In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 17-480V

(to be published)

E.S,	*	
	*	Filed: November 13, 2020
Petitioner,	*	
	*	Chief Special Master Corcoran
v.	*	
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Human Papillomavirus Vaccine; Type I Diabetes; Influenza Vaccine; Narcolepsy; Postural Orthostatic Tachycardia Syndrome; Chronic Fatigue; Reliable Theory; Aggravation of Diabetes; Onset
	*	
	*	
	*	
Respondent.	*	
	*	
	*	

Robert J. Krakow, Law Office of Robert J. Krakow, New York, NY, for Petitioner.

Sarah Duncan, U.S. Department of Justice, Washington, D.C., for Respondent.

DECISION[1]

On April 4, 2017, E.S filed this action seeking compensation under the National Vaccine Injury Compensation Program (the "Program").[2] ECF No. 1; *see also* Amended Petition, filed Apr. 4, 2017 (ECF No. 64-1). Petitioner alleges that she suffered autonomic dysfunction, manifesting in a wide variety of conditions and symptoms (including headaches, chronic fatigue syndrome ("CFS"), postural orthostatic tachycardia syndrome ("POTS") and small fiber neuropathy ("SFN"), after receipt of the human papillomavirus ("HPV") and hepatitis A vaccines in July 2014, with the same symptoms plus a cardiac condition and aggravation of preexisting diabetes mellitus after receiving another HPV vaccine dose along with the influenza ("flu") vaccine in August 2015.

[1] This Decision will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means the Decision will be available to anyone with access to the internet**. As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the published Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen (14) days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire Decision will be available to the public in its current form. *Id.*

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

Id. at 1. After the filing of multiple expert reports, I invited Respondent to request the claim's dismissal, and the matter is now fully briefed. Resp.'s Brief in Support of Dismissal, filed Sept. 13, 2019 (ECF No. 103-1) ("Mot."); Pet.'s Brief in Opposition of Dismissal, filed Dec. 2, 2019 (ECF No. 112) ("Opp."); Resp.'s Reply Brief in Support of Dismissal, filed Feb. 4, 2020 (ECF No. 114-1)("Reply"); Pet.'s Sur-Reply Brief in Opposition of Dismissal, filed Apr. 2, 2020 (ECF No. 118) ("Sur-Reply").

Petitioner's medical history establishes that she has experienced a variety of conditions and symptoms, but many of her alleged injuries (in particular POTS and myocardial ischemia) are not preponderantly established, nor are all related, as she seems to assume. In addition, those symptoms she *can* establish having experienced appear attributable to her preexisting diabetes, or occurred too long after vaccination to be deemed causal. And overall, Petitioner's theories—that the HPV vaccine or flu vaccine can either cause or aggravate (a) dysautonomia and/or POTS, (b) small fiber neuropathies, (c) chronic fatigue syndrome, (d) narcolepsy, or (e) diabetes—reiterate contentions that have rarely been successful in the Program, and are medically and scientifically unreliable based upon the evidence offered in this case. I therefore find that Petitioner's claim merits no further consideration, and dismiss it on the basis of the existing filings.

I. Factual Background

A. *Pre-Vaccination Health History*

Ms. E.S. was born on January 2, 1996 (and was thus eighteen years old when she received the first vaccines at issue in this case). Ex. 1 at 1. She was a strong student by her accounts, and an accomplished athlete as well, who swam competitively and won top positions at regional swim competitions during high school. Ex. 103; Ex. 43; Ex. 44. Ms. E.S. held summer employment as a lifeguard and was reportedly considered for membership on college swim teams, although it is unclear from the filed documentary evidence if she did in fact swim for the university she ultimately attended (Villanova University). Ex. 103; Ex. 104 at 2.

The record, however, also reveals that Petitioner had her share of medical problems before the relevant vaccinations, and some of these bear on her claim. In particular, Ms. E.S. was diagnosed with type I diabetes mellitus ("DM-1") when she was five years old (although she had good control of it in the time before receiving the first vaccines alleged to have injured her).[3] Her medical records also reflect problems with persistent lower back pain, intermittent hematuria,[4] flank pain, kidney stones, surgery for hemorrhagic right ovarian cyst, irregular menses, selective

[3] *See* Mot. at 3 n.7 ("Petitioner's DM-1 was under fair control prior to receiving the first HPV vaccine with a hemoglobin A1c ("HbA1c") typically in the range of 7-8% (ideal for a child being <7%) since 2008") (citing Ex. 19 at 81–110).

[4] Hematuria (or erythrocyturia) is blood (erythrocytes) in the urine. *Dorland's Illustrated Medical Dictionary* 824 (33rd ed. 2020) (hereinafter, "*Dorland's"*).

immunoglobulin A deficiency, and rheumatoid arthritis. Ex. 19 at 50, 54, 66, 69; Ex. 4 at 152; Ex. 3 at 5, 8; Ex. 23 at 5.

Additionally, there are several documented instances from the record in which Ms. E.S. sought emergency treatment for ambiguous complaints that did not result in any significant findings or explanations. Thus, in July 2011, Petitioner visited the emergency room complaining of two days of mid-sternal chest pain, weakness, and shortness of breath. Ex. 17 at 198–204. However, her vital signs, chest x-ray, and EKG[5] were normal, her chest pain resolved, and she was discharged. *Id.* at 198–204, 207, 210. Later on, in the fall of 2012 (now about two years before her relevant vaccinations), Ms. E.S. went two more times to the ER complaining of flank pain. Ex. 4 at 152–196. At these visits she recounted similar episodes in the past and a prior history of kidney stones. *Id.* at 152, 159. She also reported that blood in her urine was (at least at that time) a "chronic problem." *Id.*

Petitioner reported several health problems to her pediatrician in the months before her July 2014 receipt of the HPV and hepatitis A vaccines. She complained of recurring headaches and sore throat in the fall of 2013. Ex. 3 at 16. A strep test came back negative and her treater diagnosed her with adenopathy and acute pharyngitis. *Id.* She was directed to return if symptoms worsened. *Id.* In March 2014, she visited her pediatrician, Dr. Rebekah Lipstein, for nausea and sore throat, and was diagnosed with a viral infection. Ex. 3 at 13–15. She weighed 159 pounds at this visit. *Id.* Then, in April 2014 she went to the ER again, this time complaining of blood in her urine, back and flank pain, and hyperglycemia. Ex. 4 at 117–31. Her blood glucose was 349 (an extremely high level for a diabetic[6]), she had glucose and ketones in her urine, and she now weighed 150 pounds. *Id.* at 118–20.

B. *July 15, 2014: Petitioner Receives HPV and Hepatitis A Vaccines*

At a well visit with Dr. Lipstein on July 15, 2014, Ms. E.S. received the first vaccines at issue—the HPV and hepatitis A vaccines. Ex. 3 at 8–12. She weighed 164 pounds at this visit, and a urine dipstick test showed trace glucose (an indication of elevated serum glucose levels). *Id.* at 11. The record reveals no immediate vaccine reaction. In fact, as indicated below, there was a subsequent, several-month gap before Petitioner again sought medical treatment. Thus, there is no evidence from this period that she was experiencing symptoms of any kind.

Ms. E.S. began college in the fall of 2014. On September 2, 2014, she visited the student health center for treatment of increased blood sugars that she had observed from her own self-

[5] Electrocardiogram ("EKG" or ECG) is a graphic tracing of the variations in electrical potential caused by the excitation of the heart muscle and detected at the body surface. *Dorland's* at 593.

[6] In children two years to adult, normal "casual" (meaning any time of day) blood glucose levels are ≤ 200 mg/dL or 11.1 mmol/L. *Mosby's Manual of Diagnostic and Laboratory Tests* 253 (6th ed. 2018) (hereinafter, "*Mosby's*").

monitoring, and a sore throat. Ex. 14 at 88–90. Petitioner tested positive for group A streptococcus and was prescribed antibiotics. *Id.* However, there is no evidence from this particular record that any treater associated her strep infection or diabetes resurgence with her July vaccinations (which had been administered nearly seven weeks before). Later that same month, from September 22–24, 2014, Ms. E.S. visited the health center multiple times for high glucose levels and a cough (later diagnosed as bronchitis). *Id.* at 84–87. About ten days later, on October 2, 2014, she visited the emergency room ("ER") at Bryn Mawr Hospital for an abnormal glucose level of 338. Ex. 9 at 3–12. She denied having previous similar symptoms (despite her history in the immediate weeks prior), and although she complained of headache and sinus pressure, she did not identify the onset of these symptoms occurring much before the ER visit. *Id.* Four days later, on October 6, 2014, Petitioner visited her university health center for nausea and elevated blood sugars. Ex. 14 at 70. Meanwhile, more than ten weeks had passed from the time in July when Petitioner received the relevant vaccines.

No records have been filed establishing any additional visits by Ms. E.S. to medical treaters in November 2014. Then, on December 5, 2014, Petitioner made a second visit to the Bryn Mawr ER, now complaining of constant vomiting and diarrhea that she reported began about one and a half weeks before her visit (late-November). Ex. 9 at 27–35. This was the first time in the medical record Petitioner reported this combination of symptoms and based on her presentation she was diagnosed with gastroenteritis. *Id.* Throughout December, Petitioner visited the Villanova student health center multiple times for increased glucose levels, diarrhea, vomiting, and abdominal pain. *See, e.g.*, Ex. 14 at 68–69; Ex. 17 at 12–21, 102–05.

On December 11, 2014, Petitioner saw Dr. Keith Benkov, a gastroenterologist. Ex. 11 at 1–2. She reported that in late September 2014 she had experienced several viral infections, high blood sugars, and back pain. *Id*. She also told Dr. Benkov that in November 2014 she began vomiting daily and having loose stools. *Id.* Dr. Benkov ordered labs, doubled Petitioner's Protonix[7] dose, considered performing an endoscopy, and took Petitioner's weight (now 172 pounds). *Id.* Petitioner's celiac and thyroid profiles were negative, and she was also negative for thyroid antibodies, FSH, testosterone, estradiol, and DHEAS.[8] *Id.* at 6. The records from this time reflect some treater concerns that Petitioner may have suffered from a pancreatic condition, although this was not confirmed. *Id.* at 10. Later that same December, Ms. E.S. was again hospitalized after complaining of persistent headaches, and testing performed on her revealed elevated liver enzymes plus some evidence of a possibly enlarged liver. Ex. 17 at 97, 99, 113. Dr. Benkov concluded that

[7] Protonix is the trademark for preparations of pantoprazole sodium. *Dorland's* at 1513. Pantoprazole sodium is a proton pump inhibitor used in the treatment of erosive esophagitis associated with gastroesophageal reflux disease. Pantoprazole Sodium, *Dorland's Online Medical Dictionary*, https://www.dorlandsonline.com/dorland/definition?id=36645&searchterm=pantoprazole+sodium (last visited Oct. 9, 2020).

[8] Dehydroepiandrosterone sulfate ("DHEAS") is a steroid secreted by the adrenal cortex, the major androgen precursor in females; it is often present in excessive amounts in body fluids of patients with adrenal virilism. *Dorland's* at 476.

Petitioner had poor diabetic control as well as poor gastric emptying, and a fatty liver. *Id.* at 105.

On January 6, 2015, Petitioner's glycated hemoglobin (HbA1c)[9] level was 9.8% and 10.2% on different readings taken that day—both highly elevated and evidence of ongoing diabetes. Ex. 19 at 114, 119. Later that month, on January 27, 2015, she visited Dr. Elizabeth Wallach, an endocrinologist. *Id.* at 28–31. Petitioner's mother was concerned about Ms. E.S. 's increasing HbA1c levels (9.8% that day) and increasing weight (12 pounds since she began college). She privately discussed with Dr. Wallach that Petitioner was eating a lot and not always testing her blood sugar. *Id.* at 29. Dr. Wallach felt Petitioner was doing well on her insulin pump, but discussed the possibility of taking her off it (something Petitioner expressed a desire to do). *Id.* at 28.

C. *Additional Vaccines Deemed Causal and Onset of Novel Symptoms*

More than three months passed before Ms. E.S. again required medical treatment. On May 1, 2015, Petitioner sought emergency room treatment at Bryn Mawr Hospital for the fourth time, complaining of abrupt onset of right flank pain, nausea, and vomiting. Ex. 9 at 54. Petitioner's blood glucose at the point of care was 129 mg/dL, and urine glucose was 500 mg/dL. *Id.* at 70. Three months passed before Petitioner's next doctor visit which was for her annual pediatric exam on August 19, 2015. Ex. 3 at 5–7. She now weighed 168 pounds, and a urine dipstick showed 3+ blood and no glucose.[10] *Id.* During this exam, she received her second HPV vaccine dose, and a flu vaccine. *Id.* Petitioner's filed medical history reveals she had in the past repeatedly received the flu vaccine with no complications. Ex 2; Ex. 17 at 185. There is no evidence of any immediate/close-in-time reaction to these vaccinations.

Over the fall of 2015 and into early 2016, Ms. E.S. continued to seek emergency care on a regular basis, with most treater visits seemingly oriented toward addressing diabetes-related issues or complications. Approximately two months passed since the second set of vaccinations before Petitioner had two ER visits. At the first visit (October 10, 2015), she complained of nausea, vomiting, loose stools, and high blood sugar. Ex. 9 at 79, 81–82. However, she had a normal EKG, and the discharge assessment was nausea and vomiting. *Id.* at 83. She was instructed to drink plenty of fluids, avoid alcohol and certain over-the-counter pain relievers, and to adjust her insulin pump

[9] In adults, about 98 percent of the hemoglobin in the red blood cell is hemoglobin A. About seven percent of hemoglobin A consists of a type of hemoglobin (HbA_1) that can combine strongly with glucose in a process called glycosylation. As the red blood cell circulates, it combines its HbA_1 with some of the glucose in the bloodstream to form glycohemoglobin (GHb). The amount of GHb depends on the amount of glucose available in the bloodstream over the RBC's 120-day life span. Therefore, determination of the GHb value reflects the average blood sugar level for the 100- to 120-day period before the test. The more glucose to which the RBC is exposed, the greater the percentage. *Mosby's* at 266.

[10] Urine reagent strips or dipsticks are used for the estimation of glucose, albumin, hemoglobin, and bile concentrations, as well as urinary pH, specific gravity, protein, ketone bodies, nitrates, and leukocyte esterase. *Mosby's* at 909. Dipstick testing is considered preliminary or for screening. *Id.* Often more definitive and quantitative studies are necessary to confirm the results. *Id.*

as directed by her diabetes physician. *Id.* Similarly, on her second ER visit (October 21, 2015) she presented with high blood sugar and abdominal pain occurring since the prior visit. Ex. 12 at 1, 10, 75. A CT scan of the abdomen and pelvis was performed with no significant findings. *Id.* Petitioner's treater noted that her symptoms sounded like acid reflux and that she had a positive response to such treatment. *Id.* at 36.

Vomiting and diarrhea prompted a third ER visit in early December 2015, and although Petitioner's blood sugar was now a bit lower, she was diagnosed with hypokalemia,[11] and instructed to follow-up with her GI doctor about her visit and her potassium levels. Ex. 9 at 106, 108, 109. Petitioner reported a similar constellation of symptoms at a January 10, 2016 visit. Ex. 7 at 5, 8–9. None of the relevant treaters proposed that Petitioner's receipt of the second HPV dose or flu vaccine in August 2015 might have played a role in Petitioner's illness, however, treaters did consider her high blood sugar as causal. Ex. 12 at 39.

Petitioner again sought specialized treatment in early 2016. On February 16, 2016, she saw Dr. David Lefkowitz, a cardiologist, for evaluation of chest pain. Ex. 5 at 1–4. She reported the pain she was experiencing was "generally exertional" in nature, and that she also suffered from occasional night sweats, decreased exercise tolerance, new onset migraines, and episodes of tachycardia not experienced in the past.[12] *Id.* She also claimed that she had felt poorly since receiving the HPV vaccine, two other vaccines, and a tuberculosis skin test. *Id.* at 1.

A physical exam performed by Dr. Lefkowitz showed regular heart rhythm, a mid-systolic click, absent jugular venous pressure, normal carotid upstrokes and no lower extremity edema.[13] Ex. 5 at 2. Pericardial[14] thickening was noted on Petitioner's echocardiogram, and an EKG showed "sinus rhythm, inferior and lateral repolarization abnormality compatible with pericarditis[15] versus early repolarization." *Id.* at 3–4, 13. A stress EKG revealed distal inferoseptal hypokinesis[16] at peak stress, which (as Dr. Lefkowitz noted) might suggest a possible jeopardized myocardium,[17]

[11] Hypokalemia is abnormally low potassium concentration in the blood resulting from excessive potassium loss by the renal or the gastrointestinal route, from decreased intake, or from transcellular shifts. *Dorland's* at 891.

[12] Tachycardia is excessive rapidity in the action of the heart and is usually applied to a heart rate above 100 beats per minute in an adult. *Dorland's* at 1838.

[13] Edema is the presence of abnormally large amounts of fluid in the intercellular tissue spaces of the body, usually referring to subcutaneous tissues, which may be localized. *Dorland's* at 587.

[14] The pericardium is the fibroserous sac that surrounds the heart and the roots of the great vessels, comprising an external layer of fibrous tissue and an inner serous layer. *Dorland's* at 1391.

[15] Pericarditis is inflammation of the pericardium. *Dorland's* at 1391.

[16] Hypokinesis or hypokinesia is abnormally decreased mobility/motor function or activity. *Dorland's* at 891.

[17] The myocardium is the middle and thickest layer of the heart wall, composed of cardiac muscle. *Dorland's* at 1204.

although the stress test was cut short when Petitioner complained of chest pain. *Id.* at 2, 4, 15. The positive stress test prompted the doctor to order cardiac CT angiography,[18] but that test produced normal results. *Id.* at 16–18 (performed on March 3, 2016). There was no immediate follow-up with Dr. Lefkowitz (moreover, Petitioner did not return to him for an entire year).

On February 17, 2016, Petitioner visited Dr. Benkov again (whom it does not appear from the records she had seen for more than a year). Ex. 11 at 3. Although she reported experiencing less severe gastrointestinal issues overall, she still had occasional episodes of nausea, diarrhea, and vomiting. *Id.* Records from this visit establish that Petitioner's mother now expressed the view that Ms. E.S. 's symptoms were associated with the second HPV dose she had received in August 2015. *Id*. The medical record, as discussed above, does not support this conclusion. However, it does reveal that throughout this time period Ms. E.S. 's diabetes was not under good control. *Id*. Additionally, Petitioner reported that she continued to gain weight despite monitoring of her diet. *Id*. Moreover, Petitioner's mother informed Dr. Benkov that Petitioner's sister seemed to have gotten sick after receiving the HPV vaccine,[19] and that both sisters had developed pericarditis as a result. *Id.*

In contrast to the mother's statements, Dr. Benkov noted on exam that Petitioner "actually looked pretty well off." Ex. 11 at 3. However, she now weighed 177 pounds and her hemoglobulin A1C was elevated (9.8%), and remained so even when tested again in early March.[20] *Id.* at 3, 7; Ex. 19 at 145. An abdominal ultrasound revealed two non-obstructing stones in Petitioner's right renal collecting system. Ex. 11 at 10. Dr. Benkov noted that Petitioner's condition "could be some form of pancreatitis" and suggested doubling her current dose of Protonix. *Id.* at 1, 2.

On May 12, 2016, Ms. E.S. visited Dr. Edith Schussler, a Clinical Fellow in the Division of Allergy and Immunology at Icahn School of Medicine at Mount Sinai, for an immune dysfunction consultation. Ex. 23 at 5–8. The records from this visit include a condensed medical history, addressing her long-standing struggle with diabetes among other things. *Id*. at 5. The history also stated that beginning in the summer of 2014, Petitioner had started to experience repeated throat infections, cyclic vomiting (four times a day), diarrhea, racing heart, and fatigue. *Id*. During this period, her athletic pursuits were curtailed, she experienced extreme weight gain and poor glucose control, and she now claimed she had been diagnosed with a non-alcoholic fatty liver. *Id*.

Petitioner asserts she had improved the following summer, but then worsened after receiving

[18] Angiography is the radiographic visualization of blood vessels following introduction of contrast material; used as a diagnostic aid in such conditions as stroke syndrome and myocardial infarction. *Dorland's* at 83.

[19] *See* Opp. at 15.

[20] Petitioner visited the ER on March 2, 2016 for non-radiating, waxing and waning abdominal pain that was aggravated by menstruation diagnosed as a ruptured ovarian cyst. Ex. 14 at 13–14.

her second HPV vaccine in August 2015. She also reported "running in the 300-400 glucose range," but had better control after recently seeing her endocrinologist. Ex. 23 at 5. A physical examination was mostly normal, although Dr. Schussler recommended that Petitioner not get the Rubella or hepatitis B vaccines—the only two she needed at the time—while she was not feeling well. *Id*. at 7–8.[21] Dr. Schussler, based on HLA testing,[22] concluded that Petitioner did not appear to be a vaccine "non-responder," and that she should continue to be vaccinated in the future. *Id.* at 13.

At the end of May 2016, Petitioner visited Dr. John Wells for a neurologic evaluation. Ex. 24 at 6–7. She reported a number of medical problems within the last year. *Id*. at 6. Her primary neurological complaint was a headache sensation, which had been persistent since starting college and was characterized by constant pressure and "weird feelings in her head that come and go." *Id*. Ms. E.S. recounted the same general medical history post-2014 vaccinations, adding that she had taken a leave of absence from school starting in March 2016. *Id.* Her neurological exam and brain MRI/MRA were normal. *Id*. at 7 (MRI/MRA performed on June 27, 2016). Dr. Wells concluded that Petitioner had persistent headaches despite a normal neurological exam and a normal brain MRI/MRA, and suggested that she follow up with her cardiologist and endocrinologist and try therapy for her anxiety. *Id*. at 7 (MRI/MRA performed on June 27, 2016).

In August 2016, Petitioner followed up with Dr. Wallach, her endocrinologist. Ex. 19 at 2–3. She generally reported doing better, with an improved HbA1C level of 8.7%, down from more than 9%, and some weight loss. *Id*. at 2. Dr. Wallach noted that Petitioner was ready to go back to college after taking the prior semester off for health issues. *Id.* A treater thereafter (whom Petitioner first saw that spring—and hence long after the vaccinations in question) recommended that Petitioner not receive the flu vaccine again due to a "history of adverse reaction," although (as revealed by the record above) this assertion is not well-supported by either the bare medical record or any informed treater opinion not solely reliant on Petitioner's self-reported history. Ex. 15 at 1.

Petitioner obtained some mental health counseling in October 2016. Ex. 13 at 5–6. Later that same month, Petitioner visited Dr. Sanjeev Kothare at NYU's Langone Health System for evaluation of possible seizures and sleep problems. Ex. 22 at 5. Although this is the first time such symptoms are mentioned in Petitioner's medical record, she now reported daytime sleepiness and insomnia for the past *two years* (which would place onset in October 2014, or nearly three months after the first vaccines in dispute), plus sleep paralysis, vivid/violent dreams, panic attacks, and depressed mood—all of which she attributed to her receipt of the flu vaccine in 2015. *Id.* at 6;

[21] Notes from that visit also briefly discussed Petitioner's sister—who allegedly had her own reaction to the HPV vaccine and has filed a petition in the Program. Ex. 23 at 8 ("[t]here is some confusion about what the sister had, and what [Petitioner] has had: while racing heart was noted as ventricular tachycardia in the sister by a monitor, [Petitioner] who has similar complaints has not had this. . . . The relationship between the reactions to Gard[a]sil [sic] in the sisters, if any is also unclear").

[22] Human leukocyte antigen (HLA) testing is a blood test that identifies antigens on the surface of cells and tissues. *Mosby's* at 306–07. These antigens can identify patients who are allergic to certain medications or to confirm diagnosis of certain diseases in which the antigens are present. *Id.* at 306.

Statement of Pet., filed Apr. 14, 2017 (ECF No. 7-1), at 3.

