert report from pediatric rheumatologist, Dr. Carlos Rose, and a Rule 4(c) report recommending against compensation. (ECF No. 26; Exs. E-F.) Petitioner's parents responded to respondent's Rule 4(c) report on December 3, 2014, with a supplemental expert report from Dr. McCurdy (Ex. 34-35 (later struck)), a letter from immunologist Dr. Joshua Davidson (Exs. 36-37), a letter from petitioner's pediatrician, Dr. Demonteverde (Ex. 38), a letter from petitioner's gymnastics coach (Ex. 39), and a presentation from petitioner's father responding to the government's report (Ex. 40).[5] (ECF No. 31.) The medical literature accompanying Dr. McCurdy's expert report and Dr. Davison's letter was filed later.[6] (ECF Nos. 33, 35.) Respondent then filed supplemental expert reports on March 26, 2015. (ECF No. 37; Exs. G-I.)

On May 20, 2015, after petitioner had reached the age of majority, petitioner's parents filed a motion to amend the caption to make her the sole petitioner in her adult capacity. The motion was granted on the same day. (ECF Nos. 39, 40.)

On April 1, 2015, Special Master Millman ordered the parties to propose mutually agreeable dates for an entitlement hearing. (ECF No. 38.) However, in an email to Special Master Millman's law clerk on June 29, 2015, petitioner indicated that she was attempting to secure a new expert and pursuing additional neurological exams to more

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[4] Anaphylaxis is a Table Injury for the Tdap vaccine if it occurs within four hours of vaccination. 42 C.F.R. § 100.3(a)(I). The amended petition does not invoke anaphylaxis but does allege that there was an immediate vaccine reaction consisting of fatigue, headache, fever, and arm swelling, beginning one hour after the vaccination. (ECF No. 12, p. 3.) In the interest of completeness I note that based on my review of the record evidence petitioner did not suffer anaphylaxis as defined by the Qualifications and Aids to Interpretation ("QAI") that define the Table Injury of anaphylaxis. 42 C.F.R. § 100.3(c)(1). Nor did petitioner establish that she suffered anaphylaxis caused-in-fact by her vaccination. Rather, petitioner's expert, Dr. Shoenfeld, later indicated that these symptoms constituted an arthus reaction. (Ex. 97, p. 31.)

[5] This presentation is not a sworn witness statement. Rather, it is a rebuttal to the medical opinions provided by respondent's experts. Mr. F. confirms in his presentation that he is an engineering manager rather than a medical doctor. Especially because petitioner subsequently provided expert medical opinion to support her claim, I need not address the content of this report further. I do note, however, that I have reviewed the presentation and considered any factual representations as unsworn fact witness declarations.

[6] These articles were identified as numbered "references" from Dr. Davidson's and Dr. McCurdy's submissions. They were not given exhibit designations.

specifically diagnose her injury. (ECF No. 42.) Petitioner subsequently filed additional medical records marked as Exhibits 41-42. (ECF No. 46.) However, petitioner's first attorney, Ms. Moss was then removed from the case by consented motion to substitute counsel on October 12, 2015. (ECF No. 49.)

Petitioner then proceeded with her second attorney, Ms. Stadelnikas. (ECF No. 49.) From October 12, 2015, to September 22, 2016, petitioner continued to see different specialists, collect updated medical records (Exs. 43-45, 47, 50-51),[7] and attempted to secure additional expert support for her claim. (*See* ECF Nos. 53, 62-65, 70-74.) However, on January 5, 2017, a status conference was held where petitioner notified the court that Ms. Stadelnikas intended to withdraw as petitioner's attorney. (ECF No. 75.) Petitioner filed additional medical records marked as Exhibits 52-54 on January 13, 2017, but otherwise made no filings until her attorney filed a motion to withdraw as counsel on February 6, 2017. (ECF Nos. 76, 78.) Ms. Stadelnikas was removed as the attorney of record in this case on April 6, 2017. (ECF No. 82.)

Petitioner's current counsel, Ms. Gentry, entered this case on May 9, 2017. (ECF No. 88.) In March of 2018, petitioner filed further medical records (Exs. 55, 95) and subsequently secured an expert report coauthored by Drs. Mikovits and Ruscetti (Ex. 56) and supporting literature (Exs. 57-94) to further support her claim of Tdap-induced ASIA. (ECF Nos. 90, 93, 95, 97, 98, 108, 109-111, 115-118.) (This report and supporting literature would later be struck from the record by petitioner's own motion as discussed below.)[8] Petitioner filed further medical records in February of 2019. (ECF No. 116; Ex. 96.)

This case was then assigned to my docket on June 5, 2019. (ECF No. 119.) Thereafter, petitioner filed an expert report from immunologist Dr. Yehuda Shoenfeld on September 9, 2019, and the accompanying medical literature on November 12, 2019. (ECF Nos. 122, 125-27; Exs. 97-124.) In response, respondent filed supplemental reports from Drs. Whitton and Rose on February 28, 2020. (ECF No. 130; Exs. J-K.)

On September 10, 2019, I ordered petitioner to file a status report identifying mutually agreeable dates in January or February of 2021 to hold an entitlement hearing. However, the parties requested a status confernece to discuss which experts would testify. (ECF No. 128.) During the conference, petitioner indicated that she no longer intended to rely on the opinions of either Drs. Mikovits and Ruscetti or Dr. McCurdy. However, to the extent their reports remained in the record, respondent maintained that he had a right to cross examine these experts. (ECF No. 131.) Accordingly, petitioner moved to strike the Mikovits and Ruscetti report and accompanying literature from the

[7] Exhibit designations 46, and 48-49 were used for procedural filings related to issuance of subpoenas and an invoice from Dr. McCurdy.

[8] Exhibit designations 55-58 were initially used by prior counsel in connection with a motion for interim attorneys' fees and costs. These designations were then duplicated by subsequent counsel. Exhibits 56-58 were subsequently struck. Accordingly, only Exhibit 55 remains duplicated. For purposes of this decision Exhibit 55 refers to the medical records from Torrance Memorial Medical Center as filed at ECF No. 97.

record and that motion was granted. (ECF No. 132; Order (Non-PDF) granting motion at ECF No. 132, 3/31/2020.) The parties initially intended for Dr. McCurdy to testify during the entitlement hearing due to her additional status as a treating physician, but ultimately determined that her testimony was not necessary. (ECF No. 164.) Instead, the parties agreed to also strike Dr. McCurdy's expert opinion from the record. (ECF No. 165.)

A three-day entitlement hearing was ultimately set to commence on March 12, 2021. (ECF No. 145.) Petitioner subsequently submitted several additional pieces of medical literature to support her claim on January 29, 2021, and an updated curriculum vitae for Dr. Shoenfeld. (ECF No. 151; Exs. 124-136.) A three-day entitlement hearing was held beginning March 12th, 2021, and continuing to March 17th and 18th, 2021. (*See* ECF Nos. 188, 190, 192, Transcript of Proceedings ("Tr"), filed 03/26/2021, 04/09/2021.) Petitioner presented testimony from herself and Dr. Shoenfeld. Respondent presented testimony from two of his experts, Drs. Rose and Whitton. The parties submitted their post-hearing briefs on May 18, 2021, September 29, 2021, and October 25, 2021. (ECF Nos. 195, 200, 202.)

This case is now ripe for resolution.

III. Factual History

a. As Reflected in Petitioner's Medical Records

Petitioner was born on May 19, 1997. (Ex. 1.) Prior to her June 18, 2011, Tdap vaccination, she was a healthy child who received 20 vaccinations between May 22, 1997 and July 12, 2002. (*See* Ex. 2, p. 1.) Her medical history was largely unremarkable beyond a eustachian tube disorder diagnosed during infancy and several acute sinus issues arising during 2009 and 2010. (Ex. 25, p. 4, 7, 8, 29; *See generally* Ex. 25.)

Petitioner received the Tdap vaccination in question on June 18, 2011. (Ex. 2, p. 1.) Four days later on June 22, she was seen by Dr. Peter J. Georgio for left arm pain. (Ex. 4.) Petitioner reported progressively improving pain and swelling in her left arm with no rash. (Ex. 4.) On exam, Dr. Georgio observed full range of motion and strength with a painful sensation. (Ex. 4.) Petitioner was assessed of having a possible reaction to the preservative in the Tdap vaccination and advised to continue using over the counter pain medication to manager her symptoms. (Ex. 4.)

Petitioner reported to her pediatrician, Dr. Maria Lui on June 28, 2011 for a routine well check. (Ex. 5, p. 1-3.) She had her blood pressure taken on her left arm. (Ex. 5, p. 1.) Petitioner reported that after her Tdap injection she became feverish and suffered a headache. (*Id.*) She further reported that her arm was red and swollen, and that she had been experiencing episodes of vertigo and pixelated peripheral vision, which occasionally occurs when she is ill. (*Id.*) Petitioner explained to Dr. Lui that she had swine flu the previous year and that ever since it felt as if her immune system was

becoming weaker.[9] (*Id.*) During this visit, petitioner's physical exam was normal. Dr. Lui ordered tests for petitioner's thyroid function and sedimentation rate, advised petitioner to monitor her headaches, and made differential diagnoses of delayed allergic reaction to the preservative in the Tdap vaccination and optical migraines. (*Id.* at 3.) Petitioner's test results were returned the following day with no abnormal findings other than slightly elevated sedimentation rate. (*Id.* at 5-6.) This was interpreted as "a small sign of inflammation which is probably due to her allergic [reaction]" and repeat test of the sedimentation rate was recommended. (*Id*. at 4.) Subsequently on July 18, 2011, petitioner's sedimentation rate was within normal limits. (*Id*. at 7.)

Dr. Lui referred petitioner to pediatric neurologist Dr. Pantea Sharifi Hannauer on July 19, 2011 for "post-vaccine reaction and headaches." (Ex. 6, p. 2.) Petitioner reported that her left arm became very swollen with a reduced range of motion and painful to the touch following her Tdap vaccination. (*Id.*) Petitioner reported that this condition lasted for about two weeks and that ice and ibuprofen "helped only a little." (*Id.*) Petitioner also reported that while her headaches waxed and waned, she was consistently fatigued, and that in the five days preceding this visit, the pain had increased again. (*Id.*) She no longer reported vertigo but was now suffering from light sensitivity and intermittent nausea. (*Id.*) Petitioner's physical and neurologic exams were both normal. (Ex. 6, p. 3-4.) Dr. Hannauer believed that petitioner had "a tendency for migraine headaches" and that "it is likely that the post-vaccine reaction triggered her headaches and extreme fatigue." (*Id.* at 4.) She recommended Prednisone for petitioner's headaches, Zofran for nausea, and over the counter antacid to address any potential side effects. (*Id.*)

Petitioner returned to Dr. Hannauer for a follow up on July 28, 2011. (Ex. 6, p. 5.) During this visit, petitioner reported that while the Prednisone was effective in reducing the severity of her headaches, they still occurred on a daily basis. (*Id.*) Petitioner's neurological exam was normal. (*Id.* at 6.) Dr. Hannauer prescribed Topamax and Indomethacin and scheduled a 2-week follow up. (*Id*.)

Petitioner was next seen by immunologist Dr. Joshua Davidson on August 8, 2011 for further testing.[10] (Ex. 7, p. 1.) Petitioner's bloodwork, reported on August 11, 2011, was normal apart from a somewhat elevated Helper/Suppressor Ratio of 2.96, and slightly lowered CD3 and CD8 cells at 59% and 14%, respectively.[11] (*Id.* at 3.) Dr.

[9] I asked petitioner about this notation during the hearing. She indicated that both she and her brother had a flu-like illness at about the same time, but that she was never tested and has no confirmation it was swine flu specifically. (Tr. 80.)

[10] As explained in the procedural history above, Dr. Davidson also wrote a letter in support of petitioner's claim. (Ex. 36.) Dr. Davidson's letter expressed support for the notion that petitioner's claim can satisfy the three-prong *Althen* test based on the ASIA theory. Because this was more fully addressed by Dr. Shoenfeld, Dr. Davidson's opinion will not be discussed further. Dr. Davidson's records do not contain any specific reference to ASIA. (Ex. 7.)

[11] A notation dated August 23, 2011 explains that petitioner's gender was incorrectly reported as male when conducting these tests, but that the "reference range" remained unchanged and the results remained the same once the error was corrected. (Ex. 7, p. 3.)

Davidson wrote a letter on August 24, 2011, explaining that petitioner was unable to participate in her physical education courses at school. (*Id.* at 4.)

Petitioner initially submitted a VAERS report on July 11, 2011, with supplemental updates made on August 1, 2011, and August 22, 2011. (Ex. 3.) In the report, petitioner explains that within one hour of her June 18, 2011, Tdap vaccination, she "developed a headache, [felt] tired and had a temperature of 101 Fahrenheit." (*Id.* at 4.) She further explained that the following day, "her left arm started to swell and for 3 days she could not lift [her] left arm," but that it "was better within 2 weeks." (*Id.*) Petitioner also included her June 28, 2011, visit to Dr. Lui, and her subsequent visit to Dr. Hannauer. (*Id.*) Her August 22, 2011, supplemental update explained that she was continuing to see an immunologist and neurologist and that occasionally her arms and legs felt like they were falling asleep. (*Id.*) Petitioner's diagnoses were listed as "persistent headache, nausea, vertigo, fatigue," with a history of vertigo, eustachian tube disorder, and "no change" in her progress. (*Id.*)

Petitioner returned to Dr. Lui on September 2, 2011 for flu symptoms that began the night before. (Ex. 5, p. 8.) She explained to Dr. Lui that she awoke at 2 AM with nausea but could not vomit. She also reported myalgias, arthralgias, and ongoing headaches since her June Tdap vaccination. Petitioner's physical exam revealed mild epigastric tenderness. She was ultimately diagnosed with acute gastroenteritis ("viral unlikely flu") and prescribed anti-nausea medication and over the counter painkillers for joint pain. (*Id.*)

On September 26, 2011, petitioner saw neurologist Dr. Mary Kay Dyes on referral by Dr. Lui. (Ex. 8.) Petitioner reported that her arm swelling and fever had ultimately resolved, but that she was still experiencing daily headaches and fatigue. (*Id.* at 1.) She described her headaches as "throbbing and occasionally 'stingy'" with varying intensity and occasional dizziness. (*Id.*) She was undergoing acupuncture and felt that it provided relief, albeit temporarily. She denied any present numbness but noted that her extremities would "fall asleep easily" and sometimes spontaneously. (*Id.*) Petitioner reported that the steroids Dr. Lui prescribed did not help her headaches. Dr. Dyes noted that petitioner had been seen by an immunologist who suggested a trial of IVIG and that although petitioner was prescribed Topamax by her previous neurologist, she had not taken it due to concerns regarding the side effects. Dr. Dyes exam did not reveal any abnormal findings. (*Id.*) Dr. Dyes ultimately diagnosed petitioner with Chronic Daily Headache ("CDH") and recommended a brain MRI and lab work for vitamin B12 and Monospot. (*Id*. at 2.) Dr. Dyes also recommended a trial of nortriptyline and scheduled a one-month follow up appointment. (*Id.*)

The following day, September 27, 2011, petitioner was seen by allergist/immunologist Dr. Helen Mawhinney. (Ex. 9, p. 1.) At this visit petitioner continued to report the same history of present illness as she had to her previous treating physicians but noted that her fatigue was slowly resolving. Petitioner also reported that she was no longer experiencing light sensitivity, and that she was tested for allergies to the inactive Tdap vaccine ingredients of aluminum phosphate, formaldehyde, glutaraldehyde, and 2-phenoxethanol with no allergic reactions. (*Id.*)

Petitioner's exam was unremarkable and revealed no additional symptoms beyond those reported in her history of present illness. (*Id at 2.*) Dr. Mawhinney did not believe that petitioner's history was indicative of a serum sickness reaction, nor an IgE-mediated reaction. She believed that the most likely inciting agent was the pertussis component of the Tdap vaccine that caused a "severe hypersensitivity reaction". (*Id.*) She requested antibody titers for tetanus toxoid, diphtheria, and pertussis "to see if we can identify any exaggerated responses to these components of the vaccine," but felt that beyond these tests, "further attempts to identify the nature of this reaction are unlikely to be helpful." (*Id.*) She recommended against future Tdap vaccinations. Dr. Mawhinney stated that she did "not believe that [she could] shed any further light on the nature of [petitioner's] headaches" but that "[i]t would appear that in some way the reaction to Tdap [was the trigger]." (*Id.*)

Petitioner underwent a brain MRI without contrast on October 8, 2011. (Ex. 8, p. 3.) The results were "degraded by dental/orthodontic hardware" but otherwise appeared "unremarkable." (*Id.*) On October 19, 2011, petitioner visited Dr. Lui for headache, sinus pressure, and one week of ear discomfort. She was diagnosed with Eustacian Tube Disorder and prescribed flonase, Claritin, and etodolac for her headache. (Ex. 5, p. 9.)

