In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 16-1278V

Filed: April 26, 2021

L.P., Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	TO BE PUBLISHED Influenza Vaccine; Postural Orthostatic Tachycardia Syndrome (POTS); Dismissal Decision

Andrew D. Downing, Van Cott & Talamante, PLLC, for Petitioner
Daniel A. Principato, U.S. Department of Justice, Washington, DC, for Respondent

DECISION ON ENTITLEMENT[1]

Oler, Special Master:

On October 5, 2016, L.P. ("Petitioner") filed a petition for compensation under the National Vaccine Injury Compensation Program, 42 U.S.C. § 300aa-10, *et seq*.[2] (the "Vaccine Act" or "Program"). The petition alleges that Petitioner developed postural orthostatic tachycardia syndrome ("POTS") as a result of the influenza ("flu") vaccine she received on September 25, 2015. Pet. at 5-6, 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 in 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the Decision's inclusion of certain kinds of confidential information. To do so, each party may, within 14 days, 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, this Decision will be available to the public in its present form. *Id.*

[2] National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

Upon review of the evidence in this case, I find that Petitioner has failed to show that POTS is her correct diagnosis or that the influenza vaccine she received on September 25, 2015 caused her condition. The petition is accordingly dismissed.

I. Procedural History

On October 10, 2016, Petitioner filed her Petition. ECF No. 1. She filed medical records and a statement of completion on December 19, 2016. ECF No. 14.

On January 17, 2017, Respondent filed a Rule 4(c) Report, presenting his analysis of Petitioner's claims and concluding this case is not appropriate for compensation under the terms of the Vaccine Act. ECF No. 16.

On March 13, 2017, Petitioner filed an expert report from Dr. Jill Schofield as well as Dr. Schofield's curriculum vitae. ECF No. 18, Ex 30-31. On March 24, 2017, Petitioner filed the medical literature associated with Dr. Schofield's report. ECF Nos. 19-21, Exs. 32-49.

On October 5, 2017, Respondent filed an expert report from Dr. Thomas Leist, Dr. Leist's curriculum vitae, and the medical literature associated with his report. ECF No 28, Ex. A; Ex. A Tabs 1-2.

On December 5, 2017, this case was assigned to my docket. ECF No. 32.

On August 13, 2018, Petitioner filed a supplemental expert report from Dr. Schofield. ECF No. 36, Ex. 50. On April 29, 2020, and March 17, 2021, Petitioner filed additional medical literature in support of Dr. Schofield's reports. ECF No 53, Ex. 56; ECF No. 62, Ex. 57.

On October 15, 2018, Respondent filed a supplemental responsive expert report from Dr. Leist, and the associated medical literature. ECF No. 37, Ex. B; Ex. B, Tab 1.

On August 20, 2019, Petitioner filed a Statement of Completion. ECF No. 48.

On December 20, 2019, Petitioner filed her Motion for Decision on the Record. ECF No. 49. On March 20, 2020, Respondent filed a Response. ECF No. 50. On April 29, 2020, Petitioner filed a Reply brief. ECF No. 54.

On June 18, 2020, the parties filed a Status Report stating that the record in this matter was complete. ECF No. 57. This matter is now ripe for adjudication.

II. Medical Records

A. Relevant Pre-Vaccination History

Prior to her vaccination on September 25, 2015, Petitioner had a history of heart palpitations, exercise induced asthma, anxiety, scoliosis, allergic rhinitis, eustachian tube dysfunction, premenstrual and menstrual irregularities, iron deficiency anemia, Vitamin D

deficiency, and a sensitivity to sunlight. She had suffered from allergic rhinitis since the age of four, and she was diagnosed with exercise induced asthma in 2001. Ex. 10 at 17-19. In 2002, Petitioner had a left breast biopsy. Ex. 5 at 1. In September 2012, an x-ray of Petitioner's spine revealed lumbar scoliosis measuring 20 degrees. Ex. 18 at 55.

In the two years leading up to Petitioner's alleged vaccine injury, Petitioner regularly visited various doctors with complaints of heart palpitations, back pain, allergy related symptoms, and menstrual issues.

On February 27, 2013, Petitioner saw Dr. Yeash, her primary care physician, complaining of irregular heartbeats occurring daily, sometimes at night, which seemed to trigger anxiety. Ex. 18 at 28. An EKG was non-diagnostic *Id.* at 29. Dr. Yeash assessed Petitioner with palpitations and referred her to a cardiologist. *Id.* at 28.

On March 20, 2013, Petitioner saw Dr. Benedict, a cardiologist, complaining of heart palpitations mostly when sleeping or sitting still, usually occurring one week before and during her period and sometimes accompanied by a flushed or clammy feeling and lightheadedness. Ex. 5 at 8-9. Dr. Benedict ordered an EKG, an echocardiogram, and a Holter heart monitor. *Id.* at 8. The results of the EKG and echocardiogram were non-diagnostic/normal. *Id.* at 11, 26.

On April 15, 2013, Petitioner saw Dr. Yeash for a medication check. Ex. 18 at 26. Her bloodwork revealed low levels of Iron and Vitamin D. Dr. Yeash recommended supplements. Ex. 18 at 52.

On April 22, 2013, Dr. Benedict provided Petitioner with the results of her Holter monitor test. Ex. 5 at 2. Seven total events of "fluttering in the chest" were recorded over a period of 30 days which did not correlate with premature atrial contractions ("PACs")[3]. *Id.*

Petitioner visited Dr. Yeash on May 6, 2013 complaining of fatigue and constipation. Ex. 18 at 23. Dr. Yeash assessed Petitioner with anemia and premenstrual disorder and prescribed 0.5mg of Alprazolam every eight hours or as needed. *Id*. at 24.

Petitioner again visited Dr. Yeash on November 18, 2013 complaining of heavy periods, trouble sleeping and tinnitus. Ex. 18 at 21. Dr. Yeah assessed Petitioner with an iron deficiency, Vitamin D deficiency, metrorrhagia, tinnitus and insomnia. *Id.* He recommended that Petitioner undergo an endometrial ablation to relieve her heavy periods and perhaps resolve her iron deficiency. *Id.* Dr. Yeash recommended that Petitioner see an ENT for her tinnitus. *Id.*

[3] Atrial Premature Complex is a single ectopic atrial beat arising prematurely, manifesting electrocardiographically as an abnormally shaped premature P wave, usually with a slightly increased PR interval. It occurs in normal hearts, sometimes associated with the use of stimulants, but may be associated with structural heart disease. *Dorland's Illustrated Medical Dictionary*. (33 ed. 2019), https://www.dorlandsonline.com/dorland/definition?id=66296 (last visited April 19, 2021) (hereinafter "Dorland's").

On March 26, 2014, Petitioner saw Dr. Schkade, an ENT, complaining of allergies and exercise induced asthma. Ex. 10 at 11. She reported an oral allergy to walnuts and tomatoes and that Nasacort made her anxious. *Id.* at 12. Dr. Schkade noted a history of rhinoconjunctivitus, pruritus and eustachian tube dysfunctions, which he indicted was probably secondary to her allergic rhinitis. *Id.* at 12.

Petitioner returned to Dr. Schkade on April 12, 2014 for allergy testing and desensitization injections. Ex. 10 at 13. Skin testing revealed that she was allergic to grass and Dr. Schkade diagnosed her with chronic rhinitis due to non-allergenic symptoms in the winter. *Id.*

On April 24, 2014, Petitioner presented to Westside Women's Clinic complaining of heavy periods and insomnia due to having to get up at night to address her menstrual flow. Ex. 52 at 13. Petitioner also reported a lack of libido. *Id*. She was assessed with dysmenorrhea. *Id.*

Petitioner saw Dr. Schkade on July 16, 2014 reporting a 50 percent improvement in her allergic rhinitis since she started desensitization injections. Ex. 10 at 21. She reported that Flonase changed her menstrual cycle and caused breast discomfort. *Id*. Dr. Schkade recommended continued immunotherapy and both a nasal and ocular antihistamine. *Id.*

On October 15, 2014, Petitioner saw Dr. Schkade complaining of ear discomfort and a pruritic skin rash in sun exposed areas. Ex 10 at 23. Dr. Schkade noted that Petitioner's asthma and allergic symptoms were under control and that her ear discomfort could be related to her eustachian tube dysfunction. *Id.* at 24. He recommended that she see a dermatologist for possible photosensitivity. *Id.*

Petitioner visited Dr. Maybach as a new patient on December 3, 2014. Ex. 18 at 19. Petitioner reported having abnormal TSH levels but indicated she had never been on medication. *Id.* She attributed her iron deficiency to her heavy periods and reported suffering from constipation as a result of taking iron supplements. *Id.* Dr. Maybach assessed Petitioner with an iron deficiency (chronic anemia), Vitamin D deficiency, and metrorrhagia. *Id.*

On February 11, 2015, Petitioner presented at Westside Women's Care complaining of pain on her left side and excessively heavy periods. Ex. 21 at 6. Petitioner reported having tried every kind of birth control for her symptoms, but she reported they were either ineffective or caused side effects. *Id.* Petitioner rejected trying an IUD because she was concerned about hormone issues. *Id*. Her doctor found the pain on Petitioner's left side to be consistent with constipation. *Id.* An ultrasound showed a normal uterus with no abnormalities. *Id*.

Petitioner presented to Arvada Sports and Spine Group on April 8, 2015 complaining of left side low back pain for the past three to four weeks possibly due to falling while walking her dog. Ex. 11 at 1. Petitioner was also concerned that the pain might be related to her ovaries, internal organs, or pre-menopausal hormone issues. *Id.* She also reported an irregular heartbeat and constipation. *Id.* at 1-2. The therapist recommended a home exercise regime combined with physical therapy once a week for six to eight weeks. *Id*. at 4. The therapist noted that Petitioner "appeared to be anxious." *Id.* at 2.