Dr. Kothare noted a history of snoring, dry mouth, mouth breathing, leg twitching, abnormal arousals (sleep walking and confusional arousals), and daytime sleepiness were also present. Ex. 22 at 6. However, Petitioner had a normal neurological exam with no evidence of sensory deficits in response to light touch, pin prick, position, and vibration. *Id*. at 8. It was also noted (at a follow-up visit in December 2016) that there were no reported instances of cataplexy.[23] *Id.* at 11. As of the initial visit, Dr. Kothare diagnosed Petitioner with narcolepsy type 2, non-REM parasomnia, and REM sleep disorder. *Id*. at 9.

Petitioner underwent a nocturnal polysomnography test on November 21, 2016. Ex. 22 at 27. The results were interpreted to reveal the existence of mild sleep apnea and "upper airway resistance syndrome," both of which were considered treatable. *Id.* Then, in January 2017, Ms. E.S. had a multiple sleep latency test ("MSLT"). Ex. 36 at 33, 35. The results were deemed by Dr. Kothare to reveal "evidence of excessive daytime sleepiness" which "could be consistent with narcolepsy under the appropriate clinical circumstances," leading him to propose follow-up clinical confirmation. *Id.* at 35. Dr. Kothare noted mild obstructive sleep apnea but normal baseline oxygenation, normal CO_2, normal EKG, and no significant periodic leg movements. *Id.* at 24. Dr. Kothare saw Petitioner again in March 2017, and after review of the MSLT results and another exam, he again confirmed his earlier diagnosis of type 2 narcolepsy (i.e. without cataplexy). Ex. 36 at 46–50.

D. *2017 and Post-Filing Treatment*

In January 2017, laboratory results from CellTrend and GmbH were sent to Petitioner's mother. Ex. 16 at 1. Ms. E.S. was found to be positive for anti α-1-adrenergic antibodies and anti-muscarinic cholinergic receptor 4 antibodies.[24] Ex. 16 at 1. She was also "at risk" for anti-muscarinic cholinergic receptor 3 antibodies. *Id.*

On February 23, 2017, Petitioner saw Dr. Lefkowitz again, who expressed the view that the potentially cardiac-associated symptoms were *not* likely the product of coronary disease. Ex. 18 at 14 ("[s]he had a thorough workup which revealed ultimately that she had no evidence of coronary artery disease on CT angiography"). Dr. Lefkowitz concluded that any cardiac risk factors that Ms. E.S. faced were most credibly associated with her existing diabetes. *Id.* Petitioner still sought treatment for her overall complaints, however, with some treaters allowing the possibility of a link

[23] Cataplexy is a condition in which there are abrupt attacks of muscular weakness and hypotonia triggered by an emotional stimulus such as mirth, anger, fear, or surprise and is often associated with narcolepsy. *Dorland's* at 298.

[24] Dr. Steinman (one of Petitioner's experts) has referenced a recent study that associates certain autoantibodies, including adrenergic receptor antibodies, with ME/CFS and fibromyalgia. Steinman Second Report, filed on Jan. 14, 2019 (ECF No. 85-1), at 26. Dr. Steinman has also maintained that elevated muscarinic receptor antibodies are also associated with ME/CFS, POTS, CRPS, and fibromyalgia. *Id.*

to the HPV vaccine. *See, e.g.*, Ex. 19 at 3 (March 2017 visit to Dr. Wallach).

This case was subsequently initiated in April 2017, although the period thereafter continued to be punctuated by urgent care or emergency treater visits, as Petitioner grappled with the same overall constellation of symptoms that she had confronted since the fall of 2014. In May 2017, for example, Petitioner visited the ER for chest pain—described as sharp, mild, ongoing, and exacerbated by movement and palpitation. Ex. 33 at 57–71. An EKG showed possible left arterial enlargement but no evidence of ischemia. *Id*. at 65. Ms. E.S. was diagnosed with non-specific chest pain and hypoglycemia.[25] *Id*. at 71.

Four days later, on May 24, 2017, Petitioner returned to the ER. Ex. 33 at 24. She stated that "[s]he drank a lot and her insulin pump is going crazy." *Id*. On intake, Petitioner reported a tingling in her chest and chest pain for the last two days. *Id*. 24–25. Labs reported that Petitioner's blood alcohol level was 0.137,[26] and a urine screen was positive for cannabinoid. *Id*. at 17, 21, 40. An EKG mostly was normal but did detect a prolonged QT.[27] *Id.* at 8, 23. Petitioner was discharged and diagnosed with hypoglycemia and nausea. *Id*. at 11.

There is a lengthy records gap through January 2018, when Petitioner returned to the ER with abdominal, rectal, and chest pain with nausea. Ex. 34 at 1. An EKG test was borderline but showed normal sinus rhythm and a rightward axis. *Id*. at 72. A few months later, in April 2018, Petitioner sought more treatment for her purported narcolepsy and sleep issues. Ex. 102 at 1. Dr. Rodriguez, a board-certified sleep medicine specialist, noted that Petitioner had paralysis and hallucinations at night. *Id.* He recommended 0.25-0.5 mg of Clonazepam, and Petitioner was advised to follow up in three months. *Id.*

Then, in late June 2018, Ms. E.S. visited Dr. Susan Levine, a specialist in infectious disease and internal medicine. Ex. 98 at 27. A subjective exam showed weakness, fatigue, palpitations, upset GI, and numbness of lower extremities. *Id*. During an objective exam, Dr. Levine noted that Petitioner had "[n]euro-diminished sensory over L4/L5 and L5/S1 deformities; 5/+5 good motor strength in both lower extremities; [and] slightly diminished patellar reflexes bilaterally." *Id*.

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[25] Hypoglycemia is an abnormally diminished concentration of glucose in the blood, which may lead to tremulousness, cold sweat, piloerection, hypothermia, and headache; when chronic and severe it may cause central nervous system manifestations that in rare cases can even be fatal. *Dorland's* at 890.

[26] A blood alcohol concentration ("BAC") of 0.10-0.12 causes significant impairment of motor coordination, including balance, speech, vision, and control, as well as loss of judgment. Stanford University, Office of Alcohol Policy and Education, *What is BAC?*, https://alcohol.stanford.edu/alcohol-drug-info/buzz-buzz/what-bac (last visited Nov. 2, 2020). A BAC of 0.13-0.15 causes gross impairment of motor control, blurred vision, and major loss of balance, as well as dysphoria, which includes anxiety and restlessness. *Id.*

[27] Long QT syndrome ("LQTS" or "prolonged QT") is a heart rhythm condition that can potentially cause fast, chaotic heartbeats. These rapid heartbeats might trigger you to suddenly faint. Mayo Clinic, Long QT syndrome, https://www.mayoclinic.org/diseases-conditions/long-qt-syndrome/symptoms-causes/syc-20352518 (last visited Nov. 10, 2020).

Relying on the above, but also on prior test results, Dr. Levine assessed Ms. E.S. with inflammatory neuropathy, autonomic dysfunction,[28] gastroparesis, and endometriosis. *Id*. Notably, EMG and nerve conduction study tests performed on September 12, 2018 only supported a mild radiculopathy rather than true neuropathy. Ex. 49 at 27. Not long after this visit, Dr. Levine prepared the one-page report that Petitioner has submitted in support of her claim. Ex. 85.

Petitioner followed up with Dr. Levine in August 2018. Ex. 98 at 26. She now reported continuing daily weakness, fatigue, palpitations, worsening ability to function, and increased panic. *Id.* Dr. Levine assessed Petitioner with ME/CFS,[29] DM1, post-HPV vaccine onset of CFS symptoms, dysautonomia, and POTS.[30] *Id.* However, the record does not include evidence of confirmatory testing for the POTS diagnosis.

In the fall of 2018, Petitioner visited Dr. Russell Chin, a neurologist at Weill Cornell medicine, for "suspected neuropathy" upon referral by Dr. Levine. Ex. 49 at 1; Ex. 48 at 1. Dr. Chin ordered EMG testing and epidermal nerve fiber density testing via skin biopsy. Ex. 48 at 1; Ex. 49 at 27. Petitioner reported that since 2015, she had noticed some intermittent tingling sensations in her mid-chest region, and since early 2018 tingling and "chilled" sensations to her scalp, neck, and shoulders (complaints that, as the review of records to this date should reveal, are not especially reflected in her overall history). Ex. 49 at 2. Although Petitioner has claimed that Dr. Chin "suspected" she had progressing small fiber neuropathy in her body since 2015, Dr. Chin merely expressed the view that her symptoms were possibly related to other dysautonomic/autoimmune issues (such as her diabetes, inflammatory arthritis, or an IgA deficiency). Ex. 86 at 34–37. However, he ultimately acknowledged that the "[e]tiology of these symptoms is unknown." Ex. 49 at 7.

An EMG/nerve conduction study performed at this time suggested to Dr. Chin carpal tunnel and ulnar entrapment of the right arm, a mild radiculopathy of the lower extremities, but no evidence of neuropathy. Ex. 49 at 27–34. However, extensive laboratory tests for causes of neuropathy yielded normal results with the exception of Petitioner's known diabetes and elevated cholesterol levels. *Id.* at 21–26. The two skin biopsies performed at this time showed reduced sweat gland nerve fiber density and a reduced intra-epidermal nerve fiber density at one site. Ex. 48. A brain MRI

[28] The autonomic nervous system is the portion of the nervous system concerned with regulation of the activity of cardiac muscle, smooth muscle, and glandular epithelium; usually restricted to the two visceral efferent peripheral components, the sympathetic nervous system, and the parasympathetic nervous system. Autonomic nervous system, *Dorland's Medical Dictionary Online*, https://www.dorlandsonline.com/dorland/definition?id=111779 (last visited Oct. 26, 2020).

[29] People with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) have overwhelming fatigue that is not improved by rest. ME/CFS may get worse after any activity, whether it's physical or mental. Other symptoms can include problems with sleep, thinking and concentrating pain, and dizziness. Centers for Disease Control and Prevention, Myalgic Encephalomyelitis/Chronic Fatigue Syndrome, What is ME/CFS? (last visited Nov. 10, 2020).

[30] At a December 2018 follow-up Dr. Levine's assessment was ME/CFS and dysautonomia. Ex. 98 at 26.

performed on Ms. E.S. on September 24, 2018 revealed "a 4 X 4 X 3 mm nonenhancing lesion along the pituitary gland" and a "punctate focus of T2 hypointensity." Ex. 49 at 20. The radiologist who obtained the imaging deemed it to potentially "reflect the provided history of a pituitary adenoma,"[31] adding that no prior imaging was available to make any comparisons or further assessments. *Id.* at 21. I am unaware of any additional documents filed in this case relating to any subsequent exams or treatments conducted by Dr. Chin.

On August 12, 2019, Petitioner saw Dr. David S. Younger, a neurologist, for additional evaluation. Dr. Younger reviewed Petitioner's medical history and past studies as well as performed a physical examination. Ex. 105 at 3. The examination showed sensory loss, hyporeflexia, distal leg weakness, Romberg sign,[32] and tandem imbalance. *Id.* Upon review of past studies, Dr. Younger noted that a 2012 MRI showed degenerative changes. *Id.* Although, tests from 2016 appeared normal, the 2018 pituitary MRI studies suggested a microadenoma. *Id.* at 2. Dr. Younger recommended additional screening studies. *Id.* On November 7, 2019, Dr. Younger saw Petitioner for a follow-up visit. *Id.* at 6. Dr. Younger now reported that skin changes suggested possible vasculopathy. *Id.* Petitioner's neck and shoulder pain and chest discomfort suggested combined cervicogenic and autonomic disturbances. *Id.* Dr. Younger again recommended additional screening studies as well as a psychiatric assessment. *Id.*

II. Expert Reports and Other Evidence

Thirteen expert reports have been filed in this matter, totaling more than 200 pages of opinion. Hundreds, if not thousands, of pages in supporting medical research and literature have also been offered. As of today, Petitioner has presented six reports from three different experts, and Respondent has filed seven reports from four individual experts. Each expert, their credentials, and opinions are considered in turn.

A. *Petitioner's Experts*

1. Dr. Lawrence Steinman

Dr. Steinman prepared three reports in support of Petitioner's claim. Report, dated Mar. 2, 2018, filed as Ex. 39 (ECF No. 47-1) ("First Steinman Rep."); Report, dated Jan. 14, 2019, filed as Ex. 86 (ECF No. 85-1) ("Second Steinman Rep."); Report, dated Feb. 15, 2019, filed as Ex. 99 (ECF No. 90-1) ("Third Steinman Rep."). Dr. Steinman inconsistently focuses on different aspects

[31] A pituitary adenoma is a slow-expanding growth deemed benign in the vast majority of cases. Mayo Clinic, Pituitary Tumors, https://www.mayoclinic.org/diseases-conditions/pituitary-tumors/symptoms-causes/syc-20350548 (last visited Oct. 26, 2020).

[32] Romberg sign/syndrome, or facial hemiatrophy, is a condition of unknown etiology, characterized by progressive atrophy of the tissues of one side of the face, frequently with pigmentation disorders and alopecia. Sometimes it can spread to involve both sides of the face or the ipsilateral trunk, viscera, or limbs.

of Petitioner's case, depending on the date of his report and whether the report was reacting to the assertions of one of Respondent's experts.

Dr. Steinman currently serves as the chairman in immunology and professor in the departments of neurology, pediatrics, and genetics at Stanford University. Steinman Curriculum Vitae, filed as Ex. 40 (ECF No. 52-1) ("Steinman CV") at 1. He obtained his bachelor's degree from Dartmouth College before earning his medical degree from Harvard University. *Id.* He then completed his internship and residency in surgery, pediatrics, and pediatric and adult neurology at Stanford University. *Id.* He has also completed several fellowships in the area of immunology. *Id.* He is board certified in neurology, though much of his work in the field also involves immunological concepts and theories. *Id.* at 2. However, he has no demonstrated expertise in treating or diagnosing diabetes or conditions attributable to autonomic dysfunction.

a. *First Steinman Report*

In his first report, Dr. Steinman limited his opinion solely to whether the HPV vaccine doses Petitioner received in 2014 and 2015 and/or the flu vaccine from 2015, could have caused the narcolepsy and headaches Petitioner asserts she experienced. First Steinman Rep. at 1. He began by considering when such symptoms likely first manifested. Dr. Steinman opined that onset of Ms. E.S.'s headaches could be placed in early October 2014 (based on an ER note associated with that visit). Ex. 9 at 3. Other medical records, however, reveal that Petitioner complained of headaches well *before* her first HPV dose in July 2014. *Id*. at 30; Ex. 3 at 16 (headache listed among chief complaints on September 19, 2013). Onset of narcolepsy, in contrast, was by Dr. Steinman's admission harder to pinpoint. *Id*. at 30–31. The first mention of any sleep issues appears in an October 2016 record—where Petitioner reported that she had been experiencing such symptoms in the two-plus years since receiving the flu vaccine. *Id.* at 31. This contention is not only uncorroborated by the record but is partially in conflict with it (since Petitioner had received the flu vaccine in August 2015—hence only 14 months prior). Ex. 22 at 5.

Dr. Steinman proposed that Petitioner's narcolepsy could have been caused specifically by the HPV vaccine. First Steinman Rep. at 6. He relied on molecular mimicry as the biologic mechanism for how this occurred, basing this contention on what is known about how narcolepsy likely occurs. *Id.* at 22. Dr. Steinman explained that decreased levels of hypocretin[33] and/or abnormalities in hypocretin receptor 2 in the brain are scientifically understood to play a central role in the occurrence of narcolepsy. *Id*. at 8 (citing Ex. 39, references 9 and 10). Aberrant immune responses are thought to possibly explain such circumstances. First Steinman Rep. at 8 (discussing

[33] Hypocretin, also known as orexin, is "either of two neuropeptides (orexin A ad orexin B) produced in the hypothalamus and regulating behavior as well as the sleep-wake cycle." Orexin, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=35458 (last visited Aug. 13, 2020).

references 11–17). Decreased hypocretin neurotransmission is thought to be due to autoimmune-mediated destruction of hypocretin-containing neurons in the lateral hypothalamus. Ex. 39, Ref. 9, at 39.

One possible way the immune response could create conditions for narcolepsy would be where an antigen presenting to the immune system (whether from a wild virus or vaccine) might mimic "various components of the hypocretin pathway, including hypocretin itself and the HCRT-R2 receptor." First Steinman Rep. at 9. Dr. Steinman estimated the HPV vaccine could accomplish this—but to bulwark this contention he relied significantly on "BLAST" searches[34] he personally performed, looking for homology between HPV vaccine components and hypocretin pathway structures. *Id.*[35] In so doing, Dr. Steinman explained that his criteria for "a meaningful molecular mimic" relied on evidence of five or more amino acids that were identical (although fewer could also trigger a cross-reaction, and the amino acids did not in his view need to be identical in sequence). *Id.* (citing Exhibit 39, references 18–20).

Based on electronic database research performed specifically for this case, Dr. Steinman maintained that several proteins in the HPV vaccine had sufficient homology to hypocretin to have the potential to induce an autoimmune cross-reaction that would trigger narcolepsy. First Steinman Rep. at 11–22. For support, he referenced a study finding increased incidence of narcolepsy following receipt of the HPV vaccination. *Id*. at 25 (citing L. Arnheim-Dahlstrom et al., *Autoimmune, Neurological, and Venous Thromboembolic Adverse Events After Immunization of Adolescent Girls with Quadrivalent Human Papillomavirus in Denmark and Sweden: Cohort Study*, British Med. J. 1, 1–11 (2013), filed as Ex. 39, Ref. 24 (ECF No. 50-4) ("Arnheim-Dahlstrom")). However, Arnheim-Dahlstrom found no supporting associations between exposure to the quadrivalent HPV vaccine and autoimmune, neurological, or venous thromboembolic adverse events. Although associations for three autoimmune events were initially observed, on further assessment these associations proved weak, and not temporally related to vaccine exposure. Arnheim-Dahlstrom at 1. Dr. Steinman acknowledged that this observed increase did not reach a level of statistical significance—but proposed (based on his layman's understanding of the legal standards applicable to Vaccine Program cases) that it was sufficient to meet the preponderance test relevant to fact determinations in this case. First Steinman Rep. at 27.[36]

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[34] Basic Local Alignment Search Tool ("BLAST") is a medical/scientific internet resource that assists researchers in finding regions of similarity between biological sequences of amino acids. The program compares nucleotide or protein sequences to sequence databases and calculates the statistical significance. BLAST, U.S. National Library of Medicine, https://blast.ncbi.nlm.nih.gov/Blast.cgi (last visited Oct. 6, 2020).

[35] In other cases, Dr. Steinman has characterized the research undertaken to identify such homology as an "in silica" study—by which he means that he used a desktop or personal computer, and access to scientific databases, to identify the comparable amino acid sequences that he references to establish homology. *See, e.g.*, *Blackburn v. Sec. of Health & Hum. Servs.*, No. 10-410V, 2015 WL 425935, at *10 (Fed. Cl. Spec. Mstr. Jan. 9, 2015). This kind of research is clearly case-oriented, and is not equivalent to lab or clinical research that an expert might perform and/or rely upon for an opinion.

[36] In his second report, Dr. Steinman went to great lengths to cast doubt on the lack of statistical significance he had

In addition, Dr. Steinman generally seemed to embrace a loose timeframe for narcolepsy onset as medically acceptable—in effect suggesting that any onset "weeks to months" from the date of vaccination to the time Petitioner obtained a formal sleep test confirmed narcolepsy diagnosis was reasonable, since it was literally *after* the vaccines were administered in 2014 and 2015. *Id.* at 31. Dr. Steinman more specifically suggested that onset within eight months of vaccination would be a generally reasonable timeframe for narcolepsy to first manifest (relying on studies about the flu vaccine and narcolepsy). *Id*.

Further, Dr. Steinman opined that Petitioner's headaches were attributable to the HPV vaccine. First Steinman Rep. at 30. In support, he noted that the vaccine's package insert lists headaches as a frequent symptom (although it specifically envisions them as a *transient* response, likely occurring close in time to vaccination, and does not identify headache as a *chronic* post-vaccination concern). *Id*.; Gardasil [Package Insert]. Whitehouse Station, NJ: Merck & Co., Inc.; 2011, filed as Ex. 39, Ref. 7 (ECF No. 48-7) ("Gardasil Package Insert").

Dr. Steinman also noted the existence of "strong evidence that calcitonin-gene-related-peptide (CGRP) is involved in chronic headache, particularly migraine." First Steinman Rep. at 28. Based on sufficient evidence of homology between the antigenic components of the HPV vaccine and CGRP, Dr. Steinman reasoned that the vaccine might plausibly trigger an autoimmune cross-reaction sufficient to produce headaches. *Id.* at 28–29. The headaches could later become chronic, due to the fact that the vaccine's alum additive (used as an adjuvant, to cause a more robust immune response)[37] has been demonstrated to persist for up to a year (albeit in animal studies). *Id.* at 30 (citing Z. Khan et al., *Slow CCL2 Translocation of Biopersistent Particles from Muscle to Brain*, 11 BMC Medicine (2013), filed Mar. 5, 2018 as Ex. 39, Ref. 27 (ECF No. 50-7)). This, plus the fact that the immune response to HPV vaccine itself can be long-lasting, lent further support to his conclusion that chronic headaches could be propagated by the vaccine. First Steinman Rep. at 30 (citing C. MacIntyre et al., *Immunogenicity and Persistence of Immunity of a Quadrivalent Human*

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seemingly admitted in his first report about Arnheim-Dahlstrom's conclusions, making arguments about the mathematic guidelines used in evaluating whether a given statistical finding had significance that (by his own admission) exceeded his expertise. Second Steinman Rep. at 22–23.

[37] The argument that the alum adjuvant ingredient in a vaccine can remain in the body for extended periods of time post-vaccination, and thereafter cause or contribute to immunologic harm, is perilously close to a discredited theory often posed by unsuccessful petitioners, termed "ASIA," or "autoimmune/inflammatory syndrome induced by adjuvants." *See, e.g.*, *Yalacki v. Sec'y of Health & Hum. Servs.*, No. 14-278V, 2019 WL 1061429, at *24 n.30 (Fed. Cl. Spec. Mstr. Jan. 31, 2019), *mot. for review den'd*, 146 Fed. Cl. 80 (2019) (noting several prior decisions in which special masters rejected the ASIA theory as scientifically unreliable). The evidence that a vaccine's adjuvants can act in this manner (as opposed to merely increase the immunogenicity of the vaccine generally) is thin to none and has little acceptance in the medical community otherwise as a reputable theory. *See, e.g.*, *Rowan v. Sec'y of Health & Hum. Servs.*, No. 10–272V, 2014 WL 7465661 (Fed. Cl. Spec. Mstr. Dec. 8, 2014); *mot. for review den'd*, 2015 WL 3562409 (Fed. Cl. 2015); *D'Angiolini v. Sec'y of Health & Hum. Servs.*, No 99–578V, 2014 WL 1678145 (Fed. Cl. Spec. Mstr. Mar. 27, 2014), *mot. for review den'd*, 122 Fed. Cl. 86 (2015), *aff'd*, 645 F. App'x 1002 (Fed. Cir. 2016).

Papillomavirus (HPV) Vaccine in Immunocompromised Children, 34 Vaccine 4343, 4343–45 (2016), filed Mar. 5, 2018 as Ex. 39, Ref. 28 (ECF No. 50-8)).

b. *Second Steinman Report*

Dr. Steinman's second report was of comparable length to his first, but largely aimed at responding to counter-arguments (discussed in more detail below) that had been lodged by two of Respondent's experts. *See generally* Second Steinman Rep.