Petitioner visited rheumatologist Dr. Deborah McCurdy on November 30, 2011, for further exam regarding her Tdap reaction.[12] (Ex. 11A, p. 7.) In addition to the history of present illness that she had reported to her previous treating physicians, petitioner also noted that the most helpful treatment for her headache had been acupuncture, and that she now feels "very cold at times." (*Id.* at 8.) Petitioner also explained to Dr. McCurdy that she had abandoned competitive gymnastics ever since she "blacked out mid vault and landed on her head" shortly after receiving her Tdap vaccination. (*Id.* at 7.) Dr. McCurdy's exam showed no abnormalities beyond possible problems with weight gain. (*Id.* at 8-9.) According to Dr. McCurdy, petitioner's lab results showed a mildly elevated sedimentation rate in June that returned to normal by July. (*Id.* at 12.) Dr. McCurdy did note that petitioner's tetanus antibodies were "very high suggesting an exaggerated response to the vaccine," and "moderately positive anti-histone antibodies suggesting an immune reaction to the vaccine." (Ex. 11A, p. 12.) Petitioner's immune workup was "basically within normal limits" with minor deviations of peripheral blood B and T lymphocytes from normal limits that were "likely not of clinical significance." (*Id.*)

Dr. McCurdy believed that, based on the immediate reaction, petitioner had suffered an arthus reaction, stating that:

> The reaction to the injection was immediate suggesting an arthus reactions (type III hypersensitivity reactions) perhaps to previous vaccines. Although

[12] As discussed in the procedural history above, petitioner also submitted an expert opinion by Dr. McCurdy to support her claim. However, she ultimately determined that she would not rely on Dr. McCurdy's opinion and filings associated with Dr. McCurdy's opinion have been struck. Accordingly, only Dr. McCurdy's opinion as a treating physician as reflected in her medical records has been considered.

> arthus reactions are rare after vaccinatio[n], they may occur after tetanus toxoidcontaining [*sic*] or diphtheria toxoidcontaining [*sic*] vaccines. An arthus reaction is a local vasculitis associated with deposition of immune complexes and activation of complement. Immune complexes form in the setting of high local concentration of vaccine antigens and high circulating antibody concentration. Arthus reactions are characterized by severe pain, swelling, induration, edema, hemorrhage, and occasionally by necrosis. These symptoms and signs usually occur 412 [*sic*] hours after vaccination. They usually abate over time, however, care should be used with vaccinations, especially Tdap in the future.

(Ex. 11A, p. 12.) However, Dr. McCurdy noted that because petitioner's immune complexes were negative, her headaches were likely unrelated to an immune disorder. (*Id.* at 13.) She explained to petitioner's parents that IVIG therapy would likely be ineffective due to the fact that petitioner's condition was unrelated to earlier immune complexes that may have resulted from her Tdap vaccine but had now cleared. She recommended medications for chronic migraine headaches, including those in the anti-depressant and anti-convulsant groups. She also recommended aqua or physical therapy, continued acupuncture, sleep hygiene, and a diet adjustment. (*Id.*)

Petitioner saw Dr. McCurdy six times between February 1, 2012, and February 15, 2013, without any significant improvement in her symptoms or developments in her diagnosis. (Ex. 11A, pp. 24-28, 29-31, 32-36, 37-39, 40-42, 43-46.) Dr. McCurdy ordered Antinuclear ab labs, which demonstrated normal ANAs. (Ex. 11B, pp. 6-7, 27, 41, 47.) Additionally, petitioner began physical and occupational therapy at Body Dynamics on December 6, 2011. (Ex. 18, p. 1.) She attended at least 82 sessions between December 6, 2011 and March 26, 2013, however, there is no record of a specific discharge date. (*See* Ex. 18, pp. 1-87.)

On March 8, 2012, petitioner was seen by ear, nose, and throat specialist Dr. Quinton Gopen upon referral by Dr. McCurdy for "pressure problems in her ear" and accompanying dizziness. (Ex. 12, p.1.) Petitioner's mother reported that petitioner had been diagnosed with drug-induced lupus, but this diagnosis is not recorded in any of petitioner's medical records.[13] (*Id.*) Petitioner otherwise reported the same symptoms that she had previously reported, and Dr. Gopen diagnosed her with eustachian tube disorder and recommended using flonase more regularly. (*Id.* at 2.)

Petitioner next saw Dr. Lonnie Kaye Zeltzer at the UCLA Pediatric Pain Clinic on referral by Drs. Lui and McCurdy on July 16, 2012. (Ex. 13.) Petitioner continued to report symptoms consistent with her prior visits but also included to a year and a half of joint pain. (*Id.* at 1.) Petitioner's physical and mental exams were both within normal limits. (*Id.* at 3.) Dr. Zeltzer assessed petitioner with "post-vaccination syndrome . . . with persistent headache, dizziness, and fatigue. Likely central headaches now, with

[13] Many of petitioner's records indicate a history of lupus based on this report of drug induced lupus, but she has not submitted any records indicating that she ever formally or definitively carried such a diagnosis. This summary does not include all such repeated references to lupus.

heightened SNS stress responsivity," and "secondary amenorrhea, likely related to the vigorous exercise of gymnastics." (*Id.*) Dr. Zeltzer recommended education about petitioner's pain and stress, continued acupuncture and Pilates, additional physical therapy and yoga, and Elavil or Neurontin. (*Id.*)

Petitioner's records next describe a visit to Dr. Colin Robinson at UCLA's Pediatric Rheumatology Clinic roughly a year later on July 31, 2013. (Ex. 31, p. 2.) During this visit, petitioner reported that she had been better since school had let out, that her fatigue had improved throughout the school year, and that her more severe headaches occurred less often. (*Id.*) Petitioner noted that her headaches were more severe when she had to "focus mentally." (*Id.*) She reported arthralgias in her left knee, wrist, and elbow, as well as continued numbness in her arms and legs approximately twice a week. (*Id.*) Petitioner's physical exam was normal and Dr. Robinson assessed chronic headaches, chronic fatigue, and "[p]ositive antihistone antibody, possibly as a response to TDaP vaccination, most recent titer 1.4 (weak positive), improving symptoms, stable Ab level over past two visits." (*Id*. at 4.)

On October 23, 2013, petitioner was referred to Dr. Gopen once more for throat pain and bilateral ear pain. (Ex. 31, p. 5.) Dr. Gopen erroneously noted that petitioner had a history of drug-induced rheumatoid arthritis. (*Id.*) He believed that petitioner "may have reflux or other diagnosis causing irritation at the back of her throat that she is having as referred otalgia." (*Id.*)

Petitioner was next seen by Dr. Jennifer Long at UCLA's Head and Neck clinic on October 30, 2013 with a chief complaint of throat pain. (Ex. 31, p. 6.) Petitioner explained that this pain was different from a typical sore throat as it involved the bilateral sides of the larynx. (*Id.*) Dr. Long's impression was that petitioner showed "signs and symptoms of laryngopharyngeal reflux" but that her diet was "actually quite good from a reflux standpoint given the degree of laryngeal swelling present." (*Id.* at 7.) She also believed that petitioner had likely suffered from "a component of muscle tension dysphonia that is worsening her pain especially after voice use." (*Id.*) Dr. Long prescribed omeprazole and referred petitioner to voice therapy. (*Id.*)

Petitioner also had a follow-up appointment with Dr. McCurdy on October 30, 2013. (Ex. 31, p. 7.) During this visit, petitioner reported that her fatigue had been worse since she started home schooling in September, and that she felt "too tired to do anything" in spite of sleeping regularly throughout the night. (*Id.* at 7-8.) Her headaches continued to improve, as did her arthralgias and numbness. (*Id.* at 8.) Dr. McCurdy assessed petitioner as suffering from sore throat and ear pain, feeling of being in a fog, and positive antihistone antibodies as a possible response to her Tdap vaccination. (*Id.* at 16.)

Dr. Long referred petitioner to Speech and Language Pathologist ("SLP") Lisa Joy Bolden on November 14, 2013, with a diagnosis of mild dysphonia. (Ex. 31, p. 16.) SLP Bolden noted that petitioner's throat pain began approximately one week after she began taking Omega-3 supplements with Gamma Linolenic Acid (GLA) which could be

contributing to her pain. (*Id.* at 17.) SLP Bolden felt petitioner's rehabilitation potential was excellent based on successful trial therapy and recommended an additional three months of voice therapy. (*Id.* at 18.)

Petitioner next saw Dr. McCurdy on February 5, 2014. (Ex. 31, p. 19.) Dr. McCurdy noted that in addition to petitioner's earlier symptoms of headache, fatigue, brain fog, and abdominal pain, her symptoms now included an almost 20-pound weight loss (98 lb, 5.2 oz), muscle loss, vision changes, and myopathy. (*Id.* at 20.) Petitioner had discontinued GLA, which helped with her throat pain, but made her joint aches worse. (*Id.*) Petitioner was also suffering from significant constipation at that time, had changed her diet, and used calcium citrate to no effect. (*Id.*) Dr. McCurdy noted that petitioner's positive anti-histone antibodies persisted "despite treatment with Plaquenil, which she discontinued in 2013." (*Id.* at 23.) Dr. McCurdy recommended continued physical therapy, aqua therapy if physical therapy did not work, a follow up with Dr. Zeltzer for pain management, laxative until her constipation subsided, possible Provigil, physical exercise, and a neuro-ophthalmology evaluation. (*Id.*)

Petitioner saw Dr. Long again on February 19, 2014 for a video laryngoscopy with stroboscopy and medical speech evaluation. (Ex. 31, p. 25.) Petitioner's videolaryngostroboscopy was normal apart from mild edema and erythema. (*Id.*) Dr. Long's impression was that petitioner's dysphonia had resolved. (*Id.*)

Petitioner was next seen by Ophthalmologist Dr. Stacy Pineles on April 14, 2014, for problems related to blurry vision, occasional black spots, and difficulty in dark lighting. (Ex. 31, p. 26.) Dr. Pineles explained that she believed petitioner's symptoms were caused by migraine based on her normal eye exam. (*Id.*) Dr. Pineles referred petitioner to Dr. Lekha Rao to discuss migraine treatment and suggested an electroretinogram could be done to rule out retinal disease. (*Id.*)

Petitioner was seen by Dr. Joyce Matsumoto at UCLA's neurology department on April 24, 2014, with a chief complaint of headache. (Ex. 31, p. 27.) Petitioner had lost an additional 12 pounds, weighing in at 85 lbs, 8.6 oz. (*Id.* at 28-29.) Dr. Matsumoto believed that petitioner's chronic headache/migraine was "likely triggered by her reaction to the vaccine" and that they were "likely [a] large component" of her other symptoms. (*Id.* at 29.) Petitioner reported that she was also suffering from disrupted sleep, was eating smaller meals, not drinking enough fluids, and occasionally experiencing "presyncopal/lightheaded feeling." (*Id.*) Dr. Matsumoto emphasized the importance of adequate nutrition and augmented petitioner's migraine medication regimen with B2 and magnesium supplements. (*Id.*)

On April 28, 2014, petitioner was seen by pediatric allergist Dr. Maria Garcia-Lloret for a consultation on her weight loss. (Ex. 31, p. 30.) Petitioner explained that she was experiencing adverse reactions to an increasing number of foods which was causing difficulties maintaining a nutritious diet. (*Id.*) Petitioner had lost 30 pounds since 2012, explained that she was hungry and wanted to eat, but that she would feel full very quickly regardless of what she was eating. (*Id.* at 30-31.) Petitioner denied any

ongoing fevers, joint pain, weakness, or malaise. (*Id.* at 31.) Dr. Garcia-Lloret assessed petitioner with a history of multiple pollen and food allergies, oral allergy syndrome, food restriction with weight loss with an "unclear etiology but allergic process unlikely to be a main cause." (*Id.*) Dr. Garcia-Lloret wanted to rule out inflammatory bowel disease or other systemic inflammatory processes and referred petitioner to a pediatric gastrointestinal specialist for a delayed gastric emptying study. (*Id.* at 32.) She recommended CBC and ESR labs, a chemical panel, and an Immunocap for various foods. (Ex. 31, p. 32.) She also prescribed a trial of Loratadine, and potentially montelukast. (*Id.*)

Petitioner next saw Dr. Zeltzer on May 7, 2014, for further evaluation of her headache and fatigue. (Ex. 31, p. 32.) Petitioner's mother reported that petitioner passed out for the first time the week before, and petitioner reported that her head would pulse for a long time and her vision and hearing would go out when she would stand up. (*Id.* at 33.) Petitioner's primary complaint during this visit was disruptions with her sleep schedule, stating that she could take up to two hours to fall asleep and that she would wake up once or twice a night. (*Id.)* Dr. Zeltzer noted "no evidence of SLE but rather post-vaccination reaction with multiple symptoms, normal ANA, normal ESR, and weakly positive histone." (*Id.* at 32.) Dr. Zeltzer prescribed melatonin to help petitioner sleep and referred her to Dr. Bruce Levine for biofeedback.[14] (*Id.* at 35.)

Petitioner was next seen at the UCLA Pediatric Rheumatology department on May 13, 2014. (Ex. 31, p. 35.) At this point petitioner's weight had decreased to 79 lbs, 2.3 oz and she was in the 0-percentile BMI for her age. (*Id.* at 36.) Beyond these updates, the medical record is an almost verbatim copy of Dr. McCurdy's February 5, 2014 report of petitioner's condition and treatment recommendations. (*Compare* Ex. 31, p. 9 *with* Ex. 31, p. 39.) Petitioner's April 28, 2014 lab work indicated slightly elevated MCH concentration, reduced neutrophil and lymphocyte percent, reduced glucose, slightly elevated albumin, slightly elevated ALT (SGPT), and normal ESR. (Ex. 31, pp. 36-39.)

Following her visit to pediatric rheumatology, petitioner was seen by pediatric gastroenterologist Dr. Elaheh Vahabnezhad on May 21, 2014. (Ex. 31, p. 40.) Petitioner reported that since November, she was feeling full for longer periods of time and described herself as having an appetite but feeling like she could not eat. (*Id.*) She was recorded as losing roughly 33 pounds over the past year weighing in at about 78lbs. (*Id.* at 40, 42.) Petitioner's constipation had resolved. (*Id.*) She developed a "cyst like" raised bump along her left buttock that "comes and goes on its own" but lasts for several weeks at a time. (*Id.*) She felt that her throat would feel tight at times and explained that she was experiencing irregular menstruation. (*Id.* at 41.) Dr. Vahbnezhad made differential diagnoses of potential gastroparesis, inflammatory bowel disease, celiac disease, potential fatty acid deficiency, and potential malignancy based on enlarged lymph nodes. (Ex. 31, p. 44.) Dr. Vahbnezhad recommended nutritional therapy and a 3 to 4 week follow up after analyzing the results of petitioner's gastric emptying study. (*Id.*)

[14] Petitioner has not submitted any records from Dr. Levine.

On May 23, 2014, petitioner was seen by Dr. Reena Gupta at Osborne Head and Neck Institute with a chief complaint of throat pain. (Ex. 53, p. 16.) Dr. Gupta observed symptoms of decreased vocal range and difficulty projecting. (*Id.*) Dr. Gupta diagnosed petitioner with dysphonia, throat pain, and an unclassified autoimmune disease. (*Id.* at 19.) Based on petitioner's complicated medical history, Dr. Gupta thought that petitioner's throat symptoms were related to her general health and it was therefore best to defer to petitioner's rheumatologist and GI specialists. (*Id.* at 18.)

Petitioner was seen by Drs. Benjamin Kretzmann and McCurdy at UCLA pediatric rheumatology on June 10, 2014. (Ex. 44, p. 51.) Dr. Kretzmann recommended that petitioner stick to Dr. McCurdy's earlier recommendations of physical therapy and exercise. Dr. McCurdy reviewed petitioner's medical history and confirmed that there "had been no change." (*Id.*) Petitioner did believe that she was eating more, however. (*Id.*)

On August 16, 2014, petitioner reported to the UCLA Emergency Department with hypothermia and severe weight loss. (Ex. 44, p. 55.) Upon admission petitioner weighed approximately 60 pounds. (*Id.* at 52.) The attending physician concluded that petitioner was severely malnourished and recommended inpatient treatment in order to explore the source of her condition as either psychological or biological. (*Id.* at 56.) Petitioner had "exponentially elevated" LFTs which the attending physician believed could be a sign of liver failure even though she was showing that her liver still had capacity to have synthetic function. (*Id.*) Petitioner was observed to have dry-scaly skin, lanugo-like hair on her abdomen, gross hyperpigmentation patches over her arms and legs, and petechiae. (*Id.* at 61.) She was put on IV nutrition and monitored over the course of about three weeks. (*See generally Id.* at 52-242.)