On April 10, 2015, Petitioner visited the Saint Anthony Hospital Emergency Department complaining of a reddened sharp stabbing left lower quadrant abdominal pain over the past one month as well as constipation. Ex. 25 at 5. The results of a pelvic ultrasound were normal. *Id.* at 7. The attending physician doubted diverticulitis and considered constipation to be likely. *Id.* at 7.

Petitioner presented to Hafner Chiropractic on April 14, 2015, complaining of sharp burning stabbing pain and stiffness radiating down her left buttock that started after a workout one month prior. Ex. 13 at 1. She reported having some anxiety and feeling hypermobile at times. *Id*. Petitioner treated with Dr. Hafner from April 2014 through October of 2015. *See generally*, Ex. 13. Over the course of her treatment, she alternately reported her symptoms as either unchanged or improved. *Id*.

On April 15, 2015, Petitioner retuned to Arvada Sports and Spine Group. Ex. 11 at 10. She reported having gone to the ER concerned about a "burst ovarian cyst," and that she was feeling better after seeing a chiropractor yesterday. *Id.* at 10. An MRI revealed lumbar scoliosis and level 4-5 degeneration. *Id.* at 11. The therapist again noted that Petitioner "appeared anxious." *Id.* Petitioner treated with Arvada Sports and Spine Group from May 2015 through July 2015. *See generally*, Ex. 11. Over the course of her treatment, Petitioner rated her pain as a 1/10 and noticed that her pain seemed to coincide with her menstrual cycle. *Id.*

Petitioner visited Westside Women's Care on April 17, 2015 complaining of severe symptoms associated with premenstrual dysphoric disorder ("PMDD"), mainly anxiety, and stated to her doctor: "I am losing my mind." Ex. 21 at 5. Petitioner reported that she had been diagnosed with PACs related to "hormones." *Id.* Petitioner continued to resist any type of hormonal therapy and reported that she had a bad reaction to SSRIs. *Id.* She eventually agreed to try a low dose of Citalopram[4] for her anxiety. *Id*.

On June 10, 2015, Petitioner saw Dr. Schkade and recounted an episode of pruritus while on a trip to San Francisco. *Id.* at 27. She reported that a dermatologist told her she might have polymorphous light eruption. *Id*. Petitioner felt that her current treatment was adequate and did not feel the need to make any changes. *Id.*

Petitioner returned to Westside Women's Care on June 16, 2015 complaining of issues with PMDD; that Citalopram made her more anxious and jittery; and that she thought she had a small umbilical hernia from straining due to constipation. Ex. 21 at 3. Her doctor refilled a prescription for Xanax; Petitioner refused to try 10 micrograms of birth control for PMDD. *Id.* Petitioner's blood work indicated that she had a vitamin D deficiency. *Id.*

On July 15, 2015, Petitioner saw Dr. Maino at Centura Health complaining of lower back pain and an umbilical hernia. Ex. 22 at 1. Dr. Maino recommended an MRI for her back pain and referred Petitioner to Dr. Brew. *Id.* at 3.

[4] Citalopram hydrobromide is a selective serotonin reuptake inhibitor (SSRI), chemically unrelated to other SSRIs and consisting of a racemic mixture of two stereoisomers (S- and R-, the S-isomer being pharmaceutically active); used as an antidepressant, administered orally. Dorland's, https://www.dorlandsonline.com/dorland/definition?id=9949) (last visited April 19, 2021).

Petitioner visited Dr. Brew at Surgical Specialists of Colorado on August 3, 2015 complaining of chronic constipation, palpitations and back pain. Ex. 15 at 1. Dr. Brew assessed Petitioner with a very small asymptomatic umbilical hernia; he recommended observation and not surgery. *Id.* at 3.

B. Post-Vaccination History

Petitioner received her flu vaccination at Costco in Westminster, Colorado on September 25, 2015. Ex. 2 at 1-4.

On October 6, 2015, Petitioner presented to Dr. Schkade and reporting having trouble with her ears for the past week. Ex. 10 at 30. She stated she was hearing a new lower tone in her left ear and it felt full like she couldn't pop it. *Id.* Dr. Schkade noted increased post-nasal drainage and some facial swelling which could indicate a low-grade viral infection. *Id.* at 30-31.

Petitioner presented to Taos Urgent Care on October 17, 2015 while in Taos, New Mexico. She stated that she awoke in the middle of the night with her heart racing, pressure in her left ear and tinnitus. Ex. 7 at 1. The results of her lab work and EKG were essentially normal, but she was advised to follow up with her cardiologist. *Id.* at 5.

On October 20, 2015, Petitioner saw Dr. Hartemink, an ENT, reporting sudden hearing loss and a sense of fullness in her left ear that began three or four days prior. Ex. 3 at 1. She reported having a 20-year history of high frequency tinnitus in both ears but was hearing a new low frequency thumping in her left ear that had since resolved. *Id.* An audiogram revealed mild sensorineural low frequency hearing loss in the left ear. *Id.* at 2. Dr. Hartemink's differential diagnosis was sudden sensorineural hearing loss (SSHL), unilateral, verses atypical Ménière's disease. *Id.* at 1. Petitioner reported having issues with nasal steroid sprays, and Dr. Hartemink decided on a low dose of prednisone - 20mg 2x a day for 7 days, then one tablet per day for 14 days. *Id.*

On October 28, 2015, Petitioner saw Dr. Kreutzer, another ENT, for a second opinion. Ex. 4 at 1. Petitioner reported having a 17-year history of high frequency tinnitus after suffering whiplash in a car accident and occasional pressure in her left ear for over a decade. *Id.* She reported a new low frequency sound in her left ear, fullness, and hyperacusis on October 1, 2015. *Id.* She denied having vertigo but did feel "spacey." *Id.* An audiogram showed resolution of the low frequency hearing loss, and Dr. Kreutzer's differential diagnosis was either bilateral endolymphatic hydrops or Ménière's disease as opposed to bilateral autoimmune inner ear disorder. *Id.* Dr. Kreutzer recommended a balance test, the results of which were unremarkable. *Id.* at 5. "The caloric results indicated a unilateral weakness in the left ear" indicative of a left peripheral pathology consistent with Ménière's disease. *Id.*

Petitioner saw Dr. Yeash on November 2, 2015 reporting that she completed a course of prednisone for ear issues and that she was having a lot of anxiety, elevated pulse, and mood swings. Ex. 18 at 16. She also reported a history of PACs. *Id.* Dr. Yeash recommended that Petitioner

follow up with Dr. Benedict. *Id.* Dr. Yeash prescribed 0.5mg of Xanax and instructed her to take either a half or whole tablet, every eight hours as needed. *Id.* at 17.

On November 4, 2015, Petitioner saw Dr. Hafner for pain in her left hip. Ex. 13. at 19. She reported having increased panic attacks after being treated with steroids for an ear issue. *Id.*

Petitioner visited Dr. Benedict on November 6, 2015 recounting her episode in Toas, New Mexico. Ex. 5 at 26, 38. Petitioner told Dr. Benedict that she had been treated with steroids for possible Ménière's and "went crazy on these." *Id.* at 26. Dr. Benedict noted that the incident in Taos occurred mid-cycle, and that Petitioner was still having periods and hot flashes. *Id*. Petitioner was exercising and reported having no palpitations in the past two weeks. *Id.* at 38. An EKG performed at Taos Urgent Care revealed a long QT which Dr. Benedict attributed to Petitioner being on antihistamines at the time. *Id*. A subsequent EKG was normal. *Id.* at 37. Dr. Benedict ordered a repeat Holter monitor. Ex. 5 at 36.

On November 10, 2015, Petitioner saw Dr. Yeash and informed him that two ENTs had assessed her with possible Ménière's disease. Ex. 18 at 14. Petitioner reported having dizziness but no vertigo. *Id.* Dr. Yeash recommended that she continue seeing Dr. Benedict and prescribed an anti-inflammatory for ongoing lower back pain. *Id.*

Petitioner returned to Dr. Hartemink on November 12, 2015 reporting that her hearing was better and that the fullness was mostly gone. Ex. 3 at 5. She told him that the prednisone had caused her severe anxiety and that she was experiencing mood swings, sleep issues and menstrual issues. *Id.* Considering that Petitioner's hearing issues had returned to normal after treatment with prednisone, Dr. Hartemink's differential diagnosis was sensorineural hearing loss, unilateral, or Ménière's disease. *Id.* at 6. Dr. Hartemink suggested a low salt diet and a prescription for dyazide. *Id*. Petitioner declined the medication because her cardiologist told her that dyazide would make her palpitations worse. *Id.*

On November 17, 2015, Petitioner saw a third ENT reporting that she developed a humming sound in her left ear, hearing loss and hyperacusis four to six weeks prior. Ex. 17 at 4. She informed the ENT that she completed treatment with steroids but was still having anxiety, sleeping problems, unintentional weight loss, ringing in her ears/head noise, post-nasal drainage, and an irregular/fast/pounding heartbeat. *Id.* The ENT assessed her with tinnitus, sensorineural hearing loss, and labyrinth dysfunction. *Id.* at 6.

On November 19, 2015 Petitioner visited Swedish Medical Center ER complaining of intermittent and worsening palpitations for the past month and an onset of paresthesia/tingling in her fingers earlier that day. Ex. 23 at 42, 49. She reported that she was working at her desk and couldn't get her heart to stop racing. *Id.* at 28. She informed the treating team that her cardiologist prescribed propranolol but she could not take it due to her asthma. *Id*. at 48. She reported having been recently treated with Prednisone which made her anxious. *Id.* at 42. She informed the treating team that her cardiologist ordered a Holter monitor, but that was she could not complete the testing due to an adverse reaction to the adhesive. *Id.* Her EKG and lab tests came back normal. *Id.* at 45. The treating physician noted, "discussed lab results with patient. Patient improved spontaneously.