Dr. Steinman began by referencing some new research relevant to the biological processes underlying narcolepsy (specifically pertaining to the hypocretin pathway) that he maintained was additionally supportive of his previously-asserted opinion. Second Steinman Rep. at 1–4; D. LaTorre et al., *T cells in Patients with Narcolepsy Target Self-Antigens of Hypocretin Neurons*, Nature 1, 1–23 (2018), filed Jan. 14, 2019 as Ex. 87 (ECF No. 85-2) ("Latorre"). Latorre observed the existence of "peptides that attacked orexin [another term for hypocretin] and were found in the spinal fluid," and that these amino acid sequences showed homology with HPV vaccine antigens (based on Dr. Steinman's BLAST searches). Second Steinman Rep. at 1–3; Latorre at 5[38]. As a result, Dr. Steinman concluded that "this degree of homology is sufficient to induce clinically relevant neuroinflammation." Second Steinman Rep. at 3. He later emphasized literature he felt underscored the legitimacy of BLAST searches to establish potentially significant homologies (for purposes of establishing the potentiality of pathologic autoimmune cross-reactions). *Id.* at 16–18.

Next, Dr. Steinman attempted to rebut arguments attacking various aspects of his theory. He acknowledged that Petitioner did not have (and was never diagnosed with) type I narcolepsy—the kind that is more definitively understood to have an autoimmune character. Thus, she was not positive for the HLA molecules most associated with type I narcolepsy, and had otherwise not been tested for hypocretin levels either. Second Steinman Rep. at 7. However, Dr. Steinman still contended that type II narcolepsy could have an autoimmune character or etiology—although in doing so he devoted many pages of his second report to a detailed defense of research he had previously cited, or had been involved with, rather than citing evidence that more directly supported his opinion. *Id.* at 5–15. At bottom, Dr. Steinman proposed that the rarity of a vaccine-induced narcolepsy excused the need for more statistically-significant or robust evidence supporting his argument. *Id.* at 14, 22.[39]

[38] Page five of the Latorre article filed by Petitioner appears to be blank. Dr. Steinman, however, provides a copy of the referenced table on page two of his second report.

[39] Dr. Steinman similarly diminished the need for epidemiologic evidence linking the HPV vaccine to narcolepsy, maintaining that it was "not the proper tool to decide whether, in a given individual with a given disease, the vaccine did NOT trigger the disease in that individual." Second Steinman Rep. at 18. This completely misstates the relevant evidentiary burden (and underscores why Dr. Steinman should avoid commenting on the legal standards employed in adjudicating Program claims). Although it is very true that petitioners are *never* compelled to present epidemiologic evidence, and can thus prevail without it, it is a petitioner's ultimate burden to establish preponderantly that a vaccine *caused* an injury. The Respondent is not tasked with proving a negative (that the vaccine could *not* have caused the

Dr. Steinman reiterated prior arguments regarding the purported link between the HPV vaccine and Petitioner's chronic headaches. He emphasized that an association between the two was not only established by the vaccine's package insert, but also by VAERS[40] reports identifying headache as a commonly reported adverse event. Second Steinman Rep. at 18–19. He elaborated on how he proposed the headaches could become chronic, noting that the vaccine's antigenic particles would bind with alum contained in it, and thereby persist in the body for as long as the alum did. *Id.* at 19–20. This argument seems to assume that because there is some limited evidence that alum can persist, that the vaccine's initial immune-stimulative impact would last for the same timeframe; however, Dr. Steinman did not offer evidence showing this beyond items referenced in his initial report suggesting that the vaccine had created long-lasting immunity against HPV (*not* that its components would continuously stimulate the immune system in a pathologic manner, and specifically cause chronic headaches in the process).

In addition to defending previously expressed opinions regarding Petitioner's purported narcolepsy and headaches, Dr. Steinman addressed some of the additional diagnoses she had obtained after the case's filing (including CFS and SFN). Second Steinman Rep. at 24. He noted that testing performed on Ms. E.S. in the fall of 2016 (over a year from the time she received the second HPV dose) and obtained in January 2017 established she possessed elevated levels of muscarinic[41] antibodies associated with CFS. Second Steinman Rep. at 24–25. He maintained that these antibodies played a significant role in the pathogenesis of CFS. *Id.* In contrast, the literature offered for this proposition was less certain. M. Loebel et al., *Antibodies to β Adrenergic and Muscarinic Cholinergic Receptors in Patients with Chronic Fatigue Syndrome,* 52 Brain, Behavior, and Immunity 32–39 (2016), filed Jan. 15, 2019 as Ex. 97 (ECF No. 42-4) ("Loebel"). Loebel, for example, noted that there was evidence of elevated levels of these antibodies in only a "subset" of CFS patients, and also that the function of the antibodies remained unclear (and thus could not

injury), but may offer evidence that undercuts the success of a claimant's showing. As a result, reliable epidemiologic studies can be evaluated—and can undermine a petitioner's showing—even if they cannot preponderantly *disprove* the possibility of causation by itself.

[40] The Vaccine Adverse Event Reporting System ("VAERS") is a national early warning system to detect possible safety problems in U.S.-licensed vaccines. VAERS, https://vaers.hhs.gov/about.html (last visited Oct. 7, 2020). VAERS was established in 1990 and is co-sponsored by the Centers for Disease Control and Prevention (CDC), and the Food and Drug Administration (FDA), agencies of the U.S. Department of Health and Human Services (HHS). *Id.*

[41] Muscarinic receptors are a type of cholinergic receptor that is stimulated by the alkaloid muscarine and blocked by atropine; it is found on autonomic effector cells as well as central neurons in the thalamus and cerebral cortex. Muscarinic Receptor, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=102569 (last visited Oct. 7, 2020). Different types may be distinguished on the basis of pharmacologic specificity or molecular structure; a number of differing nomenclatures have been applied to these types. *Id.* Cholinergic receptors are a type of cell-surface receptor that binds the neurotransmitter acetylcholine and mediates its action on postjunctional cells. Cholinergic Receptor, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=102541 (last visited Oct. 7, 2020). Types include parasympathetic autonomic effector cells, sympathetic and parasympathetic autonomic ganglion cells, striated muscle, and certain central neurons. *Id.*

definitely be said to contribute to CFS's pathogenesis). Loebel at 38.

Dr. Steinman also proposed that these antibodies (that would potentially attack the same neuroreceptors relevant to autonomic dysfunction that could in turn produce CFS, POTS, or other similar conditions) could be produced as part of an autoimmune, cross-reactive process instigated by the HPV vaccine, and cited literature purportedly to that effect. S. Ikeda et al., *Autoantibodies against Autonomic Nerve Receptors in Adolescent Japanese Girls after Immunization with Human Papillomavirus Vaccine*, 2 Annals of Arthritis and Clinical Rheumatology 1, 1–6 (2019), filed Nov. 24, 2019 as Ex. 107 (ECF No. 106-1) ("Ikeda"). Ikeda (in a case-control comparison of young girls who received the HPV vaccine versus those who did not) did observe increased levels of these autoantibodies directed against the relevant nerve receptors in those who had received the HPV vaccine. Ikeda at 3. However, Ikeda's authors also frankly admitted that "[t]here was no significant association between the major symptoms including dysautonomic symptoms and the serum levels of autoantibodies" (*Id.* at 4)—a lynchpin of the argument that these autoantibodies are pathogenic.[42]

Nevertheless, Dr. Steinman proposed that the antibodies associated with chronic fatigue were also mimics of HPV antigens, similarly citing additional BLAST search evidence in support as with prior representations about homology between HPV vaccine components and hypocretin pathway-associated amino acid sequences. Second Steinman Rep. at 26–33. Thus, this could again establish a mechanism by which the vaccine might promote this additional injury. Dr. Steinman also noted that Petitioner's visit to Dr. Chin in the fall of 2018 (after his first report was prepared and filed) corroborated the chronic fatigue and small fiber neuropathy diagnoses with reliable testing (such as a skin biopsy for the latter). *Id.* at 35–38.

c. *Third Steinman Report*

A month after his second report had been filed, Dr. Steinman prepared an additional, final report solely to address the question of onset of Petitioner's CFS or SFN. *See generally* Third Steinman Rep. He asserted that the onset of these conditions (which were not even diagnosed until *three years* after the second round of relevant vaccines administered in August 2015) was medically acceptable, invoking his prior findings about post-vaccine headache onset (early October 2014, hence two and one-half months after vaccination), and narcolepsy (in the fourteen months after receipt of the flu vaccine in August 2015). *Id.* at 1–2.

To support the medical acceptability of onset for such varied conditions, Dr. Steinman referenced an item of literature specific to the HPV vaccine. Third Steinman Rep. at 2; K. Ozawa

[42] In addition, further undercutting the reliability of any determinations in Ikeda is the fact that its authors approvingly cited to the ASIA theory discussed above to support the contention that vaccines can "occasionally trigger the development of POTS, CRPS, and CFS." Ikeda at 5 n.38 (referencing an article written by the creator of the ASIA theory, Dr. Yehuda Shoenfeld). Dr. Shoenfeld is a frequent Program expert, and has offered the opinion that the HPV vaccine can cause dysautonomic injuries like POTS or chronic fatigue—although not credibly. *See, e.g.*, *Johnson v. Sec'y of Health & Hum. Servs.*, No. 14-254V, 2018 WL 2051760, at *22–23 (Fed. Cl. Spec. Mstr. March 23, 2018).

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 1, 1–11 (2017), filed Feb 15, 2019 as Ex. 100 (ECF No. 90-2) ("Ozawa"). Ozawa was an observational study from Japan that considered the symptoms reported by 120 female subjects who had received the HPV vaccine in the 2013-16 timeframe. Ozawa at 1. Ozawa observed that certain symptoms (including fatigue, headaches, sleep disturbance, and autonomic dysfunction) manifested on average within 360 days of vaccination—supporting a lengthy, post-vaccination timeframe. Ozawa at 9. Ozawa itself, however, notes that the average time for onset observed was "very long in comparison with the adverse effects of conventional vaccinations," and attributed this in part to the fact that "it is rather difficult to determine the exact time of onset" for the symptoms it considered. *Id*. More importantly, the overall probative value of Ozawa's findings was limited by other deficiencies in the study *readily acknowledged by its authors*, including but not limited to (a) a lack of an unvaccinated control group, (b) its generally small sample size, and (c) the self-selection of studied subjects, all of whom specifically sought out the medical institution for which Ozawa's authors worked to report their concerns that the vaccine had caused their symptoms. *Id.* at 2, 9.

2. Dr. Sin Hang Lee

Dr. Lee, a pathologist, prepared two expert reports on Petitioner's behalf, both of which sought to establish that (a) her preexisting diabetes was exacerbated by the two HPV vaccine doses she received in 2014 and 2015, and (b) she developed myocardial ischemia due to those same vaccines. Report, dated Mar. 23, 2018, filed as Ex. 41 (ECF No. 55-1) ("First Lee Rep."); Report, dated Oct. 30, 2018, filed as Ex. 50 (ECF No. 78-1) ("Second Lee Rep.").

Dr. Lee studied at Wuhan Medical College and Tongji University College of Medicine from 1951 to 1956. Sin Hang Lee Curriculum Vitae at 1, filed on Mar. 23, 2018 (ECF No. 61-1). In 1966, he earned his F.R.C.P. (C) from the Royal College of Physicians and Surgeons of Canada. *Id*. He participated in several post-graduate training programs and held several teaching positions in China, Hong Kong, Canada, and the United States—several of which focused on pathology. *Id*. at 1–2. He is licensed to practice medicine in Connecticut and is boarded in pathology. *Id*. at 2. Dr. Lee is currently the director of Milford Molecular Diagnostics Laboratory, in Milford, Connecticut, which performs DNA sequencing-based diagnostic testing to confirm conditions like Lyme disease. *Id*.; Milford Molecular Diagnostics, http://www.dnalymetest.com/ (last visited Oct. 6, 2020). His first report acknowledges that the opinions he has provided were based on a review of Petitioner's medical history and his own research into "the science available in the public domain," (as opposed to professional research or expertise pertaining to the issues in dispute). First Lee Rep. at 1.

a. *First Lee Report*

Dr. Lee described type 1 (or "insulin-dependent") diabetes generally as an autoimmune-

induced condition, mediated by T cells and autoantibodies, in which insulin-producing beta cells (responsible for regulating blood sugar) in the pancreas are destroyed, resulting in downstream sequela attributable to the inability of the body in the absence of insulin to monitor and control blood sugar levels. First Lee Rep. at 6; M. Cnop et al., *Mechanisms of Pancreatic β-Cell Death in Type 1 and Type 2 Diabetes: Many Differences, Few Similarities*, 54 Diabetes S97, S97–S107 (2005), filed Mar. 23, 2018 as Ex. 41, Ref. 6 (ECF No. 56-6). Dr. Lee proposed that the HPV vaccine had significantly exacerbated Petitioner's DM-1, based on several independent points. First Lee Rep. at 5.

First, Dr. Lee noted that federal safety disclosures relating to the HPV vaccine's approval for use revealed instances in which the vaccine may have been associated with new cases of diabetes—although to reach this conclusion, Dr. Lee relied on tortuous math that is almost facially incorrect from a scientific/epidemiologic standpoint. He cited to the fact that in the HPV vaccine's clinical trials, the same number of vaccinated individuals (two out of 10,706) reported new cases of type 1, insulin-dependent diabetes (measured at fourteen days after each vaccine dose administration) as the unvaccinated placebo group (two out of 9,412)—suggesting no statistically-significant greater incidence of vaccine-associated cases (18.7 cases per 100,000 for vaccinated individuals, versus 21.2 for the control group). *Id.;* Gardasil [Package Insert]. Whitehouse Station, NJ: Merck & Co., Inc.; 2011, filed as Ex. 41, Ref. 4 at 8 ("Gardasil Package Insert"). This finding might seem *not* to support Petitioner's overall claim.

Dr. Lee, however, compared these rates to a "national statistics report" from 2016, which showed an incidence of 19.9 cases of diabetes total per 100,000 unvaccinated individuals for the entirety of 2005 (prior to the HPV vaccine's approval). Although this earlier incidence rate exceeds what was observed for even *vaccinated* individuals from the HPV vaccine trials, Dr. Lee maintained (without demonstrating his methodology)[43] that this figure "translates" into a far lower incidence of .74 cases per 100,000 after two weeks—thus establishing a "25 fold" increase in the incidence rate for vaccinated individuals as reflected in the safety study data. How this calculation can be possibly reliable (since Dr. Lee has not shown that the 2005 data identifies diabetes onset as reasonably occurring in the span of two weeks—and if so, based on what starting point, since it does not measure time from a vaccination or placebo event) is not explained, although Dr. Lee's report rapidly moves on.

Next, Dr. Lee maintained that based upon what was understood about how the HPV vaccine mechanistically "works" (coupled with some speculative points of his own about an inadvertent byproduct of its manufacture), a reliable theory could be proposed for how the vaccine's components might worsen a preexisting case of DM-1. First Lee Rep. at 6–14. The relevant formulation of the HPV vaccine, he contended, contains purified "virus-like particles," or VLPs,

[43] Presumably, Dr. Lee took the data for 2005, divided it by 365 (for the total days in a year), and then multiplied that sum by 14—although doing so does not precisely produce the rate he cites in his report.

derived from the L1 capsid[44] for the HPV wild virus. *Id.* at 6; Gardasil Package Insert at 12. To provoke an immune response to the presentation of these VLP antigens after vaccination, the HPV vaccine includes alum as an adjuvant. First Lee Rep. at 7–9. Some vaccines have also begun to incorporate toll-like receptor ("TLR") agonists, a different kind of biologic adjuvant that helps stimulate a greater immune response (although this distinct form of adjuvant has primarily been used to date in anticancer therapies). *Id.* at 8–10. However, Dr. Lee admitted TLR agonists are *not* an intentional component of the HPV vaccine's formulation. *Id.* Nevertheless, Dr. Lee maintained that the process by which HPV vaccine was manufactured likely resulted (inadvertently) in the inclusion of some "viral DNA fragments" that would in effect "serve as potent long-acting TLR9 agonist"—and hence acting as "the actual functional adjuvant." *Id.* at 12.

From the above, Dr. Lee attempted to explain how the HPV vaccine could aggravate type I diabetes. Although much remains unknown about the pathogenesis of this form of diabetes, Dr. Lee proposed that some new research establishes that TLR ligands (which can function like agonists) play a "key role in initiation or aggravation of type 1 diabetes." First Lee Rep. at 13 (citing A. Limmer et al., *Stimulation of Autoimmunity by Toll-like Receptor Ligands*, 64 Annals Rheumatic Diseases 15, 15–18 (2005), filed Mar. 23, 2018 as Ex. 41, Ref. 31 (ECF No. 59-1); S. Ferris et al., *The Islet-Resident Macrophage is in an Inflammatory State and Senses Microbial Products in Blood*, 7;214(8) J. Experimental Med. 1, 1–17 (2017), filed Mar. 23, 2018 as Ex. 41, Ref. 32 (ECF No. 59-2) ("Ferris"); J. Dowling & A. Mansell, *Toll-like Receptors: The Swiss Army Knife of Immunity and Vaccine Development*, 5 Clinical Translational Immunology 1, 1–10 (2016), filed Mar. 23, 2018 as Ex. 41, Ref. 33 (ECF No. 59-3)).

Of these cited articles, only Ferris addresses diabetes head-on. In Ferris, researchers examined the transcriptional profiles of macrophages in diabetic mice. The mice demonstrated an increased inflammatory signature, including elevated expression of chemokines[45] and chemokine receptors and an oxidative response. Ferris at 1. Researchers concluded, among other things, that macrophages have the capacity to sense blood-born stimuli. *Id.* at 10. Nevertheless, because type I diabetes is believed to have an autoimmune component, activation of TLRs in such a person would (in Dr. Lee's view) occur by "augment[ing] production of all autoantibodies against self-antigens," including those autoantibodies thought to attack the insulin-producing beta cells—thus exacerbating an existing case of diabetes. First Lee Rep. at 14.

Dr. Lee attempted to set his theory within the context of Ms. E.S.'s actual experience. First Lee Rep. at 14–15. Relying on an overview of the medical history (*Id.* at 1–4), he observed that

[44] Gardasil is the trade name for the Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant, a non-infectious recombinant quadrivalent vaccine prepared from the purified virus-like particles (VLSs) of the major capsid (L1) protein of HPV Types 6, 11, 16, and 18. The L1 proteins are produced by separate fermentations in recombinant *Saccharomysces cervisiae* and self-assembled into VLPs. Gardasil Package Insert at 12.

[45] Chemokines are regulators of the immune system and may also play a role in the circulatory and central nervous systems. *Dorland's* at 335.

Petitioner appeared to have fair control of her diabetes prior to her receipt of an initial HPV vaccine dose. *Id.* at 1–2, 14. But, her diabetic-associated symptoms greatly worsened in the months thereafter, as reflected in the many ER and doctor visits she had (at which time her glucose levels were consistently determined to be high). *Id*. Then, after her second HPV vaccine dose in August 2015, Petitioner started to develop chest pain and experienced additional worsening symptoms, including vomiting. *Id*. at 14. He specifically deemed the timeframe between the second HPV dose (administered August 19, 2015) and her October 10, 2015 ER visit—a more than seven-week period—as medically acceptable, although (incongruously) in so doing he referenced his prior arguments about the HPV clinical trials revealing post-vaccination onset as possible within two weeks. *Id.*; Gardasil Package Insert at 14–21.

Besides exacerbation of type I diabetes, Dr. Lee's first report included the opinion that the HPV vaccine could outright trigger a myocardial ischemia due to low blood perfusion, and did so to Petitioner. First Lee Rep. at 15. Dr. Lee explained that if and when immune cells are activated as a result of receipt of the HPV vaccine, and then reach sufficient number in the myocardium, the cytotoxic cytokines generated by these immune cells can cause myocardial depression with reduced cardiac outputs and low blood profusion through the myocardium, leading to irreversible myocardial damage in certain genetically and physically predisposed individuals. *Id.* at 16–17; *See also* Second Lee Rep. at 7. He noted that (again referencing the HPV vaccine package insert) syncope (resulting from insufficient blood flow to the brain attributable in turn to low blood pressure (hypotension) is the most commonly-reported adverse reaction after receipt of the vaccine. *Id;* Gardasil Package Insert at 27. He did not, however, specify the expected timeframe for such an adverse event (and syncope itself is expected to occur very close-in-time, if at all, to vaccination—not months or years later). Gardasil Package Insert at 1.

Syncope is a feature of orthostatic intolerance—a category that includes POTS, and that has been associated with receipt of the HPV vaccine. However, by Dr. Lee's admission this association "has not received much attention of [sic] the medical community." First Lee Rep. at 15. Dr. Lee cited a post-licensure survey study observing (for a 2006 to 2008 timeframe) that out of 12,424 reported adverse events, there were 32 deaths, six of which could be shown to have been cardiac-related. First Lee Rep. at 15; B. Slade et al., *Postlicensure Safety Surveillance for Quadrivalent Human Papillomavirus Recombinant Vaccine*, 302 JAMA 750–57 (2009), filed Mar. 23, 2018 as Ex. 41, Ref. 36 (ECF No. 59-6) ("Slade") (medical and autopsy reports on 20 of the 32 deaths confirmed there were 4 unexplained deaths and 6 cardiac-related deaths). From this, Dr. Lee concluded that vaccine-induced hypotension could in turn reduce blood flow to the heart, thereby incurring a "jeopardized myocardium." First Lee Rep. at 15.

Dr. Lee offered a causation theory for how the HPV vaccine might initiate such a process, which paralleled or relied on his theory addressing aggravation of diabetes. He reiterated his prior contention that the vaccine likely contained "a set of ready-made instant DNA immune 'mediators'" (in the form of the purported TLR agonist attributable solely to the vaccine's manufacture, rather

than an actual ingredient), which enabled the innate immune system's macrophages to transport vaccine antigens throughout the body—including across the blood-brain barrier. First Lee Rep. at 16. He offered a case report as evidence of the latter. F. DiMario et al., *A 16-year-old Girl with Bilateral Visual Loss and Left Hemiparesis Following an Immunization Against Human Papillomavirus*, 25 J. Child Neurology 321–27 (2010), filed Mar. 23, 2018 as Ex. 41, Ref. 39 (ECF No. 59-9) ("DiMario"). However, DiMario is factually distinct in that it involved localized encephalomyelitis and a biopsy-confirmed tumefactive demyelinating lesion. In addition, Dr. Lee referenced a Program case in which it was purportedly established that the HPV vaccine caused a child's death from a silent myocardial infarction (however, the facts and circumstances of that case are readily distinguishable). First Lee Rep. at 18; *Gomez v. Sec'y of Health & Hum. Servs.*, No. 15-160V, 2016 WL 6072391 (Fed. Cl. Spec. Mstr. Sept. 21, 2016).[46]

Dr. Lee proposed that the stimulation of TLRs induced by vaccination could equally promote upregulation of a variety of proinflammatory cytokines, some of which (like tumor necrosis factor alpha (TNF-α or Il-1β)) are "recognized myocardial depressants" which can cause damage to the myocardium in physically predisposed individuals. First Lee Rep. at 16–17; J. Parrillo et al., *A Circulating Myocardial Depressant Substance in Humans with Septic Shock: Septic Shock Patients with Reduced Ejection Fraction have a Circulating Factor that Depresses in Vitro Myocardial Cell Performance*, 76 J. Clinical Investigation 1539–53 (1985), filed Mar. 23, 2018 as Ex. 41, Ref. 40 (ECF No. 59-10). A sufficient number of these "cytotoxic cytokines" would be capable of causing myocardial depression and low blood perfusion, resulting in "irreversible myocardial damage." First Lee Rep. at 16–17.