During her treatment, petitioner was seen by a variety of specialists including general pediatricians, gastroenterologists, nutritionists, rheumatologists, and psychiatrists. (Ex. 44, p. 243.) Petitioner's discharge summary explained that she was diagnosed with hepatitis during her stay and received work-ups for autoimmune, infectious, and toxic etiologies of the disease, all off which were negative. (*Id.*) The most likely etiology for petitioner's hepatitis was thought the be malnutrition caused by anorexia nervosa, however the treating physicians found it difficult to make this specific diagnosis due to petitioner and her family becoming defensive when the topic was approached.[15] (*Id.*) During her stay, petitioner received IV nutrition, her LFTs were reduced considerably, and although she remained hypothermic upon discharge, she did

[15] It was noted in the discharge summary that petitioner:

> [h]as a dietary history strongly concerning for restrictive eating behavior and there is a strong concern for anorexia nervosa (BMI 10.5, wt loss of 27kg over 1 yr, restrictive eating behavior, lack of medical cause found). Pt does not have insight into her condition. Parents have poor insight into their daughter's condition. Rather than accepting fully that she has an eating disorder, they choose to believe that she has an eating disorder, but that it is 2/2 TDap Vaccine induced gastroparesis and feelings of fullness.

(Ex. 44, pp. 243-44.)

show an improved overall temperature curve. (*Id.*) The discharge summary noted that petitioner's malnutrition was due to "inadequate intake from restrictive eating habits vs organic due to symptomatic gastroparesis," but the ultimate discharge diagnosis was "eating disorder NOS." (*Id*. at 242, 244.)

After she was discharged from the hospital, petitioner saw Dr. Chiaki Jutabha for regular follow-ups regarding her eating disorder. (*See generally* Ex. 42, pp. 2-21.) Petitioner's first visit to Dr. Jutabha was on September 8, 2014. (*Id.* at 2.) Petitioner reported that she was feeling much better and that she was able to eat "better foods and more variety." (*Id.*) She had gained 7 pounds since being discharged and was taking in about 2100 kcal/day. (*Id.*) Petitioner noted that she had severe lower back pain on her left side the day before, but that it had resolved, she was also experiencing dysuria. (*Id.*) Petitioner's AST was within normal limits and ALT was "returning back to normal." Dr. Jutabha ultimately assessed petitioner with an "eating disorder of unknown etiology." (*Id.* at 4.) Petitioner was asked to follow up in 3-4 days for a weigh check with a plan to do biweekly weight checks until petitioner's weigh stabilized, in which case she the weight checks would be reduced to once per week. (Ex. 42, p. 4.) On October 22, 2014, petitioner received an abdominal ultrasound on a referral from Dr. Jutabha. (Ex. 45, p. 12.) Comparing this ultrasound to one conducted on August 18, 2014, during petitioner's inpatient treatment at UCLA, the impression was that petitioner had improved hepatic echotexture compared to the prior study, suspected gallbladder sludge or cholesterol polyps, and bilateral heterogeneous renal echotexture and indistinct corticomedullary differentiation suggesting either medical renal disease, right renal sinus cyst, or hydroureter. (*Id.*) Petitioner continued to see Dr. Jutubha through May of 2015 and continued to regain weight. (Ex. 42, p. 35.)

Petitioner was seen by Dr. Dana Kennedy at Torrance Memorial Medical Center's emergency department on November 8, 2014, with a chief complaint of chest pain and tightness. (Ex. 55, p. 19.) She denied any other symptoms, including any headaches or gastrointestinal symptoms. (*Id.*) Petitioner underwent a chest X-ray which appeared normal, with "[n]o definite evidence of acute infiltrate, effusion, or pneumothorax." (*Id.* at 37.) Petitioner was ultimately discharged with orders to take Tylenol or ibuprofen for pain while monitoring for future chest pains and breathing difficulties. (*Id.* at 43.) Petitioner underwent a kidney and bladder ultrasound study by Dr. Theodore Hall study on December 3, 2014. (Ex. 45, p. 11.) Dr. Hall did not find any remarkable results. (*Id.*)

On December 17, 2014, petitioner was seen again by Dr. McCurdy. (Ex. 42, p. 21.) Petitioner was found to have consistently improved since her hospitalization in August and reported eating around 2,400 calories per day. (*Id.*) Her physical exam was normal, she weighed almost 90 pounds, but reported that she was still experiencing regular headaches. (*Id.* at 21-22.) Petitioner noted minor arthralgias in her toes but explained that physical therapy was helping. (*Id.* at 21.) Petitioner was on a regiment of ascorbic acid, cholecalciferol, magnesium oxide, and omega-3 fatty acids which seemed to be helping her symptoms. (*Id.* at 21-22.) Dr. McCurdy recommended that

petitioner continue physical therapy, continue taking her medication, and an ANA and anti-histone antibody study with her next round of lab work. (*Id.* at 22-23.)

On February 27, 2015, petitioner was seen by Dr. Ana Lopez-O'Sullivan at the Torrance Memorial Medical Center Emergency Department with a chief complaint of headache. (Ex. 55, p. 78.) Petitioner explained that she was not taking pain medication because she did not believe in it, denied fever, cough, congestion, rash, neck pain, changes in her hearing or vision, nausea, vomiting, photophobia, and any weakness or numbness of her extremities. (*Id.*) Dr. Lopez-O'Sullivan noted that she did not suspect any serious causes for petitioner's symptoms and convinced petitioner and her parents that there was no need for a CT scan, but that if petitioner's symptoms became severe she could order an outpatient MRI to explore any causes that she had not yet considered. (*Id.* at 79.) Petitioner was discharged with a diagnosis of "headache" and advised to take over-the-counter pain medication as needed and to return to the emergency department if the symptoms became severe. (*Id.* at 109.)

On March 4, 2015, petitioner underwent a Pulse Wave Profiler study to measure her Heart Rate Variability, a Surface EMG study to measure her muscle tone and balance, and a thermal scan to measure her organ and glad control. (Ex. 51, p. 25.) The results of these studies were compiled to generate a "personal neural efficiency index" measured by a "CORE Score" rating. (*Id.* at 36.) Petitioner showed a score of 73 for her heart rate variability, 68 for her muscle tone and balance, and 52 for her organ and gland control resulting in an aggregate CORE Score of 66, indicating an overall "challenged" neural efficiency index. (*Id.* at 37.)

Petitioner saw Dr. McCurdy for another follow up visit on March 18, 2015. (Ex. 42, p. 26.) During this visit petitioner reported that she was having trouble focusing, suffering from continued headaches, fatigue, and nausea, throat pain on her left side, constant urination, sensitivity to smell and light, and easy indentation of her skin. (*Id.* at 26-27.) Petitioner had not followed up with psychology. (*Id.* at 26.) She weighed just under 102 pounds but was having trouble gaining more weight. (*Id.* at 26, 28.) Dr. McCurdy recommended consults with ophthalmology, neurology, and psychology, continued physical therapy and vitamins, additional B vitamins for headache and focus issues, and cortisol, ANA, and anti-histone antibody labs. (*Id.* at 30-31.) Petitioner next saw Dr. Sande Okelo for pulmonary function testing on April 15, 2015. (Ex. 42, p. 31.) Petitioner's spirometry, lung volume, and diffusion capacity tests did not reveal any abnormalities. (*Id.* at 32.)

Petitioner began seeing psychologist Dr. Kelly Mothner, PhD on May 19, 2015. (Ex. 52, p. 30.) Petitioner saw Dr. Mothner once to twice a week until at least December 20, 2016. (*See* Ex. 52, pp. 2-30; Ex. 54.) Notably, Dr. Mothner and petitioner explored somatic responses to petitioner's anxiety on July 13, 2015, suggesting that she physically feels "tight" when she is anxious versus feeling "loose" when she is not. (*Id.* at 26-27.) However, beyond this notation, Dr. Mothner's records are largely unremarkable and focus on petitioner's progress with dealing with her anxiety disorder. (*See generally* Ex. 52.)

On June 17, 2015, petitioner was seen by gastroenterologist Danice Hertz on referral from Dr. Simone Gold.[16] (Ex. 45, p. 2.) Dr. Hertz's preliminary impression was a reported history of severe reaction to a Tdap vaccination with possible Systemic Lupus Erythematosus leading to severe malnutrition. (*Id.*) Dr. Hertz noted that petitioner was slowly improving but dealing with constipation lasting for two months. (*Id.*) Dr. Hertz recommended continuing a high fiber diet, increased fluids, and increased magnesium, citracel caplets, and miralax. (*Id.*)

Petitioner saw Dr. Bette Geller Jackson, Ph.D. throughout June and July of 2015 for a series of Neuropsychological-Educational Assessments. (Ex. 50, p. 181.) Petitioner's parents requested these evaluations in order to determine whether petitioner suffered from any learning, processing, or psychological disorders. (*Id.* at 197.) Dr. Geller Jackson's diagnostic impression included generalized anxiety disorder, somatic symptom disorder, and attention deficit hyperactivity disorder. (*Id.* at 197.) She recommended that petitioner be given additional time and extended breaks on standardized tests, that she be evaluated for an anxiety disorder, attend individual psychotherapy to "help alleviate her feelings of anxiety and to deal with her somatic issues," engage in extracurricular enrichment activities, and participate in mindfulness training, yoga, meditation, and exercise. (*Id.* at 197-98.)

On July 21, 2015, petitioner was seen by gastroenterologist Dr. William Stuppy for an expanded GI panel. (Ex. 51, p. 1.) Petitioner's results were normal, with a borderline low result for her total intestinal SIgA (Stool). (*Id.*) Petitioner was also seen by Dr. Johannes Czernin for a gastric emptying study at the UCLA Nuclear Medicine Clinic. (Ex. 51, pp. 7-8.) Dr. Czernin concluded that petitioner had "[b]orderline abnormal gastric emptying at 49%" but that this was a marked improvement to a prior study that noted only 22% after 90 minutes. (*Id.* at 7.) On July 31, 2015, petitioner underwent an exhaled air analysis conducted by Dr. Jorge Vargas. (Ex. 42, pp. 36-37.) Dr. Vargas interpreted petitioner's results as normal with a slightly lower than predicted BMR. (*Id.* at 37.) Petitioner tested negative for Lyme Disease on August 18, 2015. (Ex. 51, pp. 5-6.)

Petitioner was seen by Dr. Ryan F. Osborne at Osborne Head and Neck Institute on September 18, 2015, with a chief complaint of ear clogging. (Ex. 53, p. 9.) She described her symptoms as moderate to severe, beginning three weeks earlier, with a sudden onset following a hyperbaric oxygen treatment. (*Id.*) Dr. Osborne diagnosed petitioner with impacted cerumen, dysfunction of eustachian tube, candidal otitis externa, and conductive hearing loss, external ear. (*Id.* at 10.) He conducted a left ear debridement and cleansing and prescribed ciprodex otic suspension drops and a clotrimazole 1% solution. (*Id.* at 10, 13.) Petitioner was again seen by Dr. Osborne on a follow-up for her ear complaint the following week on September 24, 2015. (*Id.* at 4.) She explained that her symptoms persisted were slightly improved but that she did not believe the medicated ear drops were working. (*Id.*) Dr. Osborne treated patient with boric acid powder which she requested be removed and conducted an "extensive

[16] Although this record suggests that petitioner was previously being treated by Dr. Gold, she has not submitted any records of this treatment beyond a letter written on October 15, 2015. (Ex. 43.)

debridement" and disimpaction of petitioner's left ear. (Ex. 53, pp. 7-8.) Dr. Osborne suggested that petitioner may need to return for weekly debridement, but no further records of treatment for petitioner's ear problem exist. (*Id.* at 7.)

On October 15, 2015, Dr. Simone Gold wrote a letter detailing petitioner's symptoms and her suspected diagnosis. (Ex. 43.) Dr. Gold notes that petitioner's most severe symptom was her gastrointestinal slowing which led to her malnourishment and weight loss. (*Id.* at 1.) Dr. Gold explained that she believed that petitioner suffered from an uncommon condition called "dysautonomia," triggered by her Tdap vaccination. (*Id.* at 1-2.)

Petitioner saw Dr. Michael Arata on October 23, 2015, with chief complaints of "severe mental fog, chronic fatigue, weakness, chronic headaches, urinary urgency, digestive discomfort, malnutrition, sleep disturbances, and visual disturbances." (Ex. 47, p. 1.) Petitioner's physical exam was normal; however, based on her subjective reports, Dr. Arata diagnosed petitioner with an unspecified disorder of the autonomic nervous system, mild cognitive impairment, fatigue, chronic headache disorder, constipation, bloating, urinary urgency, unspecified sleep disturbance, paresthesia of skin, blurred vision, unspecified protein-calorie malnutrition, and gastroparesis. (*Id.* at 5.) Dr. Arata recommended an organic acids test and a PLA-2 "to see what's going on in the body," noting that:

> Abnormally high levels of these microorganisms can cause or worsen behavior disorders, hyperactivity, movement disorders, fatigue and immune function. Many people with chronic illnesses and neurological disorders often excrete several abnormal organic acids. The cause of these high levels could include: oral antibiotic use, high sugar diets, immune deficiencies, and genetic factors.

(*Id.*) Dr. Arata also recommended a qEEG assessment with neurofeedback, adjusting petitioner's diet to include more protein and less carbohydrates, and for petitioner to continue her organic diet. (*Id.*)

Petitioner next saw Dr. Robert Roberts and Suzanne Cambou on November 4, 2015 for an allergy and immunology consultation. (Ex. 95, p. 313.) Dr. Cambou described petitioner's earlier diagnoses of drug induced lupus and dysautonomia as "questionable" on this visit. (*Id.* at 314.) Petitioner's physical exam was normal, and Dr. Roberts recommended a variety of labs including Tetanus toxoid antibodies, ESR, CRP, Rubella antibodies, Measles antibodies, B and T Cell subsets, IgM, IgG, IgE, IgA, Gelatin IgE, Diphtheria toxoid antibodies, CBC with differential, B pertussis antibodies, and Almond IgE testing. (*Id*. at 318.)

Petitioner saw Dr. Arata on December 16, 2015, for a follow up on blood work and an evoke assessment. (Ex. 47, p. 7.) Petitioner was reported that her metabolism was changing and that she was losing weight again. (*Id.*) Dr. Arata noted that petitioner's blood work revealed low progesterone and estrogen. (*Id.* at 8.) Her

quantitative EEG revealed elevated levels suggestive of ADD. (*Id.*) Dr. Arata recommended progesterone, screen toxicity testing, hair toxin screening, adding broccoli or other cruciferous vegetables to petitioner's diet, eliminating bananas, neurofeedback training, and a 7-day food diary. (*Id.*)

Petitioner returned to Dr. Arata the following week on December 23, 2015, to follow up on her evoke results, discuss her 7-day food diary, and discuss her GPL results. (Ex. 47, p. 10.) Dr. Arata explained that petitioner reverse T3 hormone was "on the higher side," and listed diagnoses of an unspecified disorder of the autonomic nervous system, mild cognitive impairment, fatigue, chronic headache disorder, bloating, unspecified protein-calorie malnutrition, and headache. (*Id.* at 13.)

Petitioner returned to Dr. McCurdy on July 12, 2016. (Ex. 95, p. 319.) She continued to complain of mental fog and headaches. (*Id.*) Dr. McCurdy noted that petitioner was "doing neuro feedback in Playa del Rey," which seemed to be helping. (*Id.*) Petitioner's lab work was normal besides an elevated vitamin D level, and she was advised to stop taking Vitamin D supplements. (*Id.* at 323.) Dr. McCurdy recommended that petitioner continue her therapies to decrease pain, to check ANA and anti-histone antibodies, and to look for a dysautonomia specialist or treatment. (*Id.* at 322.)

Petitioner was seen by Drs. McCurdy and Terwa Yong on January 24, 2017, for a follow up to her July 12 visit. (Ex. 95, p. 323.) Petitioner reported that she was enjoying college and doing well, but that she was recently having issues sleeping on account of her headaches becoming more severe. (*Id.* at 323-24.) She was still taking vitamin D despite having been advised to stop. (*Id.* at 324.) Her antihistone antibodies remained slightly elevated. (*Id.* at 326.) Dr. Yong recommended a renewed physical therapy prescription, discontinuing vitamin D supplements, continued neurofeedback, massage, and acupuncture as needed, and lab work including fungal culture urine, antinuclear antibodies, sedimentation rates, CBC analysis, a comprehensive metabolic panel, c-reactive protein, and histone antibody IgG testing (*Id.* at 328.)