Tachycardia and tingling resolved." *Id.* at 46. The attending physician suspected some component of anxiety contributed to Petitioner's symptoms and prescribed Diltiazem. *Id.*

Petitioner returned to Dr. Yeash to discuss her heart issues on November 30, 2015. Ex. 18 at 12. Dr. Yeash suspected that Petitioner's palpitations were due to anxiety. *Id.* Nevertheless, he recommended that Petitioner continue taking propranolol as needed. *Id.* He prescribed letrozole for GE reflux, and recommended Pepcid at bedtime. *Id*.

On November 30, 2015, Dr. Benedict provided Petitioner with the results of her Holter monitor testing. Ex. 5 at 51. The monitor recorded nine total events over the course of 14 days, and that Petitioner was in sinus bradycardia (less than 60bpm) 24% of the time and sinus tachycardia (greater than 100bpm) only 2% of the time. *Id.* at 52. Dr. Benedict concluded that her symptoms were not associated with dysrhythmia and recommended that Petitioner continue taking propranolol. *Id.*

Petitioner returned to Arvada Sports and Spine Group on December 3, 2015 reporting that she had been feeling great until two or three months ago when she developed increased tinnitus, low back pain, left hip pain, and tingling of the pubic symphysis. Ex. 11 at 23. She rated her pain as a 1/10. *Id.* She also reported feeling constipated and that steroid treatment for possible Ménière's caused her to feel ill, lethargic, and weak. *Id*. The physical therapist noted that Petitioner "appeared anxious." *Id.* at 23. She was referred to Dr. Sabin at Precision Orthopedics for evaluation of her hip and low back pain. *Id.* at 24.

On December 4, 2015, Petitioner presented to Precision Orthopedics complaining of six months of lower back pain, intermittent left hip pain, and numbness/tingling. Ex 8 at 1. She also reported hearing loss, arrythmia, asthma, constipation, and anemia. *Id*. Dr. Sabin found no palpable trigger points. *Id.* at 2. An x-ray of Petitioner's left hip appeared normal with no evidence of impingement or degeneration. *Id.* Dr. Sabin's overall impression was "questionable hip impingement, left side." *Id.* at 5.

Petitioner returned to Arvada Sport and Spine Clinic on December 16, 2015 reporting improvement in her left hip and groin pain since her previous visit. Ex. 11 at 26. Petitioner rated her pain as 1/10. *Id.* She reported that she tested positive for hip joint dysfunction. *Id*. Her therapist noted that she "appeared anxious." *Id.*

On December 31, 2015, Petitioner returned to Arvada Sport and Spine Clinic and reported improvement in her left hip pain over the past two weeks, possibly due to a new mattress. Ex. 11 at 28. She rated her pain as 1/10, was compliant with her home exercise regime, and noticed less tingling in her pubic region. *Id*. Her therapist noted that she "appeared anxious." *Id.*

Petitioner saw Dr. Yeash on January 15, 2016 reporting that she had not had a period for the last few months. Ex. 18 at 10. Dr. Yeash noted that Petitioner had some signs and symptoms of paroxysmal orthostatic tachycardia syndrome. *Id.* at 9. He noted that Petitioner was "fairly anxious and that may be a cause of her palpitations as well." *Id*. For the first time, the record states that Petitioner's history of palpitations was particularly related to standing. *Id.* at 10.

On January 20, 2016, Petitioner returned to Arvada Sport and Spine Clinic and reported: "Overall, I've been feeling really good. My exercises have been getting easier and I haven't really had too many symptoms so I was hoping to go through some new exercises in order to continue with my strengthening to keep my pain at bay." Ex. 11 at 30.

Petitioner met with a physician assistant at Dr. Yeash's office on January 25, 2016 and reported that she was still having palpitations, and that it was becoming difficult for her to work. Ex. 18 at 7. Petitioner stated that she would like to see a cardiophysiologist and a neurologist, and specifically requested a referral to Dr. Jill Schofield at University of Colorado Hospital. *Id*. The PA noted that Petitioner remarked "on paper she looks good and physically she may look good, but she says inside she does not feel good." *Id*.

On January 26, 2016, Petitioner presented to Boulder Community Health ER complaining of "epigastric abdominal pain and early satiety" beginning in November 2015. Ex. 12 at 2. Petitioner's husband reported that she began having abdominal pain and digestive issues after completing a 10-day course of prednisone for a eustachian tube dysfunction in her left ear. *Id*. All of her lab work came back normal and an examination revealed a benign abdomen, non-tender to palpitation. *Id.* The attending physician referred her to a gastroenterologist. *Id*. His differential diagnosis included gastritis, H. pylori, pancreatitis, peptic ulcer disease, celiac disease, and depression. *Id.* at 4.

Petitioner saw Dr. Hartemink on February 2, 2016 complaining of dizziness and a lightheaded "rocking motion." Ex. 23 at 9. She requested that Dr. Hartemink re-check her for vertigo. *Id*. She also reported the following new symptoms: heart palpitations, GI issues, bowel movement issues, increased heart rate when standing up, increased car sickness, and intermittently hearing her heartbeat in her left ear, especially when laying down at night. *Id*. Dr. Hartemink assessed Petitioner with (1) sensorineural hearing loss, unilateral, and (2) inactive Ménière's disease. *Id.* at 10.

On February 4, 2016, Petitioner saw Dr. Mandagere, an endocrinologist, for concerns about possible thyroid disease. Ex. 9 at 1. Petitioner reported having palpitations, alternating issues with diarrhea and constipation, general weight loss, heat and cold intolerance, poor sleep, sore throat, nausea, nighttime urination, diminished libido, abnormal periods, numbness/tingling and anxiety. *Id.* at 2. Dr. Mandagere noted that Petitioner had "nonspecific complaints that are not thyroid related." *Id.* at 3. Petitioner's TSH level was normal, "not even equivocal," and Dr. Mandagere did not find an endocrine cause for her palpitations. *Id.*

Petitioner visited Dr. Schkade to review her allergy and asthma treatment on February 9, 2016. Ex. 10 at 34. She reported having a rapid heart rate that increased when she stood up, "although she did not appear to have any hypotensive symptoms." *Id*. She reported that propranolol caused her dyspnea due to her asthma, "although she had not used her inhaler for exercise induced apnea in years." *Id*. She also reported feeling flushed at times, having loose stools and headaches associated with her rapid heart rate. *Id*. She did not want to resume her allergy injections. *Id*.

On February 10, 2016, Petitioner saw Dr. Moon, a neurologist, for a POTS evaluation. Ex. 15 at 16. Petitioner was concerned about a possible autoimmune disorder and reported that she

started having palpitations in September 2015. *Id*. She reported treatment with steroids for fullness and hearing loss in her left ear in October 2015. *Id.* She reported that she then developed tachycardia upon standing up first thing in the morning, anxiety, panic attacks, lightheadedness, poor sleep, significant fatigue, indigestion, diarrhea, decreasing sweating, heat and cold intolerance, low grade headache, nausea, decreased appetite, and phonophobia. *Id.* She reported that tachycardia sometimes woke her up at night. *Id*. Dr. Moon assessed Petitioner with dysautonomia, migraine headaches and anxiety. *Id.* Dr. Moon did not see any clear evidence of POTS but recommended an MRI of the brain, a tilt table test, dysautonomia laboratory studies and a repeat trial of propranolol. *Id*.

Petitioner saw a nurse practitioner at Rocky Mountain Gastroenterology on February 15, 2016 where she complained of intermittent stomach burning, heartburn, nausea, gas, constipation and burping beginning after treatment with prednisone for possible Ménière's disease. Ex. 6 at 1. She reported losing ten pounds initially but had regained the weight. *Id.* She noted tomatoes, onions, garlic, and fatty foods as triggers. *Id.* All of her lab work came back normal. *Id.* The NP suspected that prednisone caused her some esophagitis, gastritis and possibly duodenitis. *Id.* at 4. Petitioner elected conservative treatment with Zantac, Tums, H2 blocker and a restricted diet. *Id.*

On February 25, 2016, Petitioner underwent a tilt table test at Swedish Medical Center. Ex. 23 at 19. The contemporaneous notes indicate that Petitioner showed no symptoms of POTS when tilted 70% for 40 minutes, and no signs of syncope. *Id.* Her heart rate remained in the low 100s and her blood pressure was stable. *Id.*

Petitioner underwent an MRI at Touchstone Imaging on March 10, 2016 pursuant to Dr. Moon's orders. Ex. 3 at 12. The contemporaneous notes state that the results were normal with the exception of one indication of a prior microhemorrhage in the right cerebrum. *Id.*

On March 15, 2016, Petitioner had a follow-up appointment with Dr. Moon regarding dysautonomia. Ex. 16 at 13. Dr. Moon noted that autonomic laboratory testing and extensive neuropathy laboratory testing were unremarkable; that the results of Petitioner's tilt table test were not conclusive; and that her MRI was normal with the exception of was one small area of possible microhemorrhage in the right hemisphere. *Id.* Dr. Moon noted: "At this point we do not have definitive POTS." *Id.* Dr. Moon's differential diagnosis was dysautonomia, migraine headache and anxiety. *Id.* Dr. Moon recommended that Petitioner retry propranolol, explaining that a lower dose should not interfere with her asthma, and that Petitioner should not expect to see results for approximately one month. *Id*. Alternatively, Dr. Moon considered treating Petitioner for migraines and anxiety, which he noted could either be co-morbidities to her autonomic complaints or the actual primary problem. *Id.*

Petitioner saw Dr. Yeash on March 18, 2016 for dizziness, vertigo, poor concentration, tachycardia when standing up, extreme fatigue, and weakness. Ex. 18 at 5. Petitioner requested paperwork for short term disability. *Id.* Dr. Yeash's notes state that Dr. Moon had diagnosed Petitioner with dysautonomia and POTS. *Id*.

