In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 17-542V
(to be published)

* *

ASHLEY AMERICA,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

* *

Chief Special Master Corcoran

Filed: January 4, 2022

Renee J. Gentry, Vaccine Injury Clinic, George Washington Univ. Law School, Washington, DC, for Petitioner

Amanda Pasciuto, U.S. Department of Justice, Washington, DC, for Respondent.

DECISION DENYING ENTITLEMENT[1]

On April 17, 2017, Maria and Rui America, on behalf of their then-minor child, Ashley, filed a Petition under the National Vaccine Injury Compensation Program (the "Vaccine Program"[2]), alleging that as a result of receiving the human papillomavirus ("HPV") and influenza ("flu") vaccines, Ashley developed neurocardiogenic syncope ("NCS"). Petition (ECF No. 1)

[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 Ruling'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. 3755 (codified as amended at 42 U.S.C. §§ 300aa-10–34 (2012)) (hereinafter "Vaccine Act" or "the Act"). All subsequent references to sections of the Vaccine Act shall be to the pertinent subparagraph of 42 U.S.C. § 300aa.

("Pet.") at 1–2. Ms. America became the named petitioner after she turned 18 years old. ECF No. 8. She has since restricted her claim to alleging only an off-Table significant aggravation claim of her preexisting NCS. ECF No. 55 at 13.

Having reviewed the record, all expert reports, the parties' briefs, the medical records, and associated literature, I hereby deny an entitlement award. As discussed in greater detail below, Petitioner has not preponderantly established that the HPV vaccine (the primary allegedly-causal vaccine focused upon by her expert) can aggravate NCS, or that it did so to Ms. America in the relevant timeframe.

I. Factual Background

Pre-Vaccination Health History

Ms. America was born on January 28, 1996. Pet. at 1. Her medical history was significant for hypothyroidism, obesity, hyperlipidemia/hypertriglyceridemia, anxiety disorder, thyroid nodule, and (most significant for purposes of this case) episodic syncope. Ex. 3 at 7. Her syncope episodes consisted of occasional convulsive arm movements, but were largely characterized by instances where her eyes were rolling back as she fell to the floor, losing consciousness for a few seconds, and then regaining consciousness when one of her parents lowered her head or put some salt on her tongue. Ex. 8 at 39. After these episodes, she would recover almost immediately, but she would not feel like herself for several minutes. *Id.* Ms. America's first such syncopal episode is reported to have occurred in 2009, during the first week of her menstrual cycle, where she collapsed while standing in a hot kitchen. Ex. 10 at 1. She had four additional episodes from 2010 to September 2014. *Id* at 1–2. The 2010 and July 2011 episodes involved heat, like her first episode. *Id.*

After the August 2013 episode, Ms. America was seen by Karameh Hawash, M.D., a neurologist, at Boston Children's Hospital, who deemed them syncopal in nature rather than evidence of seizure activity. Ex. 8 at 39–40. Ms. America was thereafter reportedly referred for cardiology evaluation, but no documentation was recorded. *Id.* After the September 2014 episode (which occurred twenty-four days before her first receipt of the HPV vaccine), Ms. America was taken to the emergency room at Faxton St. Luke's in New Hartford, New York. Ex. 5 at 287. She was diagnosed with a sinus infection and syncope. *Id*. at 286, 288. A CT scan performed on September 26, 2014, revealed partial opacification of the left mastoid air cells, but other test results were deemed normal. Ex. 5 at 307. Prior to this final pre-vaccination episode, Ms. America reported that she felt an "itch in [her] brain," which she stated had not occurred during any of the previous episodes. Ex. 5 at 301. She also reported that her episodes typically occurred around menstruation. Ex. 5 at 287. Ms. America's mother informed treaters that she had experienced similar symptoms as a child. *Id.*

During these episodes, Ms. America's family had moved several times. Ex. 8 at 39; Ex. 10 at 1–2. In July 2011, the family relocated from Portugal to Massachusetts; then from Massachusetts to Sauquoit, New York in September 2013; and then finally from Sauquoit to Westmoreland, New York in September 2014.[3] Ex. 10 at 1–2. Ms. America's mother stated that these moves were "somewhat stressful" for her daughter. *Id.* at 2. Moreover, Dr. Hawash documented that Ms. America's family planned to move again. Ex. 8 at 39. Dr. Hawash also documented that at that time, Ms. America's parents had lost their jobs, and that one of her brothers had been diagnosed with bipolar disorder. *Id.*

Receipt of the HPV Vaccine

Ms. America received her first HPV vaccine dose (along with the flu vaccine) on October 20, 2014, from her primary care physician, Dr. Quazi Islam, M.D. Ex. 1 at 1. The following day, she felt dizzy at school and went to the nurse's office, where she passed out. Ex. 5 at 278. That same day she had also started taking Levothyroxine. *Id.* at 278. She was sent to Faxton St. Luke's emergency room and was diagnosed with vertigo. *Id.* at 268.

The next day, October 22, 2014, Ms. America passed out again and went back to Faxton St. Luke's emergency room, where she complained of dizziness, shortness of breath, and a headache. Ex. 5 at 225. The physicians believed she had syncope. *Id.* at 226. While at the hospital Ms. America had another episode and passed out again, but her vitals remained stable. *Id.* at 241.

Testing performed on Ms. America at this time was not fully corroborative of syncope. Her blood pressure was 137/74 while laying down, 143/74 standing, and 138/60 standing. Ex. 5 at 238. In cases of typical vasovagal syncope, however, a patient's blood pressure and heart rate would *fall*, which differs from what happened to Ms. America on this visit. *Id.* at 241. In addition, during the episode in question a nurse conducted a "drop test,"[4] but Ms. America moved her hand to avoid hitting herself. *Id.* After this episode, the emergency room physician suggested a mental health evaluation, and diagnosed Ms. America with a potential conversion disorder.[5] *Id.* at 266. Ms.

[3] Ms. America had a previous history of losing consciousness when she was living in Portugal and was apparently evaluated for seizures, although prior work-up records were not documented. Ex. 8 at 39. A neurologist in Portugal determined that she did not have seizures. *Id*.

[4] A drop test involves a treater holding a patient's hand over her head, and then dropping the hand to see if the patient is truly unconscious. Ex. 5 at 241. If so, the hand would strike her head; if not, she would move her hand to avoid hitting herself. *Id.*

[5] Conversion disorder is "a mental disorder characterized by conversion symptoms (loss or alteration of voluntary motor or sensory functioning suggesting physical illness, such as seizures, paralysis, dyskinesia, anesthesia, blindness, or aphonia) having no demonstrable physiological basis and whose psychological basis is suggested by (1) exacerbation of symptoms at times of psychological stress, (2) relief from tension or inner conflicts (primary gain) provided by the symptoms, or (3) secondary gains (support, attention, avoidance of unpleasant responsibilities)

America's mother has alleged that over the following days Petitioner experienced four additional episodes (on October 23, 27, 30, and 31, respectfully), but she was not again taken to the emergency room. Ex. 10 at 2.

At the start of the following month - November 6, 2014 - Ms. America visited Ramzi Nassif, M.D., a cardiologist, for a work-up, which included physical examination, electrocardiogram, and echocardiogram. Ex. 7 at 4–6. Ms. America's blood pressure at that time was 130/76 laying down, 112/76 sitting, and 110/78 standing. *Id.* at 2. She weighed 200 pounds with a body mass index[6] ("BMI") of 36.6. *Id.* at 3. Dr. Nassif also ordered an event monitor to evaluate her for arrhythmia, and it demonstrated a normal sinus rhythm with a rate of 60. *Id.* at 4, 6. There were no auto-triggered events, but occasional isolated premature atrial contractions. *Id.* at 5–6. During this time, Ms. America's mother witnessed an episode and filmed it. Ex. 7 at 6. Dr. Nassif proposed the video taken of the episode was suggestive of a partial complex seizure, though there were no changes in heart rate. *Id.*

Petitioner's mother has alleged that less than a week later, on November 12, 2014, her daughter complained of a severe headache and dizziness after picking her up from school. Ex. 10 at 2. On November 13, 2014, Dr. Islam performed an ultrasound evaluation of the thyroid, where a solid hypoechoic nodule was present on the right lobe of her thyroid. Ex. 5 at 170. The cardiac echocardiogram also showed trace to mild regurgitation in all valves. Ex. 7 at 5. Petitioner's mother maintains that her daughter had three additional episodes thereafter, beginning that same day, although medical records do not corroborate these assertions. Ex. 10 at 2.

The following month, on December 2, 2014, Ms. America underwent evaluation by Allen Gerber, M.D., a neurologist, who saw nothing of concern. Ex. 8 at 5. On December 6, 2014, Ms. America underwent additional testing, which included a normal sleep study. Ex. 8 at 24–25. It revealed no evidence of obstructive sleep apnea, however, and it showed a normal 24-hour ambulatory EEG. *Id*. A few days after, on December 11, 2014, Petitioner purportedly experienced yet another episode, but again opted not to seek treatment at the emergency room. Ex. 10 at 3.

Increase in Observed Symptoms, 2014 to 2015

Throughout the course of 2015, Ms. America is alleged (primarily by her mother) to have experienced over 20 additional syncopal episodes. Ex. 10 at 3. However, the medical record in this case largely provides no clear evidence of an etiology or other explanation for these occurrences.

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provided by the symptoms." *See Dorland's Illustrated Medical Dictionary* (33d ed. 2020) at 543 [hereinafter *Dorland's]*.

[6] An individual's BMI is a measure of body fat and is a formula for determining obesity. *See Mosby's Medical Dictionary* (10th ed. 2017) at 228.

From January 14-15, 2015, Ms. America had a 24-hour ambulatory EEG and a continuous EKG recorded, but no interictal epileptiform morphologies were identified, and no electrographic seizures were seen. Ex. 8 at 23. The overseeing neurologist, Anthony Ritaccio, M.D., concluded that the study was normal. *Id.*

On February 10, 2015, Ms. America had a follow-up appointment with Dr. Gerber, who reported that Ms. America's 24-hour Holter, 24-hour EEG, cardiology consult, and sleep study were normal. Ex. 8 at 4. Ms. America and her mother brought in several videos purportedly showing her experiencing seizures. *Id.* In the videos, Ms. America had twitching in either hand and she would enter a state that appeared as if she were sleeping, and then would completely pass out. *Id.* Her mother appeared to slap her to wake her up. *Id.* Dr. Gerber stated that "one time she awoke because the slap was too heavy and another time, she appeared to awake when the dog greets her." *Id.* Dr. Gerber opined, however, that these events most likely represented pseudoseizures.[7] *Id.* Dr. Gerber increased her Keppra dosing as an anti-epileptic therapy. *Id.*

On March 31, 2015, Ms. America saw ophthalmologist Patrick Costello, M.D., who reported that her evaluation was normal. Ex. 8 at 37. On April 23, 2015, she received her second HPV vaccine dose. Ex. 1 at 1. After this second dose, Petitioner is alleged to have experienced six additional episodes over the following months. Ex. 10 at 3. There is, however, limited record corroboration for these subsequent events—and no proof establishing an event close-in-time to this second dose.

From June 2-4, 2015, Ms. America underwent a long-term video Epilepsy Monitoring Unit ("EMU") study using a digital video EEG for assessment. Ex. 8 at 20–22. Her Keppra medication was stopped during this procedure. *Id*. at 20. Her prior routine EEG was normal. *Id.* Observing neurologist Kevin McMahon, M.D., wrote at this time that no interictal epileptiform discharges occurred during the EEG. *Id.* at 21. Ms. America's first episode during the study occurred on June 3, 2015, where the following information was provided:

> On June 3, 2015 at 08:43:48 the [Ms. America] was lying in bed with her eyes closed. At 08:44:03 the mother was sitting at [her] bedside, [and] asked her if she could speak but she shook her head, "no". Her mother then pushed the event button. Approximately 10 seconds later, a nurse entered the room and asked her a series of orientation questions; however, the patient did not answer any of these questions nor follow[ed] commands. The nurse also attempted to raise her arm [] on multiple occasions. The patient just dropped it to the bed and remained motionless for the majority of the event with her eyes closed. Throughout

[7] A pseudoseizure is "an attack resembling an epileptic seizure but being a type of conversion disorder; it lacks the electroencephalographic characteristics of epilepsy and the patient may be able to stop it by an act of will." *Dorland's* at 1522.

> the event she did not answer to voice or follow any verbal commands. The event appeared to be over at 08:45:00 when she resumed speaking and following commands appropriately.

Id. Dr. McMahon wrote that there were no correlative EEG changes before, during, or after the event. *Id.* Dr. McMahon's determination was thus that Ms. America's EEG was normal, and that she had likely experienced a non-epileptic event. *Id.* Based on these findings, Dr. McMahon recommended that Ms. America see a psychiatrist and be taken off her anti-epileptic medication. *Id.* Bridget Frawley, M.D., a neurologist, who reviewed the study alongside Dr. McMahon, agreed with his findings. *Id.* at 22.

Treatment in 2016 and Beyond

Ms. America had subsequent psychiatric evaluations in January and February 2016, and the relevant treaters opined that she might be experiencing an adjustment disorder. Ex. 11 at 15–16, 18–19, 27–28. In May 2016, however, Ms. America was discharged for non-compliance of attendance at her therapy sessions, as she had not contacted her clinician for two months. Ex. 11 at 27–28.

Ms. America appears to have continued throughout this period to report episodes of syncope. Ex. 5 at 4–34. In August 2016, emergency medical services were called to her school for concern of a possible seizure. *Id.* at 4. She stated that she had a lump on the right side of her neck that was causing her to be "more dizzy than normal." *Id.* at 13.

In the Fall of 2016, Ms. America began community college. Ex. 12 at 1. The Coordinator of Accessibility Resources in the Office of Services to Students with Disabilities described Ms. America's episodes as being non-responsive, with Ms. America unmoving and displaying shaking limbs plus muscle tension, and the events being preceded by pallor and "limited facial expression." *Id.* at 2. The episodes would last ten seconds to two minutes, and were brought on by bright lights or flickers on computer screens. *Id*. Afterwards, Petitioner would complain of fatigue, tingling, numbness, extreme pain, dizziness, poor concentration, and memory problems. *Id.* She also reported accompanying migraines. *Id.* This reportedly led to increased avoidance of social involvement due to potential "seizure triggers." *Id.*

In late January 2018, Ms. America's primary care physician, Dr. Islam, obtained lab studies during a routine physical examination. Ex. 15 at 1–3. Abnormal findings included a complete blood count with a low mean corpuscular volume and mean corpuscular hemoglobin, an abnormal lipid panel, and a low vitamin D level. Ex. 14 at 1–10. She was given a prescription for vitamin D 50,000 units to be taken once weekly. Ex. 15 at 1–2.

Neurology Consults with Petitioner's Causation Expert

Ms. America has had two consulting sessions with her causation expert, Dr. Svetlana Blitshteyn, M.D., since the date of the case's initiation in April 2017. *See* Consult, dated December 23, 2017, filed as Ex. 13 (ECF No. 24-3) ("Blitshteyn First Consult"); Consult, dated April 4, 2018, filed as Ex. 16 (ECF No. 26-2) ("Blitshteyn Second Consult").