On October 11, 2017, petitioner was seen by nephrologist Dr. Patricia Weng for a consultation on her polyuria. (Ex. 95, p. 329.) Petitioner reported that six months prior to this visit she had experienced gross hematuria, right flank pain, and felt that she had possibly passed a kidney stone. (*Id.* at 330.) She also reported that she was experiencing gross hematuria as recently as a week and a half earlier. (*Id.*) Dr. Weng believed that petitioner may have had a kidney stone and recommended urinalysis, complete metabolic profile, complete blood count, osmolality and iron studies, a renal ultrasound, and a litholink 24 hour urine collection. (*Id.* at 334-35.) Dr. Weng added an addendum to this record noting that petitioner showed normal renal function, elevated vitamin D levels, microscopic hematuria, and a slightly elevated calcium-creatinine ratio which would not explain the polyuria or gross hematuria. (*Id.* at 335.) Dr. Weng noted that petitioner's polyuria had an unclear etiology and further recommended a follow up renal ultrasound if petitioner tested negative for kidney stones because in that case, her gross hematuria may indicate lower GI tract bleeding. (*Id.*)

Petitioner was seen by Dr. Ellen Baker at the Torrance Memorial Medical Center Emergency Department on November 30, 2017, with chief complaints of right flank pain and lower abdominal pain. (Ex. 55, p. 141.) Petitioner's urine was positive for trace leukocytes and sent for urinalysis and culture; her chemistry panel was normal. (*Id.* at 142.) Dr. Baker ordered Rocephin, IV fluids, and an ultrasound for completeness. (*Id.*) Petitioner's testing did not reveal that she was passing a kidney stone. (*Id.*) Petitioner was prescribed ciprofloxacin and told to follow-up with her primary care physician. (*Id.*)

Petitioner followed up on her polyuria issues with Dr. Steven Lerman on December 3, 2017. (Ex. 95, p. 335.) Dr. Lerman believed that petitioner's kidneys looked "relatively stable and structurally fine." (*Id.*) His assessment was that the best plan of action was to monitor petitioner's symptoms over the next six to twelve months, with a repeat ultrasound after that time. (*Id.*) Dr. Lerman made two addendums to this record. The first was on December 22, 2017, where he noted that petitioner's ED ultrasound raised the question of nonobstructing kidney stones and that her urinalysis revealed red and white blood cells but with a negative culture. (*Id.* at 336.) He recommended hydration, possibly pyridium and/or ditropan if petitioner's symptoms persisted, and a non-contrast CT scan to assess for stones. (*Id.*) Dr. Lerman's second addendum was made on January 5, 2018. (*Id.*) He noted that petitioner was clinically better with random episodes of polyuria. (Ex. 95, p. 336.) Petitioner's CT scan revealed a "4mm non obstructing left lower pole stone." (*Id.*) Dr. Lerman recommended observation and a similar CT scan in 2 years. (*Id.*)

Petitioner saw Dr. McCurdy again on March 7, 2018. (Ex. 96, p. 47.) Dr. McCurdy reported that petitioner had developed Raynaud's Syndrome "over the last few months," that only involved one finger or toe. (*Id.*) Petitioner reported that she was in pain, but Dr. McCurdy did not observe any necrotic lesions. (*Id.*) Dr. McCurdy did however, observe small skin lesions that take a long time to heal, very dry skin on petitioner's face that she reported does not clear up, and a lesion that would not heal. (*Id.*) Petitioner also reported that for two to three days it had felt like she had a hair in her throat. (*Id.*) Dr. McCurdy recommended Derma-Smooth for petitioner's face, a renewed physical therapy prescription, continued alternative treatments, and a variety of labs. (*Id.* at 52.) Petitioner received a bilateral kidney ultrasound on January 9, 2019, which did not reveal any abnormalities or detectable kidney stones. (Ex. 96, p. 94.) No further medical records have been filed.

b. As reflected in witness statements

i. Petitioner's parents' letter to the court

Petitioner filed a letter from her parents on October 15, 2013, providing an assessment of her condition up to that point. (Ex. 26.) This letter indicates that, prior to her vaccination, petitioner was a high performing competitive gymnast, training four to five hours each day, six days per week. (*Id.* at 2.) She would spend much of her time outside and with her family, she was physically fit, and had reached puberty. (*Id.*) Her parents explain that since her vaccination, petitioner is unable to engage in much

physical activity, has been provided handicap parking access, and suffers from debilitating headaches that limit her daily productivity. (*Id.* at 3.) According to this letter, petitioner was, at the time, only able to engage in normal walking or riding her bike for a few blocks, as more rigorous physical activities would exacerbate her symptoms. (*Id.*)

Petitioner's parents list out the symptoms that she experienced following her vaccination including: headaches that spikes under stress, inability to focus for long periods of time, chronic fatigue, mental fogginess, anxiety, inability to sleep, leg pain, numbness of the legs, bone pain, random bruising and tenderness, arthralgias, nausea, and allergies to fruits and vegetables. (Ex. 26, p. 3.) They explain that petitioner was enrolled in driver's ed, but that she was worried about her physical ability to drive due to her symptoms, specifically, her anxiety which they report worsened all of her other symptoms. (*Id.*) They also explain that she ceased taking prednisone and plaquenil after becoming "puffy looking," and that her complexion had become "more erratic" since the vaccination. (*Id*.)

Petitioner's parents indicate that prior to her vaccination, petitioner had a "pretty normal diet" and ate reasonably for a person her age, with no dietary restrictions and regular meals. (Ex. 26, pp. 3-4.) However, after her vaccination, petitioner parents report that she developed allergic reactions to a variety of fruits and vegetables that cause lesions in her mouth lasting a week or more depending on the amount of food she had eaten. (*Id.* at 4.) Notably, petitioner developed an "aversion to cold foods" and would become emotional when asked to heat up her leftovers, explaining to her parents that she could not "look at or be around cold leftovers, she can be around and eat them once they have been heated, but not cold." (*Id.*) Additionally, petitioner's parents report that sweets tended to make petitioner more anxious and irritable. (*Id.*)

Petitioner's parents also describe a change in petitioner's emotional state following her Tdap vaccination. Prior to petitioner's vaccination, they describe her as a "well-connected and respected friend, daughter, sister, niece, granddaughter etc.," who made "a positive impression on anyone she met." (Ex. 26, p. 4.) After her vaccination, however, they report that she has developed significant anxiety after being forced to quit gymnastics and leave the "stable environment and base of friends" that she had formed at her gymnastics gym. (*Id.* at 4-5.) Petitioner's parents also write that petitioner had become "disconnected from her friendships." (*Id.* at 5.) They indicate that her social life changed dramatically. (Ex. 26, p. 5.) Petitioner's parents explain that petitioner had developed significant anxiety issues following her vaccination and she had become significantly needy and demanding of her parents' time. (Ex. 26, pp. 6-7.) Petitioner's parents describe a level of dependency that they believe is not normal and believe that this adversely impacted their family dynamic. (*Id.*)

Prior to her vaccination, petitioner's parents describe her as a high achieving student who was able to focus intently on her studies and thus earn top grades. (Ex. 26, p. 8.) She would spend the early morning finalizing homework assignments, go to school at 8:30 am, and go to gymnastics from 2:30 to 8:00 pm. (*Id.*) She would then eat her dinner on the drive home from gymnastics, and then complete her homework

from 9:00 pm to 11:00 pm. (*Id.*) Petitioner's parents write that this was a schedule that petitioner was happy with and she would "adamantly" deny any desire to cut back on her gym hours. (*Id.*) After her vaccination, petitioner's parents describe her as bright, but challenged by her condition, needing to "take a step back from regular coursework . . . as her symptoms . . . [did] not allow her to keep mentally focused to endure a heavier coursework . . . ." (*Id*. at 8-9.) They explain that "she now has to study in short bursts as her headache escalates when she has to intently focus on the task at hand." (*Id.* at 9.) Petitioner ultimately needed to be placed on a special curriculum at school and would often leave early due to exhaustion and mental fatigue. (*Id.*)

ii. Petitioner and her brother's letters to the court

Petitioner also submitted her own letter to the court and a letter from her younger brother on October 15, 2013. (Ex. 27.) She breaks her letter down into two sections, a "before" section and an "after" section. (*Id.* at 1.) Before her vaccination, petitioner reports that she was "doing gymnastics every day from 2:30-8 during the school year and 12:30-7 during the summer." (*Id.*) She spent every day with her closest friends at the gym and viewed that group as a family. (*Id.*) She enjoyed school, received good grades, and rarely missed class. (*Id.*) She would always finish her homework even though she would work late into the night. (Ex. 27, p. 1.) She reports that she was "athletic and strong." (*Id.*) She also reports that she "had never had a headache in her life and besides from a small cold here and there was rarely sick." (*Id.*)

After her vaccination, petitioner reports that she rarely sees her friends, has quit gymnastics, doesn't "usually feel good enough to do any activities with [her] friends," has difficulties in school, has a hard time retaining information and focusing, and is unable to handle the long school day so only attended class for half of the day. (Ex. 27, p. 1.) Further, petitioner reports that she lost a lot of strength, had constant headache and nausea, suffered from anxiety to the point that she needed her mother to sleep in her room with her for a year, and would wake up frequently throughout the night. (*Id.*) She also notes symptoms including numbness of her extremities, dizziness, extreme fatigue, muscle and joint pain, and that she "never felt good." (*Id*.) She indicates that she was unable to focus enough to drive and unable to get her license. (*Id.*)

Petitioner's brother states in his letter that prior to vaccination she was in gymnastics, had great attendance at school and gymnastics, was very healthy, and had very few doctor appointments. (Ex. 27, p. 2.) He further writes that after petitioner's vaccination, her illness made petitioner's gymnastics training "hazardous" to her and her teammates. (*Id.*) He also notes that petitioner was only attending school for half of the day because she would be overcome by her headache and nausea and that she could no longer maintain good health. (*Id.*) He also explains that petitioner's doctor appointments were "through the roof" and that their parents now focus much more on petitioner "especially because of her anxiety." (*Id.*)

iii. Gymnastics coach's letter to the court

Petitioner submitted a short letter from her former gymnastics coach on December 3, 2014. (Ex. 39.) She writes that:

> [Petitioner] was a competitive gymnast training at All Olympia Gymnastics Center from the period of September 2006, through July 2011. [She] was a level 4 State Champion and competitive gymnast with the best scores in her age category through 2011. When [petitioner] unexpectedly had to leave gymnastics for an illness, she was training level 8 and well on her way to compete at the college level. All her coaches and fellow gymnasts have missed her. J. was bright, consistent, focused and motivated, her attendance was consistent and she was a role model for young gymnasts and a joy to coach.

(*Id.* at p. 2.)

iv. Petitioner's Testimony

Petitioner explained that prior to the vaccination in question, she was generally healthy with no major illnesses and received the typical childhood vaccines. (Tr. 11-12.) She noted that she excelled academically and participated in a demanding gymnastics program, training around six to seven hours each day. (*Id.* at 13.) Petitioner further testified that after receiving the Tdap vaccine in question, she experienced a headache, swollen arm, nausea, fatigue, tingling in her fingers and arms, leg numbness, joint pain, anxiety, photophobia, and brain fog. (*Id*. at 23-28.) She testified that her symptoms did not occur simultaneously, but spiked at different times, with some remitting entirely as she learned to treat and manage her condition. (*Id.* at 30-32.) Due to her symptoms, petitioner was unable to learn how to drive, forced to continue living with her parents, limit her social engagement due to fatigue, and seek special accommodations at school, including standing up for the majority of classes and extra time on exams. (*Id.* at 32-36.) Petitioner further testified that she currently experienced headaches, brain fog, fatigue, limb numbness, photophobia, difficulty sitting for long periods, myofascial tightening, kidney stones, and rarely, gastrointestinal symptoms. (*Id.* at 36-39)

Petitioner also recounted her 2014 hospitalization, stating that she was hospitalized for three weeks and confined to a wheelchair for a period after. (Tr. 39-40.) Petitioner also testified that as her physical symptoms progressed, she developed symptoms of anxiety which she felt were primarily due to the uncertainty surrounding her condition and loss of social outlets like gymnastics. (*Id.* at 40-44.)

On cross examination, petitioner clarified that she began to experience episodes of numbness around October of 2011. (Tr. 68-69.) The remainder of petitioner's testimony recounts her symptoms and the progression of her condition consistent with the medical records recorded above.

IV. Expert Opinions

a. Petitioner's Expert, Yehuda Shoenfeld, M.D., FRCP[17]

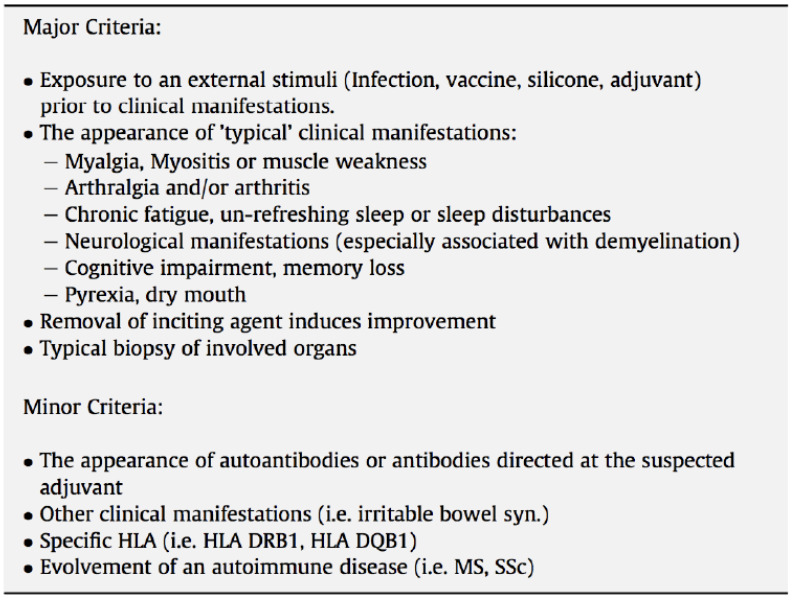
Dr. Shoenfeld identifies "autoimmune/inflammatory syndrome induced by adjuvants" or "ASIA" as a pertinent medical condition that can explain petitioner's medical history.[18] (Ex. 97, pp. 21, 30-31.) According to Dr. Shoenfeld, this is a syndrome developed in 2011 that posits that exposure to an adjuvant, which is an agent that enhances an antigen-specific immune response, can lead to an aberrant autoimmune response. (*Id*. at 21.) During the hearing, Dr. Shoenfeld explained ASIA as a collection of symptoms and signs in a genetically susceptible person[19] that join together prior to development of a full-blown, well-defined autoimmune disease. (Tr. at 110-113.) In other words, ASIA is a syndrome that follows an insulting agent but precedes manifestation of the final autoimmune disease. (*Id.*)

Citing to his own 2011 publication, Dr. Shoenfeld provides a set of relevant diagnostic criteria and indicates that diagnosis of ASIA requires fulfillment of either two major or one major and two minor criteria. (Ex. 97, p. 22 (citing Yehuda Shoenfeld & Nancy Agmon-Levin, *'ASIA' – Autoimmune/inflammatory syndrome induced by adjuvants*, 36 J. OF AUTOIMMUNITY 4 (2011) (EX. 98).) Specifically:

[17] After striking previously filed expert reports, petitioner relies on the expert opinion of immunologist Dr. Yehuda Shoenfeld. (Ex. 97.) Dr. Shoenfeld filed one report and also testified at the entitlement hearing. He was proffered at the hearing without objection as an expert in immunology and autoimmunity. (Tr. 104-05.) Dr. Shoenfeld received his medical degree from Tel Aviv University in 1978. (Ex. 124, p. 1.) He served as senior resident in the internal medicine department and outpatient clinic of hematology and immunology at Beilinson Medical Center in Petach Tikva, Israel from 1976 to 1978. (*Id.*) He has held several fellowships in hematology and oncology and has served as a senior physician or department head at five separate hospitals throughout Israel and Russia. (*Id.*) Dr. Shoenfeld has over 40 years of experience researching immunology, has held multiple academic positions, and currently serves as an Appointed Professor of Medicine with Tel-Aviv University's Sackler Faculty of Medicine. (*Id.* at pp. 3-4.)

[18] Further to this, Dr. Shoenfeld indicates that "[a]ccording to her clinical presentation and the assessment by pediatric rheumatologist – the diagnosis of myofasciitis was raised which is related to ASIA syndrome. It is worth noting that the treating physicians highlight the possibility of the relationship of the vaccine administration and disease development." (Ex. 97, p. 28.) In discussing his own opinion of petitioner's case, Dr. Shoenfeld at turns discusses her presentation as "ASIA/MMF," but never discusses MMF as a standalone explanation for petitioner's condition nor ever explicitly confirms that petitioner can be properly diagnosed as having MMF. Accordingly, MMF will be discussed to the extent it purportedly contributes to the evidence supporting ASIA, but will not be discussed further vis-à-vis petitioner's own medical history.

[19] According to Dr. Shoenfeld, HLA-DRB1 is the haplotype gene most commonly associated with autoimmune disease, while TPTN22 has been found to be associated to a lesser extent. (Tr. 113-116.) However, regarding petitioner's own condition, Dr. Shoenfeld conceded that genetic testing was never completed and thus there is no evidence that petitioner was indeed a genetically prone individual carrying the HLA-DRB1 haplotype. (*Id.* at 116-18.)