On April 12, 2016, Petitioner saw Dr. Foster, an ENT, at University of Colorado Hospital. Dr. Foster noted that Petitioner had a history of low-grade dizziness with hearing loss, low pitched

tinnitus but no true vertigo, and premenstrual migraines. Ex. 24 at 20. Upon examination, Dr. Foster did not find any abnormalities. *Id.* at 21. Dr. Foster's diagnosis was probable progressive vestibulopathy affecting the left inner ear. *Id.* Dr. Foster noted that the Petitioner's migraines might be associated with Ménière's disease, and that her low frequency sensory neuro hearing loss suggested hydrops[5] but that recurrent spells were required to confirm. *Id.* She noted that Petitioner's dizzy spells were premenstrual and advised Petitioner to avoid migraine triggers. *Id.*

Petitioner saw Dr. Moon on April 13, 2016 and reported that she was feeling better; however, she stopped taking the propranolol because it gave her nightmares. Ex. 16 at 12. Petitioner indicated that she was taking riboflavin and magnesium and had found an exercise regimen that seemed to help, but she was still having anxiety. *Id.* Dr. Moon assessed Petitioner with dysautonomia and migraine headache. *Id.* In Dr. Moon's opinion, the exercise regime would improve Petitioner's dysautonomia as well as her vertigo. Dr. Moon noted that Petitioner had endolymphatic disease which can cause vertiginous dizziness separate from her dysautonomia issues. *Id.*

On May 6, 2016, Dr. Yeash provided Petitioner with the results of blood work ordered on March 24, 2016. Ex. 18 at 32. The results were normal, but Dr. Yeash recommended that Petitioner continue taking an iron supplement. *Id.*

On May 13, 2016, Petitioner saw Dr. Yeash to obtain paperwork necessary for her to return to work. Ex. 18 at 1. Dr. Yeash reported that Petitioner had no significant physical restrictions other than those related with her balance issues due to Ménière's and vestibular issues. *Id.* Dr. Yeash noted that Petitioner's POTS, Ménière's, migraines and vertigo were all stable, and that she was no longer taking Xanax for anxiety. *Id.*

Petitioner saw Dr. Schofield, on June 8, 2016. Dr. Schofield noted that Petitioner was previously healthy with underlying joint hypermobility until an acute onset of quite severe postural tachycardia syndrome, hearing loss and tinnitus one week following influenza vaccination. Ex. 24 at 35. Dr. Schofield indicated that "her clinical picture is very suspicious for an immune mediated etiology possibly molecular mimicry secondary to influenza vaccination." *Id.* Dr. Schofield's diagnosis included antiphospholipid syndrome ("APS") with hearing loss, tinnitus and migraines. Her differential diagnosis included celiac disease and autoimmune Ménière's. *Id.* at 35. She noted that Petitioner had joint hypermobility but no chronic joint pain or spontaneous joint dislocation to suggest Ehlers-Danlos syndrome and thus did not refer Petitioner to a geneticist. *Id.*

On June 11, 2016, Petitioner visited Dr. Schkade to review her allergy treatment. Ex. 10 at 37. Petitioner did not want to continue her allergy shots. *Id.*

[5] Ménière's disease is a defined as hearing loss, tinnitus, and vertigo resulting from nonsuppurative disease of the labyrinth with edema. It may also be referred to as endolymphatic hydrops, labyrinthine hydrops, and recurrent aural vertigo. Dorland's, https://www.dorlandsonline.com/dorland/definition?id=70588 (last visited April 19, 2021).

Petitioner presented to Westside Women's Clinic on July 28, 2016 complaining of incapacitating menstrual migraines and vestibular migraines. Ex. 52 at 7. The doctor noted that her symptoms were likely due to a sudden drop in her estrogen level. *Id*. Petitioner was prescribed Prometrium for her menstrual symptoms. *Id*.

On September 12, 2016, Petitioner presented at Westside Women's Clinic reporting that she noticed an improvement in her PMDD and PMS on the Prometrium. Ex 52. at 7.

Petitioner saw Dr. Yeash on September 16, 2016. He assessed Petitioner with (1) POTS, (2) dysautonomia, (3) migraine with vertigo (4) Vitamin D deficiency, and (5) Vitamin B12 deficiency. Ex. 54 at 23. Dr. Yeash directed Petitioner to continue taking metoprolol and prescribed 5mg Adderall to help with the neurovascular instability of POTS as well as 5mg Maxalt for headache. *Id*. Petitioner reported that she was generally feeling a lot better and was able to return to work. *Id*.

On October 14, 2016, Petitioner again saw Dr. Schofield. She complained of fatigue and lack of focus. Ex. 28 at 4. Dr. Schofield recorded Petitioner as having a disorder of the autonomic nervous system, unspecified. *Id*. at 3. Dr. Schofield noted that Petitioner was working full time, and "possibly this is making her worse, but not nearly as severe as last year when she was trying." *Id*. Petitioner was using an exercise bike at home but was still experiencing migraines once a month and oscillopsia[6] when moving, but no dizziness or vertigo. *Id*. She tried taking aspirin but it did not help and caused bruising and nosebleeds. *Id*. Dr. Schofield prescribed a daily Vitamin D supplement and 10mg Vyvanse[7] daily and suggested that Petitioner cut back from 40 hours per week to 30. *Id*. Petitioner declined. *Id*. Dr. Schofield recommended repeat APS testing. *Id*.

Petitioner presented at Westside Women's Clinic on October 20, 2016 reporting that her lab work for APS was negative, but that she was working on controlling her symptoms of dysautonomia. Ex. 52 at 7.

On March 16, 2017, Petitioner saw Dr. Schkade reporting that when she eats eggs for several days in a row it seems to cause some vestibular symptoms. Ex. 51 at 12.

On April 10, 2017, Petitioner presented to Westside Women's Clinic indicting that she wanted to stop her Promethium because her specialist thought she had Ehlers-Danlos syndrome or possibly Ménière's disease. Ex 52 at 5. She reported that an echocardiogram done four years ago

[6] Oscillopsia is a symptom in which objects appear to wiggle, jerk, or move back and forth; it sometimes accompanies nystagmus, especially the downbeat type. Oscillopsia is also called oscillating vision. Dorland's, https://www.dorlandsonline.com/dorland/definition?id=35681&searchterm=oscillopsia (last visited April 19, 2021).

[7] Vyvanse is a central nervous system stimulant prescription medicine used to treat Attention-Deficit/Hyperactivity Disorder (ADHD) and Binge Eating Disorder (BED). *RxList - The Internet Drug Index for Prescription Drugs, Medications, and Pill Identifier* (2017), https://www.rxlist.com/vyvanse-drug.htm (last visited April 19, 2021).

was abnormal, that she had extreme laxity in the ligaments in her arms, and severe joint and muscle pain. *Id*. Petitioner reported that Prometrium made her symptoms worse. *Id*.

On May 31, 2018, Petitioner saw Dr. Yeash for a medication evaluation. Ex. 54 at 14. Dr. Yeash assessed Petitioner with (1) anxiety (2) acid reflux disease (3) migraine with vertigo (4) POTS (5) Ehlers-Danlos, hypermobile type (6) neutropenia and (7) iron deficiency anemia. *Id*. Dr. Yeash noted Ménière's disease had been ruled out. Petitioner felt that her vertigo was related to her migraines. *Id*. Dr. Yeash remarked that Petitioner was managing her POTS very well. *Id*.

On July 19, 2018, Petitioner saw Dr. Yeah for a medication check. Ex. 54 at 11. Dr. Yeash assessed Petitioner with (1) dysautonomia (2) Ehlers-Danlos, hypermobile type (3) concentration deficit (4) acid reflux disease (5) decreased white blood cell count and (6) migraine with vertigo. *Id*. Dr. Yeah prescribed 10mg Vyvanse for concentration deficit related to dysautonomia and Ehlers-Danos syndrome. Petitioner tried Adderall and Concerta but reported that they were either ineffective or caused side effects. *Id*.

Petitioner presented to Westside Women's Clinic on July 26, 2017 reporting that her physician thought she had a variant of Ehlers-Danlos syndrome, not involving the cardiovascular system, but causing laxity in her joints and ligaments. Ex. 52. at 6. She reported having no libido but reported that Promethium was helping with her PMDD as well as her dysautonomia. *Id*.

Petitioner presented to Westside Women's Clinic for her annual visit on August 14, 2018. Ex. 52 at 1. Her only complaint was having no libido. *Id*. Her periods were normal. She was taking Vyvanse and a multivitamin and exercising on a regular basis. *Id*. She reported that she had been diagnosed with Ménière's disease, but that she was not having many symptoms at that time. *Id*.

On October 15, 2018, Petitioner saw Dr. Yeash for a medication check. Ex. 54 at 8. Dr. Yeash assessed Petitioner with (1) concentration deficit (2) muscle contraction headache (3) cervicogenic headache and (4) decreased white blood cell count. *Id.* Dr. Yeash noted that Petitioner's muscle contraction headaches were thought to be secondary to cervicogenic disc disease. *Id.*

On April 15, 2019, Petitioner saw Dr. Yeash for a medication check. Ex. 54 at 4. Dr. Yeash assessed Petitioner with (1) fatigue (2) concentration deficit (3) neutropenia (4) iron deficiency anemia (5) subclinical hypothyroidism and (6) daytime somnolence. *Id*. Petitioner complained of nonrestorative sleep, morning dry mouth, and excessive daytime somnolence. *Id*. Dr. Yeash recommended that Petitioner be evaluated for sleep apnea. *Id.*

III. Petitioner's Affidavit

Petitioner signed her affidavit on October 2, 2016. Ex. 1 at 4. In the affidavit, she stated that she received her flu vaccine on September 25, 2015 and the following week, she began to experience "a strange sensation" in her left ear. *Id.* at 1. She noted that the sensation was distinct from the tinnitus she had previously experienced, in that she felt "a low hum, vibrating noise in [her] left ear that would not go away." *Id.*

Petitioner went on a trip to Taos soon thereafter, and during this trip, her feeling of fullness in her left ear and tinnitus continued to worsen. Ex. 1 at 1. She also felt that her heart was beating in an erratic manner and that it was racing. *Id.* at 2. She noted, "I had been diagnosed with PACs, or extra heartbeats, years before, but this sensation felt very different and I was worried." *Id.*

On October 19, 2015, Petitioner experienced hearing loss in her left ear and was diagnosed with possible Meniere's disease. Ex. 1 at 2. She was prescribed steroids and her hearing recovered. *Id.*

In early November 2015, Petitioner began to notice that her heart was racing with a change in position. Ex. 1 at 2. She indicated that her various symptoms impacted her work. *Id.* at 3. Petitioner stated that she was able to work "sporadically through November and December of 2015 due to taking many vacation days, holidays, and a low number of clients." *Id.* She further indicated that her symptoms continued to worsen into January 2016. *Id*. On January 25, 2016, Petitioner stated that she was forced to take a leave of absence from her job. *Id.*

Petitioner indicated that she experienced the following symptoms at the worst of her illness:

> Orthostatic Tachycardia, palpitations or pounding heart, cold hands and feet, inability to regulate body temperature, sweating irregularities, constipation, diarrhea, loose stool, severe GERD, nausea, unexplained weight loss, nervousness, anxiety, depression, flushing, heat intolerance, increased blood pressure, hair loss, dry skin, adrenaline rushes, hearing loss, tinnitus, dizziness, motion intolerance, extreme motion sickness, hyperacusis, brain fog/cognitive struggles, blurred vision, tingling in my legs, feet, and face, exercise intolerance, fatigue, insomnia, and reduced stress tolerance.