The first, one-hour telephonic consultation occurred in December 2017. Blitshteyn First Consult at 1–3. Dr. Blitshteyn described Ms. America's medical history as "daily syncope, constant headaches, dizziness, balance difficulty, and recurrent numbness of the legs and arms." *Id.* at 1. Further, Ms. America informed Dr. Blitshteyn that after she received the first HPV vaccine dose in October 2014, she had dizziness and was instructed by a nurse to lie down for 15 minutes. *Id.* However, she stated the dizziness "never resolved, [and] she has been dizzy ever since." *Id.* She reported episodes of syncope, sometimes supine, lasting up to 30 minutes. *Id.*

Dr. Blitshteyn's working diagnosis was NCS, an autonomic nervous system disorder, migraine with and without aura, and chronic daily headaches. Blitshteyn First Consult at 2. She proposed that perhaps Ms. America previously had experienced mild recurrent syncope, but that the HPV vaccination exacerbated it, coupled with other neurologic manifestations. *Id.* at 2. To rule out secondary causes, Dr. Blitshteyn recommended Ms. America undergo a large number of antibody and serum tests, and also undergo a "tilt table" test to evaluate the degree of Ms. America's orthostatic intolerance.[8] *Id.* at 2. She also proposed a corticosteroid course and some non-pharmacologic interventions (exercise, increased salt and fluid intake, etc.). *Id.* It does not appear from the record in this case, however, that the tilt table test ever occurred.

Several months later, on April 4, 2018, Dr. Blitshteyn held a follow-up telephone consultation and evaluation with Ms. America and her mother. Blitshteyn Second Consult at 1–3. During the call, Ms. America complained of syncope occurring every two weeks, headaches occurring every other day, dizziness, photophobia, phonophobia, and recurrent numbness.[9] *Id.* at

[8] A tilt table test is used to evaluate syncope by measuring heart rate and blood pressure in response to the body's change in position. *Tilt Table Test*, Mayo Clinic, https://www mayoclinic.org/tests-procedures/tilt-tabletest/about/pac-20395124 (last accessed Nov. 19, 2021). During the test, the patient lies flat on a table for around 15 minutes. *Id.* The table is then quickly tilted upright to change the body's position from lying down to standing up. *Id.* The table generally remains upright for 45 minutes to allow the doctor to monitor the patient's cardiovascular response. *Id.*

[9] In her initial report, Dr. Blitshteyn stated that there were also two additional follow-up telephonic consultations, held on February 16, 2018, and July 11, 2018. Ex. 17 at 3. However, no records were ever filed confirming that in fact these consultations occurred. During the purported February 16, 2018 consultation, Dr. Blitshteyn alleges that that Ms. America "reported 40% improvement in her symptoms with non-pharmacologic therapy alone, and with the addition of Florinef, all of her symptoms have improved significantly, including daily headache and syncope."

1. Dr. Blitshteyn's working diagnosis was NCS, migraine with and without aura, chronic daily headaches, and vitamin D deficiency. *Id.* at 2. But the nature of this follow-up was almost identical to the first neurology consult in terms of recommendations as Ms. America had not undergone any of the diagnostic tests ordered in Dr. Blitshteyn's first consult back in December 2017. *Id.* at 2.

II. Expert Reports

A. *Petitioner's Expert – Svetlana Blitshteyn, M.D.*

Dr. Blitshteyn, a neurologist specializing in autonomic disorders, conducted the aforementioned telephone neurology consults and prepared two written causation reports as well. Report, dated September 10, 2018, filed as Ex. 17 (ECF No. 29-2) ("Blitshteyn First Rep."); Report, dated March 5, 2019, filed as Ex. 39 (ECF No. 36-2) ("Blitshteyn Second Rep."). Dr. Blitshteyn opines that Ms. America had NCS, and that the HPV vaccine more likely than not was the causative factor in the exacerbation of it. Blitshteyn First Rep. at 6–7; Blitshteyn Second Rep. at 4.

Dr. Blitshteyn obtained her undergraduate degree in biochemistry from the State University of New York at Buffalo, and her medical degree from the State University of New York School of Medicine and Biomedical Sciences. CV, filed as Ex. 38 (ECF No. 32-4) ("Blitshteyn CV") at 1. She is a Clinical Assistant Professor of Neurology at the State University of New York at Buffalo School of Medicine and Biomedical Sciences. Blitshteyn CV at 1. She is also the Director and Founder of the Dysautonomia Clinic, where she provides neurologic care to adolescents and adults with autonomic and other neurologic disorders. *Id.* Dr. Blitshteyn became licensed to practice medicine in New York State in 2007, and became board certified in Neurology by the American Board of Psychiatry and Neurology in 2010. *Id.* Dr. Blitshteyn has also published in peer-reviewed scientific literature and co-authored a book on autonomic disorders. *Id.* at 6–8.

First Expert Report

Dr. Blitshteyn relied on a common definition for syncope embraced by the Heart Rhythm Society: "a transient loss of consciousness associated with inability to maintain postural tone, rapid and spontaneous recovery and the absence of clinical features specific for another form of transient loss of consciousness, such as epileptic seizures." Blitshteyn First Rep. at 4; Chew et al., *Vasovagal Syncope in 2016: The Current State of the Faint*, Arrhythmia: Open Access 1–4, 1 (2016), filed as Ex. 18 on Sept. 14, 2018 (ECF No. 30-2) ("Chew").[10] Specifically, she defined vasovagal syncope

Blitshteyn First Rep. at 3. However, During the July 11, 2018 consultation, Ms. America supposedly reported that she had occasional headaches, but dizziness, palpitations, nor syncope. *Id*.

[10] Petitioner filed the Chew article twice—as Exhibits 18 and 46.

(a term Dr. Blitshteyn proposed was synonymous with NCS) as a syndrome that typically "1) occurs with upright posture greater than 30 seconds, or with exposure to emotional stress, pain, or medical settings; 2) features diaphoresis, warmth, nausea, and pallor; 3) is associated with hypotension and relative bradycardia, when known; and 4) is followed by fatigue." Blitshteyn First Rep. at 4; Chew at 2. The NCS diagnosis usually rests on an individual's medical history and physical examination, and thus does not typically require further investigation or corroboration in Dr. Blitshteyn's view. First Blitshteyn Rep. at 4.

Although NCS often occurs after prolonged standing or sitting, it can be triggered even in the supine position, which Dr. Blitshteyn viewed as likely having occurred during Petitioner's hospitalization at the EMU, when she experienced an episode of unresponsiveness while her EEG remained normal. Chew at 2; Ex. 5 at 225. Treatment for NCS involves both non-pharmacologic measures and drugs akin to what Petitioner received (and which in this case proved efficacious). Chew at 3; Blitshteyn First Rep. at 3–4.

Based on an in-depth overview of Petitioner's medical history, Dr. Blitshteyn embraced the NCS diagnosis, opining as well that the HPV vaccine had a causal role. Blitshteyn First Rep. at 2–3. Dr. Blitshteyn highlighted several records of significance. *Id.* at 2, 4. Petitioner only experienced a total of five syncope episodes between 2009 and September of 2014, and overall was generally healthy. *Id.* at 5; Ex. 10 at 1–2. Additionally, Petitioner had no documented symptoms of chronic dizziness, headache, presyncope or fatigue prior to vaccination. Blitshteyn First Rep. at 5. Yet, only one day after vaccination, Petitioner began to experience recurrent episodes of syncope—six in the ten days thereafter. *Id*. at 2. She also developed a chronic headache condition, which she had not experienced before vaccination.

Then, at Petitioner's subsequent visits to cardiologist Dr. Nassif, Petitioner's displayed blood pressure was 130/76 with a heart rate of 68 bpm while laying down, but her blood pressure decreased to 110/78 with a heart rate of 68 bpm when standing. Ex. 7 at 2. And although the results of the 30-day cardiac event monitor (reviewed on December 18, 2014) demonstrated no evidence of cardiac arrhythmia, Petitioner's symptoms were deemed consistent with vasovagal syncope. *Id.* at 6. Ms. America's visits to neurologist Dr. Gerber were also considered by Dr. Blitshteyn to be highly relevant to causation. Although Dr. Gerber had entertained the possibility that Ms. America's symptoms could reflect a seizure disorder, he ultimately concluded that his initial impression (that her multiple episodes of loss of consciousness sounded "more like cardiac") was correct. Ex. 8 at 4-6, 23.

The record also (in Dr. Blitshteyn's view) established that Petitioner had experienced orthostatic hypotension, which occurs when an individual experiences (upon standing) a decline in blood pressure coupled with dizziness or other syncopal-like symptoms.[11] Petitioner's history

[11] *Dorland's* at 894.

revealed continued episodes of presyncope with a normal heart rate and rhythm. Blitshteyn First Rep. at 4. According to the Heart Rhythm Society, syncopal episodes can be associated with normal sinus rhythms, possibly due to several disorders such as orthostatic hypotension. Chew at 2. Dr. Blitshteyn specifically proposed that Ms. America evidenced orthostatic hypotension upon physical examination at Ms. America's cardiology evaluation on November 6, 2014 (although the record itself from Dr. Nassif's work-up at that time did not so conclude). Ex. 7 at 5.

Further evidence in the record of the HPV vaccine's causal role could, in Dr. Blitshteyn's view, be seen after Petitioner's second dose on April 23, 2015. Thereafter, Petitioner continued to have episodes of syncope at a greater frequency (occurring on average about once a week) than what she had experienced in the past. Blitshteyn First Rep. at 4; Ex. 10 at 3.

Approximately two years later, Dr. Blitshteyn herself was consulted in this action in December 2017. Blitshteyn First Rep. at 3. Based on the telephone consult, she reached the working diagnosis that Petitioner had NCS and a chronic headache condition. Blitshteyn First Consult at 2. At the next consult in February 2018, Petitioner then reported that her symptoms had improved significantly with medication and non-pharmacologic therapy.[12] Blitshteyn First Rep. at 3. On her most recent follow-up consultation on July 11, 2018, Ms. America reported having only occasional headaches, but no dizziness, palpitations, or syncope.[13] *Id.* And ultimately, a variety of alternative causes—seizure disorder, cardiac arrhythmia. and psychiatric disorders—had been considered but ruled out for Ms. America through appropriate testing and consultations.[14] Ex. 7 at 4, 6; Ex. 8 at 21, 23.

Dr. Blitshteyn next explained the basis for her opinion that NCS could be vaccine-caused or aggravated. She differentiated the kind of acute/abrupt syncope known to occur after virtually any vaccination (recognized as the most common vaccination adverse event) from recurrent syncope, acknowledging that evidence for the latter was much harder to find. Blitshteyn First Rep. at 5. However, Dr. Blitshteyn nevertheless proposed that reliable scientific and medical evidence *could* establish an association between the HPV vaccine and NCS, even though the incidence of chronic and recurrent syncope after vaccination was currently unknown. *Id.*; B. Slade et al., *Postlicensure Safety Surveillance for Quadrivalent Human Papillomavirus Recombinant Vaccine*, 302 JAMA 750–57, 753–56 (2017), filed as Ex. 19 on Sept. 14, 2018 (ECF No. 30-3) ("Slade") (concluding that most of the reported rates of adverse events following vaccination were not

[12] No medical records were filed confirming that this consultation occurred.

[13] No medical records were filed confirming that this consultation occurred.

[14] It was unclear from the medical records whether psychiatric disorders were in fact "ruled out," as Ms. America never completed her psychologic treatment—but the records from the sessions she did attend include nascent treater views that her symptoms were reflective of some kind of mental health issue. Ex. 11 at 15–16, 18–19, 27–28.

greater than the background rates of other vaccines, although the authors note disproportionate reporting of syncope and venous thromboembolic events).

Dr. Blitshteyn did not offer independent support directly establishing that chronic, recurrent syncope can occur after vaccination. Blitshteyn First Rep. at 5. But she noted that a variety of *related* autonomic disorders, such as Postural Tachycardia Syndrome ("POTS") or autonomic neuropathy, featuring similar symptoms, had been reported to occur after receipt of various vaccines. *See,* e.g., S. Vernino et al., *Autonomic Ganglia: Target and Novel Therapeutic Tool,* Neurology 1–11, 1, 2, 5 (2009), filed as Ex. 20 on Sept. 14, 2018 (ECF No. 30-4) ("Vernino"). Although a precise incidence of these disorders after vaccination is unknown, this was in Dr. Blitshteyn's view likely because many patients are undiagnosed or misdiagnosed with other conditions involving altered consciousness and awareness.

Another study similarly looked at passive surveillance evidence derived from the U.S. Vaccine Adverse Event Reporting System ("VAERS").[15] DuVernoy et al., *Hypotonic–Hyporesponsive Episodes Reported to the Vaccine Adverse Event Reporting System (VAERS), 1996–1998*, Pediatrics 1–9 (2000), filed as Ex. 22 on Sept. 14, 2018 (ECF No. 30-6) ("DuVernoy"). But DuVernoy is less supportive of causation than asserted because it in fact observed that children with hypotonic-hyporesponsive episodes experienced only benign, self-limited, nonrecurrent episodes after vaccination. DuVernoy at 8. DuVernoy otherwise focused on the administration of the DTaP vaccine and other vaccines like Hepatitis A and B for young children—not the HPV vaccine. *Id.* at 6.

Dr. Blitshteyn noted in particular that the HPV vaccine was specifically recognized as a possible trigger of several specific autonomic disorders, such as POTS, complex regional pain syndrome ("CRPS"), and small fiber neuropathy. Blitshteyn First Rep. at 5. She herself was the author of a relevant item of literature, involving a case series of six patients who developed POTS after HPV vaccination. S. Blitshteyn, *Postural Tachycardia Syndrome Following Human Papillomavirus Vaccination*, European Journal of Neurology 135–39, xx (2014), filed as Ex. 21 on Sept. 14, 2018 (ECF No. 30-5) ("Blitshteyn Article"). Two of the relevant patients discussed in the Blitshteyn Article had also been diagnosed with NCS. Blitshteyn Article at 1–2.[16]

[15] VAERS is a database maintained by the Center for Disease Control ("CDC") to compile information from reports about reactions to immunizations listed on the Vaccine Injury Table, 42 U.S.C. § 300aa–14(a).