Major Criteria:

- Exposure to an external stimuli (Infection, vaccine, silicone, adjuvant) prior to clinical manifestations.
- The appearance of 'typical' clinical manifestations:
  - Myalgia, Myositis or muscle weakness
  - Arthralgia and/or arthritis
  - Chronic fatigue, un-refreshing sleep or sleep disturbances
  - Neurological manifestations (especially associated with demyelination)
  - Cognitive impairment, memory loss
  - Pyrexia, dry mouth
- Removal of inciting agent induces improvement
- Typical biopsy of involved organs

Minor Criteria:

- The appearance of autoantibodies or antibodies directed at the suspected adjuvant
- Other clinical manifestations (i.e. irritable bowel syn.)
- Specific HLA (i.e. HLA DRB1, HLA DQB1)
- Evolvement of an autoimmune disease (i.e. MS, SSc)

(EX. 97, p. 24.) Dr. Shoenfeld asserts that petitioner meets two major and one minor criteria, because she experienced typical clinical manifestations of neurological manifestations (tingling), fogginess/forgetfulness, fever, dizziness, blurred vision, lethargy (which he equates to chronic fatigue), weakness, sleeping disturbances, arthralgia, and cognitive impairment, as well as relevant autoantibody findings. (Tr. 125.) According to Dr. Shoenfeld, the validity of these diagnostic criteria for ASIA have been validated through the registry that he had his research group created and the resulting publications. (Tr. 120-27, 196-97 (citing Abdulla Watad et al., *The autoimmune/inflammatory syndrome induced by adjuvants (ASIA/Shoenfeld's syndrome: descriptive analysis of 300 patients from the international ASIA syndrome registry,* 37 CLIN. RHEUMATOL. 483 (2018) (Ex. 121); Abdulla Watad et al., *Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) demonstrates distinct autoimmune and autoinflammatory disease associations according to the adjuvant subtype: Insights from an analysis of 500 cases,* 203 CLIN. IMMUNOL. 1 (2019) (Ex. 122)).) Later papers have refined these criteria, however.[20] (*Compare* Shoenfeld & Agmon-Levin, *supra*, at Ex. 98 (Table 2) and Watad et al, *supra*, at Ex. 121 (Table 1).) In fact, Dr. Shoenfeld testified that he is still developing different diagnostic parameters for ASIA. (Tr. 140.)

Overall, Dr. Shoenfeld believes petitioner developed ASIA based on her pre-vaccination health, post-vaccination condition, antihistone antibody levels, and the fact that at least two of petitioner's treating physicians mentioned ASIA and that her condition was a possible vaccine reaction. (Tr. 144-46.) Dr. Shoenfeld concluded that petitioner's condition fell within the typical two-to-42-day window for onset of an

[20] In fact, the 2011 paper lists the major and minor criteria, but does not explicitly explain what the thresholds for diagnosis are (i.e., how many major and minor criteria are required to label a case as ASIA). (Shoenfeld & Agmon-Levin, *supra*, at Ex. 98.) The threshold identified by Dr. Shoenfeld was developed later. (Tr. 126.)

autoimmune reaction. (Tr. 172.) However, he also testified that ASIA symptoms could manifest anywhere from immediately after insult to years later. (*Id.* at 225-26.)

Dr. Shoenfeld explained that petitioner exhibited a mildly elevated sedimentation rate ten days after her vaccination which would indicate an acute inflammatory condition. Petitioner's sedimentation rate returned to normal levels roughly a month after her vaccination, but Dr. Shoenfeld indicated that this typically occurs when inflammation becomes chronic. (*Id.* at 150-51.) Dr. Shoenfeld testified that he believed petitioner's appropriate diagnosis was ASIA, encompassing aspects of dysautonomia,[21] undifferentiated connective tissue disease ("UCTD"),[22] and "unspecified vaccine reaction." (Tr. 151.) Dr. Shoenfeld testified that petitioner also suffered from joint pain which satisfies a second diagnostic criteria of ASIA. (*Id.* at 164-65.) Dr. Shoenfeld also noted that petitioner's brain fog, chronic fatigue, sleep abnormalities, vision changes, allergies, and extremity tingling were all consistent with ASIA. (*Id.* at 167-68.) He testified that his conclusions were further supported by the fact that some of petitioner's treating physicians also diagnosed her with ASIA, that her VAERS report documented symptoms of ASIA (headache, fatigue, and fever), and that other physicians believed that her condition, while not necessarily ASIA, was nonetheless vaccine related. (*Id.* at 169.)

Dr. Shoenfeld states that the efficacy of most vaccines currently in use for humans or animals depends on "the presence of an adjuvant in conjunction with the infection antigen." (Ex. 97, p. 22.) Adjuvants increase efficacy and length of the immune response to the infectious antigen and enable increased vaccine production by allowing manufacturers to use less antigen per dose. (*Id.*) However, Dr. Shoenfeld writes, the use of adjuvants can "also provoke an enhanced immune response." (*Id.* citing Sunita Awate et al., *Mechanisms of action of adjuvants*, 4 FRONT IMMUNOLOGY 114 (2013) (Ex. 101).) Because of this, "newer more effective and perhaps safer adjuvants" such as virosome, new oil based adjuvants, and "adjuvants that utilize [t]oll-like receptor signaling pathways" have been developed. (Ex. 97, pp. 22-23 (citing Shoenfeld & Agmon-Levin, *supra,* at Ex. 98).) He writes that on rare occasions vaccines may induce the appearance of "autoantibodies, enigmatic inflammatory conditions and overt autoimmune disease," that can cause non-specific manifestations like arthritis, neuronal damage, fatigue, encephalitis, and vasculitis. (Ex. 97, p. 22.) Dr. Shoenfeld suggests that these events have been documented in case-reports, case series, studies, and

[21] He opined that petitioner's gastroparesis confirmed her dysautonomia due to the fact that the GI tract is fully autonomic and therefore, the dysfunction of the GI tract suggests dysfunction of the autonomic nervous system, also known as dysautonomia. (Tr. 159-60.) Dr. Shoenfeld conceded however, that he was unable to determine what exactly led to petitioner's dramatic weight loss during her treatment, and only suggests that she suffered from gastroparesis because her records did not point to malabsorption. (*Id.* at 160-63.) Dr. Shoenfeld further explained that dysautonomia has a variety of etiologies, including autoimmunity, and that in this case, petitioner suffered from autoimmune dysautonomia, manifesting as gastroparesis.

[22] However, upon cross examination he was unable to cite to a record supporting this assertion. (Tr. 200-02.) Additionally, he explained that a diagnosis of UCTD requires a positive ANA test, but conceded that petitioner had two negative ANA tests, and still suggested that she suffered from UCTD based only on her symptoms. (*Id.* at 202-03.)

VAERS reports weeks, months, and even years following vaccination. (*Id.*) He further cites the causal link found between the 1976 swine flu vaccine and an increase in occurrences of Guillain-Barre syndrome ("GBS"). (*Id.*)

Dr. Shoenfeld asserts that a number of animal studies have been conducted showing a causal link between vaccines and autoimmune conditions. (Ex. 97, p. 22.) He refers to one study of immunizations in puppies that "resulted in production of 9 different autoantibodies including lupus-associated ones."[23] (*Id.*) A second study Dr. Shoenfeld relies on is focused on specific vaccination protocols of diabetic prone newborn mice and rats which resulted in an increased incidence of diabetes. (*Id.* (citing J. Bart Classen, *The Timing of Immunization Affects the Development of Diabetes in Rodents*, 24 AUTOIMMUNITY 137 (1996) (Ex. 99)).) Dr. Shoenfeld cites a more recent study of intra-peritoneal immunization of salmon with oil-adjuvanted vaccines that resulted in the production of several autoantibodies and autoimmune diseases evidenced by "granulomatous diseases of the liver and peritoneum, thrombo-embolic disease and immune mediate glomerulonephritis."[24] (Ex. 97, p. 22 (citing Minoru Satoh et al., *Polyclonal hypergammaglobulinemia and autoantibody production induced by vaccination in farmed Atlantic salmon*, 30 FISH & SHELLFISH IMMUNOLOGY 1080 (2011) (Ex. 100)).)

Dr. Shoenfeld explains several mechanisms by which the human immune system can turn on itself to trigger autoimmune responses to vaccines. The first and most common mechanism is "molecular mimicry between infectious antigens and self-antigens . . . ." (Ex. 97, p. 26.) The second is "epitope spreading, whereby invading antigens accelerate an ongoing autoimmune process by local activation of antigen presenting cells and over processing of antigens . . . ." (*Id.*) The third and final mechanism is bystander activation of B lymphocytes "which enhances cytokine production and further induce the expansion of auto reactive T-cells." (*Id.*) Dr. Shoenfeld then argues that because vaccine adjuvants such as alum generate an increased immune response, vaccines "may provoke more exaggerated, anarchic immune responses than infections." (Ex. 97, p. 27 (citing Eitan Israeli et al., *Adjuvants and Autoimmunity*, 18 LUPUS 1217 (2009) (Ex. 111)).)

Dr. Shoenfeld testified that the reason ASIA progresses to different defined autoimmune diseases is because different autoantibodies are generated in response to different insults, and those autoantibodies attack the host in different ways via molecular mimicry, causing the variety of autoimmune diseases seen following ASIA. (Tr. 135-38.)

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[23] Dr. Shoenfeld does not provide a citation to this study.

[24] It should be noted that this study, appearing in the Journal of Fish & Shellfish Immunology, relates to vaccine efficacy for vaccines used to support aquaculture by preventing infection in farmed salmon stock. Nothing in this paper purports to have any implications outside of that context. (Classen, *supra,* at Ex. 99.) During the hearing I asked Dr. Shoenfeld directly if it was appropriate to use a fish model (i.e., non-mammalian) to evidence what happens in the human immune system. He did not directly address my concern, instead contending that ASIA is supported by animal models broadly. (Tr. 233-34.) However, the other animal modes he cited were mammals. (*Id.* at 233-38.) I am not prepared to credit Dr. Shoenfeld's reliance on this article on this record.

Dr. Shoenfeld opines that petitioner received the Tdap vaccine, and that the alum adjuvant in that vaccine hyperstimulated her immune system, leading to her symptoms. He further testified that he believed petitioner will ultimately develop molecular mimicry in response to the vaccine ingredients which will determine whether her condition ultimately becomes a specific autoimmune disease. (Tr. at 143.) Dr. Shoenfeld testified that he was unable to say with any certainty whether petitioner's condition was induced via molecular mimicry, and that it would require petitioner to develop a distinct autoimmune disease in order to say for sure, but he opines based on petitioner's symptoms that there is a possibility that molecular mimicry was occurring. (*Id.* at 223.)

Dr. Shoenfeld suggests that post-vaccination adverse immune responses can occur over a wide period of time, ranging from months to years after the vaccination. (Ex. 97, p. 24 (citing Charles M. Poser & Peter O. Behan, *Late Onset of Guillain-Barre Syndrome*, 3 J. OF NEUROIMMUNOLOGY 27 (1982) (Ex. 106)).) He acknowledges that in some cases, a period of 4 to 6 weeks has been considered plausible in the onset of autoimmune diseases following vaccination but cites a study by Ozawa et al to contend that post-vaccine adverse effects can manifest as late as several years following vaccination. (Ex. 97, p. 25 (citing Kazuki Ozawa et al., *Suspected Adverse Effects After Human Papillomavirus Vaccination: A Temporal Relationship Between Vaccine Administration and the Appearance of Symptoms in Japan*, 40 DRUG SAFETY 1219 (2017) (Ex. 108)).) Dr. Shoenfeld explains that the Ozawa study observed 120 female patients who received the HPV vaccine over two and a half years. The authors observed definite or probable vaccine-related symptoms in 72 of those patients. The researchers observed onset of symptoms occurring between 1 and 1532 days with an average of 319.7 ± 349.3 days. (Ex. 97, p. 25 (citing Ozawa et al., *supra*, at Ex. 108).) Dr. Shoenfeld relies on these findings to suggest that "post vaccination symptoms could start with [a] quite long latency period post vaccination." (Ex. 97, p. 26.)

Dr. Shoenfeld further stresses a causative role for aluminum oxyhydroxide ("alum") adjuvants in the emergence of macrophagic myofasciitis. (Ex. 97, p. 27.) Alum is specifically used as an adjuvant in the Gardasil HPV vaccine and has been "implicated . . . in several autoimmune phenomena." (*Id.*) Dr. Shoenfeld explains that concerns regarding alum adjuvants originally arose "following recognition of their causative role in the so-called macrophagic myofasciitis (MMF) lesion detected in patients with myalgic encephalomyelitis/chronic [fatigue syndrome]." (*Id.* (citing Naval Daver & Hagop Kantarjian, *Malignancy-Associated Haemophagocytic Lymphoistiocytosis in Adults*, 18 THE LANCET 169 (2009) (Ex. 112)).) He notes that "[i]t was previously shown that poorly biodegradable aluminum-coated particles injected into muscle are promptly phagocytosed in muscle and the draining lymph nodes," which "can disseminated within phagocytic cells throughout the body and slowly accumulate in [the] brain." (Ex. 97, p. 27.) According to Dr. Shoenfeld, "[t]his strongly suggests that long-term adjuvant biopersistence within phagocytic cells is a prerequisite for slow brain translocation and delayed neurotoxicity." (*Id.*) Dr. Shoenfeld cites "macrophagic myofasciitis syndrome" or "MMF" as a "the most evaluated post-vaccination condition . . . in which a causal link was clearly delineated." (Ex. 97, p. 23 (citing Romain Gherardi et al., *Macrophagic myofasciitis: an emerging entity*, 352 THE LANCET 347 (1998) (EX. 102);

Romain Gherardi et al., *Macrophagic myofasciitis lesions assess long-term persistence of vaccine-derived aluminum hydroxide in muscle,* 124 BRAIN: A J. OF NEUROLOGY 1821 (2001) (EX. 103); Christopher Exley et al., *A role for the body burden of aluminum in vaccine-associated macrophagic myofasciitis and chronic fatigue syndrome,* 72 MED. HYPOTHESES 135 (2009) (Ex. 104).)

Based on all of the above, Dr. Shoenfeld opines in his report that petitioner's own medical history can be explained as "ASIA/MMF, Dysautonomia, and/or simply [a] vaccine reaction and subsequent autoimmune symptoms" caused by her June 18, 2011 Tdap vaccine. (Ex. 97, p. 31.) He opines that she suffered an initial arthus reaction within one hour of vaccination that included headache, fever, and arm pain, and then developed new progressive symptoms of brain fog, gastroparesis, limb tingling/numbness, face blisters, and Raynaud's syndrome. (*Id*.)

b. Respondent's Experts[25]

i. Edward W. Cetaruk, M.D., FACMT[26]

Dr. Ceteruk's opinion is most notable for challenging the role of aluminum in the ASIA theory. Dr. Cetaruk charges that the ASIA theory does not differentiate between the "chemical composition of the different adjuvants or their mechanism of interaction with the immune system to exert their adjuvant effect . . . [and the] theory that all adjuvants are immunologically, pharmacologically and toxicologically equivalent and

[25] As explained above, petitioner did not file Dr. Shoenfeld's report until September of 2019. (ECF No. 122.) Before that she had relied on expert opinions that she ultimately moved to strike from the record. Accordingly, most of the expert reports submitted by respondent are responsive to expert opinions that are no longer a part of the record. This includes both of the reports respondent filed by Dr. Cetaruk as well as the first two reports filed by both Drs. Rose and Whitton. Nonetheless, these reports remain a part of the record. Moreover, despite the change in experts, petitioner has consistently pursued her claim under the ASIA theory. Accordingly, these earlier reports from respondent's experts remain at least partially relevant. However, there is substantial overlap among respondent's expert opinions. Each expert opines from a different perspective (toxicology, immunology, and rheumatology respectively), but all three address their criticisms of Dr. Shoenfeld's ASIA concept broadly. The resulting reports will be addressed selectively so as to avoid what is cumulative.

[26] Respondent filed two reports by toxicologist Dr. Edward W. Cetaruk to discuss ASIA and why he believed the ASIA theory fails to support petitioner's claim. (Exs. A, G.) Both reports were filed before Dr. Shoenfeld became involved in the case and Dr. Cetaruk was not subsequently called to testify at the entitlement hearing. Dr. Cetaruk's first report is discussed herein; however, Dr. Cetaruk's supplemental report responds directly to Dr. McCurdy's report, which has now been struck. (Ex. G.) That report focuses largely on contesting Dr. McCurdy's own underlying understanding of the ASIA theory, a point that is now moot, as well as on contesting the general acceptance of ASIA, which is further addressed by Drs. Whitton and Rose. (*Id*.) Accordingly, that report will not be discussed further. Dr. Cetaruk received his medical degree from New York University School of Medicine. (Ex. B, p. 2.) He is board certified by the American Board of Emergency Medicine with Special Qualifications in Medical Toxicology and the National Board of Medical Examiners. (Ex. B, p. 1.) He currently holds a position with Toxicology Associates in Denver, Colorado and as an Assistant Clinical Professor of Medicine in the Department of Medicine, Section of Clinical Pharmacology and Toxicology at the University of Colorado Health Sciences Center. (*Id.*)

can all cause autoimmune disease is not supported by the medical and scientific literature." (Ex. A, p. 2.) Dr. Cetaruk explains that adjuvants can be derived from a number of very different classes of chemical compounds. Only aluminum salts are used in the United States; however, "Dr. Shoenfeld generalizes that all vaccine adjuvants, regardless of their chemical composition, mechanism of action or administered dose are potential causes of autoimmune disease." (*Id*. at 4.)