Ex. 1 at 3. Petitioner further stated that since the worst of her illness, she has seen some improvement, but she continues to experience daily symptoms and to have flares. *Id.* at 3-4.

IV. Expert Opinions and Qualifications

A. Expert Qualifications

1. Dr. Schofield's Qualifications

Dr Schofield graduated from the University of Colorado School of Medicine with Honors in 1995 and completed her internship and residency in internal medicine at the Johns Hopkins Hospital in Baltimore from 1995 to 1998. Ex. 31 at 2 (hereinafter "Schofield CV"). She worked for 16 years as an attending physician at St. Joseph Hospital in Denver where she developed an interest in autoimmune disease, specifically autonomic disorders in the antiphospholipid syndrome. Schofield CV at 1. As there is currently no formally accredited fellowship training in multi-specialty autoimmune disease, she designed a curriculum and completed training with Professor Yehuda Shoenfeld at the University of Colorado from January 2015 to July 2016. Ex 30 at 1. She researches, publishes, and presents on the topics of autoimmune disease and

antiphospholipid syndrome. Schofield CV at 2-3. Of note, in 2014 she co-authored an article with Professor Shoenfeld, and Dr. Graham Hughes entitled *Postural tachycardia syndrome (POTS) and other autonomic disorders in antiphospholipid (Hughes) syndrome (APS)*. 2014 LUPUS 23, 697-702 (2014). *Id.* at 2. Dr. Schofield maintains a clinical practice in antiphospholipid syndrome ("APS") and the emerging area of autoimmune dysautonomia at the IMMUNOe Health and Research Center in Denver, Colorado. *Id.* at 1. She is also a Clinical Assistant Professor of Autoimmune Disease at the University of Colorado in the Department of Medicine. *Id.*

2. Dr. Leist's Qualifications

Thomas P. Leist, MD, PhD, is Professor of Neurology, Chief of the Division of Clinical Neuroimmunology, and Director of the Comprehensive Multiple Sclerosis Center at Jefferson University in Philadelphia, PA. Ex. A, Tab 2 at 1 (hereinafter "Leist CV"). Dr. Leist also directs the Jefferson Medical College fellowship program in clinical neuroimmunology. Leist CV at 2. He earned a PhD from the University of Zurich in Switzerland and received his medical degree from the University of Miami School of Medicine. *Id*. at 1. Dr Leist completed his residency at Cornell Medical Center and Memorial Sloan-Kettering Medical Center in New York, and he trained as a fellow at the National Institutes of Health in Bethesda, MD. *Id*. He conducts research in multiple sclerosis and other autoimmune and infectious conditions of the CNS. He serves on the editorial board for *Practical Neurology* and is an ad-hoc reviewer for several journals including *Neurology, Annals of Neurology,* and *Journal of Neuroimmunology*. *Id*. He has been published in a multitude of peer-reviewed publications and frequently presents on the topics of multiple sclerosis and other autoimmune and infectious conditions of the CNS. *Id*. at 2-5, 6-11.

B. Expert Opinions

1. Dr. Schofield's First Report

Dr. Schofield opined that Petitioner's flu vaccination in September 2015 triggered an autoimmune response that caused Petitioner to develop symptoms associated with an autoimmune clotting disorder known as antiphospholipid syndrome (APS). *See generally*, First Schofield Rep. According to Dr. Schofield, all of Petitioner's clinical manifestations have been associated with APS, and "[t]he clear temporal association of her illness with the influenza vaccination and the time course of her antibody production and decrease in C4 level make it very likely that her illness arose as a complication of the vaccination." *Id*. at 8.

Dr. Schofield reported that prior to 2015, Petitioner "had enjoyed good health her whole life;" but that dramatically changed when she received her flu vaccination. First Schofield Rep. at 3. Dr. Schofield's review of Petitioner's medical records revealed that one week after her vaccination, Petitioner began to experience tinnitus and hearing loss in her left ear which was diagnosed in late October 2015 as suspected Ménière's disease. *Id*. In April of 2106, Dr. Schofield noted that another ENT diagnosed Petitioner with possible Ménière's disease as well as progressive vestibular disorder. *Id*.

Dr. Schofield observed that Petitioner developed a number of other systemic symptoms "at the same time" including vestibular migraines, cognitive dysfunction, tachycardia, heart rate

lability, adrenaline surges at night, insomnia, severe fatigue, flushing, heat intolerance, difficulty regulating her temperature, polyuria, nausea, paresthesia in her legs, orthostatic tachycardia and POTS. First Schofield Rep. at 3-4. Dr. Schofield noted that symptoms of dysautonomia such as migraine headaches, cognitive issues, sensorineural hearing loss and Ménière's disease "may all occur in association with APS." *Id.* at 5.

Upon examination, Dr. Schofield discovered that Petitioner had other symptoms related to APS including reduced tear production, Livedo reticularis, joint hypermobility, abdominal bruit, and POTS. First Schofield Rep. at 5. Dr. Schofield referred to four articles, one of which she authored herself and another which she co-authored, in support of the theory that many of Petitioner's symptoms are common in patients with APS. *See* Schofield, et al., *Postural tachycardia syndrome (POTS) and other autonomic disorders in antiphospholipid (Hughes) syndrome (APS),* 23 LUPUS 7, 697-702 (2014) (filed as Ex. 45, Ref. No 14) (hereinafter "Schofield-1); JR Schofield, *Autonomic neuropathy—in its many guises—as the initial manifestation of the antiphospholipid syndrome,* IMMUNOL RES. (2017) (filed as Ex. 46, Ref. No. 15) (hereinafter "Schofield-2"); DA Mouadeb & MJ Ruckenstein, *Antiphospholipid inner ear syndrome*, 115 LARYNGOSCOPE 5, 879-83 (2005) (filed as Ex. 47, Ref. No. 16) (hereinafter "Mouadeb & Ruckenstein"); GRV Hughes, *Heparin, antiphospholipid antibodies and the brain*, 21 LUPUS 10, 1039-40 (2012).

When Dr. Schofield first evaluated Petitioner in June of 2016, she noticed "a clear temporal relationship to the onset of her symptoms and the influenza vaccine she received." First Schofield Rep. at 4. Suspicious of an immune-mediated mechanism triggered by the vaccination, Dr. Schofield ran a number of tests to determine the cause of Petitioner's POTS. *Id*. Initially, she found Petitioner to be "indeterminate or low positive at 18 MPL" for anticardiolipin IgM antibody, one of the antibodies associated with APS. *Id*. However, repeated testing came back negative. *Id*. at 6.

Dr. Schofield observed that APS is also associated with a low C4 level and testing revealed that Petitioner had a low C4 level on three serial occasions, "suggestive of either active autoimmunity or a genetic predisposition to autoimmunity." First Schofield Rep. at 6. By January of 2017, Petitioner's C4 level had normalized, indicating that her autoimmunity was transient as opposed to genetic. *Id.* at 6-7. Dr. Schofield referred to several articles suggesting that "transient production of anticardiolipin antibodies and clinical manifestations of APS (including stroke) as occurred in [Petitioner's] case has [sic] been reported in more than one publication." *Id*. at 8; *see also,* Perdan-Pirkmajer, et al., *Autoimmune response following influenza vaccination in patients with autoimmune inflammatory rheumatic disease,* 21 LUPUS 2, 175-83 (2012) (filed as Ex. 34, Ref No. 3) (hereinafter "Perdan-Pirkmajer"); Agmon-Levin, et al., *Influenza vaccine and autoimmunity,* 11 ISR MED ASSOC J. 3, 183-5 (2009);11(3):183-85 (filed as Ex. 41, Ref. No. 10) (hereinafter "Agmon-Levin"); Toplak, et al., *Autoimmune response following annual influenza vaccination in 92 apparently healthy adults,* 8 AUTOIMMUN Rev. 2 134-38 (2008) (filed as Ex. 42, Ref. No. 11) (hereinafter "Toplak").

Dr. Schofield claimed that "it is well recognized that APS may be triggered by vaccination and infection." *Id*. at 4. In support of that statement, Dr. Schofield referred to the Cruz-Tapias article, but offered no explanation or discussion of that article's findings. S*ee* Cruz-Tapias, et al., *Infections and vaccines in the etiology of antiphospholipid syndrome,* 24 CURR OPIN RHEUMATOL

4, 389-93 (2012) (filed as Ex. 49, Ref. No. 18) (hereinafter "Cruz-Tapias"). Dr. Schofield stated that the "most widely recognized mechanism by which infections or vaccines may trigger autoimmunity is that of molecular mimicry;" she further stated that there are "surprisingly few examples by which molecular mimicry has been demonstrated and the reality is that infection or vaccination-induced autoimmunity is likely much more complex in most instances." *Id*. at 9. Dr. Schofield suggested other proposed mechanisms by which a vaccine may trigger autoimmunity such as cell damage that causes an infection, revealing antigens to the immune system that were previously hidden, as well as alteration of a host antigen such that it becomes recognized as foreign. *Id*. at 10.