[16] Dr. Blitshteyn also referenced a study purporting to find that recurrent syncope was more likely to occur in patients who had received the HPV vaccine than in the age-matched controls who did not. Blitshteyn First Rep. at 6; D. Geier & M. Geier, *Quadrivalent Human Papillomavirus Vaccine and Autoimmune Adverse Events: A Case–Control Assessment of the Vaccine Adverse Event Reporting System (VAERS) Database*, Env't & Autoimmunity 46–54, 49 (2016), filed as Ex. 37 on Sept. 14, 2018 (ECF No. 32-3) (the "Geier Article"). I note, however, that the authors of the Geier Article have been almost wholly discredited as experts in the Vaccine Program. *See, e.g., Hooker v. Sec'y of Health & Hum. Servs.*, No. 02-472V, 2017 WL 3033940, at *17 (Fed. Cl. Spec. Mstr. Apr. 11, 2017) (noting the complete lack of qualifications of David Geier and the condemnations of Dr. Geier the medical boards and subsequent revocation of his medical license in 2012); *King v. Sec'y of Health & Hum. Servs.,* No. 03-584V, 2011 WL 5926126,

In addition, articles from Japan, Denmark, Spain,[17] and Italy all reported larger numbers of young women developing autonomic disorders like POTS after receiving the HPV vaccine. *See, e.g.,* T. Kinoshita, *Peripheral Sympathetic Nerve Dysfunction in Adolescent Japanese Girls Following Immunization with the Human Papillomavirus Vaccine*, Internal Med. 2185–200, 2185 (2014), filed as Ex. 23 on Sept. 14, 2018 (ECF No. 30-7) ("Kinoshita") (Japan); L. Brinth et al., *Orthostatic Intolerance and Postural Tachycardia Syndrome as Suspected Adverse Effects of Vaccination against Humanpapilloma Virus*, Vaccine 1–4, 1 (2015), filed as Ex. 24 on Sept. 14, 2018 (ECF No. 30-8) ("Brinth I") (Denmark); M. Martinez-Lavin, *HPV Vaccination Syndrome: A Questionnaire-Based Study*, Clinical Rheumatology 1–4, 1 (2015), filed as Ex. 25 on Sept. 14, 2018 (ECF No. 30-9) ("Martinez-Lavin") (Spain); B. Palmieri, *Severe Somatoform and Dysautonomic Syndromes after HPV Vaccination: Case Series and Review of Literature*, Env't & Autoimmunity 1–11, 9 (2016), filed as Ex. 26 on Sept. 14, 2018 (ECF No. 30-10) (Italy).

There are, however, deficiencies in each of these articles (observed in comparable prior Vaccine Program cases in which they have been relied upon), calling into question the evidentiary weight they merit. For example, Brinth I and Martinez-Lavin utilized subjective self-reporting questionnaires to record the purported autonomic symptoms, even though there is evidence that autonomic symptoms are prone to exaggerated self-reporting that cannot be correlated to objective findings. *See Balasco v. Sec'y of Health & Hum. Servs.*, No. 17-215V, 2020 WL 1240917, at *31 (Fed. Cl. Spec. Mstr. Feb. 14, 2020). The Martinez-Lavin article even noted that a "clear limitation of [the] study is the *lack of direct medical examination of affected individuals*." Martinez-Lavin at 3 (emphasis added).

Kinoshita, which proposed an association between the HPV vaccine and injuries involving the sympathetic nerve system, like POTS, has equally been called into question. *See Combs v. Sec'y of Health & Hum. Servs.*, No. 14-878V, 2018 WL 1581672, at *7, 18 (Fed. Cl. Spec. Mstr. Feb. 15, 2018). Kinoshita also involved a limited number of case studies, making it difficult to draw reliable causal conclusions from its determinations. *See R.V. v. Sec'y of Health & Human Servs.*, No. 11–504V, 2016 WL 3882519, at *41 (Fed. Cl. Spec. Mstr. Feb. 19, 2016), *mot. for rev. denied*, 127 Fed. Cl. 136 (2016). Indeed, Petitioner herself has filed literature that directly opposes

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at *15 (Fed. Cl. Sept. 22, 2011) (finding it noteworthy that the Geiers have had a long track record of producing data analyses and articles supportive of the theory that vaccines can contribute to causing autism, but which have been persistently found to be severely defective); *Doe/03 v. Sec'y of HHS,* 2007 WL 2350645, at *3 (Fed. Cl. Spec. Mstr. July 31, 2007) ("I found that the articles authored by Dr. Geier unpersuasive and not scientifically sound. . . I am also aware that Dr. Geier is trained as a geneticist and obstetrician, not an immunologist, epidemiologist, or rheumatologist, and that my fellow special masters and several other judges have opined unfavorably on his qualifications and testimony as an expert."); *Daly v. Sec'y of HHS,* No. 90–590V, 1991 WL 154573, at *7 (Cl. Ct. Spec. Mstr. July 26, 1991) (calling into question Dr. Mark Geier's qualifications, credibility, and credentials as early as 1991).

[17] Although Dr. Blitshteyn stated that the relevant article involved a study in Mexico, in fact it involved subjects from Valencia, Spain.

reliance on this set of articles, since none of them used control subjects, and ultimately do not stand as robust proof in support of causation. Z. Chustecka, *Case Reports of 'Syndrome' Appearing After HPV Vaccination*, Medscape 1–4, 1 (2018), filed as Ex. 28 on Sept. 14, 2018 (ECF No. 31-3) ("Chustecka").

Dr. Blitshteyn did acknowledge that some later articles expressly rebutted her causation contentions. *See* R. Chandler et al., *Current Safety Concerns with the Human Papillomavirus Vaccine: A Cluster Analysis of Reports in VigiBase*, Drug Safety 81–90 (2017), filed as Ex. 29 on Sept. 14, 2018 (ECF No. 31-4) ("Chandler"). Chandler references the fact that the European Medicines Agency ("EMA") had concluded that there was no evidence of an increased prevalence of POTS or CRPS after HPV vaccination, regardless of the findings in articles like Brinth I or Kinoshita. Chandler at 82.[18] Dr. Blitshteyn, however, argued that such studies were not rigorous enough to eliminate the *possibility* of an HPV vaccine association. Blitshteyn First Rep. at 5.

Next, Dr. Blitshteyn outlined potential mechanisms for how the HPV vaccine might produce dysautonomic conditions like NCS. Although the pathogenesis of new-onset chronic and recurrent NCS after HPV vaccination is unknown, she opined that molecular mimicry (in which antibodies generated by vaccination would cross-react against potential targets of the autonomic or vascular components due to antigenic similarity/homology) was the most probable mechanism. *See, e.g.,* Blitshteyn First Rep. at 5–6; Blitshteyn Article at 138; Vernino at 5. To support this contention, she referenced a study where NCS and other comparable orthostatic intolerance disorders, like POTS, were viewed as potentially reflective of autoimmune disease processes. M. Ruzieh et al., *The Role of Autoantibodies in the Syndromes of Orthostatic Intolerance: A Systematic Review*, 51 Scandinavian Cardiovascular J. 243–47 (2017), filed as Ex. 31 on Sept. 14, 2018 (ECF No. 31-6).

In particular, Dr. Blitshteyn highlighted literature discussing anti-adrenergic autoantibodies as potentially causal of some kinds of dysautonomia or orthostatic injuries. X. Yu et al., *Autoantibody Activation of Beta-adrenergic and Muscarinic Receptors Contributes to an "Autoimmune" Orthostatic Hypotension: Reception Autoantibodies in Orthostatic Hypotension*, J. Am. Soc'y Hypertension 1–10 (2012), filed as Ex. 32 on Sept. 14, 2018 (ECF No. 31-7) ("Yu"); H. Li et al., *Agonistic Autoantibodies as Vasodilators in Orthostatic Hypotension: A New Mechanism*, 59 Hypertension 1–18 (2012), filed as Ex. 33 on Sept. 14, 2018 (ECF No. 31-8) ("Li"). Adrenergic receptors in the autonomic nervous system play a role in modulating cardiovascular function and reaction, and so "antagonists" to these receptors (which would potentially include

[18] Petitioner never filed the official report from the EMA. Another Program decision has noted, however, that after Brinth I the EMA conducted a study finding "that the incidence rate for the number of patients with post-vaccination POTS (1 reported per 10,000) proved to be *smaller* than predicted, resulting in an assessment that disputed associating the HPV vaccine to POTS." *McKown v. Sec'y of Health & Hum. Servs.,* No. 15-1451V, 2019 WL 4072113, at *29 (Fed. Cl. Spec. Mstr. July 15, 2019).

autoantibodies capable of a cross-reaction) could interfere with the receptors, resulting in syncopal symptoms or other orthostatic problems. Blitshteyn First Rep. at 5–6. Additionally, Li found that 75 percent of studied patients (with orthostatic hypotension (15 out of a total sample of 20) possessed autoantibodies specific to beta 2-adrenergic or M3 muscarinic receptors. Li at 5.

However, articles like Li and Yu remain silent on how the HPV vaccine might produce the autoantibodies they discuss. Additionally, Dr. Blitshteyn admitted that (at least as of the filing date of her first report) there were no testing facilities in the United States that could identify the presence of adrenergic and muscarinic antibodies; indeed, these antibodies were seldom tested in other countries. Blitshteyn First Rep. at 6. Nevertheless, Dr. Blitshteyn proposed that these studies pointed to a possible autoimmune explanation for some kinds of dysautonomia that could bear on this matter.

Other literature, Dr. Blitshteyn noted, provided alternative mechanisms for how the HPV vaccine could cause the injury at issue. One case study, for example, showed that vaccinated patients with neurologic symptoms developed abnormalities in their spinal fluid consistent with neuro-inflammation and neuro-immune processes. Y. Takahashi, *Immunological Studies of Cerebrospinal Fluid from Patients with CNS Symptoms after Human Papillomavirus Vaccination*, J. Neuroimmunology 71–78, 77–78 (2016), filed as Ex. 34 on Sept. 14, 2018 (ECF No. 31-9) (focusing on patients with central nervous system symptoms after HPV vaccination). Dr. Blitshteyn also brought up an animal study suggesting that HPV vaccines may cause brain changes through anti-HPV antibodies cross-reacting to protein structures in the brain. R. Inbar, *Behavioral Abnormalities in Female Mice Following Administration of Aluminum Adjuvants and the Human Papillomavirus (HPV) Vaccine Gardasil*, Env't & Autoimmunity 1–14, 8 (2016), filed as Ex. 35 on Sept. 14, 2018 (ECF No. 31-10) (studying whether vaccine adjuvants and vaccines could induce autoimmune and inflammatory manifestations resulting in a few instances of symptoms like syncope and a single diagnosis of POTS).

There were also case reports referenced by Dr. Blitshteyn in which patients displayed post-vaccination syncopal symptoms comparable to Petitioner's experience. Blitshteyn First Rep. at 6. In particular, Dr. Blitshteyn highlighted a case series report from Denmark consisting of 53 patients presenting with symptoms of dysautonomia after HPV vaccination. L. Brinth, *Suspected Side Effects to the Quadrivalent Human Papilloma Vaccine*, Danish Med. J. 1–5 (2015), filed as Ex. 36 on Sept. 14, 2018 (ECF No. 32-2) ("Brinth II"). A quarter of the studied patients in Brinth II experienced typical dysautonomic symptoms; 45 percent of that subgroup reported syncope, while all complained of a new-onset headache.[19] Brinth II at 2. Another figure cited in Brinth II indicated that 98 percent of the entire sample (52 out of 53 patients) reported that their activities

[19] Additionally, Dr. Blitshteyn reported that 96 percent of the 53 patients experienced dizziness, including syncope, although this could not be confirmed in Brinth II. Blitshteyn First Rep. at 6.

of daily living were seriously affected, and 75 percent had to quit school for more than 2 months due to their symptoms. *Id.* at 3.

Finally, Dr. Blitshteyn discussed the timeframe in which Ms. America experienced her post-vaccination syncope, deeming it medically acceptable. Blitshteyn First Rep. at 6–7. The Petitioner's increased tempo of symptoms occurred within days of the first and second HPV vaccine doses, a timeframe that was in Dr. Blitshteyn's view consistent with how long the immune challenge would take to become pathologic.[20] *Id.* at 7. Dr. Blitshteyn also claimed that Ms. America's history arguably revealed a re-challenge[21] because her syncope and chronic daily symptoms worsened more demonstrably and quickly after the second dose from April 2015, resulting in admission to the EMU study just 6 weeks after vaccination. Ex. 8 at 20–22. (As the above review of the record shows, however, evidence of the onset of symptoms after the second dose is far thinner in the record than the evidence of a reaction after the first dose, and thus Dr. Blitshteyn seems to rely on the contentions of fact witnesses like Petitioner's mother for this aspect of her opinion).

Second Expert Report

Dr. Blitshteyn's second report largely attempted to respond to the contentions of Respondent's expert.[22] Blitshteyn Second Rep. at 1–6. Dr. Blitshteyn argued that there was "clear evidence" that Ms. America had recurrent NCS, and that her symptoms became much more severe and complex after receiving the HPV vaccine. *Id.*

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[20] Dr. Blitshteyn did not support this argument with any citations to medical literature.

[21] As noted in prior cases, "[c]hallenge-rechallenge happens when a person (1) is exposed to one antigen, (2) reacts to that antigen in a particular way, (3) is given the same antigen again, and (4) reacts to that antigen similarly. Typically, the second reaction is faster and more severe." *Nussman v. Sec'y of Health & Human Servs.*, 83 Fed. Cl. 111, 119 (Fed. Cl. 2008) (internal citations omitted) (quoting *Nussman v. Sec'y of Health & Human Servs.*, No. 99-500V, 2008 WL 449656, at *9 (Fed. Cl. Spec. Mstr. Jan. 31, 2008)).

[22] Dr. Blitshteyn's second report also tried to clarify the importance of her role as a neurologist, differentiating the scope of her relevant expertise from Dr. Boris's pediatric cardiology qualifications. Blitshteyn Second Rep. at 1. She allowed that Dr. Boris was clearly familiar with POTS, since children and adolescents present with its typical features and manifestations and thereafter seek cardiac specialists. *Id.* However, because Ms. America did not present with typical features of POTS or NCS, Dr. Blitshteyn maintained that neurologists like herself were better trained to investigate the etiology and differential diagnosis of such symptoms, which often require detailed evaluation workups. *Id.* To support her point she referenced two pieces of evidence, only one of which was filed. *See* D. Hindley et al., *Diagnoses Made in a Secondary Care ''Fits, Faints, and Funny Turns'' Clinic*, Arch. Dis. Child 214–18 (2006), filed as Ex. 40 on March 15, 2019 (ECF No. 37-2). Dr. Blitshteyn argued that Dr. Boris's lack of expertise in this kind of neurologic presentation might explain why he attributed Ms. America's "atypical" spells to psychogenic causes, while neglecting a number of important neurologic etiologies. Blitshteyn Second Rep. at 1.

Ultimately, this is not a case in which competing expertise was the basis for my conclusion to give one side's expert opinion more weight. To the contrary—even had I concluded that Dr. Blitshteyn's expertise on the relevant topic exceeded that of Dr. Boris, I would *still* determine that her opinion was consistently unreliable.

Dr. Blitshteyn made four arguments to challenge Dr. Boris's diagnosis of psychogenic pseudosyncope ("PPS")[23] or conversion disorder and support her own diagnosis of NCS. First, she noted that Ms. America's cardiologists and neurologists seemed to concur that her episodes were due to syncope rather than reflective of some other condition, like seizures. Blitshteyn Second Rep. at 2. Second, based on Ms. America's multiple evaluations, there was no support for a diagnosis of PPS or conversion disorder, which directly conflicted with Dr. Boris's opinion. *Id.* at 2, 5. Third, Ms. America had improved with targeted therapies for NCS, which would not have occurred if her episodes were psychogenic. *Id.* at 2. Fourth, evaluation by a psychiatrist and psychologist between 2015 and 2016 ruled out conversion disorder. *Id.* at 1. (This argument is inaccurate, as medical records indicated that Ms. America had a working diagnosis of conversion disorder that was never refuted, with Petitioner failing to complete this aspect of her treatment). Ex. 11 at 15, 20, 27.