Dr. Lee supported his theory pertaining to Petitioner's purported heart issues with the medical record. As before, he deemed significant the before/after vaccination distinction in Ms. E.S.'s health, focusing particularly on the growing evidence that she might have a cardiac disorder after the August 2015 second HPV vaccine dose. First Lee Rep. at 17. He took particular note of the cardiac consultation Petitioner received from Dr. Lefkowitz in the winter of 2016 (six months from receipt of the second dose), at which time a stress EKG revealed the possibility of a jeopardized myocardium. *Id;* Ex. 5 at 3. However, Dr. Lee acknowledged that this determination was not conclusively made at this time. *Id.* Nevertheless, Dr. Lee maintained that literature supported an association of the kind of abnormality observed at this time with moderate ischemia. First Lee Rep. at 17; L. Shaw et al., *Comparative Definitions for Moderate-Severe Ischemia in Stress Nuclear, Echocardiography, and Magnetic Resonance Imaging*, 7 JACC Cardiovascular Imaging 593–604 (2014), filed Mar. 23, 2018 as Ex. 41, Ref. 50 (ECF No. 60-7). In addition, Dr. Lee drew attention to the fact that as of March 2016, Petitioner's serologic testing revealed heightened levels of white blood cells, which he deemed "indicative of an augmented immune reaction . . . probably with associated increased discharge" of the cytokines he previously maintained were known myocardial

[46] In *Gomez* (a matter in which Dr. Lee also offered an expert report), a 14-year old male died *a day after* receipt of a second dose of HPV vaccine—a far cry from the present facts. Moreover, that case settled, and therefore no reasoned causal determination was issued that could shed light on this matter's disposition. *Gomez,* 2016 WL 6072391, at *1.

depressants. First Lee Rep. at 18.

To support the timing for an association between the August 2015 second HPV dose and the February 2016 diagnostic evidence as proof of Petitioner's vaccine-caused cardiac issues, Dr. Lee noted again the post-licensure studies, like Slade. First Lee Rep. at 18; Slade at 750. Of the 32 post-HPV vaccine deaths observed (approximately .26 percent of the 12,424 reported adverse events), the timeframes for fatality were from 2 to 405 days. Slade at 755. As a result (although without any showing specific to the cardiac-associated deaths), Dr. Lee concluded that a six-month lag in this case was medically acceptable.

b. *Second Lee Report*

In reaction to arguments lodged by Respondent's experts in opposition to his theories, Dr. Lee prepared a second report even lengthier than his first (although it was padded with large sections featuring wholesale reproduction of other articles, portions of websites, or similar authorities). *See generally* Second Lee Rep.[47]

Much of the supplemental report addresses Dr. Lee's prior contentions that Petitioner's alleged cardiac injuries were caused by the HPV vaccine. Second Lee Rep. at 1–16. He strenuously defended his conclusion that Petitioner had in fact experienced an "untoward cardiac event," referencing the February 2016 stress test cited in his first report, and noting that Dr. LaRue (Respondent's cardiologist expert) had acknowledged that some "ST segment elevation" was observed from the stress test, which could "represent acute ischemia." *Id.* at 1–2. Dr. Lee (who lacks comparable cardiac expertise) fiercely attacked Dr. LaRue's diminishment of the importance of these findings as medically incorrect. *Id.* at 2–5; A. Ali et al., *Early Repolarization Syndrome: A Cause of Sudden Cardiac Death*, 7 World J. Cardiology 466, 466–75 (2015), filed Nov. 16, 2018 as Ex. 51 (ECF No. 79-1). He also observed that Petitioner had additional abnormal EKG results after her ER visits in May 2017 and January 2018, thus corroborating the proposed diagnosis. Second Lee Rep. at 4; Ex. 33 at 8; Ex. 34 at 72. Ultimately, he accused Respondent's expert of relying on "half-truth and twisted science" in rejecting the conclusion that Petitioner had experienced myocardia ischemia. Second Lee Rep. at 7. And he went to great lengths to defend his conclusion that the test results set forth in the record were a sufficient basis for his diagnostic opinion. *Id.* at 7–10.

To bulwark his prior contentions that Petitioner's purported myocardial ischemia occurred in a medically acceptable timeframe, Dr. Lee noted that the two cytokines even Respondent's experts admitted were associated with it (TNF-α and Il-1β) had been established to persist even six months

[47] Indeed, Dr. Lee attempted to rebut some of the criticisms and questions that Respondent's experts lodged against his first report mainly by repeating verbatim the arguments he had already set forth (rather than by homing in on how the objections were unreasonable or wrong). *See*, *e.g.*, Second Lee Rep. at 41 ("I have copied and pasted below the most relevant part" of prior report), 42–49 (reproducing five pages of the first report in the second).

from the date of vaccination. Second Lee Rep. at 14; Report, dated July 2, 2018, filed as Ex. A (ECF No. 68-1), at 6, 8; D. Herrin et al., *Comparison of Adaptive and Innate Immune Responses Induced by Licensed Vaccines for Human Papillomavirus*, 10 Hum. Vaccines Immunotherapies 3446–54 (2014), filed Mar. 23, 2018 as Ex. 41, Ref. 29 (ECF No. 58-9) ("Herrin"). In Herrin, however, blood plasma was analyzed for ten circulating cytokines and chemokines, including TNf, at pre-vaccination and post-first and third vaccination at days 1, 2, 5, 14 and 28 and at month seven, but no statistically significant trends were observed that would corroborate the conclusion that these two particular cytokines were likely to persist for as long as Dr. Lee assumed. Herrin at 3449–50.

Dr. Lee expanded on his causation theory, offering additional support for his general assertion that "aluminum adjuvant-laden macrophages" travel in the body (and thus transport the adjuvant away from the site of vaccine administration) but also could conceivably cluster in the myocardium, causing a sufficiently-harmful concentration of the cytokines specific to myocardial ischemia to propagate the condition. Second Lee Rep. at 16; M. Mold et al., *Insight into the Cellular Fate and Toxicity of Aluminium Adjuvants Used in Clinically Approved Human Vaccinations,* Nature: Science Reports 1, 1–13 (2016), filed Mar. 23, 2018 as Ex. 41, Ref. 34 (ECF No. 59-4) ("Mold"). In Mold, a comparative study was undertaken to monitor the particle size distributions of aluminum adjuvants through the process of vaccine formulation using dynamic light scattering. *Id.* at 1. Results suggested that the particle size distributions may be important for its immunological recognition and subsequent clearance from the injection site. *Id.* Dr. Lee deemed this "straightforward science." Second Lee Rep. at 16.

In addition, Dr. Lee maintained his contentions (relating type I diabetes to the HPV vaccine) in the face of Respondent's experts' criticisms. First, he strenuously argued that his treatment of the HPV vaccine licensing data (which he had cited as proof that the vaccine was associated with an increased incidence of diabetes) was legitimate (despite the obvious mistakes in his reading of this data that Respondent's experts readily pointed out). Second Lee Rep. at 17–18, 20–21. He attacked other epidemiologic studies referenced by Respondent which credibly undercut the HPV vaccine-diabetes association as biased or merely "observational" and thus not worthy of significant weight. *Id.* at 18–20; C. Chao et al., *Surveillance of Autoimmune Conditions Following Routine Use of Quadrivalent Human Papillomavirus Vaccine*, 271 J. Internal Med. 193–203 (2012), filed July 27, 2018 as Ex. C, Tab 18 (ECF No. 70-9) ("Chao"). At the same time, he referenced again Arnheim-Dahlstrom as bulwarking his argument (even though in comparison it dealt with a drastically smaller sample size of only 23 individuals). Second Lee Rep. at 18–20*;* Arnheim-Dahlstrom at 4.

Second, Dr. Lee reiterated his argument about the mechanism by which the HPV vaccine would theoretically cause injury, explaining the extent to which his theory was adjuvant-based. He repeated arguments contained in his first report about how a "proprietary aluminum salt" used in HPV vaccine's manufacture could only act as an adjuvant in concert with a TLR agonist—something purportedly found in the vaccine due to the presence of "gene DNA fragments" left over in the process of manufacture. Second Lee Rep. at 49. He referenced two items of literature he had

himself authored to support this argument. S. Lee, *Detection of Human Papillomavirus (HPV) L1 Gene DNA Possibly Bound to Particulate Aluminum Adjuvant in the HPV Vaccine Gardasil*, 117 J. Inorganic Biochemistry 85, 85–92 (2012), filed Nov. 16, 2018 as Ex. 66 (ECF No. 80-6); S. Lee, *Guidelines for the Use of Molecular Tests for the Detection and Genotyping of Human Papillomavirus from Clinical Specimens*, 903 Methods Molecular Biology 65–101 (2012), filed Nov. 16, 2018 as Ex. 67 (ECF No. 80-7); Second Lee Rep. at 49–52. As indirect support for these overall contentions, Dr. Lee referenced Nobel prize-winning research into the role that TLRs play "as the sensors of innate immunity." Second Lee Rep. at 52; Press Release, *The Nobel Assembly at Karolinksa Institutet, The Nobel Prize in Physiology or Medicine 2011* (Oct. 3, 2011), https://www.nobelprize.org/prizes/medicine/2011/press-release/ (last visited Oct. 13, 2020).

Moreover, Dr. Lee revisited different elements of the medical record to defend his opinion. He argued, for example, that the flank pain Ms. E.S. frequently reported was reflective of hyperglycemia related to her diabetes—and thus spikes in glycated hemoglobin levels caused (in his view) by the HPV vaccine would explain such symptoms. Second Lee Rep. at 24. He rejected attributing the worsening of Petitioner's diabetes to adolescence, arguing that she lacked other important risk factors linked to worsening such as an eating disorder, treatment-associated insulin restriction, or other disruptions in medical monitoring that might occur when a young person goes to college. *Id.* at 25–27. He maintained that evidence of inflammation taken from testing performed on Petitioner in March 2016, at which time she had been diagnosed with a ruptured ovarian cyst, was independent of the cyst (since the type of inflammation associated with such a cyst was absent[48]) and instead attributable to "autoimmune reaction" begun by the vaccines received no earlier than seven months before (the time of the second HPV vaccine dose). *Id.* at 29–33.

Besides defending his own conclusions, Dr. Lee endeavored to rebut the suggestions of Respondent's experts that the general picture of Petitioner's overall post-vaccination worsening (evidenced in her repeated returns to the ER beginning in the fall of 2014) could be explained by a "selective IgA [antibody] deficiency," thereby producing more frequent viral infections that could in turn trigger loss of control of blood glucose. Second Lee Rep. at 36, 37. Dr. Lee countered by pointing out the limited number of pre- versus post-vaccination ER visits (*Id.* at 37), and also that

[48] Specifically, Dr. Lee opined that in cases of what he termed "acute abdomen," an afflicted individual would display high levels of neutrophils in the blood and site of infection/injury, but normal to below-normal lymphocytes in blood tests. Second Lee Rep. at 28–30. Petitioner's CBC differential from March 6, 2016 showed the opposite, in his reading. *Id.* at 31–32. However, the article Dr. Lee cited for this proposition (although never filed into the record) related to abdominal pain *generally* rather than a burst cyst. *Id.* at 30; J. Deibener-Kaminsky, *Leukocyte Differential for Acute Abdominal Pain in Adults,* 17 Lab Hematology 1, 1–5 (2011). Moreover, one of Respondent's experts, Dr. MacGinnitie, observed that a CBC count performed just two days before the cyst incident showed *no* lymphocyte increase, consistent with an earlier blood test in November 2015—and thus totally rebutting Dr. Lee's supposition that the CBC reading he called attention to reflected some ongoing and chronic condition consistent with his theory. Ex. 19 at 142. Dr. Lee explained away these contrary results, arguing that lymphocyte levels could naturally fluctuate, and adding that the evidence he had previously offered establishing that the HPV vaccine generally caused sustained levels of inflammatory cytokines ultimately supported his contentions (disregarding the fact that the two other blood tests referenced by Dr. MacGinnitie were inconsistent with the idea that the HPV vaccine would lead to persistently-elevated inflammation due to the cytokines it encouraged). Second Lee Rep. at 33–36.

some of the support for Respondent's argument was derived from a case control study with a distinguishable study sample group (males considerably older than Petitioner). *Id.* at 38–39. He emphasized that the GI symptoms Petitioner often experienced were common by-products of uncontrolled diabetes, further limiting the likelihood that they reflected something else (although not making it more likely that the vaccine itself was to blame for the diabetes-related flares). *Id.* at 39–40.

Regarding onset, Dr. Lee acknowledged (in effect) that type I diabetes would not literally "begin" within two weeks of vaccination, but clarified that he meant to argue that its impact on a person's insulin-producing pancreatic beta cells could be discerned in such a short timeframe. Second Lee Rep. at 21. He also disputed the contention of Respondent's experts that glycated hemoglobin levels were themselves a strong biomarker for destruction of such beta cells, proposing instead that these levels were only proof of a "general trend" and not a predictor independent from the impact of vaccination. *Id.* at 23–24. He nevertheless attempted to link record instances in which testing exposed a spike in these levels to prior receipt of the HPV vaccine, maintaining that the process would "take a few months to express." *Id.* at 24.

Finally, Dr. Lee attempted to defend his opinion that the HPV vaccine could cause orthostatic intolerance (manifesting in different ways, like syncope or POTS) by arguing that it could occur on a transient basis, and thus the record (which does not establish persistent instances of POTS close in time to vaccination, or regular events comparable to it) supported his contention. Second Lee Rep. at 13–14. He again referenced VAERS reporting of such instances, along with the vaccine's package insert. Second Lee Rep. at 28.

3. Dr. Susan Levine

Dr. Levine, a board-certified specialist in infectious diseases, and one of Petitioner's more recent treaters, offered a one-page letter in support of Petitioner's claim. Letter, dated September 28, 2020, filed as Ex. 47 (ECF No. 75-1). The letter was derived from Dr. Levine's treatment of Ms. E.S. well after the filing of this case. Dr. Levine opined that Petitioner suffers from CFS, orthostatic intolerance, "brain fog," and migraine headaches, all of which interfere with her ability to "function in a predictable and consistent manner." Letter at 1. The bases for Dr. Levine's opinion seem to be derived from a review of Petitioner's medical history. Ex. 98 at 27. Dr. Levine has not provided any substantiation for these diagnoses outside of her record review, nor does her one-page letter propose that Petitioner's illnesses are attributable to the HPV or flu vaccines.

B. *Respondent's Experts*

1. Dr. Shane LaRue

Dr. LaRue is a cardiologist by training and teaches at the Washington University School of

Medicine. He prepared two reports in support of Respondent's position in this case. *See generally* Report, dated July 2, 2018, filed as Ex. A (ECF No. 68-1) ("First LaRue Rep."); Report, dated May 3, 2019, filed as Ex. G (ECF No. 94-1) ("Second LaRue Rep."). Dr LaRue maintains that Ms. E.S. does not suffer from myocardial ischemia, and denies that any of the relevant vaccines she received could cause it.

Dr. LaRue studied at the University of Wisconsin-Madison where he obtained his bachelor's degree in biochemistry before earning his medical degree from the Medical College of Wisconsin. LaRue Curriculum Vitae at 1, filed on July 27, 2018 (ECF No. 68-9). He then obtained a master's degree in population health sciences from Washington University School of Medicine. *Id.* Currently, Dr. LaRue is Assistant Professor of Medicine, Section of Heart Failure and Cardiac Transplantation, in the Cardiovascular Division at Washington University School of Medicine. *Id.* He is board certified by the American Board of Internal Medicine in Advanced Heart Failure and Transplant Cardiology. *Id.* at 2. And has authored numerous peer-reviewed manuscripts concerning various aspects of cardiology. *Id.* at 5–11.

Dr. LaRue's first report began with consideration of some of the instances of cardiac-oriented treatment documented in Petitioner's medical records. He noted the July 2011 instance (three years prior to the first HPV dose) when Ms. E.S. first appeared to complain of chest pain and associated symptoms, and at that time received some degree of medical work-up (including an EKG). First LaRue Rep.at 2; Ex. 17 at 198. Not only did treaters identify no underlying explanation for her complaints, but the EKG was deemed normal. At most, it included evidence of "early repolarization"—a benign finding that is common in young people (especially those who are athletic like Petitioner), even though the shape of the relevant wave recorded on the EKG looks similar to the pathologic wave elevation that can be seen during acute myocardial infarction or pericarditis. *Id;* Second LaRue Rep. at 1; Ex. 17 at 198; A. Goldberger, et al., *Electrocardiogram in the Diagnosis of Myocardial Ischemia and Infarction*, uptodate.com 36 (2019), Ex. G1, filed on May 7, 2019 (ECF No. 94-2). This early EKG was also in Dr. LaRue's view consistent with Petitioner's two later EKGs. Second LaRue Rep. at 1.

Thereafter, the record revealed that Petitioner next obtained treatment for possibly heart-related symptoms in February 2016, when she saw Dr. Lefkowitz. Ex. 5 at 2. However, Dr. LaRue's detailed evaluation of the records from this treatment event (as well as testing performed in its wake) suggested to him no evidence of anything significant from a cardiac standpoint, let alone myocardial ischemia. In particular, he highlighted the fact that Petitioner's pain was initially considered "exertional in nature," and thus had not appeared spontaneously, and also that her initial physical exam was normal. First LaRue Rep. at 2; Ex. 5 at 2. Dr. LaRue admitted that the 2016 EKG did reveal the possibility of an abnormality, but opined that (comparing this one to the 2011 EKG and one other Petitioner received in October 2015—both of which were deemed normal) it also included wave shapes consistent with the (normal) "early repolarization" he saw in all three EKGs. First

LaRue Rep. at 2–3, 6–7.[49]

Dr. LaRue conceded that Petitioner also received a positive EKG stress test[50], but emphasized his view that it only supported the "possible" existence of a jeopardized myocardium, adding that the stress test generally only serves as a screening device that should prompt additional testing and analysis. First LaRue Rep. at 4; *see also* Second LaRue Rep. at 4 ("positive findings of a wall motion abnormality on a stress [EKG] may not be the result of ischemia"). Its sensitivity was correlated to the general incidence for coronary issues in the relevant population—and here, Petitioner's youth made it unlikely that the result would have much predictive value. *Id.* Moreover, as a result of the positive stress test result (and consistent with its very purpose), Petitioner was subsequently referred for a cardiac CT angiography[51]—which in Dr. LaRue's reading revealed no evidence at all of "significant coronary artery disease," myocardial ischemia, or a "jeopardized"

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[49] In response to Dr. Lee's argument that the "early polarization" justification for all three EKGs' reported normal findings did not hold up (because Petitioner was no longer a college athlete as of 2016), Dr. LaRue maintained that (a) she had been a consistent athlete when the 2011 EKG was performed, and (b) the repolarization pattern was far more prevalent than the incidence of observable EKG abnormalities, thus allowing for the conclusion that the possible abnormality suggested by the repolarization pattern was only an "incidental [EKG] finding with no clinical implications." Second LaRue Rep. at 3. He also proposed that the finding in 2016 was not new in light of the two earlier EKGs, further reducing its overall significance. *Id.* at 2.

I need not decide the evidentiary significance or meaning of this aspect of the EKG performed on Petitioner in 2016. It cannot be disputed that the EKG resulted in a subsequent positive stress test, followed by a negative CT angiography, and that treating cardiologists like Dr. Lefkowitz did not (after consideration of *all* of the above) ultimately diagnose Petitioner with myocardial ischemia, or any other significant cardiac condition. The weight of the evidence is thus against the Petitioner on this aspect of her claim no matter which expert is more "right" about the significance of repolarization patterns specifically (although Dr. LaRue's demonstrated greater expertise in the field gives his opinions on these subjects additional heft).

[50] Dr. LaRue also speculated that the stress test constituted a false positive, noting that the low likelihood of obstructive coronary disease in a woman in her early twenties, even with type I diabetes, and the fact that prior studies have noted a false-positive rate of approximately 30% for stress echocardiography. First LaRue Rep. at 4. Dr. Lee termed this argument a straw man, reflective of an effort by Dr. LaRue to distract from the real issue under discussion while admitting that Petitioner did show inferior ST elevation. But (just like my evaluation of the purported early polarization evidence from the EKG) because my analysis turns on test results collectively and what on-the-ground treaters determined, the accuracy of the stress test in that process (which unquestionably led Dr. Lefkowitz to order follow-up testing) need not be evaluated, but instead can be presumed to support only the *possibility* of a cardiac problem—as in fact it was read.

[51] As noted above, Dr. Lee contested whether the testing Petitioner received constituted the best means of evaluating the presence of myocardial ischemia, noting (as Dr. LaRue acknowledged) that a different diagnostic test—coronary angiography—was the true "gold standard." First LaRue Rep. at 5. But Dr. LaRue went on to explain why a CT angiography was still a perfectly valid test when (as here) the likelihood of coronary disease was not high to begin with, and that this kind of test was generally sufficiently sensitive to identify the presence (or absence) of a more serious coronary problem. *Id.* Dr. LaRue also noted that Ms. E.S. would not have been a proper recipient for a more accurate but invasive test, and also that her treaters (who could have ordered any testing they thought appropriate) did not pursue additional testing. Second LaRue Rep. at 6.

I find that Dr. LaRue persuasively established the legitimacy of the CT angiography test that Petitioner received, and its reliable scientific value under the circumstances (especially given the lack of other evidence corroborating Petitioner's assertions in this regard).

myocardium. *Id.* at 2, 3, 5; Ex. 5 at 18. ("[a]ll coronaries are patent without evident atherosclerotic plaque"). Indeed, based on such results, Dr. Lefkowitz made no negative diagnostic finding close, in any respect, to what Petitioner alleges. *Id.* at 5; Second LaRue Rep. at 2, 5–6.[52] Thus, Dr. LaRue considered Petitioner's 2016 stress test result a false positive. First LaRue Rep. at 6.

Moving beyond Dr. Lefkowitz's 2016 exam, Dr. LaRue saw little from the subsequent records that would support the conclusion that Petitioner ever suffered from any meaningful form of cardiac issue, vaccine-caused or not. At the first of Petitioner's May 2017 ER visits (when she complained of chest pain, among other things), for example, she received a largely normal EKG result (except for the possibility of left atrial enlargement), First LaRue Rep. at 3. Her second May 2017 visit (facially prompted by an incident of drinking that caused her insulin pump to overreact) also resulted in an EKG result deemed normal, with no findings of cardiac-related problems upon discharge. *Id.;* Ex. 33 at 23.[53] Her January 2017 ER visit was comparable, with a similar nonspecific EKG (beyond the same evidence of early polarization that Dr. LaRue observed in Petitioner's prior EKGs). *Id.* at 4. And he discounted the probative value of a January 2018 EKG that was at the time interpreted as "borderline-abnormal" (Ex. 34 at 72), noting that his reading of the results did not convince him that it was in fact properly understood in this manner, and that her primary symptoms as of the date of this EKG pertained to abdominal pain ultimately attributable to a ruptured cyst. First LaRue Rep. at 6; Second LaRue Rep. at 4. Petitioner otherwise never displayed other objective evidence of ischemia, such as "elevated serum cardiac biomarkers or an abnormality seen on cardiac CT or cardiac MRI." Second LaRue Rep. at 3, 5.

Dr. LaRue commented on the persuasiveness of Dr. Lee's arguments that the HPV vaccine could be associated with myocardial ischemia (although he admitted in so doing that immunologic issues were in fact outside of his primary expertise). Second LaRue Rep. at 10. He agreed that cytokines like TNF-α and IL-1β did play a role in myocardial depression, but questioned whether they would remain sufficiently elevated months after vaccination to effect such injury (adding that the record did not establish that Petitioner had experienced *other* impacts of cytokine-driven inflammation that would be expected to exist under such circumstances, like low cardiac output or damage). First LaRue Rep. at 6, 8. He also disputed that the record supported the conclusion that these cytokines were in fact elevated as of March 2016. *Id.* at 8–9.

[52] Indeed—as Dr. LaRue observed, Petitioner was not even complaining of symptoms of ischemia at the time of her March 2016 exam, when Dr. Lee maintains the ischemia diagnosis was confirmed by EKG and other testing. Second LaRue Rep. at 2.