For example, Dr. Cetaruk explains that Dr. Shoenfeld relies in part on animal research by Reeves, et al., relating to antibody production in mice following the use of pristane, a hydrocarbon adjuvant, leading to lupus.[27] (Ex. A, p. 6.) However, he notes that there are no reports in the medical literature of lupus caused by exposure to pristane in humans and conversely no experimental studies replicating the Reeves results using aluminum-based adjuvants. (*Id*.) Dr. Cetaruk cites a study by Potter, et al., examining the dose-response relationship between adjuvants and development of plasmacytomas (malignant plasma cell tumors). Potter found that higher doses of pristane produced plasmacytomas, but neither aluminum hydroxide nor lower doses of pristane produced plasmacytomas. (Ex. A, Tab 16, p. 1.) According to Dr. Cetaruk, this study shows that contrary to Dr. Shoenfeld's generalization, aluminum salts and pristane do not necessarily have the same mechanism and do not have the same effects. (Ex. A, p. 7.)

Dr. Cetaruk stresses that aluminum salts are used as adjuvants in the United States precisely because they are considered to have fewer potential side effects. (Ex. A, p. 7.) Further, Dr. Cetaruk explains that human populations are routinely exposed to aluminum, absorbing it primarily through ingestion, with no corresponding reports of increased incidences of autoimmune disease. (*Id*.) For example, he notes that aluminum accumulation and toxicity is a significant complication for dialysis patients; however, despite being a well-studied population, there are no studies reporting increased rates of autoimmune disease among dialysis patients. (*Id*. at 8.)

Dr. Cetaruk indicates that histologic finding of aluminum at the injection site has long been recognized; however, he cites three prior studies that show that aluminum found in macrophage lysosomes is consistent with how the body handles aluminum generally (not just from vaccines) and is not indicative of any pathologic condition, let alone showing any of the subjects to suffer autoimmunity specifically. (Ex. A, pp. 8-9

[27] As noted above, Dr. Ceraruk's reports were filed in this case before Dr. Shoefeld became personally involved in this case. His references to what Dr. Shoenfeld relies upon refer to Dr. Shoenfeld's publications regarding ASIA rather than his expert report filed in this specific case. In this case, Dr. Shoenfeld does not specifically cite any study by Reeves in his report. (Ex. 97.) However, he does cite a 2013 paper by Cruz-Tapias, et al., on which he was an author. (Paola Cruz-Tapias et al., *Autoimmune (autoinflammatory) syndrome induced by adjuvants (ASIA) – animal models as a proof of concept,* 20 CURR. MEDICINAL CHEM. 4030 (2013) (Ex. 117).) The Cruz-Tapias paper is a review of prior animal model studies that purport to provide proof of concept for ASIA. (*Id.*) The Reeves study discussed by Dr. Cetaruk is in turn cited in the Cruz-Tapias et al, paper for the proposition that adjuvants broadly have been documented as inductors of autoimmunity. (Cruz-Tapias et al., *supra*, at Ex. 117, pp. 1, 6 (ref. 2); *see also* Westley Reeves et al., *Induction of autoimmunity by pristane and other naturally-occurring hydrocarbons,* 30(9) TRENDS. IMMUNOL. 455 (2009) (Ex. A, Tab 18).)

(citing Maria Fiejka, et al., *Effect of aluminium hydroxide administration on normal mice: tissue distribution and ultrastructural localization of aluminium in liver,* 78 PHARMACOL. & TOXICOL. 123 (1996) (Ex. A, Tab 6), Kiyokazu Kametani, *Detection of aluminium by energy dispersive x-ray microanalysis at high accelerating voltages with semi-thin sections of biological sample,* 51(4) J. ELECTRON MICROSCOPY 265 (2002) (Ex. A, Tab 11); Armand Verbueken, et al., *Ultrastructural localization of aluminum in patients with dialysis-associated osteomalacia,* 30(5) CLIN. CHEM. 763 (1984) (Ex. A, Tab 24)).) A further study by Verdier, et al., tested diphtheria-tetanus vaccines adjuvanted with either aluminum hydroxide or aluminum phosphate and found that histologic findings of macrophagic myofasciitis represented normal tissue changes that were not associated with abnormal clinical signs. (Ex. A, p. 9 (citing Francois Verdier et al., *Aluminium assay and evaluation of the local reaction at several time points after intramuscular administration of aluminium containing vaccines in the Cynomolgus monkey,* 23 VACCINE 1359 (2005) (Ex. A, Tab 25)).)

i. J. Lindsay Whitton, M.D., Ph.D.[28]

During the hearing, Dr. Whitton analogized ASIA to a table with four legs – the four legs being the four conditions originally leading to the ASIA concept (siliconosis, MMF, Gulf war syndrome, and post-vaccinal injuries). (Tr. 405-09.) According to Dr. Whitton each "leg" has significant short-comings and is unable to stand on its own. However, Dr. Whitton also contends that these four "legs" cannot act together to support the same table, because they implicate different adjuvants in different quantities that are not fungible. (*Id*.) Even if one "leg" were strong enough to stand on its own, that would not add any support to the remaining legs. (*Id.*)

Dr. Whitton "utterly rejects the validity of ASIA," describing it as "an invented syndrome that has been largely discredited." (Ex. J, pp. 5, 9.) He contends that ASIA is "speculative" and has "numerous flaws" that have not been rebutted by Dr. Shoenfeld as originator of the idea. He suggests that ASIA "barely deserves the title of scientific hypothesis." (*Id*. at 5.) Dr. Whitton observes that ASIA has no ICD9 or ICD10 code and is not recognized by the vast majority of the medical profession. (*Id*.; Tr. 397-99.) Moreover, he stresses writing by Dr. Shoenfeld himself that suggests ASIA constitutes unproven speculation. Specifically, he quotes Dr. Shoenfeld as noting in a 2015 paper regarding vaccines and autoimmunity that "every attempt for an epidemiological study

[28] Respondent filed three expert reports by Dr. Whitton. (Exs. C, H, J.) Dr. Whitton's third report includes a direct response to Dr. Shoenfeld's report. Additionally, Dr. Whitton testified at the entitlement hearing. At the hearing Dr. Whitton was proffered without objection as an expert in immunology and virology. (Tr. 387.) Because Dr. Whitton's third report and hearing testimony are comprehensive of his opinion, his first two reports will not be separately addressed. Dr. Whitton received his medical degree from the University of Glasgow in 1979. He is a member of the American Association of Pathologists, the American Association of Immunologists, the American Society of Virology, the American Society of Microbiology, the American Academy of Microbiology, and the American Association for the Advancement of Science. (Ex. D, p. 1.) He has held multiple teaching positions since 1986 and currently serves as a Professor in the Department of Immunology and Microbial Science at Scripps Research Institute in La Jolla, California. (*Id.*) Dr. Whitton has also published 185 pieces of medical literature covering topics on biochemistry, immunology, and virology. (Ex. D, pp. 2-13.)

has so far failed to deliver a connection."[29] (Ex. J, p. at 5 (quoting Luisa Eca Guimaraes et al., *Vaccines, adjuvants and autoimmunity,* 100 PHARMACOL. RES. 190 (2015) (Ex. J, Tab 6)).) Examining the 2011 and 2013 papers in which Dr. Shoenfeld and colleagues purport to validate the ASIA concept with a registry of patients, Dr. Whitton observes the diagnostic criteria to be "breathtakingly broad"[30] and also notes that the criteria have changed from the 2011 to the 2013 paper, charging this as evidence that "ASIA is built on shifting sands." (*Id*. at 6.)

Dr. Whitton cites a 2015 review of ASIA that concluded that:

> [i]t is also apparent that the broadness of the current ASIA criteria lack stringency and, as a result, very few cases of autoimmune disease could be excluded from a diagnosis of ASIA. The current studies involving human cases are so diverse, in both external stimuli and in resulting conditions, that there is currently a lack of reproducible evidence for any consistent relationship between adjuvant and autoimmune condition.

(Ex. J, p. 9 (quoting David Hawkes et al., *Revisiting adverse reactions to vaccines: a critical appraisal of autoimmune syndrome induced by adjuvants (ASIA),* 59 J. AUTOIMMUNITY 77 (2015) (Ex. J, Tab 13)).)

Further to this critique, Dr. Whitton cites a 2017 publication of a 5-year study of people receiving allergy shots. (Ex. J, p. 9 (citing Rohan Ameratunga et al., *Evidence refuting the existence of autoimmune/ autoinflammatory syndrome induced by adjuvants (ASIA),* J. ALLERGY CLIN. IMMUNOL. PRACT. (2017) (Ex. J, Tab 14).) Allergy shot recipients receive a higher dose of alum than do routine vacinees, yet the study subjects experienced lower rates of autoimmune disorders. The authors concluded that their data do not support ASIA by vaccine adjuvants. (Ameratunga et al., *supra,* at Ex. J, Tab 14.) Dr. Whitton also cites a review article discussing at length the methodological flaws of many animal model studies purportedly supporting ASIA. (Ex. J, p. (citing Rohan Ameratunga et al., *Perspective: scientific and ethical concerns pertaining to animal models of autoimmune/ autoinflammatory syndrome induced by adjuvants (ASIA),* AUTOIMMUNITY REV. (2018) (Ex. J, Tab 15)).) He explains that a number of studies published in support of ASIA have subsequently been withdrawn. (Ex. J, pp. 10-12.)

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[29] Not quoted by Dr. Whitton, the paper continues: "Despite this, efforts to unveil the connection between the trigger of the immune system by adjuvants and the development of autoimmune conditions should be undertaken." (Ex J, Tab 6, p. 1.)

[30] With respect to the breadth of the diagnostic criteria, Dr. Whitton explains that the first major diagnostic criteria for ASIA is exposure to an external stimuli, including either infection or vaccination, prior to clinical manifestation. This, he suggests, will capture virtually the entire global population. (Ex. J, p. 6.) He also notes that the minor criteria include both development of an autoimmune disorder and presence of autoantibodies (a common feature of autoimmune disease). Dr. Whitton suggests, therefore, that the ASIA diagnostic criteria will per se identify anyone with any autoimmune condition as suffering vaccine-related ASIA. (*Id*.) Dr. Whitton's implication is that this falls short of any kind of meaningful screening process. For example, he rhetorically posits that he, a healthy individual exposed to vaccines and having only occasional muscle aches and minor complaints, could be diagnosed with ASIA. (*Id*.)

According to Dr. Whitton, the lack of meaningful screening from the diagnostic criteria is compounded by an expansive understanding of the appropriate time interval between vaccination and disease. (Ex. J, p. 6.) Dr. Whitton cites Dr. Shoenfeld's report as accepting up to a ten-year latency for post-vaccination ASIA. (Ex. J, p. 6 (citing Ex. 97, p. 29).) Dr. Whitton charges this as effectively "unlimited." (*Id*.) Dr. Whitton offers specific criticisms of the papers Dr. Shoenfeld cites with respect to this prolonged latency. (Ex. J, pp. 7-9 (discussing Poser & Behan, *supra,* at Ex. 106; Ozawa et al., *supra,* at Ex. 108).) Dr. Whitton also explains more broadly that these papers seek to identify correlations, based on what he characterizes as extremely long timeframes and then outrageously purport to identify the remote vaccinations as initiating causes with no support.[31]

Turning to the specific contention that an adjuvant can drive the innate immune response to cause autoinflammatory disease, Dr. Whitton stresses that the safety of alum has been well established over a 90-year period of use and that the innate immune response to an adjuvant is very short lived, terminating within hours to days. (Ex. J, p. 10.) He asserts that "[t]here is no known way for a strong innate response to a vaccine adjuvant to be perpetuated, which would happen if an adjuvant were to drive a serious autoinflammatory disease." (*Id*.; Tr. 390-96.) Interestingly, Dr. Whitton cites a study by Dr. Shoenfeld (not filed by petitioner in this case) which he posits as evidence tending to disprove Dr. Shoenfeld's own theory that alum leads to autoimmunity. (Ex. J, pp. 12-13.) In a 2013 paper, Dr. Shoenfeld and colleagues tested the safety of four different adjuvants in mice that were genetically modified to be susceptible to the autoimmune condition of lupus. (Favoino et al., *Effects of adjuvants for human use in systemic lupus erythematosus (SLE)-prone (New Zealand black/New Zealand white) F_1 mice,* 175 CLIN. EXPER. IMMUNOL. 34 (2013) (Ex. J, Tab 18).) By Dr. Whitton's explanation, the study injected the mice with quantities of alum that were between 70,000-170,000 times the weight adjusted dose a human would receive from vaccination. (Ex. J, p. 13.) Even with these higher doses and a genetic susceptibility, there was no statistically significant difference in proteinuria (which was used as a gauge of disease activity). Dr. Whitton further testified, without citing any specific study, that animal models have shown that the immunostimulatory effect of alum adjuvants "is very restricted in two key ways." (Tr. 393.) First, the effect is local and not systemic, so it only impacts the area near the injection site and therefore would not be linked to any systemic disorders. Second, the immunostimulatory effect has been shown to decrease significantly in as little as 24 hours after exposure, suggesting that the adjuvants do not continuously stimulate the immune system. (*Id.* at 393-96.)

Dr. Whitton also addresses in depth the condition of MMF. (Ex. J, pp. 14-19.) MMF was cited in Dr. Shoenfeld's report as "[p]erhaps the most evaluated post-

[31] For example, Dr. Whitton explains that Dr. Shoenfeld relies on a paper purporting to show that GBS may occur from weeks to months after an initial event, citing incidences occurring up to 10 months post-vaccination. (Ex. J, p. 7 (citing Ex. Poser & Behan, *supra,* at Ex. 106).) A well-known study by Langmuir et al., however, shows that incidences of GBS post swine flu vaccination returned to background rates much earlier than that (8 weeks). (*Id*.) Dr. Whitton equates this scholarship with proposing red clothing as a cause of neurologic disease based on the fact that some people with GBS wore red clothing in the year prior to suffering their condition. (*Id*.)

vaccination condition, in which a causal link was clearly delineated." (Ex. 97, p. 23.) Quoting this same statement from literature coauthored by Dr. Shoenfeld, Dr. Whitton suggests that MMF constitutes a "cornerstone" of ASIA. (Ex. J, p. 15 (quoting Yehuda Shoenfeld & Nancy Agmon-Levin, *'ASIA' – Autoimmune/inflammatory syndrome induced by adjuvants,* 36 J. AUTOIMMUNITY 4 (2011) (Ex. J, Tab 27)).) Dr. Whitton explains that MMF is "a histological lesion that contains, and results from, the injection of alum." (Ex. J, p. 14.) The name derives from the fact that muscle biopsy of the lesions shows inflammatory infiltrate rich in macrophages (the "itis") and located in the connective tissue (fascia) and muscle (myo). (*Id*.) According to Dr. Whitton, MMF is a "small, highly-localized" lesion that results from injection of adjuvants. (*Id*. at 15.) The critical issue, per Dr. Whitton, is that this histological lesion has not been shown to cause systemic disease, as Dr. Shoenfeld suggests. (This is also consistent with Dr. Cetaruk's discussion, *supra*, of studies regarding aluminum at injection sites – Dr. Whitton also similarly cites Verdier, et al., *supra,* at Ex. A, Tab 25.)

Dr. Whitton explains that publications asserting that MMF constitutes a systemic disease come from a specific French research group and the idea has not gained any widespread acceptance. (Ex. J, p. 16.) In particular, this group produced a 1998 study that is cited by Dr. Shoenfeld in this case. (*Id.* (citing Gherardi et al., *supra,* at Ex. 102).) According to Dr. Whitton the study has a critical sampling bias. The study examined 18 individuals that were referred for diagnosis of muscle diseases. If no diagnosis was available, these individuals were then biopsied at the site of injection, found to have MMF lesions, and therefore categorized as suffering a systemic MMF condition. Dr. Whitton explains that the selection bias is two-fold. First, the subjects are preselected on the basis that they have signs and symptoms of a muscle disease. Second, only those who ultimately have idiopathic conditions are biopsied. (*Id*. at 17.) Especially given that MMF lesions are harmless and potentially common, without a control group, the authors have generated only the illusion of a correlation. Dr. Whitton notes that this same issue was replicated in a follow up study that was also cited by Dr. Shoenfeld. (*Id*.) Despite this issue, the researchers purport to diagnose MMF as a systemic disorder based on the histopathologic results. (*Id*.) Dr. Whitton stresses that this has been examined multiple times by the World Health Organization ("WHO") and has been rejected. The WHO indicates there is not association between histological MMF lesions and systemic disease. (*Id*. at 18.)

Finally, Dr. Whitton notes that even if petitioner did experience a short-lived arthus reaction, Dr. Shoenfeld has not established how that could be related to his theory of causation. An arthus reaction is mediated by antibodies of the adaptive immune response whereas Dr. Shoenfeld which contends that the persistence of alum in macrophages leads to chronic stimulation of the innate immune response. (Ex. J, p. 21.)

i. Carlos D. Rose, M.D.[32]

Dr. Rose received his medical degree from the University of Buenos Aires School of Medicine in 1977. (Ex. F, p. 1.) He completed his residency in internal medicine at the University of Buenos Aires Hospital in 1982, serving as chief resident. (*Id.* at 4.) He has held several fellowships in rheumatology and pediatric rheumatology. (*Id.* at 5.) He has held certifications in internal medicine by the Argentina Ministry of Public Health, in general pediatrics by the American Board of Pediatrics, by the State of Delaware, in adult rheumatology by the Argentine Society of Rheumatology and Ministry of Public Health, and in pediatric rheumatology by the American Board of Pediatrics. (*Id.* at 5-6.) Dr. Rose has served as staff physician in rheumatology at the Central Military Hospital in Buenos Aires, Argentina, the Spanish Hospital in Buenos Aires, and at The Alfred I DuPont Institute of the Nemours Foundation in Wilmington, Delaware. (*Id.* at 6.) He has taught biochemistry and internal medicine at the University of Buenos Aires School of Medicine, and Pediatrics at the University of Pennsylvania School of Medicine and Jefferson Medical College. (Ex. F, pp. 6-7.) Dr. Rose has published over 84 peer-reviewed articles on pediatric rheumatology, biochemistry, and internal medicine. (*Id.* at 13-18.)