In discussing other possible diagnoses, Dr. Blitshteyn expressed her understanding as to why some treaters believed Ms. America had adjustment disorder. Petitioner was a young woman dealing with chronic and disabling symptoms that prevented her from attending school or participating in extra-curricular activities. Blitshteyn Second Rep. at 1–2. However, Dr. Blitshteyn emphasized, the definition and clinical features of an adjustment disorder diagnosis, which do not include episodes of loss of consciousness or altered awareness. M.G. Carta et al., *Adjustment Disorder: epidemiology, diagnosis and treatment*, Clinical Prac. & Epidemiology in Mental Health 1–15, 2–3 (2009), filed as Ex. 41 on March 15, 2019 (ECF No. 37-3).

Additionally, this diagnosis did not include chronic dizziness or exercise intolerance. Blitshteyn Second Rep. at 2. A conversion disorder diagnosis would require symptoms that could not be "explained by a neurological or other medical condition or another mental health disorder." *Functional Neurologic Disorders/Conversion Disorder*, Mayo Clinic 1–6, 2, https://www.mayoclinic.org/diseases-conditions/conversion-disorder/diagnosis-treatment/drc-20355202 (last visited Nov. 3, 2021), filed as Ex. 42 on Mar. 15, 2019 (ECF No. 37-4). But Ms. America's symptoms *could* be explained by another neurological disorder—NCS. Blitshteyn Second Rep. at 2. Further, conversion disorder also involved evidence of premorbid personality and significant stressors, and Dr. Blitshteyn could not find either factor in Petitioner's history.[24] *Id.* Additionally, she noted that Ms. America's psychiatrist never suggested a conversion disorder diagnosis, which Dr. Blitshteyn argued was because Ms. America's only significant stressor was

[23] PPS has been defined as "a syndrome of apparent but not true loss of consciousness that may occur in the absence of identifiable cardiac, reflex, neurological, or metabolic causes." W. Shen et al., *2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope*, Circulation e60–e122, e66 (2017), filed as Ex. A, Tab 1 on Feb. 25, 2019 (ECF No. 34-2) ("Shen"). This type of syncope occurs among adolescents, and is the second most common type of syncope after neurally mediated syncope, occurring in 8-15 percent of cases. *Id.* at e89.

[24] Dr. Blitshteyn did not mention, however, the several instances in which Ms. America's family moved, even though her mother had admitted that the moves were "somewhat stressful" for her daughter. Ex. 8 at 39; Ex. 10 at 1–2.

recurrent syncope and chronic symptoms that prevented her from her normal level of functioning in society. *Id.*

Dr. Blitshteyn also defended herself against Dr. Boris's contention that Dr. Blitshteyn's failure to ensure that Petitioner underwent a tilt table test meant that his preferred diagnosis (PPS) could not be excluded in favor or some kind of NCS. Boris First Rep. at 7. In Dr. Blitshteyn's view, Ms. America's presentation did not justify such testing given her evident clinical features and established vital signs.[25] Blitshteyn Second Rep. at 5; Chew at 2; C. Chen-Scarabelli & T. Scarabelli, *Neurocardiogenic Syncope*, BMJ 336–41, 338 (2004), filed as Ex. 47 on Mar. 15, 2019 (ECF No. 37-9) ("Chen-Scarabelli").

Dr. Blitshteyn further disputed Dr. Boris's contention that post-vaccination autonomic disorders usually do not have an autoimmune basis, connecting her rebuttal of this assertion with her discussion of likely causal mechanisms such as molecular mimicry. Blitshteyn Second Rep. at 2. She noted that she had directly written on the topic, outlining evidence of autoimmunity in post-HPV vaccination autonomic disorders such as NCS and POTS. S. Blitshteyn et al., *Autonomic Dysfunction and HPV Immunization: An Overview*, Immunologic Res. 744–54 (2018), filed as Ex. C, Tab 8 on Aug. 8, 2019 (ECF No. 72-7) ("Blitshteyn & Brinth").[26] While Dr. Blitshteyn did not contest the overall safety of HPV vaccines, she maintained that a small number of patients can develop significant and disabling autonomic dysfunction after vaccination - as in the case of Ms. America. Blitshteyn & Brinth at 744–45. Dr. Blitshteyn also reiterated her prior point that testing for most of the antibodies relevant to her proposed causal mechanism (in particular the adrenergic antibodies) was unavailable in the United States (and hence their presence was generally difficult to confirm—even where an autoimmune process was a likely explanation for NCS, as here). Blitshteyn Second Rep. at 2.

Many disease processes, she argued, were understood to be mediated by an autoimmune process involving molecular mimicry—a fact she noted that Dr. Boris also seemed to accept, based on certain items of literature he filed. Blitshteyn Second Rep. at 2; P. Offit & C. Hackett, *Addressing Parents' Concerns: Do Vaccines Cause Allergic or Autoimmune Diseases?*, Pediatrics 653–59, 655 (2003), filed as Ex. A, Tab 6 on February 25, 2019 (ECF No. 34-7) ("Offit & Hackett"). In particular, a number of autoimmune disorders thought to be caused in some cases by

[25] Dr. Blitshetyn assessed the bedside vital signs from the orthostatic hypotension detected at a cardiology evaluation by Dr. Nassif on November 6, 2014. Ex. 7 at 4–6.

[26] Petitioner failed to file this piece of literature, but Respondent filed it as part of her case.

vaccination, such as Guillain-Barré syndrome[27] ("GBS") and transverse myelitis[28] ("TM"), are theorized to involve a small amount of antigen causing a robust and rapid autoimmune response, where antibodies produced in reaction to the vaccine's antigen attack the peripheral nervous system—in the case of GBS—or central nervous system—in the case of TM. Blitshteyn Second Rep. at 2.

Experimental models confirmed the reliability of the autoimmune-by-molecular mimicry mechanistic theory, and amino acid sequence homology between HPV vaccine components and the adrenergic receptors on nerves (the likely locus of cross-reactive attack, assuming here that the cause of Petitioner's NCS was driven by an autoimmune process) sufficient for a cross-reaction to occur. Blitshteyn Second Rep. at 2. This could be demonstrated by Basic Local Alignment Search Tool ("BLAST") searches. *Id.*[29] She went so far as to opine that there was significant homology between components of the HPV vaccine and the adrenergic receptors, which could result in exacerbation of preexisting NCS via amplification of the adrenergic antibodies triggered by the HPV vaccine. *Id*. at 5.[30]

Ultimately, based on the medical record in this case, Dr. Blitshteyn deemed it likely that the HPV vaccine had triggered or exacerbated Ms. America's NCS. Blitshteyn Second Rep. at 5. Ms. America had experienced a significant increase in frequency of episodes following vaccination. *Id*. Petitioner's course was distinguishable from situational syncope (an isolated episode of syncope in response to a stimulus like an injection), as Dr. Boris proposed, and instead was more akin to a chronic, if preexisting, neurologic disorder, such as NCS, that worsened due to vaccination. *Id.*

Lastly, Dr. Blitshteyn again discussed the timeframe in which Petitioner experienced post-vaccination syncope, repeating her view that it had occurred in a medically acceptable period based on how long it would take for HPV vaccine-triggered autoantibodies to be created. She referenced a treatise on vaccines from the Institute of Medicine ("IOM"), which in her recollection stated

[27] GBS is defined as "rapidly progressive ascending motor neuron paralysis of unknown etiology, frequently seen after an enteric or respiratory infection. An autoimmune mechanism following viral infection has been postulated." *Dorland's* at 802.

[28] MT is described as "myelitis in which the functional effect of the lesions spans the width of the entire cord at a given level." *Dorland's* at 1201.

[29] BLAST searches allow for an analysis of homology between two proteins, an understanding of where the homologies were located, and thus (in theory) a determination of whether this degree of homology was sufficient to trigger a clinical disease. S. Altschul, *Basic Local Alignment Search Tool*, J. Molecular Biology 403–410, 404 (1990), filed as Ex. 43 on Mar. 15, 2019 (ECF No. 37-5).

[30] To support some of her homology contentions, Dr. Blitshteyn also referenced personal communication with Dr. Lawrence Steinman (a neurologist who frequently offers testimony about molecular mimicry in Program cases) in March 2019 but did not file any proof to corroborate her assertions about these purported conversations.

"[t]he lag phase is generally 1 to 3 days; the logarithmic phase of the secondary antibody response occurs over the next 3 to 5 days."[31] Blitshteyn Second Rep. at 3. As a result, the HPV vaccine could initiate a vigorous recall response within 1 to 3 days, triggering an exacerbation of preexisting NCS. *Id.* Additionally, she once again asserted that there was evidence of a "re-challenge" after receipt of the second HPV dose. *Id.*

B. *Respondent's Expert – Jeffrey R. Boris, M.D.*

Dr. Boris, a pediatric cardiologist and Clinical Professor of Pediatrics at The Children's Hospital of Philadelphia and The Perelman School of Medicine at the University of Pennsylvania, prepared two written reports for Respondent. Report, dated February 25, 2019 filed as Ex. A (ECF No. 34-8) ("Boris First Rep."); Report, dated July 30, 2019 filed as Ex. C (ECF No. 42-13) ("Boris Second Rep."). Dr. Boris did not accept NCS as the proper diagnosis for Petitioner's symptoms, arguing instead that she had PPS, and he disputed that the HPV vaccine could have caused it, or that it did in this case within the relevant timeframe. Boris First Rep. at 4–6; Boris Second Rep. at 5.

Dr. Boris received his undergraduate degree in biology from Washington University in St. Louis in 1987, and his medical degree from Washington University School of Medicine in 1991. CV, filed as Exhibit B on February 25, 2019 (ECF No. 34-8), updated as Exhibit D on Mar. 8, 2021 (ECF No. 58-1) ("Boris CV") at 1. He completed his training in 1997 and has practiced pediatric cardiology since. Boris First Rep. at 1. He became board certified in Pediatric Cardiology in 1998 and in General Pediatrics in 1995 by the American Board of Pediatrics. *Id.*; Boris CV at 2. He has cared for patients in an outpatient clinic and served as a consult for inpatient cardiology service. Boris First Rep. at 1. He manages patients with dizziness, NCS, postural orthostatic tachycardia syndrome ("POTS"), and disorders of the autonomic nervous system. *Id.* At the time of writing his report in 2019, Dr. Boris had diagnosed and cared for approximately 550 patients with dizziness and syncope, and approximately 950 patients with POTS in the last 11 years. *Id.* He has authored or co-authored eight articles in the peer-reviewed literature on disorders of autonomic function. *Id.*; Boris CV at 11-12.

First Expert Report

Dr. Boris's first report contained a description of syncope and definitions of its different types. Boris First Rep. at 1–4. Dr. Boris defined syncope as "an abrupt, transient, complete loss of consciousness, associated with inability to maintain postural tone, with rapid and spontaneous recovery." *Id*. at 3; Shen at e64. The most common type of syncope, neurally mediated syncope,[32]

[31] Dr. Blitshteyn filed nothing to support this contention.

[32] Neurally mediated syncope is "a serious type of vasovagal syncope precipitated by a stimulus that causes either bradycardia, or a decrease in vascular tone, or both at once." *Dorland's* at 1788.

features an acute drop in blood pressure and cerebral perfusion. Shen at e89. This type of syncope is most common among adolescent females, in as much as 75 percent of cases. *Id.* Dr. Boris also discussed PPS, defining it as "a syndrome of apparent but not true loss of consciousness that may occur in the absence of identifiable cardiac, reflex, neurological, or metabolic causes." *Id.* at e66. PPS occurs among adolescents, and is the second most common form, occurring in 8-15 percent of cases.[33] *Id.* at e89.

Next, Dr. Boris reviewed the connection between the HPV vaccine and different types of syncope. Boris First Rep. at 4. In 15 percent of patients, the HPV vaccine has been associated with neurally-mediated syncope occurring close-in-time to vaccination (meaning within the first two hours of administration), but not beyond this short timeframe. Shen at e89. Other studies reached the same conclusion, noting that younger women were more likely to have a higher incidence of vaccine-related adverse events, but that post-vaccination syncope far more often than not occurred on the same day as vaccination. *See,* e.g., J. Gee et al., *Quadrivalent HPV Vaccine Safety Review and Safety Monitoring Plans for Nine-Valent HPV Vaccine in the United States*, 12 Hum. Vaccine Immunotherapeutics 1406–1417, 1407 (2016), filed as Ex. A, Tab 4 on Feb. 25, 2019 (ECF No. 34-5) ("Gee"); N.P. Klein et al., *Safety of Quadrivalent Human Papillomavirus Vaccine Administered Routinely to Females*, Archives Pediatrics & Adolescent Med. 1140–1148, 1148 (2012), filed as Ex. A, Tab 5 on Feb. 25, 2019 (ECF No. 34-6) ("Klein"); A. Naleway et al., *Reported Adverse Events in Young Women Following Quadrivalent Human Papillomavirus Vaccination,* J. Womens Health 425–432, 428 (2012), filed as Ex. A, Tab 3 on Feb. 25, 2019 (ECF No. 34-4) ("Naleway"). Indeed, as Dr. Boris pointed out, the Slade article cited by Petitioner found 90 percent of syncopal events occurred on the same day of vaccination. Slade at 753. Slade also noted that most rates of adverse events following vaccination were not greater than the background rates compared with other vaccines, including that of autoimmune disorders (although syncope was a disproportionately-reported adverse event in general). *Id.* at 750, 753.