[53] In discussing the May 24, 2017 EKG, Dr. LaRue noted (as he did when discussing the February 2016 EKG) another reason to doubt that it evidenced any potential problems. In Dr. LaRue's experience, an "auto-generated [EKG] machine" can produce unreliable results—in particular when the machine itself (via its computer programming) deems a result suggestive of injury, independent of a human treater's read of the findings. Second LaRue Rep. at 2, 5; M.E. Guglin et al., *Common errors in computer electrocardiogram interpretation*, 106 Int. J. Cardiol. 232–37 (2006). Thus, the first evidence of a problem from the February 2016 EKG was derived from the "computer generated reading" from the EKG machine (which itself included the heading "UNCONFIRMED INTERPRETATION") rather than Dr. Lefkowitz. Second LaRue Rep. at 2; Ex. 5 at 5. The same was true, in Dr. LaRue's review, of the subsequent May 2017 EKG report. Second LaRue Rep. at 4.

Besides opining on causal allegations specific to Petitioner's alleged cardiac injury, Dr. LaRue reviewed some of her other claimed vaccine-caused harms. For example, his review of the record did not lead him to conclude that Petitioner ever experienced persistent or significant hypotension. First LaRue Rep. at 6. He agreed hypotension could be a transient post-vaccination concern, but challenged that a valid and reliable mechanism existed for explaining how the HPV vaccine could produce circumstances in which it would be "transiently" experienced six to nineteen months post-vaccination. Second LaRue Rep. at 9. He also noted that Ms. E.S. 's blood pressure was measured in connection with Petitioner's March 2016 stress test, but that her readings even after the stress of exercise never measured below normal such that an orthostatic hypotension diagnosis could be supported. *Id.* Nor could the condition of cardiac ischemia be deemed to be caused by hypotension (although hypotension could *result* from "cardiac abnormalities"). *Id.* at 10.

2. Dr. Andrew MacGinnitie

Dr. MacGinnitie, a pediatrician and immunologist/allergist, prepared two reports for Respondent. Report, dated May 1, 2018, filed as Ex. C (ECF No. 69-1) ("First MacGinnitie Rep."); Report, dated May 3, 2019 filed as Ex. H (ECF No. 95-1) ("Second MacGinnitie Rep."). Dr. MacGinnitie's opinions mostly focused on Petitioner's alleged narcolepsy, POTS, and headaches, and whether the HPV vaccine could cause any of the above, nevertheless he did also address some of Dr. Lee's contentions specific to cardiac issues or mechanisms for vaccine causation.

Dr. MacGinnitie is currently an attending physician as well as Clinical Director for the Division of Immunology at Boston's Children's Hospital, where he oversees clinical operations for Allergy/Immunology, Rheumatology, and Dermatology. First MacGinnitie Rep. at 1. He obtained his medical degree and Ph.D. in Pathology from the University of Chicago Pritzker School of Medicine. *Id.* Dr. MacGinnitie is board certified in both Allergy/Immunology and Pediatrics and maintains an active clinical practice seeing more than 1,600 patients annually. *Id.* at 2. He also performs research and has published numerous articles in areas relating to Allergy/Immunology, including vaccine reactions. *Id.*

a. *MacGinnitie First Report*

After a brief overview of Petitioner's medical history, Dr. MacGinnitie endeavored to rebut Dr. Steinman's narcolepsy theory. First MacGinnitie Rep. at 4. He noted a diagnostic issue that undermined Dr. Steinman's causation theory as presented in this case. Dr. MacGinnitie conceded that at least a "plausible case" existed for the contention that a specific formulation of the *flu vaccine* (one that is adjuvanted—a form rarely administered in the U.S., and not received by Ms. E.S. in this case) could trigger narcolepsy with cataplexy, or "type 1" narcolepsy,[54] via an autoimmune

[54] Type 1 narcolepsy is caused by extensive loss of hypothalamic neurons that produce the neuropeptides orexin-A and -B (also referred to as hypocretin-1 and -2). Narcolepsy type 2 includes most of the same symptoms, but its cause is

process in which antibodies triggered by vaccine antigen presentation cross-react with the hypocretin pathway.[55] *Id.* However, Ms. E.S. had at best been diagnosed only with *type 2* narcolepsy[56]—a less severe form not accompanied by cataplexy, and not also believed to be autoimmune-driven. *Id.* at 4–5, 7*;* T. Scammell, *Narcolepsy*, 373 New Eng. J. Med. 2654–62 (2015), filed July 27, 2018 as Ex. C, Tab 1 (ECF No. 69-2). As a result, Dr. Steinman's entire causal explanation was inapplicable to the facts of this case.

In addition, Dr. MacGinnitie questioned whether (independent of the version of narcolepsy Petitioner allegedly had experienced) Dr. Steinman had even established that narcolepsy could be driven by an autoimmune process that was vaccine-triggered. First MacGinnitie Rep. at 5–6. Thus, he pointed out that many of the individual items of literature Dr. Steinman had cited did not demonstrate that persons with narcolepsy possessed sufficient amounts of the purportedly hypocretin-oriented autoantibodies for a cross-reaction, while individuals without narcolepsy had comparable quantities of the antibodies. *Id.* at 6; S. Ahmed et al., *Antibodies to Influenza Nucleoprotein Cross-React with Human Hypocretin Receptor 2*, 7 Sci. Translational Med. 1, 1–15 (2015), filed July 27, 2018 as Ex. C, Tab 3 (ECF No. 69-4). Dr. MacGinnitie deemed this to cast "considerable doubt on the importance of these antibodies." First MacGinnitie Rep. at 6.

Dr. MacGinnitie raised several other technical objections to the reliability of the causation theory that vaccination could provoke an autoimmune response sufficient to interfere with hypocretin pathways and thereby cause narcolepsy. First MacGinnitie Rep. at 6–9. But in his view a more fundamental flaw in the theory arose from the fact that such evidence, reliable or not, involved an *adjuvanted flu vaccine*—not the HPV vaccine. Regarding the latter, Dr. MacGinnitie noted that Dr. Steinman's argument relied heavily on the contention that mimicry existed between HPV vaccine amino acid sequences (the building-blocks of proteins) sufficient to interfere with hypocretin pathways, but without reliable evidence (in the form of experimentation or other research) showing this actually could occur. Instead, Dr. Steinman relied on animal studies relevant to autoimmune-driven demyelination generally, a disease pathogenesis wholly distinguishable from

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unknown, and it does not feature cataplexy. T.E. Scammell, *Narcolepsy*, 373 N. Engl. J. Med. 2654-62 (2015), filed July 27, 2018 as Ex. C, Tab 1 (ECF No. 69-2).

[55] In his second report, Dr. MacGinnitie devoted greater attention to the argument that the flu vaccine could be credibly associated with any form of narcolepsy, offering two 2018 articles that he proposed diminished the significance of prior research linking certain formulations of the H1N1 fly vaccine to type 1 narcolepsy. Second MacGinnitie Rep. at 5–8 (references omitted). But because Petitioner did not receive the form of flu vaccine even arguably associated with narcolepsy, and based on my prior reasoned determinations (mentioned below) that the non-adjuvanted flu vaccine commonly administered in the U.S. is highly unlikely to cause the condition, I do not herein devote extensive discussion to these issues. Of the theories advanced in this case, the contention that type II narcolepsy can be caused by the flu or HPV vaccines was among the least well-substantiated—no matter how robust the association between *type I* narcolepsy and *some* versions of the flu vaccine might be.

[56] People with type 2 narcolepsy do not have cataplexy and have normal orexin-A levels. Scammell, at 4. Type 2 narcolepsy may be caused by less extensive injury to orexin-A and -B transmitters, but data on the disease process are quite limited. *Id.*

the receptor blocking at issue in narcolepsy. *Id.* at 9–10. Dr. MacGinnitie also pointed out that there were in nature numerous examples of possible molecular mimicry between amino acid sequences and self-structures ("this level of overlap in protein sequence is common"), yet autoimmune diseases were not regular occurrences (thus suggesting that homology between sequences alone was no guarantee of an autoimmune/pathologic reaction). *Id.* at 10.

More significantly, Dr. MacGinnitie observed that several large epidemiologic studies (one of which Dr. Steinman himself cited in his own report) did not demonstrate any significant incidence of narcolepsy after receipt of the HPV vaccine. First MacGinnitie Rep. at 11; Arnheim-Dahlstrom at 1. Chao—a study referenced by Dr. Lee, and in Dr. MacGinnitie's report (and which has been offered in many other Program decisions)—reached a similar conclusion. Chao at 193. Chao was a peer-reviewed observational study analyzing a database comprised of the medical histories of approximately 189,000 women in California to determine whether the studied population had developed a variety of autoimmune conditions after receiving the HPV vaccine. Chao at 194.

Next, Dr. MacGinnitie evaluated the strength of Dr. Steinman's arguments that Petitioner's reported headaches could be associated with the HPV vaccine. He noted that the record did not offer substantiation for a migraine headache diagnosis for Petitioner, and also that the vaccine package inserts (which Dr. Steinman purported established headache as an expected post-vaccination adverse event) described "almost certainly acute events occurring immediately after vaccination," rather than a chronic occurrence manifesting long after. First MacGinnitie Rep. at 11. Dr. MacGinnitie expressed doubt about the proposed mechanism for the headaches, arguing that the likelihood of the small amount of presenting antigen in the vaccine could travel into the central nervous system (the "CNS") to bind with or activate receptors there associated with headache was low, and that other evidence cited by Dr. Steinman to substantiate persistence of effect over time (whether due to the alum included in the vaccine as an adjuvant, or evidence that the immunity effect of the vaccine could last) did not amount to a showing that the "vaccine proteins themselves" (which constituted tiny amounts of the vaccine) would remain in the body for the same period. *Id.* at 12; Second MacGinnitie Rep. at 12.

Besides his review of Dr. Steinman's opinion, Dr. MacGinnitie critiqued elements of Dr. Lee's arguments about the association between the HPV vaccine and worsening of diabetes or heart damage. He deemed the former to suffer from "a number of glaring weaknesses," including but not limited to the following:

- The table referenced from the HPV vaccine safety trials did not establish an increased, post-vaccination incidence of new-onset type 1 diabetes, and also used as a control group subjects who received a placebo (as opposed to the general population) (First MacGinnitie Rep. at 13);

- Epidemiologic studies like Chao or Arnheim-Dahlstrom showed no association between the HPV vaccine and type 1 diabetes (*Id.* at 13-14 (*citing* Chao at 201; Arnheim-Dahlstrom at 5)); and

- Dr. Lee's incidence calculation was not only mathematically erroneous, but proposed an unlikely, drastically high level that "if it were accurate, we would be observing an epidemic of [type 1 diabetes] in adolescent boys and girls" (First MacGinnitie Rep. at 14).

In addition, Dr. MacGinnitie offered to show, via the filed medical records, that in fact Petitioner's "worsened control" of her diabetes was not likely vaccine-related. First MacGinnitie Rep. at 14. As he observed, Ms. E.S. had one of her highest glycated hemoglobin readings in early July 2014—before receipt of the first HPV vaccine dose. *Id.; see also* Second MacGinnitie Rep. at 3 ("her control was worsening prior [to] receiving her fist HPV vaccine"). In contrast, one of her best readings came in December 2016, by which time she had received *both* doses at issue, undercutting Dr. Lee's contention that her levels would be expected to be persistently high due to vaccination. *Id.* at 14–15. Dr. MacGinnitie felt the onset of Petitioner's late adolescence, with the attendant "life changes" that might make monitoring more difficult, or other unhealthy behaviors" that occur at the college level (pointing specifically to the instance in which a drinking bout resulted in an ER visit), better explained her experiences. *Id.* at 15; Second MacGinnitie Rep. at 4.[57]

Regarding Petitioner's purported myocardial ischemia, Dr. MacGinnitie echoed Dr. LaRue, maintaining that the medical record (and more specifically EKG and CT testing Petitioner had received) did not establish either evidence of decreased blood flow or a jeopardized myocardium, nor had any treaters ultimately found otherwise. First MacGinnitie Rep. at 16-17. He disputed Dr. Lee's effort to link such problems to syncope or POTS, noting that (a) at most, the vaccine was associated with acute (one-time) episodes of post-vaccination syncope rather than chronic blood flow issues, and (b) the HPV vaccine was only linked to POTS by a single four-patient case study. First MacGinnitie Rep. at 16. Dr. Lee offered little to no other evidence reliably establishing the vaccine could injure the heart. *Id.* And the record did not suggest that Ms. E.S. had experienced heightened levels of inflammation around the time of her March 2016 cardiac consultation, with some testing done before this time revealing no abnormalities, and any higher levels revealed in

[57] As an alternative explanation for Ms. E.S.'s diabetes-related post-vaccination symptoms and associated ER visits, Dr. MacGinnitie proposed "selective IgA deficiency"—a deficiency in an immunoglobulin protective against infection that Petitioner was diagnosed with as a younger child. First MacGinnitie Rep. at 15. Dr. Lee argued in response that selective IgA deficiency could not be the cause because Ms. E.S.'s relevant ER visits were post-vaccination and not throughout her childhood. Second Lee Rep. at 37. Further, Ms. E.S's chronic tonsillitis was a health care issue only after vaccination and obviously unrelated to her SIgAD. *Id.* at 38. Both sides make reasonable points about the significance of the levels of this particular antibody, but my decision does not turn on who is "more" correct on this issue, since (as discussed in detail throughout) I ultimately do not find that any vaccine Petitioner received likely caused the exacerbation of her type I diabetes.

March 2016 likely attributable to the ruptured cyst she had experienced. *Id.* at 16–17.[58]

b. *MacGinnitie Second Report*

Dr. MacGinnitie's second report contained some more detailed evaluations of theories presented by Petitioner's experts. First, he questioned Dr. Lee's contention that the HPV vaccine doses Petitioner received in 2014 and 2015 could later cause elevated cytokine levels persisting into the winter of 2016. He highlighted the fact that articles, like Herrin, explicitly stated that they did *not* find that the specific proinflammatory cytokines (identified by Dr. Lee) became elevated over long periods of time after receipt of the HPV vaccine. Second MacGinnitie Rep. at 1–2; Herrin at 3449–50.

Dr. MacGinnitie also noted that the mere production of proinflammatory cytokines by macrophages was not a "controversial" point, but it did not mean that vaccines encouraged this process or could cause it to persist. In so arguing, Dr. MacGinnitie specifically challenged Dr. Lee's assertion that macrophages bearing alum would likely travel into the CNS, noting that the literature cited for this concept by Dr. Lee was speculative rather than supported with "actual data." Second MacGinnitie Rep. at 3. And he distinguished literature establishing that the HPV vaccine could promote a subsequent increased T-cell/immune response to the vaccine's proteins (the very purpose of vaccination) from a demonstration that the "immune system *in general* shows increased activity after vaccination," and that this increase would persist for long periods of time. *Id.* at 4 (emphasis in original).

In addition, Dr. MacGinnitie attempted to address head-on Dr. Lee's contentions about DNA matter persisting in the HPV vaccine formulation—a condition for Dr. Lee's overall causal theory that a "silent" adjuvant (the TLR agonist) found its way into the vaccine and would thereafter amplify its pathologic impact. He noted that this element of Dr. Lee's opinion was only supported by two articles Dr. Lee himself authored plus his own experiment, adding that the technique used to sense the presence of this DNA was so sensitive that it would pick up the presence of "miniscule" amounts, thereby producing false positives. Second MacGinnitie Rep. at 4–5. And in any event, Dr. Lee had offered "no evidence that the amount [of cell-free DNA] in the HPV vaccine is sufficient to stimulate a significant immune response," as his theory posited. *Id.* at 5.[59]

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[58] Inflammation is a localized protective response elicited by injury or destruction of tissue. *Dorland's* at 935. Inflammation can be acute, usually of sudden onset and predominated by vascular and exudative processes. *Id.* When chronic and slow in its progression, it is marked chiefly by the formation of new connective tissue; it may be a continuation of an acute form or a prolonged low-grade form, and usually causes permanent tissue damage. *Id.* Dr. MacGinnitie later partially granted Dr. Lee's contention that the ruptured cyst might exhibit different kinds of inflammatory immune cells, but insisted nonetheless that there was overall little evidence of "persistent inflammation." Second MacGinnitie Rep. at 4.

[59] Dr. MacGinnitie added that as a general matter, "trace amounts" of DNA in a vaccine were simply unlikely to be harmful, noting that humans already are exposed to similar DNA from bacteria and micro-organisms without aberrant impacts, and the blood itself also contains cell-free DNA. Second MacGinnitie Rep. at 5. And vaccine development

Because chronic fatigue had not been alleged as an additional vaccine injury at the time of his first report, Dr. MacGinnitie only addressed it in the second report, emphasizing that the diagnosis post-dated the vaccinations at issue by three to four years. Second MacGinnitie Rep. at 12. Also, he noted that Dr. Steinman's support for the association between the HPV vaccine and chronic fatigue came from a four-person case study, contrasting the embrace of such limited evidence (since case studies at bottom only demonstrated a temporal relationship) with Dr. Steinman's arguments that large-scale epidemiologic studies were not sufficiently powered to suggest the absence of an association. *Id.* at 13. Dr. MacGinnitie cited additional epidemiologic evidence undercutting a relationship between the HPV vaccine and chronic fatigue. *Id.;* J. Skufca et al., *The Association of Adverse Events With Bivalent Human Papillomavirus Vaccination: A Nationwide Register-Based Cohort Study in Finland*, 36 Vaccine 5226–33 (2018), filed May 7, 2019 as Ex. H, Tab 17 (ECF No. 96-8) ("Skufca"). Skufca (evaluating a different formulation of the HPV vaccine) considered the evidence of adverse outcomes for more than 240,000 females in Finland aged 11-15 who received the vaccine, finding no statistically-significant increased incidence rate for CRPS or POTS; while a slight increase was observed for chronic fatigue, it was consistent with what boy subjects experienced. Skufca at 3. Dr. MacGinnitie otherwise disputed that chronic fatigue could even be understood as an autoimmune condition in the first place. Second MacGinnitie Rep. at 13–14.

3. Dr. David Raizen

A neurologist and medical professor with specific training and expertise in sleep medicine issues, Dr. Raizen offered two written reports. Report, dated May 24, 2018, filed as Ex. E (ECF No. 72-1) ("First Raizen Rep."); Report, dated May 4, 2019, filed as Ex. I (ECF No. 97-1) ("Second Raizen Rep."). Dr. Raizen mainly addressed Dr. Steinman's contentions pertaining to narcolepsy, although he expanded his focus to include Petitioner's allegations of chronic fatigue in his second report.

Dr. Raizen is an associate professor at the Perelman School of Medicine for the University of Pennsylvania, and a practicing neurologist with a sub-specialty in sleep medicine. First Raizen Rep. at 1. He is board certified in psychiatry and neurology as well board certified in sleep medicine. *Id.* Dr. Raizen has been treating patients with sleep disorders for the past fourteen years and currently follows approximately 50 patients with narcolepsy in an outpatient clinic. *Id.* In addition, he directs a research group aimed at understanding the fundamental mechanisms regulating sleep and wake. *Id.* at 2. Dr. Raizen's reports were based on consideration of the reports offered from Drs. Steinman and Lee, his review of the medical record, and a variety of medical and scientific articles bearing on the diagnoses in question and what is known about the pathogenesis of each. First Raizen Rep. at 2–3; Second Raizen Rep. at 1.

efforts that seek to rely on the stimulative, adjuvant-like effect of this DNA employ amounts far in excess of the trace levels that would be found in the HPV vaccine. *Id.*

a. *Raizen First Report*

In discussing narcolepsy, Dr. Raizen noted that the "presence of cataplexy" (which he defined as "the sudden loss of muscle tone during wakefulness") was the main distinguishing feature between types 1 and 2. First Raizen Rep. at 4. Diagnosing narcolepsy requires consideration of medical history, a physical exam, and then the combination of a polysomnography test and a MSLT. *Id.* A sleep latency of eight minutes or less, plus proof of two or more sleep onset REM periods, is supportive of a narcolepsy diagnosis. *Id.* From a pathophysiologic perspective, Dr. Raizen emphasized that more was known scientifically about type 1 narcolepsy, and his explanation for it (loss of brain neurons that produce hypocretin, plus association with HLA antigen) was consistent with what Drs. MacGinnitie and Steinman agreed upon—as was his admission that evidence existed associating an adjuvanted form of the flu vaccine that was only administered in Europe (Pandemrix) with an increased incidence of type 1 narcolepsy. *Id.* at 5–6.

In this case, Dr. Raizen disputed the legitimacy the MSLT Ms. E.S. underwent in January 2017, arguing that critical protocols needed to ensure the accuracy of results did not occur. First Raizen Rep. at 5. In particular,

- performance of the polysomnography the night before the MSLT ("to ensure that proper sleep amount was achieved" before the MSLT) did not occur—instead, the two were performed *two months* apart;
- sleep logs were not obtained for the week before the MSLT;
- a urine drug screening (for medications that might impact sleep) was not performed; and
- the sleep apnea diagnosis Petitioner had previously obtained provided an alternative explanation for daytime sleepiness that undercut the MSLT findings.

Id. at 6–7. Thus, he disputed that the MSLT test, coupled with other exam and testing results considered by Ms. E.S.'s treaters, in fact supported the narcolepsy diagnosis she received.

Moreover, assuming the diagnosis was substantively supported, Dr. Raizen pointed out (consistent with Dr. MacGinnitie) that the distinction between types 1 and 2 narcolepsy was harmful to Petitioner's causation theory. He noted that there was "essentially no evidence for autoimmunity in the pathogenesis of type 2 narcolepsy," and therefore, what was believed plausible about the pathogenesis of type 1 narcolepsy had no relevance in explaining Petitioner's case. First Raizen Rep. at 7, 8. And (referencing Arnheim-Dahlstrom) he denied that reliable evidence connecting the HPV vaccine to *any* form of narcolepsy existed, noting that "the ratio of narcolepsy incidence between those vaccinated and those unvaccinated has a mean that is less (and not more) than 1." *Id.*

at 8 (emphasis in original); Arnheim-Dahlstrom at 5.[60]

b. *Raizen Second Report*

Dr. Raizen's second report focused on Ms. E.S.'s chronic fatigue diagnosis and its purported causal association with the HPV vaccine. He observed that the diagnosis (which came from Dr. Levine's treatment of Ms. E.S. in 2018) often featured "unrefreshing sleep" as a symptom. Second Raizen Rep. at 1–2. But he disputed that there was any overlap between this feature of chronic fatigue and narcolepsy, noting that those diagnosed with the latter often reported feeling *refreshed* after the instances in which they slept normally, with ever-present *sleepiness* more the problem they faced. *Id.* at 2; C. Baumann et al., *Challenges in Diagnosing Narcolepsy without Cataplexy: A Consensus Statement*, 37 Sleep 1035–42 (2014), filed July 27, 2018 as Ex. E, Tab 12 (ECF No. 73-3). As a result, he rejected the contention that chronic fatigue sleep-related symptoms would corroborate a narcolepsy diagnosis (and in fact maintained that Dr. Levine's findings further undercut the accuracy of Petitioner's earlier narcolepsy diagnosis). *Id.* at 2.

Dr. Raizen otherwise (consistent with his arguments about the narcolepsy-HPV vaccine causal relationship) contested Petitioner's allegations that the HPV vaccine was associated with chronic fatigue. He noted that science still did not fully understand the pathogenesis of chronic fatigue. Second Raizen Rep. at 5. As a result, he rejected Petitioner's argument that it was more likely than not an autoimmune condition. In addition, he noted that reliable studies from Europe did not observe an association between the HPV vaccine and an increased risk of chronic fatigue. *Id;* B. Feiring et al., *HPV Vaccination and Risk of Chronic Fatigue Syndrome/Myalgic Encephalomyelitis: A Nationwide Register-Based Study from Norway*, 35 Vaccine 4203–12 (2017), filed May 7, 2019 as Ex. I, Tab 5 (ECF No. 97-6); K. Donegan et al., *Bivalent Human Papillomavirus Vaccine and the Risk of Fatigue Syndromes in Girls in the UK*, 31 Vaccine 4961–67 (2013), filed May 7, 2019 as Ex. I, Tab 6 (ECF No. 97-7).