Based on his review of the medical records, Dr. Rose opines that petitioner "does not have a definable rheumatic or autoimmune disease." (Ex. E, p. 11.) He further notes that "[h]er diagnoses are primary chronic headache and chronic fatigue. These are symptom-based constructs of practical value for treating physicians but do not constitute biologic entities with a specific immunologic mechanism." (*Id.*) Dr. Rose stresses that headaches are the most common somatic complaint in children and adolescents. (*Id*. at 16.) Most often, the headaches are primary (*i.e*., the headache is the disease). (*Id*.) Even with new symptoms arising post-vaccination, Dr. Rose disagrees that there is any basis for causally attributing petitioner's symptoms to either autoimmunity or her Tdap vaccine.[33] (*Id*. at 16-17.)

Dr. Rose opines that petitioner's positive Anti-histone antibody (AHA), the one biomarker present that could theoretically point to an autoimmune condition, is likely a

[32] Like Dr. Whitton, Dr. Rose has presented three reports in this case, the third and final being a direct response to Dr. Shoenfeld's report. (Exs. E, I, K.) Dr. Rose also testified during the entitlement hearing and was proffered without objection as an expert in pediatric rheumatology. (Tr. 268.) Focus will be on Dr. Rose's initial report (Ex. E), which set forth his initial diagnostic opinion. The second report (Ex. I) was a rebuttal to Dr. McCurdy's report which has now been struck. The third report includes a summary of updated medical records and a response to Dr. Shoenfeld's report; however, the diagnostic assessment did not change and Dr. Rose's response to Dr. Shoenfeld reflected substantially the same criticisms of ASIA as advanced by Drs. Cetaruk and Whitton.

[33] Dr. Rose explains that petitioner's condition "has been labeled in different ways" by her treating physicians but notes that Dr. McCurdy in particular referenced a vaccine-reaction without providing a unifying diagnosis. (Ex. E, pp. 7-8.) Petitioner has variously been characterized as suffering pain amplification syndrome, migraine, sinusitis, Eustachian tube disorder, chronic headache, allergy syndrome, gastroparesis. (*Id*.) Given the number of diagnostic categories offered, the vagueness of symptoms, and the paucity of physical findings, Dr. Rose suggests that there should be concern for a functional mechanism. (*Id*. at 8.)

false positive. (Ex. E, pp. 12-13; *see also* Tr. 281-87.) Petitioner had "moderately" elevated AHA on November 30, 2011 – 1.7 U/ml (against a reference range of 0.0-0.9). (Ex. E, pp. 7-9 (citing Ex. 11A).) Later, on July 31, 2013, she had "weak positive" AHA of 1.4 U/ml. (Ex. E, p. 8.) AHA are a part of the family of antinuclear antibodies (ANA). (*Id*. at 12-13.) They have long been known to be found in patients with either systemic lupus (SLE) or drug induced lupus (DIL) and are used to help differentiate DIL from SLE. Dr. Rose explains that AHAs are "intricately linked" to ANAs. (*Id*.) In this case, however, petitioner was negative for ANA. According to Dr. Rose, "most rheumatologists will question the meaning of an AHA positive in the absence of ANA positivity." (*Id*.) Dr. Rose further cautions that antibody levels are variable rather than binary (positive or negative). There is some degree of antibody present in "normal" people and variable amounts in those with autoimmunity. In petitioner's case, further caution is warranted both because petitioner was positive for only a single autoantibody when tested against a large number of antibodies and had a moderate autoantibody level followed by a weak positive with no correlating change in the severity of her symptoms. Accordingly, Dr. Rose opines a false positive is likely. (*Id*.)

With respect to her initial post-vaccination presentation, Dr. Rose explained during the hearing that petitioner's first symptoms appeared four days after her vaccination and included swelling of the left arm, tenderness to palpation, and painful sensation with no rash or reduced range of motion. Dr. Rose disagrees that petitioner experienced a fever at the time of her presentation to urgent care because it was below the threshold of 37 degrees Celsius. (Tr. 270-72.) Dr. Rose noted that her white blood cell count, lymphocytes, platelets, hemoglobin, and PSH were all normal. Further, petitioner's "elevated" sedimentation rate was only moderate, at 22 and reverted to normal rates of 19 shortly after her initial test which would happen in the event of common cold or virus. (*Id.* at 274-76.) Dr. Rose also testified that arthus reactions are very rare and that the only way to affirmatively diagnose such a reaction is via biopsy of the injection site, and because petitioner did not receive a biopsy, there is nothing in the medical record to support any claims that she suffered an arthus reaction. (*Id.* at 276-77.) Dr. Rose provides data suggesting that petitioner's anti-tetanus toxoid antibody, a measure of protection against tetanus infection, is above mean for her age, but consistent with 18.6% of those studied. (Ex. E, p. 15.)

Providing critiques similar to the above, Dr. Rose submits that ASIA is "unusable" either for this petitioner or for any individual. (Ex. E, p. 19; *see also* Tr. 301-14.) During the hearing, Dr. Rose also made the point that based on the diagnostic criteria identifying both vaccinations and infections broadly as a relevant stimulus, and Dr. Shoenfeld's assertion that latency can be as long as years, ASIA is on its own terms incapable of distinguishing petitioner's Tdap vaccine, as opposed to earlier infections and vaccinations throughout her life, as *the* trigger of her condition. (Tr. 312-13.)

V. Analysis[34]

a. *Althen* prong one

Under *Althen* prong one, a petitioner must provide a "reputable medical theory," demonstrating that the vaccine received can cause the type of injury alleged. *Pafford v. Sec'y of Health & Human Servs.*, 451 F.3d 1352, 1355–56 (Fed. Cir. 2006) (citations omitted). To satisfy this prong, petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 549 (Fed. Cir. 1994)). Such a theory must only be "legally probable, not

[34] There is an extent to which ASIA is invoked in this case as both a diagnosis and a medical theory and this could cause confusion regarding the framing of the necessary legal analysis. When faced with disagreement among qualified experts regarding the identification and nature of a disputed injury, the Federal Circuit has concluded that it is "appropriate for the special master to first determine what injury, if any, [is] supported by the evidence presented in the record before applying the *Althen* test to determine causation." *Lombardi v. Sec'y of Health & Human Servs*., 656 F.3d 1343, 1351-53 (Fed. Cir. 2011). Importantly, however,"[t]he function of a special master is not to 'diagnose' vaccine-related injuries, but instead to determine 'based on the record as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the [petitioner]'s injury.'" *Andreu*, 569 F.3d at 1382 (quoting *Knudsen*, 35 F.3d at 549). Nonetheless, petitioner must "specify [her] vaccine-related injury and shoulder the burden of proof on causation." *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1346 (Fed. Cir. 2010). In that regard, respondent urges a threshold analysis of whether ASIA constitutes a defined and medically recognized injury (ECF No. 200, pp. 3-5), while also noting that "[b]ecause Dr. Shoenfeld's ASIA syndrome includes the diagnosis and cause in a single entity, the weakness of ASIA as a diagnosis and theory of causation are inextricably intertwined" (*Id*. at 8). Petitioner, on the other hand, asserts that ASIA does constitute her correct diagnosis (ECF No. 159, pp. 19-20), but nonetheless also argues that her only burden is to demonstrate injury regardless of specific diagnosis (*Id*.; ECF No. 195, p. 35 (citing *Kelley v. Sec'y of Health & Human Servs*., 68 Fed. Cl. 84, 100 (2005)). She argues that "[e]ven if the Court finds Petitioner's diagnosis of ASIA is not sufficiently recognizable for compensation under the Vaccine Act, Petitioner presents thorough, well-corroborated evidence that [petitioner] has indeed suffered an adverse autoimmune response attributable to her Tdap vaccination . . . ." (ECF No. 159, p. 20.) The two questions posed, and answered, in the following *Althen* prong one analysis are responsive to that framing. The first of those questions – whether ASIA identifies autoimmunity in those without otherwise defined autoimmune conditions – relates to petitioner's affirmative reliance on ASIA as part of her theory of causation, but also overlaps substantially with what alternatively could have been examined as a threshold issue of diagnosis consistent with *Broekelschen, supra*. The parties devoted significant portions of their briefing to debating respondent's experts' contention that ASIA is not recognized by the medical community as an established diagnosis, focusing especially on the specific assertion that ASIA does not have an ICD diagnostic code. (ECF No. 195, p. 19; ECF No. 200, p. 4.) However, I need not separately resolve that specific issue. While the attention to this question is understandable given petitioner's specific assertion that she can be diagnosed with ASIA, it is not necessarily informative for purposes of *Althen* prong one. For example, the Vaccine Injury Table recognizes "Shoulder Injur[ies] Related to Vaccine Administration" or "SIRVAs" as a category of compensable injuries while respondent simultaneously disputes that "SIRVA" is a viable clinical diagnosis. § 300aa-14(a) as amended by 42 C.F.R. § 100.3(a); *Lang v. Sec'y of Health & Human Servs.,* No. 17-995v, 2020 WL 7873272, at n. 3 (Fed. Cl. Spec. Mstr. Dec. 11, 2020). Like SIRVA, ASIA could as a concept theoretically point in the direction of causal explanation without also itself being a clinically recognized diagnostic entity. However, that is not the case as the analysis below explains that petitioner is unpersuasive in advancing ASIA as sound and reliable for any purpose and my conclusion is that ASIA fails as a concept fundamentally and in toto, including as a theory of causation. This conclusion arguably encompasses, but is broader than, a conclusion that ASIA fails merely as a diagnosis. Thus, analysis can proceed directly to the *Althen* prongs without any separate analysis of diagnosis as per *Broekelschen*.

medically or scientifically certain." *Id.* at 549. Generally, however, petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Human Servs*., 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1325-26 (Fed. Cir. 2006)).

With respect to *Althen* prong one, petitioner argues in her post-hearing brief that:

> It is a well-known tenet of autoimmunity that autoimmune conditions can be triggered by environmental factors, including exposure to chemicals or drugs. In line with this tenet Dr. Yehuda Shoenfeld's theory explains how the vaccine was the environmental factor in [petitioner's] case. Dr. Shoenfeld testified that the aluminum adjuvant (alum) in the vaccine caused an unusually strong proinflammatory response in [petitioner] that manifested in her autoimmune condition. ASIA is 'a collection of sign[s] and symptoms that can be induced in a genetically prone person to develop a nonwell-defined autoimmune disease or autoimmune rheumatic conditions.' Dr. Shoenfeld testified that autoimmunity is an overly exuberant response to a stimulus in which healthy cells attack themselves. The alum adjuvant was the environmental trigger that sparked [petitioner's] autoimmunity.

(ECF No. 195, p. 15 (citations omitted).)

It is undisputed that petitioner does not suffer from any defined autoimmune rheumatic condition. Petitioner argues instead that "the lack of a defined condition that describes patients like [petitioner] is exactly how the diagnosis of ASIA was developed and why it is used to describe patients like [petitioner]." (*Id*. at 35.) Thus, petitioner's framing leads *Althen* prong one to turn on two questions, both of which must be answered in the affirmative for petitioner to meet her burden. First, is ASIA sound and reliable as a means of identifying the presence of autoimmunity in those who are not suffering a defined autoimmune condition? And second, if so, has Dr. Shoenfeld provided a sound and reliable explanation demonstrating that the alum contained in a Tdap vaccine is a relevant environmental trigger that can kick off that autoimmune process? The answer to both questions is no.

At base, Dr. Shoenfeld and colleagues began developing the ASIA concept in 2011 with the observation that there were four conditions they viewed as being likely autoimmune conditions brought about by environmental factors that constituted adjuvants. These were siliconosis (generally discussed in the context of silicone breast implants), Gulf War syndrome, MMF, and post-vaccination phenomenon. (Watad et al., *supra,* at Ex. 121, p. 2.) The thinking was that all of these conditions had overlapping symptoms and a common denominator in following exposure to an adjuvant trigger. (Paola Cruz-Tapias et al., *Autoimmune (Auto-inflammatory) Syndrome induced by Adjuvants (ASIA) – animal models as a proof of concept,* 20 CURR. MEDICINAL CHEM. 4030 (2013) (Ex. 117).) Following on from that observation, the proponents of what

would become ASIA proposed that with the link between adjuvants and autoimmunity being established by these four conditions, ASIA therefore constituted a nosology[35] under which a number of similar symptoms previously attributed to defined autoimmune diseases could also be merged. (Maria Maslinkska, *Autoimmune-inflammatory syndrome induced by adjuvants – a new diagnostic problem or the solution of a diagnostic riddle,* 51(6) REUMATOLOGIA 437, 439 (2013) (Ex. 119).) Thus, diagnostic criteria were proposed and the hypothesis going forward was then that anyone meeting those diagnostic criteria was therefore experiencing an as of yet undefined autoimmune process consistent with ASIA. (Tr. 110-11; *see also* Watad et al., *supra,* at Ex. 121.) This hypothesis and the manner by which it was developed and tested have been roundly criticized. This decision will not attempt to catalogue these criticisms.[36] Highlighting several of the broadest critiques is sufficient to explain why ASIA is unpersuasive as a theory of causation under *Althen* prong one.

First, the starting premise that each of the four originating conditions (MMF, siliconosis, post-vaccination phenomena, and Gulf War syndrome) have been identified as conditions with well understood causes, or even in some cases as conditions at all, remains controversial. Dr. Whitton's above-discussed critique of MMF as a systemic disease is persuasive. Additionally, Court Exhibit I is a 2020 labeling recommendation by the FDA regarding silicone breast implants.[37] Although the FDA's recommended warning indicates implants are "associated" with systemic symptoms (Court Ex. I, p. 8),

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[35] Nosology refers to the classification of diseases. *Nosology,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=34361 (last accessed Sept. 7, 2022).

[36] The summaries of the expert opinions, *supra*, do not capture each and every criticism that has been leveled against ASIA itself, as well as against Dr. Shoenfeld and other proponents of the concept, within the record of this case. Dr. Whitton's strongly worded report at Exhibit J, responding directly to Dr. Shoenfeld's report, provides some barometer of the level of disagreement and controversy. Much of Dr. Whitton's strongest language can arguably be attributed to rhetorical flourish; however, Dr. Whitton also specifically charges, and discusses in detail, what he views as "major scientific problems." (Ex. J, p. 12; *see also* Ex. C.) Dr. Whitton indicates that proponents of ASIA have had to retract an unusually high number of publications relating to the concept and explains that a number of other prior publications cited in support of ASIA have important flaws as well. ASIA has been addressed in numerous prior decisions within this program and has been strongly and consistently criticized. *Decker v. Sec'y of Health & Human Servs.*, No. 15-71V, 2020 WL 7889059, at *32 (Fed. Cl. Spec. Mstr. Dec. 14, 2020); *Phillips v. Sec'y of Health & Human Servs.*, No. 16-906V, 2020 WL 7767511, at *21 (Fed. Cl. Spec. Mstr. Nov. 23, 2020); *Salerno v. Sec'y of Health & Human Servs.,* No. 16-1280V, 2020 WL 3444163, at *11 (Fed. Cl. Spec. Mstr. May 29, 2020); *Pearson v. Sec'y of Health & Human Servs.*, No. 16-9V, 2019 WL 3852633, at *13 (Fed. Cl. Mstr. Jul. 31, 2019); *Suliman v. Sec'y of Health & Human Servs.*, No. 13-993V, 2018 WL 6803697, at *27 (Fed. Cl. Spec. Mstr. Nov. 27, 2018) ("No special masters have ever found ASIA or ASIA-like theories to be persuasive"). These prior cases are provided as background information only and are not determinative of the outcome of this case.