Based on an in-depth overview of Petitioner's medical history (Boris First Rep. at 1–3), Dr. Boris accepted that Petitioner had experienced some episodes of neurally mediated syncope when she was younger. Boris First Rep. at 4. Her post-vaccination symptoms, however, were in his opinion more consistent with a diagnosis of PPS, also referred to as conversion disorder. *Id.* In so opining, Dr. Boris noted that Petitioner's earlier episodes had resolved quickly and were often associated with a warm environment. *Id.* Post-vaccination episodes, however, were distinguishable—lasting up to 30 minutes but with reported normal levels of electroencephalography, blood pressure, and electrocardiographic monitoring. *Id.* Additionally, during at least one witnessed episode in the hospital, Ms. America was able to respond to questions by shaking her head. *Id.*; Ex. 8 at 21. She was also able to avoid self-injury when her hand was

[33] Dr. Boris also mentioned other less-common syncopal variants, like cardiac syncope and arrhythmias, although they are not relevant to this matter. Boris First Rep. at 3–4.

dropped over her face during the drop test performed in October 2014, around the time of her first post-vaccination incident. Boris First Rep. at 4; Ex. 5 at 226. Had she experienced true cerebral hypoperfusion, she would have been unable to respond to external stimuli and could not have controlled her limbs. Boris First Rep. at 4. Thus, a psychogenic cause more likely explained such syncopal episodes. *Id.*

Dr. Boris questioned Dr. Blitshteyn's contrary diagnosis. Boris First Rep. at 4. He questioned whether enough testing or clinical results existed to support post-vaccination NCS (and rule out PPS). Ex. 11 at 15, 20, 27. For example, no tilt table testing to confirm the diagnosis had been performed, despite the widely-recognized utility of such evidence. Chew at 2. Chew also stated that a "recorded ECG can help provide insight into the etiology of syncope . . . However, a syncopal episode associated with normal sinus rhythm [such as was documented in the patient] may be due to . . . psychogenic pseudosyncope." *Id.* Here, ECG evidence was only recorded on November 6, 2014 at a sinus rhythm of 64 bpm, and on December 21, 2015 at a sinus rhythm of 84 bpm. Ex. 7 at 3, 8–9. Dr. Boris also questioned Dr. Blitshteyn's invocation of Chew in support of the argument that syncope could occur in the supine position (as was reported to have occurred with Ms. America). Chew at 2. However, Dr. Boris noted, Dr. Blitshteyn left out the fact that syncope would occur in a supine position usually after "exposure to medical or dental situations, pain, or scenes of injury." *Id.* Yet Ms. America was not recorded as having experienced any of these situations prior to her episodes. Boris First Rep. at 6–7. Chew also stated that "[u]nconsciousness usually lasts less than 1 to 2 minutes, but full recovery can be delayed. . . ." Chew at 2. This differs from Ms. America's episodes, which reportedly lasted far longer. *See,* e.g., Blitshteyn First Consult at 1.

Dr. Boris then outlined his understanding regarding the required conditions for an autoimmune disease to occur and weighed the different kinds of evidence that might bear on vaccine causation. He maintained that autoimmune diseases were premised on four conditions in most cases:

> First, self-reactive (auto-reactive) T or B cells must be present… Second, self-antigens must be presented to the immune system in quantities sufficient to cause autoreactive cells to divide and mature. Third, additional signals such as cytokines are required to activate autoreactive T and B cells. Fourth, regulatory T cells must fail to control destructive autoimmune responses.

Offit & Hackett at 654. Acute rheumatic fever, for example, is well understood to be an autoimmune-mediated process. There, an initial streptococcal bacterial infection "provides a large quantity of antigens that are similar to self (in a patient who is genetically predisposed) over a prolonged period of time," with the antibodies produced in reaction to these antigens (encouraged by an immune process) initiating a subsequent pathogenic cross-reaction. Boris First Rep. at 5.

However, Dr. Boris emphasized, the pathogenic process that drives rheumatic fever differs from the usual immune response to vaccination, because over the comparatively short period of time post-vaccination, only a small amount of antigens are presented, and cytokines associated with an initial innate response to a vaccine are not routinely produced in chronic form either. *Id.* Thus, vaccination will not in most cases present the kind of conditions required to produce an autoimmune process, even under Dr. Blitshteyn's theory. *Id*. at 6.

Dr. Boris also specifically disputed Dr. Blitshteyn's contention that the HPV vaccine could cause NCS, or that syncope could be understood to be a "post-vaccination autonomic disorder." Boris First Rep. at 5. First, he questioned whether the evidence from Petitioner's medical history could support the contention that an antibody-driven autoimmune cross-reaction had occurred. Dr. Blitshteyn herself admitted that, "currently, there is no available testing facility in the United States for the adrenergic and muscarinic antibodies…" Blitshteyn First Rep. at 6. As Ms. America had no demonstrated autoantibodies that could have produced her symptoms in the manner proposed, so Dr. Boris argued that she had no proof of an autoimmune disorder at all, much less one due to the HPV vaccine. Boris First Rep. at 5.

Second, Dr. Boris questioned the reliability of the independent medical literature offered to support a connection between the HPV vaccine and Petitioner's symptoms. In particular, the theories embraced in Dr. Blitshteyn's medical literature lacked corroboration in a clinical scenario. Vernino, for example, did not involve post-vaccination syncope, but autoimmune autonomic ganglionopathy—a version of a severe, rapidly progressing autonomic failure characterized by orthostatic hypotension *plus* other symptoms: gastrointestinal dysmotility, anhidrosis, bladder dysfunction, sicca symptoms, and impaired pupillary light reflex. Vernino at 2–3, 5. Ms. America showed no symptoms of an autoimmune autonomic ganglionopathy *other* than orthostatic hypotension. Boris First Rep. at 5. Kinoshita involved not only a distinguishable demographic sample (adolescent Japanese girls), but also had failed to identify the autoantibodies to the acetylcholine receptor deemed to be the target for an autoimmune attack in cases of autonomic dysfunction, and otherwise did not reliably support causation. Boris First Rep. at 5; Kinoshita at 2185, 2199. Indeed, Kinoshita's authors searched for the relevant autoantibodies, but did not locate them in the studied sample. Kinoshita at 2199.

Another article referenced by Dr. Blitshteyn could do no more than deem causation to be "suspected," using that very word in its title. L. Brinth et al., *Orthostatic Intolerance and Postural Tachycardia Syndrome as Suspected Adverse Effects of Vaccination Against Humanpapilloma Virus*, Vaccine 1–4, 1 (2015), filed as Ex. 24 on Sept. 14, 2018 (ECF No. 30-8) ("Brinth & Pors"). And other articles, like DuVernoy, involved a sample of patients significantly younger than Petitioner. DuVernoy at 3 (studying patients had a median age of four months old, with the oldest only nine); Boris First Rep. at 5.

Petitioner's medical history also undermined the conclusion that her post-vaccination syncopal episodes were due to the HPV vaccines she received. Boris First Rep. at 6. Unquestionably, Ms. America had experienced several episodes of syncope prior to vaccination, so the HPV vaccine could not have initiated the condition. *Id.*; Ex. 10 at 1. And even if her course seemed to worsen post-vaccination, this temporal relationship was insufficient to establish a logical sequence of cause and effect. *Id.* This was especially so given Dr. Boris's contention that Petitioner could not be properly diagnosed with NCS to begin with. Boris First Rep. at 6.

Finally, Dr. Boris discussed the timeframe in which Ms. America experienced post-vaccination syncope. As noted above, Dr. Boris allowed that reliable medical and scientific authority supported a very short (virtually immediate) timeframe for syncope associated with HPV vaccination.[34] J. Schiller et al., *Human Papillomavirus Vaccines*, Vaccines 430–55, 448 filed as Ex. A, Tab 8 on October 25, 2021 (ECF No. 60-2) ("Schiller") (noting that syncope would be expected to occur within 15 minutes of receipt of HPV vaccine). Ms. America's symptoms, however, were reported to have first increased in tempo or degree 24 to 48 hours after immunization, with recurrent syncope over the years thereafter. Ex. 10 at 2.

A longer timeframe lacked reliable medical support. Boris First Rep. at 6. In particular, it was contrary to persuasive evidence that the first type of antibody immunoglobulin created after vaccination, IgM, would not likely appear until *three* days post-vaccination. C. Siegrist, *Vaccine Immunology*, Section 1: General Aspects of Vaccination 16–34, 24 filed as Ex. A, Tab 7 on October 25, 2021 (ECF No. 60-1) ("Siegrist"). Moreover, medical literature did not otherwise support an association between IgM and autonomic targets, like adrenergic or muscarinic receptors, which if interfered with would adversely affect blood pressure (and thus produce syncope). *Id.* But the medical records established that Ms. America's blood pressure remained stable during her episodes. Ex. 7 at 2. It simply would take longer for the immune system to produce the antibodies theorized to be causal herein than a day—even though the record suggested that was when Ms. America's exacerbation began.

This timeframe deficiency could not, in Dr. Boris's view, be saved by focusing on a different class of antibodies, IgG, as some of the literature offered by Dr. Blitshteyn did, to establish a faster process. Yu at 1, 10; Blitshteyn First Rep. at 6. Dr. Boris reasoned that such contentions actually created a more difficult timeline for Petitioner, since other literature concluded that IgG antibodies could not appear until day *seven* post-vaccination, and are not even at peak titer until approximately 30 days post-vaccination. Siegrist at 24; Boris First Rep. at 6. And although Dr. Blitshteyn cited Brinth & Pors, which had a reported temporal relationship of zero to

[34] Dr. Boris stated that syncope typically occurs between 15 minutes to 2 hours after vaccine administration, although he did not fully corroborate this timeframe with literature. Boris First Rep. at 6. Petitioner, however, submitted literature that supported the contention that 90 percent of syncopal events occur on the same day of vaccination. Slade at 753–54.

30 days between vaccination and onset of symptoms, the same article concluded that even if there were symptoms that occurred in temporal association between the vaccine and the injury, that was by itself not reliable evidence of a causal link. Brinth & Pors at 1.

Second Expert Report

After vouching for his expertise in response to Dr. Blitshteyn's attacks,[35] Dr. Boris's second report defended his PPS counter-diagnosis. Boris Second Rep. at 4. In his view, it could be a difficult diagnosis to obtain, especially when treaters were unfamiliar with how to assess its presence. Boris Second Rep. at 4. As many as 50 percent of patients carrying a final diagnosis of PPS had earlier been diagnosed with vasovagal syncope or NCS. K. Walsh et al., *Psychogenic Pseudosyncope: Not Always a Diagnosis of Exclusion*, Pacing Clinical Electrophysiology 480–86, 481, 484 (2018), filed as Ex. C, Tab 16 on Aug. 8, 2019 (ECF No. 42-10) ("Walsh"). Walsh specifically observed that individuals diagnosed with PPS often reported multiple episodes of syncope per year, distinguishing them from those with true NCS. Walsh at 484. Ms. America has similarly claimed to experience several episodes of syncope each year, noting 13 events in 2014 and 20 events in 2015. Ex 10 at 2–3.

Dr. Boris also questioned whether the NCS diagnosis was ever adequately corroborated. Boris Second Rep. at 4. Given Petitioner's convoluted history, Dr. Boris maintained a tilt table test should have been performed to confirm the diagnosis. V. Raj et al., *Psychogenic Pseudosyncope: Diagnosis and Management*, Autonomic Neuroscience 66–72, 66, 68 (2014), filed as Ex. C, Tab 17 on Aug. 8, 2019 (ECF No. 42-11) ("Raj") ("[t]he incidence of PPS is likely under-recognized and the disorder is under-investigated in the unexplained syncope population, yet it can be diagnosed accurately with a focused history and confirmed with investigations including head-up tilt testing . . . ."). Dr. Blitshteyn's conclusion that confirmatory testing was not required relied on an article published in 2004, while the preponderance of medical literature describing evaluation and management of PPS, like Raj, had been published ten years or more after. *Compare* Chen-Scarabelli at 336 *with* Raj at 66; *see also* S. Ninni et al., *Usefulness of Head-Up Tilt Test Combined with Video Electroencephalogram to Investigate Recurrent Unexplained Atypical Transient Loss of Consciousness*, Archives Cardiovascular Disease 82–94, 90–92 (2019), filed as Ex. C, Tab 18 on Aug. 8, 2019 (ECF No. 42-12). The prevailing scientific and medical view underscored the need for tilt table testing, but such proof was wholly absent in this case.

Other record evidence was deemed by Dr. Boris to more directly rebut the proposed NCS diagnosis. During the October 22, 2014 visit to Faxton St. Luke's emergency room, for example (occurring two days post-vaccination), Ms. America purported to have experienced a syncopal

[35] In particular, he articulated his expertise as a pediatric cardiologist, contesting Dr. Blitshteyn's view that only an expert with a neurologic background could opine reliably on the case. Boris Second Rep. at 1.

episode, but displayed while supine a blood pressure reading that was significantly *elevated* (actually hypertensive in Dr. Boris's view) for any patient's age. Boris Second Rep. at 1; Ex 5 at 225, 238, 241. Such a reading was inconsistent with a diagnosis of NCS, which would require a finding of *hypotension* (low blood pressure). Shen at e66. In addition, Petitioner's other vital signs (in particular her heart rate), did not change. Boris Second Rep. at 1; B. Grubb BP et al., *Syncope and Seizures of Psychogenic Origin: Identification with Head-Upright Tilt Table Testing*, Clinical Cardiology 839-42, 841 (1992), filed as Ex. C, Tab 3 on Aug. 8, 2019 (ECF No. 42-2). Petitioner at this time also underwent a drop test but was able to move her hand before hitting her face, which suggested that she had not completely lost consciousness (as would be the case for true NCS). Ex. 5 at 241.

Ms. America's November 2014 visit was similarly inconsistent with the purported NCS diagnosis. Boris Second Rep. at 4; Ex. 7 at 2. Although Dr. Blitshteyn maintained that on this visit Ms. America displayed evidence of orthostatic hypotension, Petitioner's measured blood pressure at this time was 130/76 laying down, 112/76 sitting, and 110/78 standing, while her heart rate measurements were 68 laying down, 64 sitting, and 68 standing. Ex. 7 at 2. In Dr. Boris's view, the supine blood pressure finding was a *hypertensive* measurement given Petitioner's age, gender, and height, and therefore should have been repeated to confirm orthostatic hypotension but was not. Boris Second Rep. at 4. This was especially important here, since blood pressure readings in a person of Petitioner's weight and BMI were fraught with error. *See, e.g.,* N. Anast et al., *The Impact of Blood Pressure Cuff Location on the Accuracy of Noninvasive Blood Pressure Measurements in Obese Patients: An Observational Study*, Canadian J. Anaesthesiologists 298–306, 299 (2016), filed as Ex. C, Tab 14 on Aug. 8, 2019 (ECF No. 42-8); E. Umana et al., *Comparison of Oscillometric and Intraarterial Systolic and Diastolic Blood Pressures in Lean, Overweight, and Obese Patients*, Angiology 41–45, 44 (2006), filed as Ex. C, Tab 15 on Aug. 8, 2019 (ECF No. 42-9). Otherwise, because Ms. America's heart rate did not change from supine to seated position to standing in the face of presumed orthostasis, the NCS diagnosis was ultimately not well supported. Ex. 7 at 2; Boris Second Rep. at 4.

In the following year (June 2-4, 2015), Ms. America underwent a long-term video EMU study using a digital video EEG for assessment. Ex. 8 at 20–22. During the assessment, Ms. America had another purported episode, yet her EEG remained normal, and she was able to shake her head "no" when asked if she could speak, which once again indicated that she had not completely lost consciousness. *Id.* Dr. Boris characterized Petitioner's EEG findings as consistent with a study demonstrating that patients with PPS had a normal EEG prior to, during, and after an episode. S. Benbadis & R. Chichkova, *Psychogenic Pseudosyncope: An Underestimated and Provable Diagnosis*, Epilepsy & Behav. 106–10, 107 (2006), filed as Ex. C, Tab 4 on Aug. 8, 2019 (ECF No. 42-3). Thus, the medical record undercut Dr. Blitshteyn's assertion that there was no evidence that Ms. America was experiencing PPS or conversion disorder. Boris Second Rep. at 2.