4. Dr. Christopher Gibbons

Dr. Gibbons, a board-certified neurologist with specific expertise in both diabetes and small fiber neuropathies, prepared a single report. Report, dated May 3, 2019, filed as Ex. J (ECF No. 98-1) ("Gibbons Rep."). In it, he set forth his dim view of Dr. Steinman's contention that Ms. E.S.'s purported small fiber neuropathy was caused by the HPV vaccine.

Dr. Gibbons is an Associate Professor of Neurology at Harvard Medical School. Gibbons

[60] In his second report, Dr. Raizen revisited Arnheim-Dahlstrom in light of arguments Dr. Steinman had made about his interpretation of its findings (in particular criticisms he leveled at how the raw data was adjusted). Second Steinman Rep. at 21–22. Dr. Raizen admitted his lack of expertise in statistics or epidemiology (which Dr. Steinman shares), but deemed the adjusted figures (which he placed more faith in) to be common in reliable epidemiologic studies, and otherwise argued the results that supported his contentions were scientifically reasonable. Second Raizen Rep. at 3–4.

Rep. at 1. He completed neurological training at Johns Hopkins Hospital and subspecialty training in Clinical Neurophysiology at Harvard Medical School and Beth Israel Deaconess Medical Center. *Id.* Dr. Gibbons has previously served as the Chair of the Autonomic Section of the American Academy of Neurology and Chair of the Clinical Affairs Committee of the American Autonomic Society. *Id.* He is currently the Director of the Beth Israel Deaconess Medical Center Neurocutaneous Laboratory—the diagnostic laboratory for small fiber neuropathy—and has treated thousands of patients with small fiber neuropathy and reviewed tens of thousands of skin biopsy slides for evaluation of small fiber neuropathy. *Id.* at 2. Of particular note, Dr. Gibbons reports that he personally published the "seminal articles" on both small fiber neuropathy as well as the use of skin biopsies as a diagnostic tool, and that he has over the years treated thousands of individuals suffering from small fiber neuropathy. *Id.* at 1–2; C. Gibbons et al., *Quantification of Sudomotor Innervation: a Comparison of Three Methods*, 42 Muscle Nerve 112–119 (2009), filed May 7, 2019 as Ex. J, Tab 4 (ECF No. 98-5); C. Gibbons, et al., *Quantification of Sweat Gland Innervation: a Clinical-Pathologic Correlation*, 72 Neurology 1479–86 (2009), filed May 7, 2019 as Ex. J, Tab 5 (ECF No. 98-6).

Like the other experts before him, Dr. Gibbons initiated his report with an overview of Petitioner's medical history, noting in particular that (a) Ms. E.S. had struggled controlling her diabetes, and (b) her small fiber neuropathy diagnosis came from the time period when she began seeing Dr. Chin in September 2018 (three-plus years after the last vaccinations at issue) and was based on two skin biopsies performed at that time. Gibbons Rep. at 3; Ex. 48. He challenged the diagnosis, arguing (despite the fact that the test results themselves were in the abnormal range (Ex. 48 at 2)) that the underlying records for the actual results had not been provided, making it impossible for him to evaluate the accuracy of the diagnosis in light of the proper reading of the results. Gibbons Rep. at 4.

More so, Dr. Gibbons maintained that Petitioner had received normal neurologic exams from 2016 until her visits with Dr. Chin, that there was no filed record establishing follow-up with Dr. Chin that would confirm the accuracy of the diagnosis, and that overall the record lacked sufficient clinical proof to corroborate the small fiber neuropathy diagnosis. Gibbons Rep. at 5. In addition, Dr. Gibbons maintained that the diagnosis could not be based solely on biopsy results, which could constitute a false positive. *Id.*; B. Callaghan et al., *Better Diagnostic Accuracy of Neuropathy in Obesity: A New Challenge for Neurologists*, 129 Clinical Neurophysiology: Official J. of the Int'l Federation of Clinical Neurophysiology 654–62 (2018), filed May 7, 2019 as Ex. J, Tab 5 (ECF No. 98-6).

Dr. Gibbons highlighted the significance of Petitioner's preexisting type 1 diabetes. Neuropathies are well-known to be highly associated with diabetes (as well as other risk factors Petitioner possessed, such as an elevated body mass index and hypercholesterolemia[61]). Gibbons

[61] Hypercholesterolemia is excessive cholesterol in the blood. *Dorland's* at 876.

Rep. at 6. Indeed, the association between diabetes and *any* form of neuropathy was far better established by medical science than a link to the HPV vaccine. *Id.* Dr. Gibbons therefore opined that assuming the small fiver neuropathy diagnosis was correct, it was still far more likely that it was explained by her diabetes than her receipt of the HPV vaccine. *Id.*

Regarding Petitioner's causal theory, Dr. Gibbons rejected the contention that the HPV vaccine was associated with small fiber neuropathy. He noted that (based on his own research) there were exceedingly few publicly available articles involving the topic, no research evaluating how the vaccine would cause such a form of neuropathy, and no case reports. Gibbons Rep. at 4. At most, Petitioner had referenced "a case series from Japan with an enormous array of symptoms" from a pool of individuals who received the vaccine. T. Kinoshita et al., *Peripheral Sympathetic Nerve Dysfunction in Adolescent Japanese Girls Following Immunization with the Human Papillomavirus Vaccine*, 53 Internal Med. 2185–2200 (2014), filed May 7, 2019 as Ex. J, Tab 1 (ECF No. 98-2) ("Kinoshita"). But, Dr. Gibbons opined that Kinoshita may not even have identified actual incidents of small fiber neuropathy (conflating them with biopsy evidence of purported "nerve" damage that in his reading was merely proof of damage to nerve myelin), adding that its findings otherwise had been cast in doubt. *Id.;* S. Hanley et al., *Peripheral Sympathetic Nerve Dysfunction in Adolescent Japanese Girls Following Immunization with the Human Papillomavirus Vaccine*, 54 Internal Med. 1953 (2015), filed May 7, 2019 as Ex. J, Tab 2 (ECF No. 98-3) (letter criticizing Kinoshita as not "demonstrat[ing] any relationship between vaccination and adverse events, which are [in Kinoshita] poorly-defined and include an eclectic range of symptoms").

Dr. Gibbons also proposed that the reasonableness of the timeframe in which Petitioner's onset occurred had not been established. The earliest evidence of a diagnosis of small fiber neuropathy was from 2018—*three years* after the last HPV dose Petitioner received. Moreover (and contrary to the history provided to Dr. Chin), the record for the intervening period of 2015 to 2018 showed numerous instances in which Ms. E.S. received normal neurologic exams. As a result, the period from last HPV dose to when Dr. Gibbons speculated Petitioner might have developed a small fiber neuropathy was too lengthy to be medically acceptable. Gibbons Rep. at 6–7.

C. *Other Scientific or Medical Evidence Pertaining to Petitioner's Case*

Petitioner filed some additional items of literature (15 in all) in the course of briefing Respondent's dismissal motion. Only a small few, however, plowed new ground, and therefore merit discussion.[62] One such article was only published in the late summer of 2019, and purports to

[62] Illustrative of the misguided, "more heat than light" nature of Petitioner's overall showing in this case, the Sur-Reply was filed with *seven* additional items of literature—most of which could have been offered far earlier in the matter's life, since all but one were published before 2018, and did not otherwise reflect new scientific findings. One of the newly-filed items, Exhibit 117, was a nearly *nine-hundred-page* excerpt from the Institute of Medicine's treatise *Adverse Effects of Vaccines: Evidence and Causality*—essentially the entirety of the work. The filing of whole texts into the record of a Vaccine Act case is not a practice reflective of careful lawyering aimed at persuading the special master through focused reference to helpful evidence.

support Petitioner's contentions about the autoimmune character of POTS. *See, e.g.*, W. Gunning et al., *Postural Orthostatic Tachycardia Syndrome is Associated with Elevated G-Protein Coupled Receptor Autoantibodies*, 8 J. Am. Heart Assoc. 1–10 (2019), filed Nov. 24, 2019 as Ex. 109 (ECF No. 107-1) ("Gunning"). Gunning observed the presence of elevated G-protein coupled adrenergic autoantibodies or muscarinic autoantibodies in the majority of a group of 55 patients. Gunning at 5–6. However, its authors conceded that the significance of its findings remained "unknown" (*Id.* at 7), and although Gunning purported that an association between vaccination and POTS was "well-documented," it based this proposition on articles written by some of the same individuals that have been found unpersuasive in past cases. *Id.* at 8 fn. 47–50 (citing an article written by Dr. Shoenfeld).[63] Gunning otherwise is not strong evidence for the conclusion that *all* cases of POTS are autoimmune in origin or nature—let alone a subset.

Respondent similarly filed some additional articles bearing on the resolution of the case. First, he filed a 2019 statement from the American Autonomic Society (the "AAS"), written by certain individuals deemed leaders in the field,[64] finding specifically that "there are no data [at this time] to support a causal relationship between HPV vaccination and CRPS, chronic fatigue, and [POTS] to other forms of dysautonomia." A. Barboi et al., *Human Papillomavirus (HPV) Vaccine and Autonomic Disorders: A Position Statement from the American Autonomic Society*, Clinical Autonomic Res. 1, 1–6 (2019), filed Feb. 4, 2020 as Ex. M (ECF No. 115-2) (the "AAS Statement"), at 1. The AAS Statement references L. Brinth et al., *Orthostatic Intolerance and postural tachycardia syndrome as suspected adverse effects of vaccination against human papilloma virus*, 33 Vaccine 2602–05 ("Brinth").

Second, Respondent filed a response to the AAS Statement written by a medical expert whose work has been favorably cited by Petitioner in this case as supportive of the relationship between the HPV vaccine and POTS. S. Blitshteyn, *Human Papillomavirus (HPV) Vaccine Safety Concerning POTS, CRPS and Related Conditions,* Clinical Autonomic Res. (2019), filed Feb. 4, 2020 as Ex. N (ECF No. 115-3) ("Blitshteyn"). Dr. Blitshteyn's article proposes that vaccine-triggered, immune-mediated autonomic dysfunction could possibly lead to the development of de novo post-HPV vaccination syndrome in genetically susceptible individuals. Blitshetyn, et al., *Autonomic dysfunction and HPV immunization: an overview*, Immunologic Res., filed as Ex. 96 on January 15, 2019 (ECF No. 88-1). But in her letter, (and while maintaining that the concept of dysautonomia induced by the HPV vaccine should be taken seriously and be made the subject of

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[63] Once again, reference is made to an article on the propensity of vaccination to cause autoimmune disease written by Dr. Shoenfeld—the same expert who (a) came up with the discredited ASIA theory discussed in footnote 56 above, and (b) has repeatedly, but unpersuasively, testified that the HPV vaccine can cause POTS and other purportedly autoimmune conditions. *See* Gunning at 8.

[64] The AAS Statement's 22 authors include one of Respondent's experts, Dr. Gibbons, as well as Dr. Philip Low, a nationally-recognized expert on the autonomic nervous system who has testified previously in the Program for Respondent in cases involving POTS as a claimed vaccine injury. *See, e.g. Yalacki*, 2019 WL 1061429, at *18.

further research), Dr. Blitshteyn *acknowledged* the accuracy of the AAS's conclusions. Blitshteyn Letter at 1 (noting that Dr. Blitshteyn "agree[s] with [the AAS's] conclusion that given the existing evidence to date, a causal relationship has not been supported") (the "Blitshteyn Letter").

Finally, Respondent offered a 2018 statistical analysis from Japan (source of articles like Ozawa and Kinoshita) of approximately 30,000 female recipients of the HPV vaccine and 24 kinds of post-vaccination symptoms commonly reported in studies claiming an association between the vaccine and the kinds of injuries claimed in this case. S. Suzuki et al., *No Association Between HPV Vaccine and Reported Post-Vaccination Symptoms in Japanese Young Women: Results of the Nagoya Study*, 5 Papillomavirus Res. 96–103 (2018), filed Feb. 4, 2020 as Ex. L (ECF No. 115-1) ("Suzuki"). The sample group in Suzuki is far larger than the number of individuals considered in Ozawa, Kinoshita, or even Brinth. Suzuki's authors only noted statistically relevant increases in complaints of headache or hospitalization due to menstrual bleeding, but not the kind of symptoms that might be deemed autonomic in character (*e.g.*, fatigue, dizziness, weakness, brain fog, etc.). Suzuki at 98–100.

III. Procedural History

The Petition was initiated in April 2017. By September of that year, after the filing of medical records and a substitution of counsel, Respondent filed his Rule 4(c) Report opposing an entitlement award. ECF No. 27. For nearly two years thereafter, the parties filed back-and-forth expert reports as discussed above. By May 2019, however, I had determined (given misgivings I had regarding some aspects of the case) that certain elements of the matter might be amenable to disposition via ruling on the record. To that end, I set up an initial schedule for briefing the matter. Docket Entry Order, dated May 15, 2019. The parties completed briefing the matter with the filing of Petitioner's Sur-Reply in April 2020, and the matter is fully ripe for resolution.

IV. Parties' Respective Arguments

Respondent's Motion attacks both the adequacy of evidence establishing certain of Petitioner's claimed injuries, as well as her success in demonstrating that the HPV and/or flu vaccines could cause them in the first place. He disputes that the record supports Petitioner's claim of chronic headaches, noting a lack of such a diagnosis (Mot. at 18), and also similarly contests that the record establishes that Ms. E.S. experienced myocardial ischemia. Mot. at 28–30. He also maintains that Petitioner's type 2 narcolepsy diagnosis was based on incomplete testing (Mot. at 33–34), adding that preponderant evidence does not establish that this form of narcolepsy (which cannot be assumed to be autoimmune, in comparison to the first form) has not reliably been associated with the HPV or flu vaccine. *Id.* at 34–36.

In addition, Respondent similarly observes that Petitioner's purported diagnoses for chronic

fatigue, small fiber neuropathy, and POTS were all obtained long after the vaccinations at issue (calling into question how they could be reasonably associated with vaccines), and that the evidence offered to support each either lacks corroboration in the record or reflects an incomplete determination. Mot. at 37–42. And Respondent challenges Petitioner's ability to show that her DM1 could be significantly aggravated by either relevant vaccine, arguing that (a) no Program decision has ever held that diabetes can be caused or aggravated by *any* vaccine, (b) Petitioner's course did not necessarily reveal consistent worsening, but instead was characterized by numerous ups and downs (as reflected in varying blood sugar testing results in the timeframe after vaccination), and (c) Dr. Lee's causation theory is not credible or reliable, and comes from an individual lacking the expertise to so opine. *Id.* at 21–28.

In reaction, Petitioner opposes dismissal, arguing instead that ample matters have been presented warranting a hearing. She consistently takes note of the difference in her health overall pre- versus post-vaccination. Opp. at 3–4, 5–6. After a lengthy review of her medical history, she emphasizes the diagnostic support for autonomic-related injuries from Dr. Levine in 2018, followed by Drs. Chin and Younger. *Id.* at 17–23. The narcolepsy diagnosis, she maintains, similarly finds support in Dr. Kothare's evaluation, and she proposes that the testing evidence (that she possesses the autoantibodies that are key to her theory for how these injuries came about) is sound. *Id.* at 23–24, 29. She makes a similar argument to vouch for the skin biopsy findings of small fiber neuropathy, over the objections of Dr. Gibbons. *Id.* at 34. These injuries are all related and are in Petitioner's view bulwarked by reliable recent literature underscoring the significance of anti-adrenergic antibodies in causing autonomic harm, such as Ikeda. Opp. at 27–28.

Ms. E.S. also maintains that her myocardial ischemia and DM1 significant aggravation claims are supported by the record and reliable science and medical evidence, including the testimony of Dr. Lee. To do so, she relies on inclusion of large block-quoted sections from Dr. Lee's reports. Opp. at 36–40. And as further support for her significant aggravation of diabetes claim, Petitioner revisits again her argument that her health took a noticeable turn for the worse post-vaccination, and emphasizes Dr. Lee's assertion (logically questioned by Respondent's experts, as noted above) that there was a "25-fold increase" in the incidence of diabetes after administration of the HPV vaccine. *Id.* at 40–42.

Respondent filed a succinct reply. It emphasized my authority to resolve this matter without a hearing, noting that none of the "new" articles or more recent treatment records Petitioner filed established persuasive grounds for a hearing. Reply at 2–3. Respondent made specific comment about the unpersuasive or unreliable character of articles filed in conjunction with the Opposition Brief, like Kinoshita and Gunning, while highlighting his own newly-filed articles, such as the AAS Statement or Suzuki. *Id.* at 4–5.

Given the opportunity to offer a sur-reply, Petitioner prepared and filed a brief *twice as long* as the Reply, but which largely repeated arguments already lodged in opposing Respondent's initial

dismissal motion. Petitioner admitted that the evidence for a POTS diagnosis might not be preponderant (Sur-Reply at 3 ("Dr. Younger's medical record and testing *points in the direction of a POTS diagnosis*") (emphasis added)), but claimed the evidence suggestive of that diagnosis had to be considered in light of the other record evidence supportive of some kind of dysautonomia, which was likely related to Petitioner's receipt of the HPV vaccine. *Id.* at 3–4. The "newly emerged" evidence associating the two marshaled in favor of a hearing. *Id.* at 4. She reiterated her arguments about a decline in health post-vaccination (*Id.* at 5–9). She also raised two somewhat new injury complaints that she had not emphasized before: (1) that she had showed "[s]ymptoms of ovarian failure" after vaccination—a condition she maintained is associated with the HPV vaccine;[65] and (2) that 2018 MRI results revealed a pituitary lesion that could be associated with HPV infection. *Id.* at 9–11.

V. Applicable Law

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

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[66] In this case, Petitioner does not assert a Table claim.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause

[65] In fact, claims of post-HPV vaccine ovarian failure have been litigated several times in the Program—never to success. *See, e.g. Wright v. Sec. of Health & Hum. Servs.*, No. 15-851V, 2017 WL 8218937 (Fed. Cl. Spec. Mstr. Dec. 28, 2017); *Culligan v. Sec. of Health & Hum. Servs.*, No. 14-318V, 2016 WL 3101981 (Fed. Cl. Spec. Mstr. June 2, 2016); *Laughlin v. Sec. of Health & Hum. Servs.*, No. 13-289V, 2016 WL 3101977 (Fed. Cl. Spec. Mstr. June 2, 2016).

[66] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Hum. Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Hum. Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Hum. Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Hum. Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

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

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras*, 121 Fed. Cl. at 245 ("[p]lausibility . . . in many cases *may* be enough to satisfy *Althen* prong one" (emphasis in original)).

In discussing the evidentiary standard applicable to the first *Althen* prong, the Federal Circuit has consistently rejected the contention that it can be satisfied merely by establishing the proposed causal theory's scientific or medical *plausibility*. *See Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019); *see also LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) ("[h]owever, in the past we have made clear that simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof." (citing *Moberly*, 592 F.3d at 1322)). And petitioners always have the ultimate burden of establishing their *overall* Vaccine Act claim with preponderant evidence. *W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted); *Tarsell v. United States*, 133 Fed. Cl. 782, 793

(2017) (noting that *Moberly* "addresses the petitioner's overall burden of proving causation-in-fact under the Vaccine Act" by a preponderance standard).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

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

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must align 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 & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 F. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec.

Mstr. May 30, 2013), *mot. for rev. denied* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Significant Aggravation Claims*

Besides arguing that the HPV and/or hepatitis A vaccines directly caused her injuries, Petitioner's experts have also allowed for the possibility that the vaccines significantly aggravated her preexisting diabetes mellitus. Where a petitioner so alleges, the *Althen* test is expanded, and the petitioner has additional evidentiary burdens to satisfy. *See generally Loving v. Sec'y of Health & Hum. Servs*., 86 Fed. Cl. 135, 144 (2009). In *Loving*, the Court of Federal Claims combined the *Althen* test with the test from *Whitecotton v. Sec'y of Health & Hum. Services*, 81 F.3d 1099, 1107 (Fed. Cir. 1996), which related to on-Table significant aggravation cases. The resultant "significant aggravation" test has six components, which require establishing:

> (1) the person's condition prior to administration of the vaccine, (2) the person's current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person's current condition constitutes a "significant aggravation" of the person's condition prior to vaccination, (4) a medical theory causally connecting such a significantly worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) a showing of a proximate temporal relationship between the vaccination and the significant aggravation.

Loving, 86 Fed. Cl. at 144; *see also W.C.*, 704 F.3d at 1357 (holding that "the *Loving* case provides the correct framework for evaluating off-table significant aggravation claims"). In effect, the last three prongs of the Loving test correspond to the three *Althen* prongs.

In *Sharpe v. Sec'y of Health & Hum. Servs.,* 964 F.3d 1072 (Fed. Cir. 2020), the Federal Circuit further elaborated on the *Loving* framework. Under prong (3) of the *Loving* test, the Petitioner need not demonstrate an *expected* outcome, but merely that her current-post vaccination condition was worse than pre-vaccination. *Sharpe*, 964 F.3d at 1081. And a claimant may make out a prima facie case of significant aggravation overall without eliminating a preexisting condition as the cause of her significantly aggravated injury (although the Circuit did not alter the ability of Respondent to so prove in cases where the burden shifts). *Id.* at 1083.

C. *Legal Standards Governing Factual Determinations*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the

record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Hum. Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

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

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie*, 2005 WL 6117475, at *20. Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy*, 23 Cl. Ct. at 733 (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

There are, however, situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Hum. Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("'[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent'") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding

a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Hum. Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

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

D. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Hum. Servs*., 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 594–96 (1993). *See Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999)). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs*., 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the

persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts of his own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen*, 618 F.3d at 1347 (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)); *see also Isaac v. Sec'y of Health & Hum. Servs*., No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for rev. denied*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. Appx. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

Expert opinions based on unsupported facts may be given relatively little weight. *See Dobrydnev v. Sec'y of Health & Hum. Servs.*, 556 F. Appx. 976, 992–93 (Fed. Cir. 2014) ("[a] doctor's conclusion is only as good as the facts upon which it is based") (citing *Brooke Group Ltd. v. Brown & Williamson Tobacco Corp.*, 509 U.S. 209, 242 (1993) ("[w]hen an expert assumes facts that are not supported by a preponderance of the evidence, a finder of fact may properly reject the expert's opinion")). Expert opinions that fail to address or are at odds with contemporaneous medical records may therefore be less persuasive than those which correspond to such records. *See Gerami v. Sec'y of Health & Hum. Servs.*, No. 12-442V, 2013 WL 5998109, at *4 (Fed. Cl. Spec. Mstr. Oct. 11, 2013), *aff'd*, 127 Fed. Cl. 299 (2014).

E. *Consideration of Medical Literature*

Both parties filed medical and scientific literature in this case, but not every filed item factors into the outcome of this decision. While I have reviewed all the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case—just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of*

Health & Hum. Servs., 527 F. Appx. 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

F. *Consideration of Comparable Special Master Decisions*

In reaching a decision in this case, I have considered other decisions issued by special masters (including my own) involving similar injuries, vaccines, or circumstances. I also reference some of those cases in this Decision, in an effort to establish common themes, as well as demonstrate how prior determinations impact my thinking on the present case.

There is no error in doing so. It is certainly correct that prior decision in different cases do not *control* the outcome herein.[67] *Boatmon,* 941 F.3d at 1358-59; *Hanlon v. Sec'y of Health & Hum. Servs.*, 40 Fed. Cl. 625, 630 (1998). Thus, the fact that another special master reasonably determined elsewhere, on the basis of facts not in evidence in this case, that preponderant evidence supported the conclusion that vaccine X caused petitioner's injury Y does not compel me to reach the same conclusion in *this* case. Different actions present different background medical histories, different experts, and different items of medical literature, and therefore can reasonably result in contrary determinations.