[37] During the hearing I asked Dr. Shoenfeld to comment on this Court Exhibit. (Tr. 247-48; *Breast Implants – Certain Labeling Recommendations to Improve Patient Communication, in* Guidance for Industry and Food and Drug Administration Staff (Issued Sept. 29, 2020)(Court Ex. I).) Dr. Shoenfeld confirmed he is familiar with the document and is "very happy with this recommendation." (Tr. 247.) He acknowledged that the FDA "did not commit themselves to autoimmune systemic condition," but nonetheless expressed confidence that "eventually" the FDA will completely withdraw silicone breast implants in favor of an "alternative which do not have an adjuvant effect." (Tr. 248-49.)

the FDA explains that "[r]esearchers are investigating these symptoms to better understand their origins. The exact relationship of these symptoms with breast implants is unclear at this time." (*Id*. at 5.) The FDA specifically recommends that patients be informed that the causal link is "possible" but not yet established. (*Id*. at 16.) With respect to post-vaccinal phenomena, Dr. Shoenfeld himself writes in his expert report "[t]hese rare events were documented in case-reports, case series, studies as well as via the CDC vaccines adverse events reporting system, weeks and eve months or years following vaccination. As such it was difficult *if not impossible to delineate a causal relationship* between vaccination and the diagnosis of defined and non-defined AI/AIFD." (Ex. 97, p. 22 (emphasis added).) Respondent's earlier expert reports also cast doubt on the causes of Gulf war syndrome (Ex. A, p. 3; Ex. C, pp. 15-16), offering criticisms that are consistent with prior experience in this Program that reveals the idea that vaccines can cause fatiguing illnesses such as Gulf war syndrome to also remain controversial. *Skinner-Smith v. Sec'y of Health & Human Servs*., No. 14-1212V (Fed. Cl. Spec. Mstr. Aug. 15, 2022) (discussing literature addressing multiple factors under debate as possible causes of Gulf war syndrome and finding petitioner failed to establish a medical theory linking Tdap vaccine to chronic fatigue syndrome); *but see Bryan v. Sec'y of Health & Human Servs.*, No. 14-898V, 2020 WL 7089841 (Fed. Cl. Oct. 9, 2020) (finding petitioner preponderantly established the flu vaccine as a cause of chronic fatigue syndrome). Given that the first step in developing ASIA was to declare all of these conditions as related and place them under the same causal umbrella, any doubt as to the underlying causes of these conditions necessarily pervades the entirety of the endeavor. Thus, every subsequent step in the ASIA logic builds from a shaky foundation.

Second, even assuming each of the four underlying conditions and their causes were uncontroversial, the basis for grouping these conditions together would still remain unclear. Even if the four originating conditions did have a common denominator in the form of each having some kind of adjuvant trigger, Dr. Cetaruk persuasively explains that the mechanism of action among different adjuvants cannot be generalized. (Ex. A, p. 11.) Moreover, Dr. Shoenfeld discusses environmental triggers as a common feature of autoimmunity broadly. (Ex. 97, pp. 21.) Dr. Shoenfeld himself explains that there are multiple theoretical paths to autoimmunity and molecular mimicry alone can see different antigens mimic different body tissues to cause different autoimmune injuries. (*Id.* at 26.) In that regard, Dr. Whitton summed up all of these issues by offering the analogy of the four-legged table that cannot support itself. (Tr. 405-09.) Further still, even by Dr. Shoenfeld's own description the purportedly common clinical signs included in the ASIA diagnostic criteria are broad and include many non-specific symptoms (for example fatigue, arthralgia, memory loss or "neurological manifestations" broadly). (Ex. 97, p. 22 (Dr. Shoenfeld describing post-vaccination arthritis, neuronal damage, and fatigue as "non-specific").) So, it should not necessarily be surprising that they are seen in multiple different conditions. Accordingly, it is not clear how the identification of four separate conditions as having different environmental triggers should serve as any basis for fundamentally rethinking autoimmune conditions and generalizing their causes. This marks the basic starting premise of ASIA as questionable even before

examining whether exploration of the concept was subsequently pursued with appropriate scientific rigor.

Moreover, if the basis for grouping these four specific conditions together is unsubstantiated, then a fortiori the extension of that grouping to undefined conditions is unsubstantiated. Dr. Shoenfeld's cross-examination was very revealing on this point. During the hearing, respondent's counsel asked Dr. Shoenfeld to explain how molecular mimicry, which he had previously cited, fit into his theory for this case. First, he disclaimed reliance on molecular mimicry, explaining in pertinent part "I referred to the molecular mimicry, but in this case, because she did not develop a specific autoimmune disease, I stayed only with the adjuvant as the cause of the ASIA syndrome." (Tr. 221.) He indicated "currently we remain with ASIA syndrome and the *potential molecular mimicry in the future*." (*Id*. (emphasis added).) Thus, respondent's counsel sought to confirm, as Dr. Shoenfeld appeared to state, that the theory of causation is based on the adjuvant alone without molecular mimicry. (Tr. 222.) But in response to that question, Dr. Shoenfeld was not willing to let molecular mimicry go. He contended that "molecular mimicry may indicate – a specific sign or symptoms." (*Id*.) However, he continued "I didn't need to analyze the molecular mimicry here, and I just said that it's a combination of the adjuvant *plus molecular mimicry*, when the adjuvant is the reason for the adjuvant-induced autoimmune syndrome." (*Id*. (emphasis added).) Given this answer, respondent then sought to further clarify whether or not Dr. Shoenfeld was opining that there was molecular mimicry in this case with components of the vaccine at issue. (Tr. 222-23.) He explained:

> *[y]ou cannot say for sure in this case if molecular mimicry is not involved* in this case; therefore, *I raised also the possibility of the molecular mimicry*. I have explained how autoimmune disease are induced. You need the adjuvant. You are at a stage of the ASIA syndrome, and then, eventually, you develop a specific autoimmune disease. Therefore, *you cannot neglect the impact of molecular mimicry in this case*.

(Tr. 223 (emphasis added).) Asked to clarify if he was stating that some of petitioner's own symptoms were evidence of molecular mimicry he indicated that, for example, "when the nerves are involved, you can find molecular mimicry. We have shown it in the past. If the eye is involved, the dry eyes and dry mouth, we can find molecular mimicry." (Tr. 223.) However, when then pressed to link this to petitioner specifically, he responded

> I am not saying that it is a result. *I said a potential of molecular mimicry.* And actually, if you take all of the symptoms – so, for instance, the small fiber neuropathy can be the result of molecular mimicry. The blurred vision that she had can be a molecular mimicry result. *I said 'can be.'* And also the arthritis can be a molecular mimicry. So there are different signs and symptoms that can be *the combination of the adjuvant plus the molecular mimicry*.

(Tr. 223-24 (emphasis added).)

This testimony is at best confusing, with Dr. Shoenfeld attempting to simultaneously rely upon and not rely upon molecular mimicry and expressing it at turns as either a present or future concern, but it does clearly illustrate why ASIA does not meet the evidentiary standards of this program. It must be noted, of course, that molecular mimicry is not the only possible mechanism of autoimmunity and, in any event, petitioner is not obligated to demonstrate a mechanism of injury. *Knudsen*, 35 F.3d at 549. She is, however, obligated to state a sound and reliable theory of causation that goes beyond what is merely "possible." *Boatmon v. Sec'y of Health & Human Servs.,* 941 F.3d 1351, 1360 (Fed. Cri. 2019). Here, Dr. Shoenfeld's testimony reveals that, when pressed, he cannot and will not opine that petitioner's own symptoms are themselves confirmation of autoimmunity (at least as discussed as molecular mimicry). Rather, his actual opinion is that autoimmunity cannot be entirely excluded ("[y]ou cannot say for sure . . . it is not involved") because some of petitioner's symptoms "can be" associated with autoimmunity because they have been documented in other contexts as symptoms of conditions that do involve molecular mimicry – conditions that petitioner does not have. This is far, far closer to the type of merely "possible" or "plausible" causal opinion rejected by the Federal Circuit in *Boatmon*, than it is to anything approaching a sound and reliable scientific explanation. *Boatman,* 941 F.3d at 1360. It reveals the idea of reliance on ASIA for those who do not have defined autoimmune conditions to be entirely speculative.

Third, even if the initial starting premise for ASIA were sound, respondent's experts are also persuasive in explaining that the subsequent exploration of the concept is deeply flawed. In particular, the diagnostic criteria are vague, overbroad, and lack any kind of meaningful validation. Respondent's experts are not exaggerating when they say that virtually anyone could be diagnosed with ASIA. (Ex. A, p. 3; Ex. J, p. 6.) In her post-hearing brief, petitioner stresses that Dr. Shoenfeld provided testimony indicating that he understands the diagnostic criteria in a narrower sense than respondent's experts asserted. (ECF No. 195, p. 18.) Importantly, however, respondent's experts have applied a plain reading of the diagnostic criteria itself. Thus, petitioner's argument seeks to solve one problem (overbreadth) by highlighting another (vagueness). In fact, Dr. Shoenfeld testified that he is still tinkering with the diagnostic criteria (Tr. 140; *see also* Tr. 126-32), which would seem to suggest they should be viewed as preliminary at best.

Dr. Shoenfeld purports to have substantiated ASIA in two ways – a review of a registry of ASIA patients and citation to a number of animal model studies. Neither is persuasive. There is a limit to the utility of animal models generally. Moreover, respondent's experts have documented substantial criticism of the actual animal studies at issue. (Ex. J, p. 9; Ex. A, p. 9-10, 12; Reeves et al., *supra,* at Ex. A, Tab 18; Cruz-Tapias et al., *supra,* at Ex. 117; Israeli et al., *supra,* at Ex. 111; Verdier et al., *supra,* at Ex. A, Tab 25.) Respondent's experts' criticisms of the ASIA registry (and resulting papers) are also well-taken.

In her post-hearing brief, petitioner seeks to refute Dr. Rose's particular contention that that ASIA registry is circular – bringing subjects into the registry because they have ASIA and then using the fact that they meet the diagnostic criteria to validate the criteria. (ECF No. 195, p. 22 (citing Tr. 328-29).) Petitioner acknowledges that Dr. Shoenfeld's papers regarding the ASIA registry do not compare patients to controls or review a randomized sample but contends that Dr. Rose's criticism "misses the point" because the purpose of the registry is "to better understand the link between the different adjuvant subtypes and the spectrum of inflammation against self." (ECF No. 195, pp. 23-24 (quoting Watad et al., *supra,* at Ex. 122, p. 2).) But this begs two critical questions – whether the link has been established in the first place and, if so, whether the registry is an effective way of enhancing understanding of that link. The registry appears designed to incorporate the same selection bias Dr. Whitton observed with respect to the prior MMF studies. Petitioner contends that "Dr. Shoenfeld and his colleagues exercised good clinical judgment when determining which patients were admitted into the registry, looking at the whole patient and record when making an ASIA diagnosis. (ECF No. 195, p. 25.) However, this is incorrect. Dr. Shoenfeld testified that he never looked at any patient's medical records when compiling the registry. (Tr. 212.) And, in any event, Dr. Shoenfeld's own care in selecting cases is of no moment if the design of the study itself incorporates a selection bias.

Dr. Shoenfeld is also unpersuasive in causally linking alum in the Tdap vaccine to any injury beyond an isolated MMF lesion at the injection site. Much of Dr. Shoenfeld's discussion regarding vaccine-causation overlaps with his discussion of post-vaccination phenomenon as one of the four "legs" of ASIA, and so the criticisms of his approach to ASIA remain relevant to this secondary question. To the extent he presents specific information regarding the Tdap vaccine, he relies heavily on the toxicity and biopersistence of alum. (Ex. 97, pp. 26-27.) However, Dr. Cetaruk and Dr. Whitton are both persuasive on this point, with Dr. Cetaruk citing several studies showing that MMF lesions are consistent with how the body handles aluminum generally and are not pathologic (Ex. A, pp. 8-10) and Dr. Whitton providing further discussion refuting the extension of MMF lesion findings to any broader systemic disorder (Ex. J, pp. 16-17).

In light of all of this, and based on the record as a whole, petitioner is not persuasive in identifying ASIA as a sound and reliable means of identifying the presence of an autoimmune injury in those who are not suffering a defined autoimmune condition. Given that petitioner did not suffer any recognized autoimmune condition, this is fatal to petitioner's *Althen* prong one showing. *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1345 (Fed. Cir. 2010) (explaining that "[b]ecause causation is relative to the injury, a petitioner must provide a reputable medical or scientific explanation that pertains specifically to petitioner's case.") Assuming arguendo that petitioner did establish the presence of autoimmunity, the next question would be whether Dr. Shoenfeld provided a sound and reliable explanation demonstrating that the alum contained in a Tdap vaccine is a relevant environmental trigger that can kick off that autoimmune process. Here too, petitioner falls short of her

burden of preponderant proof. Accordingly, petitioner has failed to satisfy her burden under *Althen* prong one.

b. *Althen* prong two

The second *Althen* prong, requiring proof of a logical sequence of cause and effect, is usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant,* 956 F.2d at 1148. In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. *See* Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing ... that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted").

Petitioner's medical history demonstrates a lengthy search for a unifying diagnosis for her constellation of symptoms, but none was found. Thus, as noted above, there is no debate that petitioner does not have any defined autoimmune condition. (Tr. 221 (Dr. Shoenfeld testifying petitioner did not develop any specific autoimmune disease).) Nor is there any need to resolve any of the finer points as to whether petitioner's clinical history fits within the ASIA rubric advanced by Dr. Shoenfeld. As discussed pursuant to *Althen* prong one, that rubric does not constitute any sound and reliable basis for asserting the presence of autoimmunity.

Reliance on petitioner's positive antihistone antibody test is not enough to establish the presence of autoimmunity standing alone. Although Dr. Shoenfeld suggested that the presence of antihistone antibody levels confirmed an autoimmune process at work, Dr. Rose testified that antihistone antibodies are also found in perfectly healthy subjects, a point that Dr. Shoenfeld ultimately conceded on cross examination. (Tr. 203, 281-87.) Additionally Dr. Rose explained that the antihistone antibody result must be viewed in relation to the ANA result. (Tr. 281-87.) Petitioner tested negative for ANA. (Ex. 11B, pp. 6-7, 27, 41, 47; Ex. 31, p. 32.)

Dr. Shoenfeld, in accordance with some of petitioner's treating physicians, opines petitioner suffered a post-vaccine Arthus reaction, but he did not suggest that such a reaction explains her entire presentation. Rather, he explained that this would be a local reaction only and that petitioner's symptoms "vary and change over time." (Ex. 97, p. 28.) Respondent's experts also opined that an Arthus reaction, if even present,

would be local and temporary. (Ex. J, p. 19; Tr. 276-77.) Additionally, Dr. Whitton further explained that an Arthus reaction represents an immunologic process that is fundamentally different than the immunologic process underlying ASIA. (Ex. J, p. 21.) Nor has Dr. Shoenfeld persuasively addressed how an Arthus reaction would itself transform into an autoimmune process.

c. *Althen* prong three

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan*, 539 F.3d at 1352. The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 Fed. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

Here, petitioner experienced an alleged Arthus reaction shortly after vaccination and then began seeking treatment for what would become a broader constellation of symptoms within ten days post vaccination. (Ex. 5, pp. 1-4.) She first reported fatigue approximately one-month post-vaccination. (Ex. 6, p. 2.) Dr. Shoenfeld asserted that this falls within the typical period of up to 42 days for onset of an autoimmune condition. (Tr. 172.) However, as discussed above, petitioner has failed to preponderantly establish under *Althen* prong one that the broader ASIA concept provides any evidence of autoimmunity in the absence of an otherwise defined autoimmune condition. Additionally, petitioner has failed to preponderantly demonstrate pursuant to *Althen* prong two that she suffered autoimmunity either in the form of a defined autoimmune condition or under the broader ASIA umbrella. Accordingly, she has no basis for relying on the timing of autoimmune mechanisms to establish a temporal relationship.

Petitioner has also failed to demonstrate under *Althen* prong one that the ASIA concept in itself otherwise provides any reliable theory of causation. Therefore, she also by definition fails to establish that there is any medically-acceptable temporal relationship between vaccination and injury pursuant to her theory. But, in any event, respondent's experts are also persuasive in further criticizing Dr. Shoenfeld for seeking to establish a causal window for ASIA beyond what is reasonable. (Ex. A, p. 12; Ex. J, pp. 6-7.) For example, Dr. Shoenfeld relies on Ozawa, et al., as showing an onset period of up to 1,532 days. (Ex. 97, p. 25 (citing Ozawa et al., *supra,* at Ex. 108).) I have previously addressed the Ozawa study and have found it unpersuasive with respect to establishing what constitutes an appropriate period of onset. *Balasco v. Sec'y of Health & Human Servs.,* No. 17-215V, 2020 WL 1240917, at *30 (Fed. Cl. Feb.

14, 2020). Dr. Whitton also persuasively rebuts Dr. Shoenfeld's reliance on a study purporting to demonstrate late onset GBS in the face of a seminal study showing that post-vaccination incidences of GBS return to background rates within weeks. (Ex. J, p. 7.)

VI. Conclusion

During the hearing, petitioner explained that she has taken significant steps toward recovery, but that her condition has had a profound impact on her life. Petitioner does have my sympathy for what she has endured and nothing in this decision is intended to minimize what petitioner has experienced. However, for all the reasons discussed above, after weighing the evidence of record within the context of this Program, I find that petitioner has failed to present preponderant evidence showing that she suffered any injury caused-in-fact by her June 18, 2011 Tdap vaccination. Accordingly, this case is hereby **DISMISSED**.[38]

IT IS SO ORDERED.

s/Daniel T. Horner
Daniel T. Horner
Special Master

[38] In the absence of a timely-filed motion for review of this Decision, the Clerk of the Court shall enter judgment accordingly.