Dr. Boris agreed that Ms. America showed improvement on fludrocortisone therapy,[36] but disputed that this fact supported the NCS diagnosis, since other factors also likely contributed to the reduction of her symptoms. Boris Second Rep. at 2. Petitioner had, for example, begun non-pharmacologic therapy and routine exercise. *See* Blitshteyn Second Consult at 2. In addition, Ms. America was previously diagnosed with hypovitaminosis D in January 2018, and started on supplemental vitamin D therapy, which also could have contributed to her improved symptoms. Ex. 15 at 1–2. A vitamin D deficiency was associated with orthostatic hypotension. *See, e.g.,* M. Antiel et al., *Iron Insufficiency and Hypovitaminosis D in Adolescents with Chronic Fatigue and Orthostatic Intolerance*, Southern Med. J. 609-11, 610 (2011), filed as Ex. C, Tab 5 on Aug. 8, 2019 (ECF No. 42-4); F. Ometto et al., *Hypovitaminosis D and Orthostatic Hypotension: A Systemic Review and Meta-Analysis*, J. Hypertension 1036-043, 1038 (2016), filed as Ex. C, Tab 6 on Aug. 8, 2019 (ECF No. 42-5). The supplemental vitamin D therapy could take several months to resolve the effects of the hypovitaminosis, and the timing in this case coincided with the initiation of fludrocortisone and exercise therapy. Boris Second Rep. at 2.

At the same time, a lack of clear record support for the PPS diagnosis from counseling Ms. America received did not defeat its reasonability. Boris Second Rep. at 1. Dr. Boris noted the finding of one article that "psychological factors and trauma are not always reported by patients, nor are they specific to conversion disorder, and many patients with conversion symptoms may not have identifiable psychological stressors." M. Tannematt et al., *Managing Psychogenic Pseudosyncope: Facts and Experiences*, Cardiology J. 658-64, 660 (2014), filed as Ex. C, Tab 1 on Aug. 8, 2019 (ECF No. 42-1). He also observed that Dr. Blitshteyn had incorrectly claimed that Ms. America had no significant stressors in her life, when in fact the record established that she had moved multiple times from 2010 to 2014.

Dr. Boris then reiterated points he had made in his first report about Petitioner's causation theory, denying that her injury was attributable to a vaccine-caused autoimmune process. Boris Second Rep. at 2–3. In particular, he attacked Dr. Blitshteyn's contention that homology between amino acid sequences in components of the HPV vaccine and the alpha-adrenergic receptor was sufficient for a cross-reaction autoimmune attack via molecular mimicry. Medical literature actually established that homologic similarity was common in human biology, yet did not frequently or inevitably lead to autoimmune disease or process. Boris Second Rep. at 2-3; B. Trost et al., *Bacterial Peptides are Intensively Present Throughout the Human Proteome*, Self/Nonself 71–74, 73 (2010) filed as Ex. C, Tab 7 on Aug. 8, 2019 (ECF No. 42-6) ("past and present data tend to exclude a causal mechanistic role for molecular mimicry in the genesis of autoimmunity"). He also noted that Dr. Blitshteyn herself allowed for the fact that proof was ultimately lacking in support of her theory. Boris Second Rep. at 3; Blitshteyn & Brinth at 750, 751 (calling for "further

[36] Fludrocortisone is sold under the brand name Florinef. *Turkupolis v. Sec'y of Health & Hum. Servs.*, No. 10-351V, 2014 WL 2872215, at *2 n.4 (Fed. Cl. Spec. Mstr. May 30, 2014). Drs. Boris and Blitshteyn use both terms interchangeably throughout their expert reports. Blitshteyn Second Rep. at 1; Boris Second Rep. at 2.

investigation to determine the prevalence and possible causation between these post-vaccination syndromes and HPV vaccines," and admitting that the case reports referenced in the article to support its contention "rank low in evidence-based medicine hierarchy").

At the same time, ample reliable medical literature rebutted the contention that the HPV vaccine—or vaccination of any kind—was associated with syncopal conditions of dysautonomia. Boris Second Rep. at 4; Klein at 1148; Gee at 1414. Dr. Boris maintained that Dr. Blitshteyn was conflating association with causation, based primarily on the temporal relationship between Petitioner's reported increase in symptoms tempo and her vaccination. Boris Second Rep. at 3–4.

Finally, Dr. Boris repeated his prior contention that the timeframe for Petitioner's post-vaccination onset was not medically acceptable, based on Dr. Blitshteyn's conclusion that Petitioner had experienced syncopal worsening a day after receiving the HPV vaccine. Boris Second Rep. at 3 He noted again that it would take approximately three days for the most immediately-produced antibodies to appear (and this class of antibody was not likely involved in any cross-reaction against the alpha-adrenergic receptor). Boris Second Rep. at 3; Siegrist at 24. The different kind of autoantibodies more likely to be the cause of a cross-reaction under Petitioner's theory, by contrast, would take up to seven days to appear, and would not peak in numbers until 30 days post-vaccination. Siegrist at 24. And a speedier process was also not possible in this case, given that there was no evidence Petitioner already possessed the relevant autoantibody and/or was experiencing an autoimmune-caused form of syncope before vaccination. Boris Second Rep. at 3.

III. Procedural History

As noted above, the case was initiated in the spring of 2017. Early on in its course, the special master to whom the Petition had been originally assigned deemed the matter to lack reasonable basis, because it was unclear whether Petitioner alleged epileptic or non-epileptic seizures, or if she was simply feigning seizures. ECF No. 12. Although these concerns nearly resulted in the claim's outright dismissal, they were addressed sufficiently to move forward. ECF No. 16.

Following the filing of pertinent medical records and an affidavit, Petitioner offered Dr. Blitshteyn's first expert report in September 2018, with Respondent's first expert report from Dr. Boris filed in the winter 2019, followed by both sides offering an additional supplemental report. This matter was reassigned to me in July 2020, and I ordered Respondent to file her Rule 4(c) Report and for the parties to decide whether they wanted the case to be resolved on the record or through a hearing. Thereafter, Respondent filed her Rule 4(c) Report and the parties elected to resolve the matter on the record. ECF Nos. 50, 52. Petitioner filed a motion in support of her claim on January 8, 2021. ECF No. 55 ("Mot."). Respondent reacted, requesting dismissal in a brief filed

on March 8, 2021. ECF No. 57 ("Opp."). Subsequently, the Petitioner filed a reply. ECF No. 59 ("Reply"). The matter is now ripe for resolution.

IV. Parties' Arguments

Ms. America's brief clarifies that she is asserting only an off-Table significant aggravation claim for NCS or vasovagal syncope exacerbated by the HPV vaccine. Mot. at 8. She argues that she meets the first three prongs of the significant aggravation standard set in *Loving v. Sec'y of Health & Hum. Servs*., 86 Fed. Cl. 135, 144 (2009) because she suffered episodes of syncope prior to vaccination, but the episodes increased in frequency after vaccination, drastically impacting her life for the worse. *Id.* at 8, 9. Scientific literature, she purports, supports her contention that HPV vaccines can cause autonomic disorders, via the medically-reliable mechanistic theory of molecular mimicry. *Id.* at 9–11. Her NCS symptoms match those in other reported cases of autonomic issues after the HPV vaccine, such as that in Denmark. *Id.* 11–12; Brinth II at 2–3. Finally, the timing of her onset—one day after receiving her first HPV vaccine (and then two days after receiving her second dose in April 2015)—constitutes a medically-acceptable timeframe. Mot. 12–13. Ms. America also asserts that her claim is not comparable to *Combs v. Sec'y of Health & Hum. Servs.*, No. 14-878V, 2018 WL 1581672 (Fed. Cl. Feb. 15, 2018), as Respondent argues. Reply at 3–6.

Respondent questions the factual basis for the alleged injury, maintaining that Ms. America actually suffers from PPS or conversion disorder. Opp. at 16–25. However, even if Petitioner could establish a diagnosis of NCS or vasovagal syncope, and that her condition worsened after vaccination, the claim still fails under *Loving* prongs four through six. *Id.* at 25. Under *Loving* prong four, Petitioner has not preponderantly established a reliable medical theory casually connecting her HPV vaccination to exacerbation of vasovagal syncope, relying instead on broad generalizations and contentions inconsistent with what the medical record actually reveals. *Id.* at 25–32. Under *Loving* prong five, the record does not support the conclusion that the HPV vaccine likely caused her injury. *Id.* at 32–33. Under *Loving* prong six, onset of symptoms one day after vaccination is too soon given Petitioner's embrace of molecular mimicry as driving the antibody attack on the relevant nerve receptor targets. *Id.* at 33–35. Respondent also compares this claim to that in *Combs*, where a comparable theory was rejected in a case involving the HPV vaccine. *Id.* at 26.

V. Applicable Legal Standards

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).[37] 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 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 and 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 *Althen* prong requires a different showing and is discussed in turn along with the parties' arguments and my findings.

[37] 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).

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.

However, the Federal Circuit has *repeatedly* stated that the first prong requires a preponderant evidentiary showing. *See Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1360 (Fed. Cir. 2019) ("[w]e have consistently rejected theories that the vaccine only "likely caused" the injury and reiterated that a "plausible" or "possible" causal theory does not satisfy the standard"); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Broekelschen v. Sec'y of Health & Hum. Servs*., 618 F.3d 1339, 1350 (Fed. Cir. 2010). This is consistent with the petitioner's ultimate burden to establish his overall entitlement to damages by preponderant evidence. *W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted). If a claimant must *overall* meet the preponderance standard, it is logical that they be required also to meet each individual prong with the same degree of evidentiary showing (even if the *type* of evidence offered for each is different).

Petitioners may offer a variety of individual items of evidence in support of the first *Althen* prong, and are not obligated to 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). No one "type" of evidence is required. 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." *Andreu,* 569 F.3d at 1380. Nevertheless, even though "scientific certainty" is not required to prevail, the individual items of proof offered for the "can cause" prong must *each* reflect or arise from "reputable" or "sound and reliable" medical science. *Boatmon,* 941 F.3d at 1359–60.

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).

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & 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 also 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 Health & Hum. Servs.*, No. 06–522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356–57 (2011), *aff'd without opinion*, 475 F. App'x. 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 2013 WL 1896173 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs.*, No. 11–355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Standard for Significant Aggravation Claim*

Where a petitioner alleges significant aggravation of a preexisting condition, the *Althen* test is expanded, and the petitioner has additional evidentiary burdens to satisfy. *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. Servs.*, 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 potential cause of her significantly aggravated injury (although the Circuit's recasting of the significant aggravation standard still permits Respondent to attempt to establish alternative cause, where a petitioner's showing is enough to make out a prima facie case and thereby shift the burden of proof to Respondent). *Id.* at 1083.

C. *Law Governing Analysis of Fact Evidence*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [ ] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Hum. Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (determining that 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).

As noted by the Federal Circuit, "[m]edical records, in general, warrant consideration as trustworthy evidence." *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*, *Rickett v. Sec'y of Health & Hum. Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). A series of linked propositions explains why such records deserve some weight: (i) sick people visit medical professionals; (ii) sick people attempt to 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 v. Sec'y of Health & Hum. Servs*., No. 03–1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are often found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Hum. Servs*., 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, the Federal Circuit has also noted that there is no formal "presumption" that records are accurate or superior on their face when compared to other forms of evidence. *Kirby v. Sec'y of Health & Hum. Servs.,* 997 F.3d 1378, 1383 (Fed. Cir. 2021). There are certainly 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 may be required 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. *La Londe 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 Pharm., 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). Under *Daubert*, the 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).

However, in the Vaccine Program the *Daubert* factors play a slightly different role than they do when applied in other federal judicial settings—e.g., the district courts. Typically, *Daubert* factors are employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable or could confuse a jury. By contrast, in Vaccine Program cases

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 in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 (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 review den'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. App'x. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & 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").

E. *Consideration of Medical Literature*

Both parties filed numerous items of 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. *Disposition of Case Without Hearing*

I am resolving Petitioner's claim on the filed record, as per the parties' request. The Vaccine Act and Rules not only contemplate but encourage special masters to decide petitions on the papers where (in the exercise of their discretion) they conclude that doing so will properly and fairly resolve the case. Section 12(d)(2)(D); Vaccine Rule 8(d). The decision to rule on the record in lieu of hearing has been affirmed on appeal. *Kreizenbeck v. Sec'y of Health & Hum. Servs*., 945 F.3d 1362, 1366 (Fed. Cir. 2020); *see also Hooker v. Sec'y of Health & Hum. Servs*., No. 02-472V, 2016 WL 3456435, at *21 n.19 (Fed. Cl. Spec. Mstr. May 19, 2016) (citing numerous cases where special masters decided case on the papers in lieu of hearing and that decision was upheld). I am simply not required to hold a hearing in every matter, no matter the preferences of the parties. *Hovey v. Sec'y of Health & Hum. Servs*., 38 Fed. Cl. 397, 402–03 (1997) (determining that special master acted within his discretion in denying evidentiary hearing); *Burns*, 3 F.3d at 417; *Murphy v. Sec'y of Health & Hum. Servs.*, No. 90-882V, 1991 WL 71500, at *2 (Fed. Cl. Spec. Mstr. Apr. 19, 1991).

ANALYSIS

I. An Overview of Medical Terms and Relevant Prior Decisions

Syncope has been defined generally as "a transient loss of consciousness associated with inability to maintain postural tone, rapid and spontaneous recovery and the absence of clinical features specific for another form of transient loss of consciousness, such as epileptic seizures." Chew at 1; *see also* Shen at e64. The Vaccine Program recognizes a Table claim of post-vaccination syncope, although it requires establishing that the syncope began within an *hour* of receipt of the relevant vaccine. *See, e.g.*, § 100.3(I)(D) and (II)(D). Even in the rare cases when a petitioner has alleged an off-Table claim based on a syncopal injury, onset has commonly been found to have begun very close-in-time to vaccination. *See,* e.g., *Vanscoy v. Sec'y of Health & Human Servs*., No. 13–266V, 2013 WL 3871008, at *1 (Fed. Cl. Spec. Mstr. July 3, 2013) (lacking a definitive timeframe but noting that onset occurred immediately). Literature filed in this case stands for the proposition that a transient incident of post-HPV vaccine syncope would usually occur no more than *within 15 minutes* of vaccine administration. Schiller at 448.

Thus, the most commonly-recognized form of post-vaccination syncope involves an immediate/acute, one-time reaction—not a chronic condition, as alleged here. Of course, there *are* other causes of syncopal episodes, and conditions or illnesses in which it is a recurring event or symptom. Vasovagal syncope (which the experts in this case agreed could be used as a diagnostic term synonymously with NCS) is such a condition, and it typically "1) occurs with upright posture greater than 30 seconds, or with exposure to emotional stress, pain, or medical settings; 2) features

diaphoresis, warmth, nausea, and pallor; 3) is associated with hypotension and relative bradycardia, when known; and 4) is followed by fatigue." Chew at 2. Program cases[38] have recognized the existence of recurrent vasovagal syncope as a condition (independent from vaccine causality). *McKown*, 2019 WL 4072113, at *46; *Combs,* 2018 WL 1581672, at *19.