However, it is *equally* the case that special masters draw upon their experience in resolving Vaccine Act claims. *Doe v. Sec'y of Health & Hum. Servs.,* 76 Fed. Cl. 328, 338-39 (2007) ("[o]ne reason that proceedings are more expeditious in the hands of special masters is that the special masters have the *expertise and experience to know the type of information that is most probative of a claim*") (emphasis added). They would therefore be remiss in ignoring prior cases presenting similar theories or factual circumstances, along with the reasoning employed in reaching such decisions. This is especially so given that special masters not only routinely hear from the same experts in comparable cases but are also repeatedly offered the *same* items of medical literature regarding certain common causation theories. It defies reason and logic to obligate special masters to "reinvent the wheel", so to speak, in each new case before them, paying no heed at all to how their colleagues past and present have addressed similar causation theories or fact patterns. It is for this reason that prior decisions can have high persuasive value—and why special masters often explain how a new determination relates to such past decisions.[68] Even if the Federal Circuit does not *require*

[67] By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Hum. Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Hum. Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014). Special masters are also bound within a specific case by determinations made by judges of the Court of Federal Claims after a motion for review is resolved.

[68] Consideration of prior determinations is a two-way street that does not only inure to the benefit of one party. Thus, I would likely take into account the numerous decisions finding no association between vaccination and autism when confronted with a new claim asserting autism as an injury, and I have informed such claimants early in the life of their case that the claim was not viable for just that reason. But I would *also* deem a non-Table claim asserting GBS after receipt of the flu vaccine as not requiring extensive proof on *Althen* prong one "can cause" matters, for the simple reason that the Program has repeatedly litigated the issue in favor of petitioners.

special masters to distinguish other relevant cases (*Boatmon,* 941 F.3d at 1358), it is still *wise* to do so.

G. *Determining Matter on Record Rather Than at Hearing*

I have opted to decide this case based on written submissions and evidentiary filings, including the numerous expert reports that have been submitted. The Vaccine Act and Rules not only contemplate but encourage special masters to decide petitions (or components of a claim) on the papers rather than via evidentiary hearing, where (in the exercise of their discretion) they conclude that the former means of adjudication will properly and fairly resolve the case. Section 12(d)(2)(D); Vaccine Rule 8(d). The Federal Circuit has recently affirmed this practice. *Kreizenbeck v. Sec'y of Health & Hum. Servs.*, 945 F.3d 1362, 1365–66 (Fed. Cir. 2020). It simply is not the case that every Vaccine Act claim need be resolved by hearing—even where the petitioner explicitly so requests.

ANALYSIS

I. Several of Petitioner's Alleged Injuries Have Not Been Preponderantly Established

As reasoned Program case law instructs, a petitioner's vaccine injury claim is premised on first establishing the underlying *existence* of the claimed injury. The inability to establish an injury by preponderant evidence is fatal to the portion of a claim so dependent, since a vaccine could not have caused a non-existent injury. *Broekelschen*, 618 F.3d at 1346. It is also true in many cases that the claimant's causation theory only pertains to a particular injury, and/or the one articulated in the case. As a result, it is often necessary at the outset of analyzing a vaccine injury claim to determine whether a given alleged injury has been preponderantly established.

This case features a lengthy, ample medical record that strongly establishes that Petitioner (who unquestionably had preexisting type 1 diabetes that was not completely controlled in the time period prior to her first vaccination at issue) regularly sought medical treatment, often on an emergency basis, after her vaccinations in 2014 and 2015. However, other than complications attributable to her ongoing struggle with diabetes, the record does *not* preponderantly support some of the diagnoses that Petitioner purports to have received, and that she claims are the product of a vaccine injury. There is simply far less here than meets the eye, and certainly less proof of harm if petitioner-reported diagnoses (recounted to new treaters) contained in medical histories are ignored (as they rightfully should be).

The injuries asserted by Petitioner that find insufficient support in the record, and therefore have not been preponderantly established, include the following:

Myocardial Ischemia — the record does not preponderate whatsoever in support of the conclusion that Ms. Hughes has myocardial ischemia, or any comparable heart condition. The evidence supporting this diagnosis comes from a single encounter with a cardiologist in February 2016. Although there is some proof suggestive of a problem from the testing performed at that visit, the treater in question (Dr. Lefkowitz) ultimately did not diagnose Petitioner consistent with what she argues, as his follow-up visit with her a year later corroborates. *See* Ex. 18 at 14. Moreover, as ably demonstrated by Dr. LaRue, the overall picture (when EKGs obtained before and after the February 2016 visit are considered) does not reveal an actual cardiac problem. In contrast, Dr. Lee (who has *no* specific cardiac expertise) has offered an opinion on this matter that (like the larger problems his reports reflect, discussed below) is wholly unpersuasive. For this reason, I give no further consideration to arguments that the HPV vaccine could cause this kind of injury—the injury itself has not been proven preponderantly.

Headache — there are intermittent references in the record to Ms. Hughes experiencing headaches, whether migraine in nature or not. *See, e.g.*, Ex. 9 at 3 (On October 2, 2014 Petitioner was seen at student health center for uncontrollable high blood sugars and headache); Ex. 24 at 7 (On May 31, 2016, Petitioner was evaluated for headaches, neurological exam and brain MRI/MRA were normal). However, the thrust of her complaints, beginning in the fall of 2014, relate to *other* symptoms (abdominal pain in particular) that are distinguishable. There is also evidence of headaches predating vaccination (*see, e.g.*, Ex. 3 at 16), and no preponderant evidence that her headache complaints became more frequent beginning in the fall of 2014.

Headaches are simply not a consistent complaint herein—unlike other cases, where a claimant squarely maintains that he or she incurred a persistent and debilitating course of headaches due to the HPV vaccine. *See B.A. v. Sec'y of Health & Hum. Servs.*, No. 11-51V, 2018WL 6985218 (Fed. Cl. Spec. Mstr. Dec. 6, 2018) (petitioner suffered from chronic (at least every few days) headaches of gradual onset of 4-5 weeks within 9-10 days of vaccination). Thus, I do not find chronic headaches to have been preponderantly established such that they could be an independent basis for a finding of entitlement.

Injuries Highlighted in Sur-Reply

The claims of a pituitary injury or possible ovarian damage reflective of premature ovarian failure were not squarely posed in this case any time before Petitioner's Sur-Reply, but are no better substantiated by the medical record than those she alleged earlier in the case's existence. Petitioner maintains that either could be associated with her overall decline in health post-vaccination. Sur-Reply at 11; Ex. 121. But the former has not been demonstrated to be malign or a confirmed pathologic finding, with MRI evidence from Dr. Chin's evaluations in 2018 providing the primary evidence for it. Petitioner has not otherwise explained the *pathologic* impact of this purported injury (let alone *how* the HPV vaccine led to it). At most, she maintains that her "low cortisol levels" (Ex. 19 at 140) could be the product of pituitary failure—but no treaters seem to have embraced that

diagnostic view, or characterized the lesion as harmful. And its temporal distance from even the *second* dose of the vaccine in August 2015 make it highly improbable the lesion could be attributable to vaccination. In any event, the record does not preponderantly support pituitary failure as a cognizable injury in this case.

The arguments about ovarian failure rely too much on incidents experienced by Ms. E.S. involving ruptured cysts, and do not come close to the circumstances in other cases (cases which did *not* result in entitlement findings) in which petitioners far more credibly established some form of ovarian failure injury. *See, e.g.*, *Culligan v. Sec'y of Health & Hum. Servs.*, No. 14-318V, 2016 WL 3101981 (Fed. Cl. Spec. Mstr. June 2, 2016) (ovarian failure injury was characterized by markedly irregular periods, following a year of regular periods; periods that occurred less frequently than every 35 days; and heavier and longer periods, which may have lasted more than seven days); *Meylor v. Sec'y of Health & Hum. Servs.*, No. 10-770V, 2016 WL 3165774 (Fed. Cl. Spec. Mstr. May 16, 2016) (ovarian failure injury was characterized by irregular periods that became more irregular between first and second HPV vaccinations; sleep disturbances, including insomnia and night sweats; and depression and joint pain). Moreover, the record establishes menses issues well prior to the first vaccinations.

Purported ovarian failure is also unpersuasively intertwined with claims of an active HPV infection based on testing from Milford Molecular Diagnostics (Ex. 32 at 14), somehow interacting with the observed adenoma. But if this is an actual cognizable injury, there is scant treater support identifying it as such, let alone associating it with vaccination. Overall, these two late-alleged injuries simply typify Petitioner's overall effort to fashion her claim in the course of its adjudication, adding new arguments to replace old as the latter show weakness, and simply trying to keep the claim viable by looking for "new" injuries to allege as time passes.

By contrast, other injuries alleged in the Petition have just enough evidence supporting their existence to justify an *Althen* analysis (although some of them barely cross the preponderant line). Petitioner has unquestionably struggled with diabetes complications throughout her post-vaccination life, making it a reasonable injury for evaluation as part of a significant aggravation claim (given the undisputed fact that she had been diagnosed with type I diabetes long before the vaccinations at issue). Her claim of type 2 narcolepsy is also supported by *some* record proof. Respondent's experts raised reasonable objections to the overall validity of the testing that produced the diagnosis, but there is sufficient support for it to evaluate if her diagnosed sleep problems were

in fact vaccine-caused. In addition, diagnosis of chronic fatigue[69] and small fiber neuropathy[70] both are bulwarked by recent testing results. Although Dr. Gibbons raised credible and persuasive reasons to doubt that the uncorroborated skin biopsy results were sufficient for the latter diagnosis, these two diagnoses have reliable evidence behind them for purposes of moving forward.

The POTS injury, by contrast, is far less robustly supported by the record, and arguably should not be deemed to have been preponderantly established. It has never been corroborated by a true tilt table test (the gold standard for diagnosing POTS).[71] More significantly, Petitioner *acknowledges* that she has never even been diagnosed with POTS. Sur-Reply at 3. She maintains, however, that her POTS-like presentation is reflective of overall autonomic dysfunction, especially in light of her alleged chronic fatigue syndrome and small fiber neuropathy, all of which she considers part of the same vaccine response. *Id.* Thus, for sake of argument, and to give some credit to the "big picture" contention Petitioner advances with regard to her various autonomic-oriented symptoms, I will treat POTS as if it had been evidentiarily substantiated (although I expressly *do not* so rule), and will evaluate Petitioner's subsequent success in preponderantly establishing that the HPV vaccine could cause it.

II. Petitioner's Various Causation Theories are Unreliable and/or not Preponderantly Supported by the Evidence

Although I am considering a large number of alleged injuries (including several that arguably lack preponderant support), I universally find that Petitioner has not in *any* instance established that the HPV or flu vaccines "can cause" the relevant injury. (I consider separately whether these vaccines could have aggravated type I diabetes below).

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[69] Chronic fatigue syndrome is persistent debilitating fatigue lasting longer than 6 months, with other known medical conditions having been ruled out by clinical diagnosis, accompanied by at least four of the following: significantly impaired short-term memory or concentration, muscle weakness, pain in multiple joints without swelling or redness, sore throat, tender lymph nodes, headaches, unrefreshing sleep, and malaise that lasts more than 24 hours following exertion. Chronic fatigue syndrome, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=110414 (last visited Oct. 28, 2020). The cause is unknown and may be multifactorial; immune dysfunction has been suggested, and viral infection may be associated with it, although no causal relationship has been demonstrated. *Id.*

[70] Small fiber neuropathy is a type of neuropathy in which only the small sensory cutaneous nerves are affected. Small fiber neuropathy, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=137479&searchterm=small+fiber+neuropathy (last visited Oct. 28, 2020). The majority of patients experience sensory disturbances that start in the feet and progress upwards. John Hopkins Medicine, Neurology and Neurosurgery, Small Fiber Sensory Neuropathy, https://www.hopkinsmedicine.org/neurology_neurosurgery/centers_clinics/peripheral_nerve/conditions/small_fiber_sensory_neuropathy.html (last visited Oct. 28, 2020).

[71] The standard tilt table test entails the patient remaining in a supine position for twenty minutes, followed by ten minutes tilted upright, and that the heart rate and blood pressure should be measured minute by minute. *Yalacki*, 2019 WL 1061429, at *40, n.10.

A. *POTS*

POTS is a circulation disorder characterized by a group of symptoms (not including hypotension) that sometimes occur when a person assumes an upright position, including tachycardia, tremulousness, lightheadedness, sweating, and hyperventilation. Postural orthostatic tachycardia syndrome, *Dorland's Medical Dictionary Online*, https://www.dorlandsonline.com/dorland/definition?id=111236 (last visited Oct. 26, 2020). POTS is seen more often in women than in men, and its etiology remains uncertain. *Id.* It implicates the function of the autonomic nervous system, since it involves involuntary physical processes like heart rate. A tilt table test is often used to diagnose POTS. John Hopkins Medicine, Health Conditions and Diseases, Postural Orthostatic Tachycardia Syndrome (POTS), https://www.hopkinsmedicine.org/health/conditions-and-diseases/postural-orthostatic-tachycardia-syndrome-pots (last visited Oct. 26, 2020).[72] Treaters may diagnose a patient with POTS if all three of these criteria are met: (i) abnormal heart rate response to being upright; (ii) symptoms that worsen when upright; and (iii) orthostatic hypotension (i.e. a drop in blood pressure) does not develop in the first three minutes of testing. *Id.*

This is not the first case in which a claimant before me has alleged that POTS was vaccine-caused (and usually by the HPV vaccine). But I have never so found. *See e.g.*, *McKown v. Sec'y of Health & Hum. Servs.*, No. 15-1451V, 2019 WL 4072113 (Fed. Cl. Spec. Mstr. July 15, 2019); *Combs v. Sec'y of Health & Hum. Servs.*, No. 14-878V, 2018 WL 1581672 (Fed. Cl. Spec. Mstr. Feb. 15, 2018); *see also Otto v. Sec'y of Health & Hum. Servs.*, No. 16-1144V, 2020 WL 4719285 (Fed. Cl. Spec. Mstr. June 17, 2020) (case dismissed after hearing on claimant's request).

In deciding these prior claims, I have generally noted that POTS is most commonly *not* considered attributable to an autoimmune process interfering with the autonomic nervous system. Rather, it is thought to reflect the autonomic system functioning *properly* in response to stressors (for example, hypovolemia, in which a person's dehydrated states produces orthostatic imbalance). *See, e.g.*, *McKown*, 2019 WL 4072113, at *52. Thus, POTS can occur in the context of a functioning autonomic nervous system. Moreover, while it is true that some evidence has emerged in the last ten years that in rare cases POTS might *sometimes* be attributable to an autoimmune process involving anti-adrenergic antibodies (which can cause heart rate increases), this is the exception to the rule—and to date, not nearly enough is known about how this process works or what would initiate it, to draw conclusions in Program cases sufficient to meet the preponderance level of evidence.[73] Further,

[72] During the test, the patient is secured on a table while lying flat. *Id.* The table is then raised to an almost upright position. *Id.* The patient's heart rate, blood pressure, and often blood oxygen and exhaled carbon dioxide levels are measured during this test. *Id.*

[73] Another case I decided (although not involving the HPV vaccine specifically) is instructive on this point. *See Yalacki,* 2019 WL 1061429, at *18. In *Yalacki*, Dr. Philip Low (a world-renowned expert on the autonomic nervous system) testifying on Respondent's behalf, noted that he previously believed that a different kind of autoantibody might be important in POTS (although in only 10 percent of cases). *Id.* However, subsequent research disproved any correlation

in none of these cases was it preponderantly established, through citation to reliable scientific evidence or expert testimony, that the HPV vaccine could cause the production of anti-adrenergic autoantibodies posited to cause POTS in some limited circumstances.[74]

Against this backdrop, nothing offered in this case by Petitioner or her experts provides more recent or more reliable evidence supporting the conclusion that the HPV vaccine might cause POTS (or any associated autonomic-associated symptoms for that matter). Dr. Steinman, for example, makes the same literal arguments about theoretical homology between components of the HPV vaccine and muscarinic receptors that are always presented in such cases—but with insufficient reliable corroborative proof supporting the conclusion that the homology is *meaningful* from a pathogenic sense. Establishing the existence of potential homology based on internet-driven research performed solely for this case is not enough to meet the preponderant burden of establishing it more likely than not that the vaccine *would* cross-react as proposed. *Sullivan v. Sec'y of Health & Hum. Servs.*, No. 10-398V, 2015 WL 1404957, at *17–18, n. 30 (Fed. Cl. Spec. Mstr. Feb. 13, 2015) (while the law does not require Petitioner to "prove" homology in a Program case, mere assertion that HPV strain shares sequences with human body such that molecular mimicry might occur resulting in injury was by itself insufficient to satisfy burden). Indeed, as Dr. MacGinnitie noted, homologies are easily demonstrated to exist in nature, but they do not always establish the likelihood of concurrent cross-reactivity. First MacGinnitie Rep. at 4. Petitioner's experts also purport to show an HPV relationship to POTS and autonomic dysfunction generally by relying on the same items of literature I have reviewed numerous times in the past but found wanting. Ozawa; Kinoshita; *Johnson*, 2018 WL 2051760, at *24.

Arguments about the autoimmune character of POTS, or the possibility that the HPV Vaccine could encourage the production of autoantibodies thought to be POTS-associated, were also unreliably established. Articles like Ikeda simply demonstrated that a group of individuals possessed the proposed autonomic system-impacting autoantibodies after vaccination, not that they were *caused* by it (and Ikeda did not even establish the autoantibodies were likely pathogenic). By contrast, other recent articles undermine Petitioner's arguments about the significance of these autoantibodies, (some of which were even offered by her own experts). *See, e.g.*, Loebel at 38. At the same time, other evidence established a consensus in the relevant medical community that the vaccine is not associated with autonomic injury or interference, or that the kinds of injuries alleged herein have not been convincingly associated with the vaccine from an epidemiologic standpoint. *See* Suzuki at 1;

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to POTS. *Id.* Today, Dr. Low does not routinely test POTS patients for particular autoantibodies, "because we have not been able to demonstrate any causative antibody." *Id.*

[74] In *Yalacki*, the petitioner's experts proposed that an "adrenergic antibody," presumably produced in response to the hepatitis B vaccine, was the most likely mechanistic causal element in triggering Petitioner's POTS. *Yalacki*, 2019 WL 1061429 at *20. However, the literature offered to support this contention did not involve an actual measurement of the antibody in questions in humans. *Id.* While the petitioner was able to offer some reliable literature exploring the possibility that *some* cases of POTS might be autoimmune-mediated, Petitioner acknowledged that more recent research moved away from autoimmunity as the most likely explanation for POTS, in the majority of individuals. *Id.* at *31.

AAS Statement at 1. Large, reliable epidemiologic studies further undermine this conclusion. And it remains true that the majority of cases of POTS are likely *not* mediated by an autoimmune process—and that rare subset that might be would not likely occur months to years after the purported instigating event, such as of receipt of a vaccine. All of the above precludes me from determining that the HPV vaccine likely can cause POTS.

B. *Narcolepsy*

Several years ago, I wrote a lengthy decision evaluating the claim that the unadjuvanted flu vaccine could cause narcolepsy. *D'Toile v. Sec'y of Health & Hum. Servs.*, No. 15-085V, 2016 WL 7664475 (Fed. Cl. Spec. Mstr. Nov. 28, 2016) *mot. for review den'd*, 132 Fed. Cl. 421 (2017), *aff'd,* 726 F. App'x 809 (Fed. Cir. 2018). I denied entitlement (in a case featuring Dr. Steinman as the petitioner's primary expert), finding that although there was reliable and persuasive evidence that a *different* form of the flu vaccine (one that was adjuvanted and administered only in Europe) *had* credibly been associated with narcolepsy, the same was not true of the version widely administered in the United States and received by the petitioner in question.

Petitioner now tries to breathe new life into the same theory rejected in *D'Toile*—but with an overall *weaker* argument, supplemented by no new articles or evidence that might suggest a persuasive reason to revisit my prior rejection of the theory. She thus focuses on the HPV vaccine,[75] but without showing any literature akin to what was offered previously (and repeated in this case by Dr. Steinman). Worse, Petitioner's diagnosed version of narcolepsy, type II, is even *less considered* autoimmune in nature than type I, which the literature filed discusses at length. *See* National Institute of Neurological Disorders and Stroke, *Narcolepsy Fact Sheet*, available at https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Narcolepsy-Fact-Sheet (last visited Mar. 2, 2018), filed on Mar. 3, 2018 as Ex. 39, Ref. 6 at 2; Ex. 97. And Dr. Steinman's fallback is to rely on homology arguments proposing theoretical bases for an autoimmune cross-reaction incited by the HPV vaccine that find no real-world basis in research. In short, Petitioner's argument that the HPV vaccine can cause type II narcolepsy was woefully unsupported with reliable proof to be deemed a preponderant showing.

C. *Chronic Fatigue Syndrome*

Petitioner is on slightly more firm ground in arguing that vaccination can cause chronic fatigue. However, claimants have not been routinely successful in so arguing. *See,* e.g., *McCabe v. Sec'y of Health & Hum. Servs.*, No. 13-570V, 2018 WL 3029175 (Fed. Cl. Spec. Mstr. May 17, 2018) (denying entitlement for CFS allegedly caused by influenza vaccinations); *D'Angiolini v.*

[75] Perhaps mindful of my prior decisions involving the flu vaccine and narcolepsy, Petitioner *does not* ask me to consider again the same issue based on her receipt of the flu vaccine in 2015.

Sec'y of Health & Hum. Servs., No. 99-5788V, 2014 WL 1678145 (Fed. Cl. Spec. Mstr. March 27, 2014) (denying entitlement for adverse reaction, including CFS, allegedly caused by hepatitis B vaccination). I have also previously considered the issue but not found it preponderantly established. *Yalacki v. Sec'y of Health & Hum. Servs.*, No. 14-278V, 2019 WL 1061429, at *38–39 (Fed. Cl. Spec. Mstr. Jan. 31, 2019), *mot. for review den'd*, 146 Fed. Cl. 80 (2019) (hepatitis B vaccine was not shown to be capable of causing CFS); *Johnson v. Sec. of Health & Human Servs.*, No. 14-254V, 2018 WL 2051760 (Fed. Cl. Spec. Mstr. Mar. 23, 2018) (denying entitlement in case alleging CFS and POTS caused by HPV vaccination).

Petitioner has not succeeded here where others have failed, largely for the same reasons that her POTS-related causal theory is unpersuasive. She simply cannot establish with reliable scientific evidence of any kind (expert testimony, articles, etc.) that there is a likely association between the HPV vaccine and chronic fatigue.[76] Those articles or case studies she attempts to cite for this assertion do not reflect medically/scientifically reliable determinations, and are rebutted by larger-scale epidemiologic proof offered by Respondent, such as Chao.

D. *Small Fiber Neuropathy*

Dr. Gibbons (unquestionably the expert in this case most qualified to comment on Petitioner's small fiber neuropathy-based claim) raised reasonable points about the evidentiary strength of the diagnosis obtained when Petitioner saw Dr. Chin in 2018. But even if I assume for sake of argument that the small fiber neuropathy diagnosis has reliable/substantive medical support, the underlying claim that the HPV vaccine could cause small fiber neuropathy has itself not been reliably established.

As already noted, merely showing via BLAST searches that some homology exists between amino acid sequences in the HPV vaccine components and nerve cells does not amount to a preponderant showing that the vaccine can produce antibodies that will cross-react against those cells. Moreover, it is far from certain that small fiber neuropathy *is* an autoimmune-driven condition[77], as noted in other decisions. *See, e.g.*, *Todd v. Sec'y of Health & Hum. Servs.*, No. 15-

[76] At the same time, this set of symptoms could also be associated with Petitioner's diabetes. Fatigue is a common symptom in several medical conditions, including diabetes. Mayo Clinic, Chronic fatigue syndrome, https://www.mayoclinic.org/diseases-conditions/chronic-fatigue-syndrome/diagnosis-treatment/drc-20360510 (last visited Oct. 30, 2020). Some of signs and symptoms of type 1 diabetes are: extreme hunger, presence of ketones in the urine, fatigue, and frequent infections. Mayo Clinic, Diabetes, https://www.mayoclinic.org/diseases-conditions/diabetes/symptoms-causes/syc-20371444 (last visited Oct. 30, 2020).