In summary, Dr. Schofield reported that "everything about [Petitioner's] case is consistent with transient antiphospholipid antibody production and resultant complement activation secondary to the influenza vaccination, including the close temporal relationship of her symptom onset to the vaccination, the nature of her symptoms and the documented autonomic, hearing and vestibular dysfunction." *Id*. at 10.

2. Dr. Leist's First Report

Dr. Leist's first report challenged Dr. Schofield's finding of a close temporal relationship between Petitioner's flu vaccination and the onset of her symptoms; Dr. Schofield's statement that Petitioner was officially diagnosed with POTS in February 2016; and Dr. Schofield's contention that a borderline positive anticardiolipin IgM titer is indicative of APS. *Id*. at 11-12.

Dr. Leist did not find any notations in Petitioner's medical records of any immediate or delayed side effects in the hours and days following her flu vaccination. First Leist Rep. at 11. Dr. Leist remarked that Petitioner had a long history of palpitations, eustachian tube dysfunctions, tinnitus, intermittent pressure/fullness in her left ear, asthma, significant premenstrual symptoms and irregularities, as well as an even longer history of back pain, hip pain, and joint hypermobility for which she sought care prior to and after the administration of her influenza vaccine on September 25, 2015. *Id*. at 14-15.

Dr. Leist went on to observe that the contemporaneous records were not consistent with Dr. Schofield's claim that Petitioner was "eventually officially diagnosed with POTS in February, 2016 by tilt table testing done at Swedish Medical Center in Denver." First Leist Rep. at 14. To the contrary, Dr. Leist noted that after receiving the results of Petitioner's tilt table test, Dr. Moon specifically recorded: "At this point we don't have definitive POTS." *Id*.

Using the National Institutes of Health's diagnostic criteria, Dr. Leist also found that the results of Petitioner's tilt table test did not warrant a diagnosis of POTS. First Leist Rep. at 13. To diagnose a patient with POTS, the National Institutes of Health requires "lightheadedness or fainting accompanied by a rapid increase in heartbeat of more than 30 beats per minute, or a heart rate that exceeds 120 beats per minute, within 10 minutes of rising." *Id*. Prior to the start of the tilt test, [Petitioner]'s heart rate was measured while she was laying down, sitting, and standing. *Id*. Her heart rate did not increase by 30 beats per minute" *Id*. Dr. Leist observed that Petitioner remained asymptomatic during her test. *Id* at 14. "There was no significant change of the heart rate

between the start of the tilt table test (13:35, test minute 0; heart rate 102) and the subsequent time points (e.g., 13:45; test minute 10; heart rate 94). *Id*.

Dr. Leist noted that Petitioner had twice undergone Holter monitor testing for palpitations that she reported as occurring at night, when sitting still, and during the week prior to and during her period. First Leist Rep. at 12. In 2013, after wearing a Holter monitor for 30 days, Petitioner's cardiologist did not find any correlation with the seven events recorded by the monitor and Petitioner's subjective feelings of "fluttering in the chest". *Id*. In November 2015, after wearing a Holter monitor for 14 days, the results revealed that Petitioner's baseline heart rate was 54 to 67 bpm and that she remained in sinus rhythm throughout the monitoring period. *Id*. at 13. The Holter monitor test results, according to Dr. Leist, are further evidence that Petitioner did not fulfill the diagnostic criteria for POTS. *Id*.

Finally, Dr. Leist took issue with Dr. Schofield's reliance on the presence of antiphospholipid antibodies in support of the claim that vaccines can induce antiphospholipid syndrome, "which appears to be central to Dr. Schofield's theory of how influenza vaccine could have caused [L.P.'s] condition." First Leist Rep. at 14. Dr. Leist observed that Petitioner's first test for anticardiolipin IgM on June 8, 2016, was negative. *Id*. at 11. (Exhibit 24 at 66). The second test on September 28, 2016, was also negative, and on October 14, 2016, a third test (performed on a specimen obtained in June 2016) came back borderline positive. *Id*. Dr. Leist pointed out that a borderline positive anticardiolipin IgM titer, by itself, is not clinically significant or indicative of APS. *Id*. at 12. Moreover, Petitioner's anticardiolipin IgM titer "could have been elevated for many reasons other than, as alleged by Dr. Schofield, influenza vaccine given 9 months earlier." *Id*. at 11-12.

Upon reviewing Dr Schofield's medical literature, Dr. Leist found little to no relevant evidence supporting her opinions. For example, many of Dr. Schofield's cited articles merely provided evidence of a temporal association between flu vaccination and other unrelated diseases such as various demyelinating disorders of the central nervous system, giant cell arteritis, autoimmune inflammatory rheumatic disease, polymyalgia rheumatica, subacute thyroiditis and dyserythropoiesis, Chug-Strauss syndrome, narcolepsy, and Guillain-Barré syndrome. *Id*. at 7; *see also* Exs. 32-38, 40, 44. Dr. Leist noted that the Jeffs article concerned variants of a flu vaccine other than Afluria, the vaccine that Petitioner received. *Id*. at 8; *see also* Jeffs, et al., *Viral RNA in the influenza vaccine may have contributed to the development of ANCA-associated vasculitis in a patient following immunization*, 35 CLIN RHEUMATOL 4, 943-51 (2016) (filed as Ex. 39, Ref No. 8). Dr. Leist noted that the Agmon-Levin article discussed an increase in antinuclear antibodies and antiphospholipid antibodies in 92 healthy individuals up to six months after influenza vaccination; however, there is no evidence that Petitioner had antinuclear antibodies or antiphospholipid antibodies above the normal limit. *Id*. at 8; *see also* Ex. 41. The Toplak article also discussed an increase in antinuclear antibodies and antiphospholipid antibodies in 92 healthy individuals; however, Dr. Leist observed that none of the individuals studied was "reported to have developed clinical symptoms and the authors did not study fluctuation of the antibody markers over time in unvaccinated controls." *Id*. at 8, *quoting* Ex. 42. The Abu-Shakra article found that influenza vaccination was safe for patients with lupus; although it may trigger the generation of autoantibodies, the effect was usually short lived and not associated with clinical significance. *Id*. at 8, *see also* Abu-Shakra, et al., *Influenza vaccination of patients with systemic lupus*

erythematosus: safety and immunogenicity issues, 6 AUTOIMMUN REV. 8, 543-46 (2007) (filed as Ex. 43, Ref No. 12). The Schofield-1, Schofield-2, and Mouadeb & Ruckenstein articles relating APS with other disorders such as POTS and Ménière's did not include any mention of the flu vaccine. *Id*. at 8; *see also* Exs. 45, 46, 47, 48.

Having reviewed Petitioner's medical records, Dr. Leist opined "that Petitioner did not incur an injury due to influenza vaccine she received on September 25, 2015." First Leist Rep. at 15.

3. Dr. Schofield's Supplemental Report

In response to Dr. Leist's report, Dr. Schofield argued that Dr. Leist was not qualified to assess whether Petitioner has POTS or APS. Dr. Schofield's review of Petitioner's pre-vaccination medical history indicated that Petitioner may have been predisposed to autoimmunity, and Dr. Schofield refuted Dr. Leist's argument that a low positive anticardiolipin IgM level is clinically insignificant.

Dr. Schofield noted that while Dr. Leist may have great expertise in multiple sclerosis, he has no documented experience with autonomic disorders, APS, and vaccine induced immunity. Second Schofield Rep. at 1. In Dr. Schofield's personal experience, physicians who specialize in multiple sclerosis have limited knowledge of the emerging field of dysautonomia "for which there is not currently a formal training program." *Id*. Furthermore, Dr. Schofield stated that Dr. Leist's first report demonstrates that he has limited knowledge of the diagnostic criteria for POTS and does not know how to interpret a tilt table test. *Id*.

With respect to Petitioner's tilt table test, Dr. Leist referred to the National Institutes of Health's current diagnostic criteria for POTS; however, Dr. Schofield reported that "most specialists in the field use the 2015 Heath Rhythm Society Expert Consensus Statement on the Diagnosis and Treatment of POTS." Second Schofield Rep. at 1; *see also* Sheldon, et al., *2015 Heart Rhythm Society Expert and Consensus Statement on the Diagnosis and Treatment of Postural Tachycardia Syndrome, Inappropriate Sinus Tachycardia, and Vasovagal Syncope*, 12 HEART RHYTHM 6, 41-63 (2015) (filed as Ex. 57) (hereinafter "Consensus Statement"). The Consensus Statement, in part, characterizes POTS as "an increase in heart rate of >30 beats per minute (bpm) when moving from a recumbent to a standing position." *Id*. Dr. Schofield's review of the record revealed that Petitioner's heart rate when laying and sitting at 1300 and 1302, respectively, was 68 bpm. *Id*. at 2. When she was titled upright at 1305, her hear rate quickly rose to 94 bpm and by the end of the test was 101, 107, 108 and 111 at the last four time points. *Id*. at 2. "Thus, her HR rose from 68 to 111 – a 43 point increase" which Dr. Schofield claimed easily meets the criteria for POTS. *Id*. Regardless, Petitioner's inability to "do her job, drive, etc. with a constellation of symptoms typical of that seen in POTS and lasting more than 3-6 months . . . is what makes the unequivocal diagnosis of POTS in the context of her abnormal tilt table test" *Id*. at 2.