However, there are hardly any persuasive reasoned Program decisions finding that the HPV vaccine specifically can interfere with any aspect of the nervous system sufficiently to cause *any* form of orthostatic intolerance—whether manifesting as vasovagal syncope, POTS, or some other comparable autonomic dysfunction. On the contrary—the exact opposite conclusion has been repeatedly reached. *See,* e.g*., E.S v. Sec'y of Health & Hum. Servs.*, No. 17-480V, 2020 WL 9076620, at *42 (Fed. Cl. Spec. Mstr. Nov. 13, 2020)*, mot. for review den'd*, 154 Fed. Cl. 149 (2021) ("[a]lthough I am considering a large number of alleged injuries [specifically, headaches, chronic fatigue syndrome, POTS, and small fiber neuropathy] . . . I universally find that Petitioner has not in *any* instance established [in this case] that the HPV or flu vaccines "can cause" the relevant injury") (emphasis in original); *Balasco*, 2020 WL 1240917, at *34 (articulating that the special master "[did] not find preponderant evidence of a reliable medical theory causally connecting petitioner's HPV vaccinations to either POTS generally or her own fibromyalgia and/or vestibular migraines in particular"); *Johnson v. Sec'y of Health & Hum. Servs.,* No. 14-254V, 2018 WL 2051760, at *24 (Fed. Cl. Spec. Mstr. Mar. 23, 2018) (discussing how the petitioner failed to establish a reliable medical causation theory that the HPV vaccine established autonomic nervous system or orthostatic intolerance conditions); *Combs,* 2018 WL 1581672, at *1 ("[p]etitioner's causation theory—that the HPV vaccine could damage the autonomic nervous system—was scientifically unreliable and unpersuasive . . . ."); *K.L. v. Sec'y of Health & Hum. Servs.,* No. 12-312V, 2017 WL 1713110, at *15 (Fed. Cl. Spec. Mstr. Mar. 17, 2017) (noting that respondent demonstrated more persuasively that there was "no link between a number of neurological events, including epilepsy, and receipt of the HPV vaccine"), *mot. for review den'd,* 134 Fed. Cl. 579 (2017); *L.A.M. v. Sec'y of Health & Human Servs*., No. 11–852V, 2017 WL 527576 (Fed. Cl. Spec. Mstr. Jan. 31, 2017) (concluding that the HPV vaccine not found to cause POTS); *Turkupolis v. Sec'y of Health & Human Servs.*, No. 10–351V, 2014 WL 2872215 (Fed. Cl. Spec. Mstr. May 30, 2014) (finding that the HPV vaccine not shown to cause neurocardiogenic syncope).[39]

[38] As already noted, decisions from different cases do not control the outcome herein. *Boatmon,* 941 F.3d at 1358-59. Nevertheless, special masters reasonably draw upon their experience, and those of the other special masters past and present, 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 thus be remiss in ignoring prior cases presenting similar theories or factual circumstances, along with the reasoning employed in reaching such decisions.

[39] I also have not identified any reasoned decisions involving the claim that preexisting vasovagal syncope/NCS was significantly aggravated. At most, a petitioner has previously alleged that a chronic headache condition was aggravated by the HPV vaccine, among other things, but the claim was not successful. *See Salerno v. Sec'y of Health & Hum. Servs.*, No. 16-1280V, 2020 WL 3444163, at *8 (Fed. Cl. Spec. Mstr. May 29, 2020).

Particularly notable is the fact that in almost all these prior cases, arguments akin to what are advanced herein were considered but rejected. *See,* e.g.*, Balasco*, 2020 WL 1240917, at *13, 28, 34 (noting that petitioner (unlike in the present case) had a "positive tilt table test and tested positive for anti-alpha-1-adrenergic antibodies, anti-beta-2 adrenergic antibodies, and the anti-muscarinic cholinergic receptor 4 antibodies. . .", but unsuccessfully established that this raised the likelihood of autonomic dysautonomia, since there was not enough evidence to support the reliability or significance of the results); *McKown*, 2019 WL 4072113, at *50 (stating that molecular mimicry was not reliably invoked to explain vaccine association with syncopal symptoms); *see also Yalacki v. Sec'y of Health & Hum. Servs.*, No. 14-278V, 2019 WL 1061429, at *34 (Fed. Cl. Spec. Mstr. Jan. 31, 2019), *mot. for review den'd,* 146 Fed. Cl. 80 (2019) (commenting on petitioner's theory that the Hep B vaccine could trigger a pathogenic process resulting in an autoimmune attack leading to an injury, but finding that it was "not enough for a claimant to invoke the concept of molecular mimicry" as petitioner needed to "cite to evidence, circumstantial or otherwise, suggesting reason to find it plausible that the proposed autoimmune cross-reaction triggered by the relevant vaccine *does occur*") (emphasis in original); *K.L.*, 2017 WL 1713110, at *14 n.24 (commenting that medical theory using passive surveillance evidence derived from VAERS for support is "inherently less trustworthy than a retrospective study observing actual diagnosed instances of illness or conditions . . . following vaccination" because it contains reports that are unverified or incomplete of adverse events).

Moreover, the same items of literature (like Kinoshita or Brinth I) were offered by these former, unsuccessful petitioners to establish an association between the HPV vaccine and dysautonomia, but close review of the articles revealed that they simply did not reliably support causation. *See, e.g., E.S.*, 2020 WL 9076620, at *45 (". . . evidence offered to suggest a case study-oriented association, like Kinoshita, is weak, dependent on self-selected patient populations rather than scientifically-reliable studies."); *McKown*, 2019 WL 4072113, at *29, 51 (noting that although Brinth I was used to suggest an association between the HPV vaccine and POTS, it revealed selection bias in the studied patients in its sample, and otherwise suffered from a lack of reliable scientific basis); *Johnson*, 2018 WL 2051760, at *17, 24 (articulating that Kinoshita and Brinth I both involved self-selection and lacked scientifical reliability); *Combs*, 2018 WL 1581672, at *7 n.12, 18 (stating that the European medical institutions evaluated Kinoshita but determined that the figure supposedly showing a correlation between HPV vaccination and autonomic conditions was actually attributable to overreporting rather than a scientifically-based association).

The parties have anticipated the relevance of these prior determinations and thus addressed some of them in their briefing, with Petitioner specifically attempting to distinguish *Combs,* both in terms of her own pre versus post-vaccination history. Opp. at 26, 32; Reply at 3-6; *Combs*, 2018 WL 1581672, at *20. However, while Petitioner is correct that these prior cases are not completely congruent, and that there are differences in the theory presented by Dr. Blitshteyn as well (which

are discussed below), decisions like *Combs* still provide useful guidance on the core causation element: whether the HPV vaccine "can cause" interference in the autonomic nervous system sufficient to produce the kinds of symptoms at issue herein. Petitioner's claim is not automatically *unsuccessful* because of its similar contours to these prior determinations—but (as discussed below) it *also* is not sufficiently different, reliable, or preponderantly established to result in a favorable outcome where so many prior petitioners advanced comparable arguments, to no avail.

II. Petitioner Has Not Preponderantly Established the NCS Diagnosis

It is often appropriate for a special master to first determine which alleged injury is best supported by the evidence before applying the *Althen* test—particularly when the injury is disputed—so that "the special master could subsequently determine causation relative to the injury." *Broekelschen*, 618 F.3d at 1346. In some cases, determining the injury obviates entirely the need for any *Althen* analysis, since the petitioner's claim, and causation theory, is dependent on a finding of a specific injury. *Id.*

In this case, the parties dispute the proper diagnosis—and indeed it is the case that Petitioner's claim relies on a determination that she likely suffered from NCS/vasovagal syncope post-vaccination.[40] Respondent argues that she actually suffered from PPS or conversion disorder. The record does not permit me to identify the *most* proper identifying classification for Ms. America's post-vaccination syncopal episodes—but that same record, when evaluated in light of Dr. Boris's assertions, does *not* support Petitioner's contention that she suffered from NCS after receipt of the HPV vaccine, for several reasons.

First, there is an overall lack of treater support for Petitioner's preferred diagnosis. Taken together, the many physicians that Petitioner saw—including Drs. Nassif, Islam, Gerber, Costello, and McMahon—largely did not conclude that Petitioner was currently suffering from NCS (let alone that her symptoms were caused by the HPV vaccine), even though on some occasions some of them allowed that testing sometimes suggested that episodes were more consistent with a vasovagal syncope than clearly-rejected explanations, like seizure. Although I am never bound to accept a treater's opinion, I may give weight to their views. *Snyder*, 88 Fed. Cl. at 746 n.67. The strongest treater support that Petitioner suffered from NCS after the HPV vaccines comes from

[40] Although it is somewhat unclear whether Petitioner suffered from NCS *prior* to vaccination, the definition of NCS from Chew supports the contention that it is possible, as Petitioner was arguably exposed to emotional stressors, such as her family's moves from 2010 to 2014, and a few of her early episodes featured heat. Chew at 2. In addition, Dr. Boris seems to concede the possibility that the diagnosis had far more validity pre-vaccination. Boris Second Rep. at 4–5. Even so, a finding that Petitioner may have had NCS pre-vaccination would only satisfy the first *Loving* prong—and ultimately her claim turns on the determination that the HPV vaccine worsened it. So, the fact that Petitioner did preponderantly suffer from NCS pre-vaccination would not save her claim if it is also determined she was not likely experiencing it *post-vaccination*—meaning nothing could have been significantly aggravated.

Petitioner's expert, Dr. Blitshteyn, whose non-contemporaneous telehealth consuls deserve less weight (even disregarding her advocacy role in this matter as Petitioner's causation expert).[41]

Second, Petitioner's testing was inconsistent and incomplete, with important evaluative measures not performed that could have supported the proposed NCS diagnosis, depending on their results. Petitioner never completed a tilt table test, for example. While the experts disagreed whether such a test was necessary (*compare* Boris First Rep. at 7 *with* Blitshteyn Second Rep. at 5), there exists broad medical acceptance for the tilt table test as the best clinical test for symptoms of dysautonomia like POTS. *Yalacki*, 2019 WL 1061429, at *35. Accordingly, the fact that such testing never occurred undercuts the NCS diagnosis—even if some weight should also be given to Dr. Blitshteyn's contention that other clinical evidence supports it.[42]

Third, the record contains evidence supporting PPS as a possible diagnosis that was ineffectively rebutted by Petitioner. For example, Petitioner's October 22, 2014 visit to Faxton St. Luke's emergency room indicates that Petitioner never lost consciousness as a nurse conducted a drop test and Petitioner was able to move her hand from hitting herself. Ex. 5 at 241. Additionally, Petitioner experienced an episode during her June 3, 2015 EMU study where she was able to understand and respond by shaking her head "no" in answering her mother's question. Ex. 8 at 20–22. Again, although I do not find that the record preponderantly supports the PPS diagnosis, such evidence reduces the persuasiveness of Petitioner's showing to the contrary.

In reaching my conclusion, I am giving Dr. Boris's opinion on diagnosis somewhat more weight—and I do so despite Dr. Blitshteyn's objections to his qualifications. As a well-credentialed expert and cardiologist, Dr. Boris was in fact qualified to offer diagnostic opinions about syncope or dysautonomic/orthostatic intolerance injuries, since such matters involve both heart rate and blood pressure. Indeed, cardiologists are medically recognized to possess the proper credentials to make such evaluations, and cardiologists have been used as expert witnesses in cases alleging injuries comparable to that asserted in this case. *See, e.g., E.S.*, 2020 WL 9076620, at *21; *Yalacki*, 2019 WL 1061429, at *10. Even though I cannot conclude Petitioner had PPS, Dr. Boris's

[41] In addition, these two consultations appeared to simply accept Petitioner and her mother's statements about the nature of the episodes she reported to have experienced. Blitshteyn First Consult at 1–2; Blitshteyn Second Consult at 1–2. Otherwise, Dr. Blitshteyn's evaluations were cursory, lacked independent corroboration of her condition, and involved or relied upon no evident testing to confirm the conclusions reached. *Id.*

[42] Admittedly, there is a parallel lack of diagnostic/evaluative evidence to confirm Dr. Boris's contention that Petitioner's episodes constituted PPS, and this is one reason I do not find that PPS has been preponderantly established either. However, given Petitioner's initial burdens to establish matters like her claimed injury, the failure to corroborate the NCS diagnosis falls on Petitioner. And the fact that Petitioner was recommended to undergo psychiatric testing all the way back in June 2015 before this claim was initiated, but only attended a total of two documented sessions (equaling a total of 1 hour and 15 minutes) before being discharged for noncompliance shortly thereafter, reduces the impact of Petitioner's arguments that PPS is not itself established by the medical record. Ex. 11 at 15–16, 18–19, 27–28.

assertions about Petitioner's diagnoses were persuasive, and greatly undercut Dr Blitshteyn's diagnostic opinion.

III. Petitioner's Causation-in-Fact Significant Aggravation Claim Fails

Ms. America's causation-in-fact claim is rooted in the contention that the HPV vaccine she received in October 2014[43] caused a significant aggravation of her preexisting NCS symptoms. Mot. at 13. Because I have determined that she did not likely have post-vaccination NCS, she cannot prevail in establishing its significant aggravation.

However, even if I had been able to find on this record that Petitioner did likely suffer from NCS after the first HPV dose (and for purposes of this analysis I will so assume), I could not also find that she had established that the HPV vaccine could worsen it, or that it did so here. I address the *Loving* prongs below in order of their significance to my determination.[44]

A. *Loving Prong Six: Petitioner Did Not Show A Medically Acceptable Temporal Relationship Between Her October 2014 Vaccination and Alleged Exacerbation*

The timeframe for Petitioner's onset of increased syncopal episodes after her first HPV dose—24-48 hours post-vaccination—was too short to be medically acceptable, even accepting for sake of argument Petitioner's theory that the vaccine could have exacerbated her NCS via some autoimmune pathologic process.

As Dr. Boris persuasively observed, such a short timeframe is in fact *contrary* to Dr. Blitshteyn's theory of molecular mimicry as driving the alleged autoimmune process that led to Petitioner's symptoms. Boris First Rep. at 6. This is because the kind of antibodies that would be generated closest in time to vaccination (the IgM immunoglobulins) would likely take approximately *three days* to appear. Siegrist at 24. And the class of autoantibodies more likely to drive the relevant autoimmune process posited by Dr. Blitshteyn's theory would take nearly twice

[43] Petitioner also seems to suggest in passing that the second dose of the HPV vaccine received in April 2015 similarly caused a significant aggravation of her NCS (Mot. at 12–13), but as discussed below this assertion is mostly unsubstantiated.