[77] It should also be noted that small fiber neuropathy is a type of nerve damage that can occur as a result of uncontrolled diabetes. Mayo Clinic, Diabetic Neuropathy, https://www.mayoclinic.org/diseases-conditions/diabetic-neuropathy/symptoms-causes/syc-20371580 (last visited Oct. 30, 2020). This nerve damage, sometimes called diabetic neuropathy, is the result of high blood sugar and most often damages nerves in the legs and feet. *Id.* Depending on the affected nerves, diabetic neuropathy symptoms can range from pain and numbness in your legs and feet to problems with your digestive system, urinary tract, blood vessels, and heart. *Id.* This record is just as consistent with Petitioner's small fiber neuropathy being related to her diabetes as the result of vaccination, if not more so.

860V, 2020 WL 727973 at *21 (Fed. Cl. Spec. Mstr. Jan. 8, 2020) (denying entitlement for SFN allegedly caused by flu vaccination; petitioner failed to establish the existence of systemic inflammation that would be associated with a chronic autoimmune neuropathy); *LaPierre v. Sec'y of Health & Hum. Servs.*, No. 17-227V, 2019 WL 6490730 at *17 (Fed. Cl. Spec. Mstr. Oct. 18, 2019) (finding that Petitioner's non-specific symptoms were not a basis for entitlement despite possible overlap with known symptoms of other peripheral neuropathies). And evidence offered to suggest a case study-oriented association, like Kinoshita, is weak, dependent on self-selected patient populations rather than scientifically-reliable studies. *Johnson,* 2018 WL 2051760, at *9, 17.

III. The Medical Record Does Not Support the Conclusion that Petitioner Experienced Any of her Allegedly Vaccine-Related Injuries in a Medically-Acceptable Timeframe

For each claimed injury other than diabetes exacerbation, Petitioner asks that I find that her onset was medically reasonable. In so doing, however, she frequently relies on diagnoses made long after vaccination—between two and three years after, depending upon whether 2014 or 2015 are the focus. Thus, she implicitly relies on the idea that she was experiencing an interrelated, autoimmune-caused course of symptoms that began close in time to receipt of the HPV and flu vaccines (as evidenced by her first hospital visits in October 2014 after beginning college), but which occasionally blossomed into more self-evident.

But for none of these injuries has Petitioner reliably demonstrated that the HPV or flu vaccines could have produced the symptoms in a medically-acceptable timeframe. Her narcolepsy, for example, was not diagnosed until 2016—and although she claims her sleep problems began in the fall of 2014 (and hence a few months after receipt of the first HPV dose), the record does not reveal any sleep-related complaint prior to seeing Dr. Kothare. In addition, some of the same problems with her HPV-narcolepsy theory that plague her showing on the first *Althen* prong impact this one as well. Thus, since the type of narcolepsy with which Petitioner was diagnosed is different from the one that has been deemed autoimmune, scientific understanding about the process for hypocretin path interference that might be consistent with a lengthy post-vaccination onset is not automatically relevant herein. Dr. Steinman (the primary expert offering testimony for Petitioner on this aspect of her claim) did not provide a reliable basis for concluding that type 2 narcolepsy could be subclinical for so long before manifesting more overtly, even if difficulties in diagnosis are taken into account. He simply assumed that any period "weeks to months" after vaccination is medically acceptable.

The timeframes for Petitioner's development of chronic fatigue and small fiber neuropathy are even more problematic. Both were diagnosed no less than *three years* after receipt of the second HPV vaccine (and even after this case had been filed), and the record does not contain consistent evidence of complaints by Petitioner (who certainly sought medical care on a regular basis throughout) that might reflect incipient presentation of either injury, or that she was experiencing these symptoms throughout. Indeed, although these conditions are neurologic (with the latter more

specific to sensory nerves), Petitioner received *normal* neurologic workups in 2016-2018, before either diagnosis was ever considered. And Petitioner's meta-explanation for her course—that the HPV vaccine was somehow initiative of a pathologic process featuring interference with the autonomic nervous system, the manifestations of which unfolded over time—is not backed up by reliable and persuasive expert testimony or any other form of reasonable proof (i.e. treater views, medical record evidence of persistent/common symptoms complaints, medical or scientific articles, etc.)

Petitioner's alleged nascent POTS is also temporally attenuated from the vaccination, without a showing that a vaccination even years before it could initiate a chronic process that would manifest as it purportedly did long after. This is especially true if the timeframe inquiry focuses on the existence of the anti-adrenergic antibodies that Petitioner alleges were causal. Petitioner was not apparently tested for these before the fall of 2016, obtaining the evidence that she possessed them in January 2017. Ex. 16 at 1; Second Steinman Rep. at 24–25. Because the shortest period from the time the testing occurred to the last relevant vaccination (August 2015) was over one year, how can Petitioner's theory account for vaccine causality given that length of time? Could other factors have generated the autoantibodies in a period of time exceeding one year? And why has her POTS not yet fully manifested, such that the diagnosis could be made later? This was not the case even as of August 2018 (when Dr. Levine raised the topic)—more than eighteen months after Petitioner received the positive test results. These are not quibbles—they are reasonable questions, and the inability of Petitioner to answer them with reliable and persuasive evidence compels a finding that the timeframe is simply too long to be medically acceptable.

The lack of preponderant proof setting forth a medically-acceptable timeframe for injury due to vaccination is consistent with my overall impression of this case. Here, a person with severe and recurrent illnesses—illnesses most credibly associated with her preexisting diabetes—seeks to establish intervening vaccines as responsible for everything that came thereafter. That may have been enough of a basis for filing the claim—but a temporal association is *unquestionably* not enough for a finding of entitlement, or at a minimum for showing that the timeframe in which the (alleged) injuries occurred was medically acceptable. Petitioner simply has not demonstrated that all of these symptoms she experienced can be "tied together," such that it is medically acceptable to conclude that conditions diagnosed years after vaccination are the end-result of pathologic processes she experienced in the lead time up to diagnosis. This is especially so given my finding (discussed below) that most of what Petitioner experienced far closer in time to the relevant vaccinations reflected her worsening diabetes—and the symptoms associated with that have not been shown to be vaccine-caused.

IV. Petitioner's Preexisting Diabetes Has Not Been Shown to have Been Exacerbated by Any Vaccines She Received

Certain of Petitioner's evidentiary showing obligations for a significant aggravation claim

have readily been met. Thus, Ms. Hughes unquestionably was diabetic before her vaccinations (*Loving* prong one). Moreover, although her symptoms did plainly fluctuate over time (with her blood sugar levels inconsistently revealing the extent of her problem),[78] her overall health declined post-vaccination—satisfying the third *Loving* prong.[79] But she has not successfully shown that her DM1 *could* be worsened after receipt of the flu or HPV vaccines—or that in this case it likely *was* so worsened.

First, I note that it has repeatedly been determined in Program cases that vaccination does not likely worsen DM1. *See, e.g.*, *Hennessey v. Sec'y of Health & Hum. Servs.*, No. 01-190V, 2009 WL 1709053 (Fed. Cl. Spec. Mstr. May 29, 2009), *mot. for review den'd,* Fed. Cl. 126 (2010) (affirming the special master's opinion including that the petitioner had "failed to establish any logical connection between his hepatitis B vaccinations and his T1D [type 1 diabetes]" and this his deteriorated condition was caused by "the natural progression of insulin dependence, rather than his vaccines"); *Meyers v. Sec'y of Health & Hum. Servs.,* No. 04–1771V, 2006 WL 1593947 (Fed. Cl. Spec. Mstr. May 22, 2006) (petitioner failed to establish a causal link between DTP vaccine and type 1 diabetes); *Baker v. Sec'y of Health & Hum. Servs.,* No. 99–653V, 2003 WL 22416622 (Fed. Cl. Spec. Mstr. Sept. 26, 2003) (rejecting claim that multiple vaccinations caused type 1 diabetes). Although these decisions do not bind resolution of this case, they have persuasive value—and I am aware of no cases standing for the contrary conclusion.

Second, even if I ignore such older cases, I find that Petitioner did not establish *in this case* that the HPV vaccine itself could worsen DM1. Dr. Lee's opinion was the primary source of support for this contention, but it was poorly-reasoned, and supported by unreliable science or facially-inaccurate suppositions. Thus, Dr. Lee made arguments about the post-vaccination incidence of diabetes that were facially illogical and numerically/mathematically incorrect. He also contended that the HPV vaccine could have a pathologic impact based on assumptions about the inadvertent inclusion in it of immune mediators resulting in a specific kind of adjuvant (TLR agonists) that the vaccine *does not likely contain*—and which if it does, are found only in non-pathologic amounts.

[78] As Respondent points out, Petitioner's diabetes was *not* under fair control prior to vaccination. Regular testing also shows that her HbA1c levels spiked shortly before vaccination, returned to previous levels, and then increased again. *See* Table 2 Ex. 19 at 109; *see also* Exhibit C at 14. Her pre-vaccination glucose levels were also frequently higher than or similar to her post-vaccination levels.

[79] My determination arises somewhat from the restated legal standard for significant aggravation that the Federal Circuit established in *Sharpe*, under which a Petitioner need only establish post-vaccination worsening of the preexisting condition, and not that her course was worse than would otherwise be expected—with Respondent required (once the burden shifts due to Petitioner's success in setting forth a prima facie case) to preponderantly demonstrate that the injured party's course was actually consistent with her preexisting condition (thus making it and not vaccination responsible). Here, however, I do *not* find that Petitioner overall has carried her burden of establishing that the HPV or flu vaccines worsened her DM1 (since she cannot demonstrate that the vaccines at issue *could* worsen DM1 symptoms, or did so on this fact pattern in a medically-acceptable timeframe), and thus I do not reach the question of whether Ms. Hughes's post-vaccination course varied from what would be expected for a person with DM1. (I also do take into account fluctuations in Petitioner's symptoms, and periods in which she reported good health, since these undermine her "did cause" showing under *Loving* prong five).

He otherwise relied on long-rejected arguments about the role of alum in encouraging pathologic processes. He could not bulwark his theory with sufficient reliable evidence, drawn from his own experience or otherwise. The two articles he authored and cited for this component of his opinion were persuasively rebutted by Respondent's experts.

The "did cause" *Althen* prong two/*Loving* prong five evidence supporting the significant aggravation claim is also quite limited to nonexistent. There is no medical record proof that Petitioner was experiencing some kind of initial, if incomplete reaction to her first HPV dose before her October 2014 hospital visit—and no evidence from that visit, or several thereafter, that would corroborate the concept that the vaccine was responsible. The record reveals no undercurrent of an inflammatory response, or aberrant immune reaction, in the months from July 2014 to Petitioner's September 2014 treater visits, and the same is true when the August 2015 to October 2015 period is reviewed. Rather, it simply appears from the record that Ms. E.S. more likely experienced diabetes-related symptoms. Thus, I cannot ascertain support for the conclusion that *either* vaccine initiated an immune process (evidenced by signs of inflammation or otherwise) that later manifested in the spike in diabetes-related symptoms for which Petitioner sought repeated treatment.

In addition, no treaters who saw Petitioner at any time close to the date of vaccination (and in this case I will define "close" to mean even within six months) ever opined there could be a relationship between the vaccine and her flares—unlike cases in which treaters readily so speculate. *See, e.g.*, *R.B. v. Sec'y of Health & Hum. Servs.*, No. 13-956V, 2017 1713113, at *17 (Fed. Cl. Spec. Mstr. Feb. 22, 2017) (finding that treater's opinion can have evidentiary value in establishing a causation theory). And as Respondent notes, Petitioner's symptoms course was not *consistently* trending downward—in contradiction to her theory that her immune reactions were invariably negatively impacted by two HPV vaccine doses received months prior to the instances she references. The explanation offered by Dr. Lee—that blood sugar levels could fluctuate even if the effects of HPV vaccine doses remained persistently pathologic over the course of years—was not only inconsistent with his overall theory but facile as well.

Dr. MacGinnitie also persuasively explained that deterioration of diabetes control of the kind Petitioner experienced is often seen in late adolescence—an unrebutted point that (while not established to a sufficient degree to make a formal "factor unrelated" finding) diminished what evidence Petitioner *did* offer. Indeed, the record itself contains direct instances in which Petitioner acknowledged the role her own conduct played in causing symptoms flares (*see, e.g.*, Ex. 31 at 122 (Petitioner presented to the ER with the chief complaint of "intoxication" and reports of repetitive vomiting)). Even though not *every* occurrence in which Petitioner wound up in the ER for reasons associated with her DM1 could be so easily explained, self-monitoring or control of the condition is as likely to cause declines in health as other factors, further limiting the likelihood that a vaccine dose received months or years prior to a particular instance of a diabetes symptom flare was causal of it.

Finally, even if the fourth and fifth *Loving* prongs could be met, Petitioner has not shown that her DM1 aggravation occurred in a medically-acceptable timeframe. Petitioner's experts did not persuasively explain why the pathologic process leading to a decline in blood sugar control she experienced would reasonably have started in the two months from her first receipt of the HPV vaccine in July 2014 to her first medical visits in September 2014, especially given the lack of record suggestion of any problem in this period. The timeframe from Petitioner's receipt of a second HPV vaccine dose (August 2015) to new medical interventions that October was not much shorter, and thus does not provide the kind of "challenge-rechallenge" evidence of a faster reaction that might bulwark the purported causal role of the HPV vaccine.[80]

In addition, no medically reliable explanation has been provided for how long it would take a person with DM1 to have their disease aggravated after receipt of the HPV vaccine, or how the process would thereafter become chronic. Arguments about the persistence of alum in the body are reflective of previously-rejected claims in other cases. *Olson v. Sec'y of Health & Hum. Servs.*, No. 13-439, 2017 WL 3624085 at *20 (Fed. Cl. Spec. Mstr. July 14, 2017), *aff'd*, 758 Fed. Appx. 919 (Fed. Cl. 2018).

V. Petitioner's Experts Were Unpersuasive and/or Offered Unreliable Opinions

My determination to decide this case on the papers was motivated in no small part by the overall unpersuasive character of Petitioner's expert opinions. Her experts covered ground that they have in prior cases, to no success, or made facially-unreliable contentions that greatly diminished their credibility. The paper copies of such deficient reports told me all I needed to decide the matter—there was no need to hear from the experts directly.

Dr. Steinman's opinion, as set forth in his three written reports, illuminates the various evidentiary deficiencies that hampered Petitioner's case. As a well-credentialed immunologist, Dr. Steinman was unquestionably qualified to offer an opinion in this case, and what is more he has conducted direct research into some of the alleged injuries, such as narcolepsy. However, the *substance* of the opinion offered was almost identical to opinions he has offered repeatedly in prior Program cases, often in cases I have decided—and he employed argument and reasoning that I have consistently rejected as medically or scientifically unreliable. *See, e.g.*, *D'Toile,* 2016 WL 7664475, at *14 (discussing Dr. Steinman's opinion on the association between the flu vaccine and narcolepsy). Indeed, in this case he attempted to shoehorn a theory that had reliable scientific support in *one* context (the association between a version of the flu vaccine and narcolepsy) to a case involving a different vaccine, and where the evidence is substantially less robust.

[80] Challenge-rechallenge happens when a person (1) is exposed to an antigen, (2) reacts to that antigen in a particular way, (3) is given the same antigen again, and (4) reacts to that antigen similarly. *Nussman v. Sec'y of Health & Hum. Servs.*, 83 Fed. Cl. 111, 119 (Fed. Cl. 2008). Typically, the second reaction is faster and more severe. *Id.*

Dr. Steinman also referenced items of literature that I have in the past (and in comparable cases) noted were not deserving of substantial weight. *See, e.g.*, *Johnson*, 2018 WL 2051760, at *12, 16, and 24 (petitioner did not preponderantly establish that HPV vaccine was responsible for POTS or other autonomic dysfunction). And he repeated arguments about general homology in service of his mechanistic theory of molecular mimicry that, while somewhat logical and not outside the realm of possibility, do no more than raise plausible points that cannot satisfy the preponderant evidentiary standard required for an entitlement award. *Boatmon,* 941 F.3d 1351 at 1355. It may, for example, be scientifically *plausible* that the HPV vaccine could promote the creation of antibodies that could in turn cross-react in an autoimmune attack against self-structures in the body, but it has not *preponderantly* been shown that this is likely, given a total absence of reliable research evidence (whether drawn from Dr. Steinman's own work, other Program decisions, or articles discussing scientific/medical research bearing on the matter).

If Dr. Steinman's opinion was frequently conclusory or unconcerned with its unreliability, Dr. Lee's was far worse. To begin with, Dr. Lee is not an immunologist, cardiologist, or trained in the analysis or treatment of diabetes, rendering his insights into these general matters (which dominate this case) somewhat unpersuasive from the outset. But even ignoring his lack of relevant experience, his theory specific to the HPV vaccine barely rose to the level of plausibility, relying on the contention that a vaccine with *one* kind of adjuvant might inadvertently contain, through its processing, another kind (TLR agonists) *that the vaccine itself is not intended to include*—and that this would then be the lynchpin for the pathologic mechanistic processes allegedly occurring thereafter. Such a theory would require *either* an expert with more experience in treating or researching the illnesses alleged (such that a connection could be made between opinions about the vaccine's functioning and the injuries in question), or reference to some persuasive and reliable literature suggesting that vaccine manufacture has been shown to have this effect. Yet, Dr. Lee only proposed that general research *he had performed* was enough. He additionally over-relied on the role the aluminum adjuvant could play pathogenically—an erroneous contention that has repeatedly been rejected in prior Program cases. *McKown,* 2019 WL 4072113 at *16; *Rothenberg v. Sec'y of Health & Hum. Servs.*, No. 15-696V, 2018 WL 2731639 at *7 (Fed. Cl. Spec. Mstr. April 19, 2018); *Wolf v. Sec'y of Health & Hum. Servs.*, No. 14-342V, 2016 WL 6518581 at *4 (Fed. Cl. Spec. Mstr. Sept. 15, 2016).

Dr. Lee's opinion is also run-through with erroneous calculations and bald assumptions that collapse on close analysis. For example, his effort to contrast vaccine safety trial evidence of adverse events like diabetes against similar evidence derived from the time before the HPV vaccine was approved caused him to make an apples-to-oranges numeric comparison that shed no light at all on the actual risk posed by vaccination—especially since evidence from *the safety trial itself* showed no greater incidence of type 1 diabetes new onset for vaccinated individuals in comparison to a control group. Ex. 41, reference 4 at 8. Similarly, Dr. Lee proposed acceptable timeframes for onset of cardiac issues after HPV vaccine administration merely through reference to a tiny sample of semi-comparable instances, none of which helped establish anything other than the fact that

certain vaccinated individuals died of cardiac-related injuries at some time after vaccination.

Further detracting from Dr. Lee's opinions was the poor construction of his two written reports. His contentions were set forth in a garbled, scattershot manner, and relied on cut-and-pasted copies of articles and texts—adding considerably to each report's length, but without increasing their persuasiveness or clarity. He also repeatedly attempted to rebut in granular detail certain points raised by Respondent's more facially-qualified experts—but in so doing chased point after point down the proverbial rabbit hole, with no obvious benefit to the Petitioner. *Compare* Second Lee Rep. at 8 (disputing what Dr. LaRue defined as the "gold standard" test for diagnosing a coronary artery disease), *with* LaRue Second Rep. at 6 (explaining why Dr. Lee's points about diagnostic methods herein were unpersuasive in establishing Petitioner's alleged ischemia). These wasted, bickering efforts exemplify circumstances where an expert misses the forest for the trees—and underscore why I have deemed this matter appropriate for dismissal merely on the basis of the record.

VI. This Claim was Properly Resolved Without a Hearing

In ruling on the record, I am opting against holding a hearing. The choice of how best to resolve this case is a matter that lies generally within my discretion, but because Petitioner challenges this manner of disposition in opposing Respondent's request for dismissal, I shall explain my reasoning.

Prior decisions have recognized that a special master's discretion in deciding whether to conduct an evidentiary hearing "is tempered by Vaccine Rule 3(b)," or the duty to afford each party a "full and fair opportunity to present its case." *Hovey v. Sec'y of Health & Hum. Servs.*, 38 Fed. Cl. 397, 400–01 (citing Rule 3(b)). But that rule also includes the obligation of creation of a record "sufficient to allow review of the special master's decision." *Hovey*, 38 Fed. Cl. at 401; *see also Kreizenbeck,* 945 F.3d at 1366. Thus, the fact that a claim is legitimately disputed, such that the special master must exercise his intellectual faculties in order to decide a matter, is not *itself* grounds for a trial (for if it were, trials would be required in every disputed case). Special masters are expressly empowered to resolve fact disputes *without* a hearing—although they should only so act if a party has been given the proper "full and fair" chance to prove their claim.

In this case, no hearing was required to resolve fairly Petitioner's claim. I was able to evaluate the evidentiary strength of her expert's theories and opinions simply based on the written reports, and did not require credibility determinations to weigh the medical/scientific reliability of the theories espoused. Petitioner's arguments to the contrary are not persuasive. That part of her claim reliant on proving the aggravation of preexisting diabetes, for example, ventured into seas that numerous prior claimants have unsuccessfully navigated, without offering scientifically-reliable grounds reflecting new research or thinking on the subject that would counsel for reconsideration of the issue. The arguments Petitioner makes about the autoimmune nature, in whole or part, of that

basket of other symptoms she complains of, and their autonomic nature, is similarly not supported by new discoveries or research—as the 2019 AAS Statement makes clear. And her purported "new" diagnoses from 2018 or 2019 are either substantively less certain than meets the eye (like POTS and CFS), or reflect occurrences that cannot reliably or medically acceptably be linked to vaccines received three or more years before.

The fact that this matter resulted in the filing of numerous expert reports on both sides also is not a compelling reason to hold a hearing. Even the most obviously flimsy of theories could be "supported" with multiple experts willing to put their reputations on the line, so the fact that expert reports pile up in a case is not by itself a compelling reason to hold a trial. Indeed, I have resolved by ruling on the record science-dense cases in which both sides made credible, reasonably-contested arguments arising from multiple expert reports. *See, e.g.*, *D'Toile,* 2016 WL 7664475.[81] Here, after close review of all reports filed, I was able to discern either obvious deficiencies in the Petitioner's proffered opinion, or that the opinions repeated arguments I have rejected in the past. And these opinions were not rooted in new, previously-unconsidered scientific or medical evidence that would support re-evaluating my prior determinations on these topics.

CONCLUSION

Although some of Petitioner's purported injuries lack medical record or diagnostic substantiation, she has clearly experienced a number of overlapping symptoms and conditions over many years (most likely attributable to her struggles with DM1) that have caused her and her family considerable anguish—in their efforts to treat as well as to identify some unifying explanation for her constant need for medical care. She also no doubt has a good faith belief that the HPV and flu vaccines had to have some relationship to her injuries—if for no other reason than the increased tempo of her symptoms post-dated her receipt of the vaccines.

Nevertheless, the overall picture painted herein by the objective medical record is unsupportive of the conclusion that the HPV or flu vaccines were causal of any of her post-vaccination symptoms, despite their complex array and convoluted progression. The timeframes from vaccine to injury are too attenuated, the causation theories not persuasively established, and the expert support, plus other independent medical or scientific literature, offered for the claim largely unreliable (especially to the extent it repeats causation theories that have proven fruitless in numerous prior Program cases). The deficiencies of this claim were self-evident enough that a hearing was not required to adjudicate the matter.

[81] By contrast, I have also dismissed cases like this one, where the filing of multiple reports masked what was determined to be a wholly unreliable claim. *Kreizenbeck*, 945 F.3d at 1365–66 (dismissing on record case in which parties together offered opinions from six experts in total; petitioner attempted to convert abandoned autism injury claim into assertion that vaccines precipitated encephalopathic reaction resulting in developmental regression).

Accordingly, for the reasons set forth above, I deny compensation in this case and dismiss the matter. In the absence of a timely-filed motion for review (see Appendix B to the Rules of the Court), the Clerk shall enter judgment in accord with this decision.[82]

IT IS SO ORDERED.

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

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