With respect to Petitioner's pre-vaccination medical history, Dr. Schofield admitted that she did not originally review Petitioner's prior records because Petitioner reported to Dr. Schofield "that she 'was completely healthy', i.e., any prior medical history did not seem significant enough to her to warrant spending time on it." Second Schofield Rep. at 2. Nevertheless, having reviewed

Dr. Leist's summary of the pre-vaccination medical records, Dr. Schofield did not find them to be inconsistent with the opinions set forth in her first report. *Id*. According to Dr. Schofield, Petitioner's history indicates that she likely had mild underlying mast cell activation syndrome (MCAS),[8] which is characterized by symptoms occurring in "two or more organ systems that are of a generally allergic and/or inflammatory theme." *Id*. Dr. Schofield claimed that Petitioner's problems with "allergies, asthma, anxiety, flushing, hives, rashes and palpitations are very characteristic of MCAS." *Id*.

Dr. Schofield performed further testing on Petitioner, and although Petitioner tested negative for MCAS, Dr. Schofield's "clinical suspicion for this diagnosis remains high." *Id*. at 3. Dr. Schofield explained that diagnosis can be difficult given that it "requires capturing chemical mediators that are released from overactive mast cells and these mediators begin to break down at room temperature within 1-2 minutes." *Id*. at 3.

Dr. Schofield went on to propose that "the presence of MCAS (suspected as the cause for the milder issues in [Petitioner]'s background), a disorder of the primitive immune system, may predispose to autoimmunity as the primitive and acquired arms of the immune system interact significantly." Second Schofield Rep. at 6. Dr. Schofield reported that MCAS is often a comorbidity of dysautonomia, and that many of Dr. Schofield's patients have both MCAS and autoimmunity. *Id*. at 2-3. Also, in Dr. Schofield's experience, "many patients who develop severe autoimmune dysautonomia have much milder underlying symptoms suggesting orthostatic intolerance and/or immune dysregulations just as [Petitioner]'s history suggests." *Id*. Those symptoms do not become severe until they are triggered by an event that activates the immune system, for example, a vaccination. *Id*. at 3. It is Dr. Schofield's opinion that Petitioner likely had MCAS which predisposed her to developing an autoimmune disorder that was triggered by her flu vaccination given that "one week following her vaccination her symptoms became so severe that she struggled to function." *Id*. at 3.

Dr. Schofield stressed that even low positive/indeterminate anticardiolipin IgM levels can be significant, and "must be interpreted in the context of the patient's clinical phenotype to determine whether they are important." *Id*. at 3-4. A patient with a high titer but no signs or symptoms would only require observation; however, in a patient like Petitioner, with reported

[8] Dr. Schofield raised the potential diagnosis of MCAS in her second report. Respondent filed the Akin article, which delineates the proposed criteria for mast cell activation syndrome: 1. Episodic multisystem symptoms consistent with mast cell activation; 2. Appropriate response to medications targeting mast cell activation; and 3. Documented increase in validated markers of mast cell activation systemically (i.e., either in serum or urine) during a symptomatic period compared with the patient's baseline values. Akin C., *Mast cell activation syndromes*, 140 J ALLERGY CLIN IMMUNOL 2, 349-55 (2017) (filed as Ex. B, Tab 1) (hereinafter "Akin"). Dr. Schofield conceded that Petitioner's "first round of testing was negative" for MCAS. Second Schofield Rep. at 2. Dr. Schofield additionally described the interplay between MCAS and vaccination as follows: "MCAS--a disorder of the innate immune system--may theoretically predispose patients to a vaccine injury. As an emerging syndrome, there has not yet been a lot of research on many aspects of MCAS, so this remains a hypothesis…" *Id.* at 3. Dr. Leist did not find any support in Petitioner's medical records for a diagnosis of MCAS. Ultimately, I find that Petitioner did not present preponderant evidence that she had MCAS and further that her purported underlying MCAS predisposed her to a vaccine injury.

autonomic and vestibular dysfunctions, even a low level of antiphospholipid antibodies becomes relevant, especially considering that Petitioner's symptoms improved with antiphospholipid seroconversion. *Id*. at 4. The temporal relationship between the presence of those antibodies to Petitioner's flu vaccination suggests that they were triggered by the vaccination. *Id*.

Dr. Schofield stated that Petitioner's clinical manifestation of Ménière's disease was further evidence of the clinical significance of her anticardiolipin IgM levels. Second Schofield Rep. at 5. Dr. Schofield discussed the Mouadeb & Ruckenstein article which studied 168 adult patients suffering from progressive hearing loss with or without vertigo. *Id*. at 5; *see also* Mouadeb & Ruckenstein. The authors reported that "[f]orty-two patients (25%) had at least one elevated antiphospholipid antibody marker. . . [and of] the 42 patients, 64% (n = 27) met the diagnostic criteria for Ménière's disease." *Id*. at 5, *quoting* Mouadeb & Ruckenstein. The authors of the study concluded that the "data support the hypothesis that antiphospholipid antibodies are involved in the pathogenesis of some forms of inner ear dysfunction . . ." *Id*. Dr. Schofield reports that "while we have a lot to learn about the mechanisms by which both inner ear disease and autonomic dysfunction may occur in the context of APS, the most likely mechanism is sludging or microthrombosis of the smallest blood vessels including those that perfuse the tiny small fiber autonomic nerves and the inner ear." *Id*. at 7.

With respect to Dr. Leist's criticisms of her medical literature, Dr. Schofield responded that the purpose of the literature she cited "was to illustrate that multiple different autoimmune disorders--both neurological and non-neurological--may arise in the post vaccination period and were presumed to be triggered by the vaccination in those cases." *Id*. at 6. According to Dr. Schofield, the literature evidences that most experts in the field use a period of 30 days to define temporal association. *Id*.

In summary, Dr. Schofield opined as follows: "Based on the clear temporal relationship of the severe decline in [Petitioner]'s health to the influenza vaccination given in September 2015, the transient positivity of both antiphospholipid antibodies and the low C4 level (both seen in antiphospholipid syndrome) as well as the presence of clinical manifestations of antiphospholipid syndrome (autonomic dysfunction and inner ear disease), I believe that this represents a vaccine injury." Second Schofield Rep. at 7.

4. Dr. Leist's Supplemental Report

In his second report, Dr. Leist challenged Dr. Schofield's opinions on the grounds that Dr. Schofield failed to demonstrate that Petitioner has POTS; failed to demonstrate that Petitioner has MCAS; failed to demonstrate that Petitioner has APS; and failed to establish that there is any mechanistic link between the influenza vaccine and sensorineural hearing loss.

First, Dr. Leist refuted Dr. Schofield's interpretation of Petitioner's tilt table test. Second Leist Rep. at 3. Dr. Leist stated that the contemporaneous medical records do not support Dr. Schofield's findings, and he agreed with the contemporaneous assessment. *Id*. Dr. Leist suggested that Dr. Schofield incorrectly combined Petitioner's heart rate readings taken prior to the tilt table test with her heat rate readings taken after the tilt test had begun. *Id*. Dr. Leist noted that prior to the start of the tilt test, between 13:00 and 13:05, Petitioner's heart rate was measured while laying

down, sitting and standing. *Id*. In Dr. Leist's interpretation of the record, Petitioner's heart rate increased from 68bpm to 94bpm from lying down to standing up – a change of 26bpm – which does not satisfy the criteria set forth in the Consensus Statement, Dr. Schofield's preferred diagnostic reference. *Id*.; *see also* Ex. 57.

Dr. Leist highlighted that the tilt table test did not start until 13:35, as clearly noted on the contemporaneous chart used to record Petitioner's symptoms. Second Leist Rep. at 4. When the table was in the horizontal position, Petitioner's heart rate was 102bpm. *Id*. As the table was raised to 70 degrees, Petitioner's heart rate was measured every five minutes for 40 minutes. *Id*. Dr. Leist noted that Petitioner's heart rate fluctuated between 89 and 111; again, not meeting the criterion set forth in the Consensus Statement. *Id*. at 3; Ex. 57.

Dr. Leist noted that according to the Consensus Statement, the standing (or orthostatic) heart rate for individuals with POTS is often 120bpm or higher. Second Leist Rep. at 5; Ex. 57. Dr. Leist observed that Petitioner's heart rate never elevated to 120 bpm, either before or during the tilt table test. *Id*. Additionally, Dr. Leist reiterated that the results of Petitioner's Holter monitor test, obtained approximately 39-59 days after vaccination, were not indicative of POTS. *Id*. at 4. The results revealed that Petitioner had an average heart rate of 64 bpm, and that Petitioner's heart rate was below 60 bpm 24% of the time and above 100bpm only 2% of the time. *Id*. According to Dr. Leist, the Holter monitor results are "also not supportive of a diagnosis of [POTS]." *Id*. at 5.

Second, Dr. Leist stated that Dr. Schofield provided no discussion of the specific findings on which she based her diagnosis of Petitioner's MCAS, and no discussion of how MCAS could be caused by the influenza vaccine. Second Leist Rep. at 5.

Third, Dr. Leist stated that Dr. Schofield failed to demonstrate that Petitioner has APS. *Id*. at 1. He doubted Dr. Schofield's theory that a borderline positive anticardiolipin level is clinically relevant based on the fact that she "appears to apply personal discretionary standard when entertaining diagnosis of anticardiolipin syndrome in [Petitioner]' case. *Id*. at 2. He questioned her personal decision to no longer send samples to the University of Colorado Hospital laboratory for testing, and her criticisms of the Hospital's laboratory practices, especially considering that the University of Colorado Hospital is accredited by all the relevant federal agencies, and is certified by the Colorado Department of Public Health which has an interest in ensuring the quality of laboratory testing. *Id*. at 1-2. It is Dr. Leist's opinion that, "In absence of positive anticardiolipin antibodies it is unlikely that [L.P.] suffered from an anticardiolipin antibody related condition." *Id*. at 5. Even assuming that a borderline test result is clinically significant, Dr. Leist noted that that Dr. Schofield failed to explain how a transient borderline anticardiolipin antibody level would be related to an influenza vaccination eight months earlier as opposed to some other intervening event. *Id*. at 1.