[44] Because I have found that Petitioner has failed to carry three of the *Loving* prongs, I do not include a discussion of all six prongs. However, I have already observed that there is far better preponderant support for the finding that Petitioner had NCS prior to vaccination—thus establishing the first *Loving* prong. In addition, the record supports the conclusion that Ms. America had roughly five episodes over a span of five years before her vaccination, all of which resolved quickly or were associated with a variety of external stressors (temperature, menstruation, infection, etc.). Ex. 10 at 1–2. After vaccination, by contrast, she suffered up to 20 episodes of syncope in a single year, and these occurrences were prolonged although not associated with all (or even most) of the criteria relevant to NCS. *Id.* at 2–3. Thus, there is a distinct "worsening" post-vaccination sufficient to meet the lenient interpretation of *Loving* prong three embraced by the Federal Circuit in *Sharpe*. I have not found, however, that the post-vaccine NCS diagnosis has preponderant support—and even if I am in error on that finding, the last three *Loving* prongs are still not satisfied.

as long. Boris First Rep. at 6. Thus, even if it were the case that the HPV vaccine could trigger an autoimmune reaction in the manner Dr. Blitshteyn proposes, it would not likely occur within a one or two-day timespan.

Dr. Blitshteyn did not offer sufficient preponderant and reliable scientific or medical evidence to counter this opinion. Indeed, beyond her conclusory say-so, her timeframe contentions find scant evidentiary support. Dr. Blitshteyn did not cite to a filed piece of literature to support a two-day onset. Blitshteyn First Rep. at 6–7; Blitshteyn Second Rep. at 3. She referenced an IOM treatise on vaccines, which she stated allowed for a recall response within 1 to 3 days, but she did not file this literature to support her assertion, nor did she argue that the three-day onset discussed in the alleged article (directly supporting Dr. Boris's argument) was incorrect. In the end, Petitioner showed only a temporal observation—not enough to find that the two events were causally linked. *See Grant*, 956 F.2d at 1148.

Dr. Blitshteyn also argued that Petitioner experienced a faster immune reaction after her *second* dose of the HPV vaccine six months later, in April 2015. Blitshteyn Second Rep. at 3. Yet there is no medical evidence of Petitioner experiencing syncopal symptoms in an even closer-in-time period when compared to the one to two-day onset alleged after her first HPV dose in October 2014—as would be expected if the second dose reflected an instance of rechallenge. The primary mention of subsequent episodes is found in her mother's affidavit, which states that Petitioner had six additional episodes over the following months but does not specify exact dates. Ex. 10 at 3. It was not until June 3, 2015, during Petitioner's EMU study, where another episode was reported—but this was approximately *two months* post-vaccination. A longer time interval between vaccination and symptoms for a subsequent exposure to the relevant vaccine is not persuasive evidence that the vaccine was stimulating a pathogenic process due to rechallenge.

B. *Loving Prong Four: Petitioner's Causation Theory was Unreliable And Unsupported by Sufficient Preponderant Evidence*

Petitioner has failed to reliably demonstrate that the HPV vaccine "more likely than not" can prompt orthostatic intolerance, whether manifesting as POTS, generalized dysautonomia, or vasovagal syncope as alleged here. I have had multiple opportunities in the past to consider this causal theory, and have heard numerous experts propose in prior cases that components of the HPV vaccine can initiate an autoimmune cross-reaction sufficient to impact the autonomic nervous system and cause syncopal-like symptoms. *See, e.g., McKown*, 2019 WL 4072113, at *54; *Johnson*, 2018 WL 2051760, at *24; *Combs*, 2018 WL 1581672, at *18–19; *K.L.*, 2017 WL 1713110, at *14–15.

In such cases, I have consistently denied compensation, after considering the same items of literature offered herein (including Dr. Blitshteyn's own articles). My reasoning for doing so

arises from the determination that (a) orthostatic intolerance (in which the autonomic nervous system's background "control"' over heart rate and blood pressure goes awry) most commonly is not reflective of an autoimmune disease, but instead is usually attributable to other factors, like dehydration[45] or physical deconditioning;[46] (b) in the rare instances it might be autoimmune in nature, there is clinical evidence in an affected patient of *other* kinds of autonomic dysfunction symptoms (i.e. bladder control loss); and (c) although it can be plausibly contended that there is a subset of autonomic dysfunction driven by an autoimmune process (interference with adrenergic receptors by autoantibodies), this kind of rare condition has not reliably been shown to be associated with the HPV vaccine. *McKown*, 2019 WL 4072113, at *48 (noting the existence of "literature support … for the idea that one *particular variant* of autonomic neuropathy producing POTS symptoms might be associated with a particular autoantibody, thereby suggesting autoimmunity as a plausible pathologic mechanism" in some cases of orthostatic intolerance/dysautonomia, but that it is extremely uncommon and not likely vaccine-caused).

I have also repeatedly found in such cases that the injured claimant either did not demonstrably possess true autonomic dysfunction, or that the purported association with vaccination was merely temporal. *See, e.g., McKown*, 2019 WL 4072113, at *55 (establishing that "the lack of evidence that in this timeframe Petitioner was experiencing any autoimmune or inflammatory process, prevents a finding that the timeframe was medically acceptable"); *Yalacki*, 2019 WL 1061429, at *35, 37 (indicating in the record that it was unclear with petitioner even had POTS, and even if it did exist, it predated the Hepatitis B vaccination, but was not exacerbated by it); *Johnson*, 2018 WL 2051760, at *22–25 (noting that onset of petitioner's symptoms was not within a medically acceptable timeframe to establish that the vaccine caused petitioner's injuries); *Combs*, 2018 WL 1581672, at *19 (finding that petitioner was unable to establish that her autonomic nervous system was damaged); *K.L.*, 2017 WL 1713110, at *16 (pointing out that petitioner mainly relied on the temporal association between vaccination and symptoms onset to support a medically acceptable timeframe).

Of course, this is a different case, and my prior determinations, no matter how relevant or factually similar, do not compel the outcome herein. But Petitioner's causation theory as presented in this case did not break any new ground.

First, Dr. Blitshteyn made assumptions about the general association between the different forms of dysautonomia that were not well-founded. If anything, there is *less* associating NCS with vaccination than other forms of dysautonomia. Blitshteyn Article 1–2; DuVernoy at 8; Vernino at 2, 5. In fact, despite some overlap these conditions have many differences, and orthostatic

[45] Dehydration is "the condition that results from excessive loss of body water." *Dorland's* at 475.

[46] Deconditioning is "a change in cardiovascular function after prolonged periods of weightlessness, probably related to a shift of a quantity of blood from the lower limbs to the thorax, resulting in reflex diuresis and a reduction of blood volume." *Dorland's* at 469.

hypotension and POTS produce different responses in patients in terms of blood pressure and/or heart rate response. Yu at 2. A syncopal episode may occur without a change in blood pressure or heart rate. *Id.* Dr. Blitshteyn also admitted that although syncope occurring immediately after vaccination is well-recognized as an adverse event, chronic or recurrent syncope is not. Blitshteyn First Rep. at 5. And certainly, it is not the case that conditions resulting in syncope or POTS are by definition autoimmune—even Petitioner's own literature rebuts that contention. *Compare id. with* Brinth & Pors at 1 ("[t]hough numerous case reports have caused discussion in the medical literature as well as in the lay press on a possible association between vaccination and development of autoimmunity, these do not provide evidence for a causal link").

Second, the association between the HPV vaccine and vasovagal syncope/NCS has not been demonstrated by the medical or scientific authority Dr. Blitshteyn offers. Articles like Brinth I and Kinoshita are too unreliable or have been rebutted by subsequent literature *cited by Petitioner*, like Chustecka. Chustecka at 1 ("[h]owever, experts point out that all of these publications are case reports with no control subjects, and cannot determine causality"). And I have noted above that the same panoply of literature marshalled in this case to connect the HPV vaccine with various forms of dysautonomia has shown up over and over again in prior cases but has been deemed unreliable or unpersuasive. *See,* e.g., *Combs*, 2018 WL 1581672, at * 7, 18. In *Combs*, for example, I observed that Kinoshita involves a very limited number of case studies, and (as Dr. Boris noted) different disorders other than the alleged injury, ultimately providing no evidence of causation. Kinoshita at 15; Boris First Rep. at 5. The new recitation of such previously-rejected literature in this case, in support of a causation theory markedly similar to past rejected theories, does not give them a force of persuasiveness as they have never been found to have merit.

In addition, arguments about molecular mimicry driving the purported autoimmune process herein do not rise beyond plausibility, and are not otherwise bulwarked by reliable scientific or medical evidence establishing that components of the HPV vaccine might produce an autoimmune cross-reaction sufficient to adversely interact with adrenergic receptors. As a general matter, molecular mimicry is not a "one size fits all" theory in any Program case (even if some experts wield it as such). It is relatively easy for an expert to show (using BLAST searches)[47] that amino acid sequences in a vaccine's protein components match self-sequences found within the relevant human protein. But this does not mean that its invocation in a particular case carries the day for purposes of proving a persuasive causal theory. *McKown*, 2019 WL 4072113, at *50 (citing *Devonshire v. Sec'y of Health & Hum. Servs.,* No. 99-031V, 2006 WL 2970418, at *15 (Fed. Cl. Spec. Mstr. Sept. 2006)) ("[b]ut merely chanting the magic words 'molecular mimicry' in a Vaccine Act case does not render a causation theory scientifically reliable, absent *additional*

[47] Here, Dr. Blitshteyn has not even provided the underlying BLAST search data results to show the purported homology. Opp. at 30; Blitshteyn Second Rep at 2–3.

evidence specifically tying the mechanism to the injury and/or vaccine in question") (emphasis in original), *mot. for review den'd,* 76 Fed. Cl. 452 (2007)).

Rather, something a bit more specific must be offered—even if certainty remains out of reach (*and of course certainty is not the evidentiary standard in the Program*). But not only has Dr. Blitshteyn not done so, but she focuses on homology between the HPV L1 particle and the alpha-adrenergic receptor type 1B—even though Petitioner's literature references *beta adrenergic and muscarinic receptor antibodies* as driving the relevant purported autoimmune process.[48] *See* Yu at 2; Li at 5. And it is not likely that alpha adrenergic receptor type 1B autoantibodies are even causative of *any* condition, as Dr. Boris persuasively argued. Boris Second Rep. at 2–3.

Moreover, the literature offered by Dr. Blitshteyn that discusses alpha adrenergic and muscarinic receptor antibodies is focused upon addressing the specific symptoms seen in orthostatic hypotension and POTS—conditions in which positional change (e.g., standing up in the case of POTS) leads to tachycardia or a blood pressure change, thereby resulting in symptoms. Yu at 7; Li at 7. But even if it is correct that these receptors are relevant to some uncommon cases of orthostatic intolerance, it remains unestablished that Petitioner's own syncopal events *were the product of positional change*. Ex. 5 at 206, 241, 247. Thus, not enough has been shown to reliably establish that the HPV vaccine could promote the kind of highly uncommon, autoimmune-form dysautonomia driven by adrenergic receptor interference due to a molecular mimicry-caused cross-reaction.

The case report evidence used to bulwark Petitioner's claim generally, by associating the HPV vaccine with comparable injuries, is also wanting. Petitioner attempts to analogize her symptoms to those in other case reports purportedly linking the HPV vaccine to orthostatic intolerance, like Brinth II. Mot. at 12; Brinth II at 2. But Brinth II has been criticized for lacking any control group, and for choosing its subjects to fit the pre-specific hypothesis of an HPV vaccine-induced illness. *See Balasco*, 2020 WL 1240917, at *30–31 (noting specifically "that autonomic symptoms are prone to exaggerated self-reporting that cannot be correlated to objective findings," indicating that studies like Brinth II are not an accurate assessment of HPV vaccine-induced illnesses). Otherwise, it is recognized that case reports provide lukewarm evidentiary support for causation. *See Campbell*, 97 Fed. Cl. at 668 ("[c]ase reports do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value ... [but] the fact that case reports can by their nature only present indicia of causation does not deprive them of all evidentiary weight."). There simply is not enough in this record to accept Petitioner's contentions about causation.[49]

[48] In Dr. Blitshteyn's first expert report she noted beta 2 adrenergic or M3 muscarinic antibodies, but in her second report she discussed alpha-adrenergic receptor type 1b. Blitshteyn First Rep. at 5–6; Blitshteyn Second Rep. at 2–3.

[49] Petitioner also has not shown that the underlying wild HPV infection is associated with dysautonomia—a kind of proof that is unquestionably assistive of arguments that a particular vaccine might also cause the same injury, although

C. *Loving Prong Five: The HPV Vaccine Did Not Likely Worsen Ms. America's Syncopal Episodes*

The medical record does not support Petitioner's contention that her post-vaccination NCS (assuming, again, it existed—a finding I have not made, as noted above) worsened due to the HPV vaccine. There is no evidence that Ms. America's treaters ever associated her subsequent episodes with the vaccination. There is also no evidence of the kind of concurrent symptoms a person with an autoimmune disease provoking syncopal episodes (and in the manner alleged—by interference with adrenergic receptors) *would* display, such as an increased heart rate caused by a change in body positions resulting in dizziness and lightheadedness. Although this was not specifically tested for, there were occasions, such as an emergency room visit on October 22, 2014, and an event monitor ordered on November 6, 2014, which specifically noted an absence of changes of heart rate during Ms. America's episodes. Petitioner also does not appear to have possessed the autoantibodies deemed by Dr. Blitshteyn to be likely causal (although I do take note of Dr. Blitshteyn's point that this kind of testing is not commonly performed). Certainly, however, Petitioner's treating physicians did not suspect or propose that she suffered from any form of autoimmune disease that might be vaccine-attributable. While Petitioner may have *reported* more syncopal episodes post-vaccination, it has not at all been shown that this increase had any more than a temporal relationship to the date of vaccine administration.

IV. This Case Was Appropriately Decided on the Papers

In ruling on the record, I am choosing not to hold a hearing, consistent with the wishes of the litigants. ECF No. 52. Determining how best to resolve a case is a matter that lies generally within my discretion, and although the parties have not objected to this method of adjudication, I shall explain why a hearing was not required.

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*, 38 Fed. Cl. at 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." *Id*. 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.

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it certainly is not a prerequisite to so arguing. *Deshler v. Sec'y of Health & Hum. Servs.*, No. 16-1070V, 2020 WL 4593162, at *18 (Fed. Cl. Spec. Mstr. July 1, 2020).

The present claim could be, and was, resolved fairly without the need for live testimony from the experts. The parties did not agree on Ms. America's diagnosis, and while my determination of that issue bears on the outcome, it was a matter that could be decided on the basis of the record and written reports, without the need for live testimony. I also do not exclusively rely on that finding, further diminishing the significance of how I resolved the injury question, since the case ultimately turned on Petitioner's inability to meet three of the six *Loving* prongs. And resolution of that matter as well could be accomplished based upon the briefs and written reports (coupled with my extensive prior familiarity with theories for how the HPV vaccine can cause orthostatic intolerance or syncope, as well as the literature repeatedly offered to support them). This was not a case where live expert testimony was necessary to explain a concept, and holding a hearing would not have affected or altered the outcome.

CONCLUSION

The record does not support Petitioner's contention that the HPV vaccine she received could, or did, exacerbate her allegedly preexisting NCS. I therefore must DENY entitlement in this case.

In the absence of a motion for review filed pursuant to RCFC Appendix B, the clerk of the court **SHALL ENTER JUDGMENT** in accordance with the terms of this decision.[50]

IT IS SO ORDERED.

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

[50] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment if (jointly or separately) they file notices renouncing their right to seek review.