Finally, Dr. Leist stated that Dr. Schofield failed to propose a mechanism by which "transient low level anticardiolipin antibodies can cause a clot forming, thrombotic condition of the inner ear." *Id*. at 2. "Dr. Schofield neither provides evidence that this actually occurred in [Petitioner]'s case nor does she provide information that this is actually known to occur as a consequence of non-live influenza vaccine." *Id*. at 2. Dr. Leist discounted Dr. Schofield's reference to the Mouadeb & Ruckstein article on the grounds that the "article does not go beyond the

description that 42 of a series of 168 patients with sensorineural hearing loss had a least one antiphospholipid marker." *Id*. According to Dr. Leist, the article does not report any association between sensorineural hearing loss and the influenza vaccine. *Id*. "It is not known that influenza vaccine causes induction anticardiolipin antibodies that in turn can cause clinical disease;" thus, Dr. Leist found Dr. Schofield's theory to be nothing more than speculation. *Id*. at 5.

In conclusion, Dr. Leist observed that [Petitioner] had conditions related to her heart, ears, balance, and lungs before September 25, 2015, and continued to suffer from those conditions after September 25, 2015. Second Leist Rep. at 5. Dr. Leist reiterated: "It is my opinion that [Petitioner] did not incur an injury due to [the] influenza vaccine she received on September 25, 2015 whether listed in the Vaccine Injury Table or not." *Id.*

V. Applicable Law

A. Petitioner's Burden in Vaccine Program Cases

Under the Vaccine Act, when a petitioner suffers an alleged injury that is not listed in the Vaccine Injury Table, a petitioner may demonstrate that she suffered an "off-Table" injury. § 11(c)(1)(C)(ii).

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

Under the first prong of *Althen*, 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). Proof that the proffered medical theory is reasonable, plausible, or possible does not satisfy a petitioner's burden. *Boatmon v. Sec'y of Health & Hum. Servs*., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019).

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). However, special masters are "entitled to require some indicia of reliability to support the assertion of the expert witness." *Boatmon*, 941 F.3d at 1360, *quoting Moberly*, 592 F.3d at 1324. Special Masters, despite their expertise, are not empowered by statute to conclusively resolve what are complex scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners

in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Hum. Servs*., 121 Fed. Cl. 230, 245 (2015), *vacated on other grounds*, 844 F.3d 1363 (Fed. Cir. 2017); *see also Hock v. Sec'y of Health & Hum. Servs*., No. 17-168V, 2020 U.S. Claims LEXIS 2202 at *52 (Fed. Cl. Spec. Mstr. Sept. 30, 2020).

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 ("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"). 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. *Hibbard v. Sec'y of Health & Hum. Servs*., 100 Fed. Cl. 742, 749 (2011), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Caves 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 (2011), *aff'd without opinion*, 475 Fed. 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*., 503 F. App'x 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs*., No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. Law Governing Analysis of Fact Evidence

The parties agree that there are no medical facts in dispute with respect to Petitioner's medical records and Petitioner's timeline of symptoms. Joint Submission at 8, ECF No. 83; *see also* Ex. 11 (Petitioner Timeline of Symptoms). Accordingly, Petitioner's medical records are presumed to accurate and complete and are afforded substantial weight. *Cucuras*, 993 F.2d at 1528;

Doe/70 v. Sec'y of Health & Hum. Servs., 95 Fed. Cl. 598, 608 (2010); *Lowrie v. Sec'y of Health & Hum. Servs.*, No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005).

C. Analysis of Expert Testimony

Establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of her 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). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592-95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora. *Daubert* factors are employed by judges to exclude evidence that is unreliable and potentially confusing to a jury. In Vaccine Program cases, these factors are used in the weighing of the reliability of scientific evidence. *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").

Respondent frequently offers one or more experts of his own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen 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. 136, 146 (1997)). A "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly*, 592 F.3d at 1324. 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. *Id.* at 1325-26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations").

D. Consideration of Medical Literature

Although this decision discusses some but not all of the medical literature in detail, I reviewed and considered all of the medical records and literature submitted in this matter. *See Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though [s]he does not

explicitly reference such evidence in h[er] decision."); *Simanski v. Sec'y of Health & Hum. Servs.*, 115 Fed. Cl. 407, 436 (2014) ("[A] Special Master is 'not required to discuss every piece of evidence or testimony in her decision.'" (citation omitted)), *aff'd*, 601 F. App'x 982 (Fed. Cir. 2015).

VI. Analysis

Because Petitioner does not allege an injury listed on the Vaccine Injury Table, her claim is classified as "off-Table." As noted above, to prevail on an "off-Table" claim, Petitioner must prove by preponderant evidence that she suffered an injury and that this injury was caused by the vaccination at issue. *See Capizzano*, 440 F.3d at 1320.

In certain cases, the appropriate first step is to determine the precise nature of a petitioner's injury before engaging in the *Althen* analysis. *Broekelschen,* 618 F.3d at 1346. An injury which predates vaccination can defeat a Vaccine Program claim entirely. *Shalala v. Whitecotton,* 514 U.S. 268, 274-75 (1995) (Vaccine Act claimant who demonstrates she experienced symptoms of injury after receipt of vaccination does not succeed in her claim if the evidence indicates that she had symptoms of injury before her vaccination); *Locane v. Sec'y of Health & Hum. Servs.*, 99 Fed. Cl. 715, 727 (2011), *aff'd*, 685 F.3d 1375 (Fed. Cir. 2012) (finding that petitioner's Crohn's disease began prior to her vaccinations and therefore vaccine causation could not be established).

A. The Expert Opinion Evidence

In weighing the persuasiveness of opinion testimony, special masters may consider the background of the expert who is offering an opinion. *See Snyder v. Sec'y of Health & Hum. Servs.*, 553 F. App'x 994, 1000–02 (Fed. Cir. 2014) (special master's finding that respondent's experts were more persuasive due in part to their current practice in neurology compared to petitioner's expert who had no recent practice was not arbitrary or capricious); *see also Locane*, 99 Fed. Cl. 727. This flows naturally from a special master's duty to evaluate expert credibility in the process of weighing the evidence. *Porter v. Sec'y of Health & Hum. Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("[t]he Federal Circuit has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act"). I have evaluated the opinions of both experts in this case and find that Dr. Leist is the more persuasive of the two.

Dr. Leist is a board-certified neurologist with a Ph.D. in biochemistry. *See* Leist CV at 1. He is a professor of Neurology at Thomas Jefferson University and has been on faculty at that institution for more than 20 years. *Id.* Among other positions, he currently serves as the Chief of the clinical neuroimmunology division.

Dr. Schofield is a physician who is board certified in internal medicine. *See* Schofield CV at 3. During her time as an attending physician at St. Joseph Hospital in Denver, Dr. Schofield stated that she developed an interest in autoimmune disease. First Schofield Rep. at 1. Based on this interest, Dr. Schofield completed an informal (not accredited) fellowship training program in multi-specialty autoimmune disease from January 2015 through July 2016. *Id.* at 1-2. During this time, she also started her own clinic involving dysautonomia and antiphospholipid syndrome

(hereinafter "APS"). *Id.* at 2. She currently works as a staff physician at the IMMUNOe Health and Research Center where she performs clinical work in APS and autoimmune dysautonomia. *Id.*

Although Dr. Schofield has experience in the field of dysautonomia, she is not a neurologist. On the other hand, Dr. Leist has extensive medical training, including a three-year neurology residency at the Cornell Medical Center and the Sloan Kettering Memorial Cancer Center. Leist CV at 1. This three years of formal training, in addition to his 20 plus years of work as a neurologist, and his board certification in neurology all render him the more persuasive of the two experts, especially as his opinion relates to a condition that falls in the field of neurology as opposed to internal medicine.

B. There is not Preponderant Evidence that Petitioner Suffers from POTS[9]

The first question to be addressed is whether petitioner's medical history supports a finding that she suffered from POTS. For the reasons discussed below, I find that it does not.

Sheldon, et al. defined POTS as follows:

> POTS is a clinical syndrome usually characterized by (1) frequent symptoms that occur with standing, such as light-headedness, palpitations, tremor, generalized weakness, blurred vision, exercise intolerance, and fatigue; (2) an increase in heart rate of ≥30 beats per minute (bpm) when moving from a recumbent to a standing position…; and (3) the absence of orthostatic hypotension (>20 mm Hg drop in systolic blood pressure).

---

[9] I will note at the outset that the precise nature of Petitioner's injury as alleged throughout this case is unclear. The petition repeatedly uses the term "adverse reaction" to describe Petitioner's injury. *See* Pet. at 1, 7. The petition also states that

> At the worst of her illness, [L.P.] experienced the following symptoms: Orthostatic Tachycardia, palpitations or pounding heart, cold hands and feet, inability to regulate body temperature, sweating irregularities, constipation, diarrhea, loose stool, severe GERD, nausea, unexplained weight loss, nervousness, anxiety, depression, flushing, heat intolerance, increased blood pressure, hair loss, dry skin, adrenaline rushes, hearing loss, tinnitus, dizziness, motion intolerance, extreme motion sickness, hyperacusis, brain fog/cognitive struggles, blurred vision, tingling in her legs, feet, and face, exercise intolerance, fatigue, insomnia, and reduced stress tolerance.

Id. at 6. This list of conditions is reiterated in Petitioner's affidavit and in her Motion for a Decision on the Record. *See* Ex. 1 at 3; Pet. Motion at 18. However, in her Reply Brief, Petitioner argues that she has met *Althen* prong one and has shown that vaccination can cause POTS (stating "the growing body of medical literature since this case was filed in 2016 increasingly suggests an autoimmune basis for POTS."). *See* Reply at 7-8. Further, Dr. Schofield opined as follows: "During my initial evaluation, there was a clear temporal relationship to the onset of her symptoms and the influenza vaccine she received and I was suspicious of an immune-mediated mechanism for her dysautonomia triggered by the vaccination. I ordered serological testing for autoimmune and non-autoimmune causes for her POTS…" First Schofield Rep. at 4. Accordingly, I have evaluated whether Petitioner suffered from POTS in conducting my analysis in this case.

Sheldon, et al., *2015 Heart Rhythm Society Expert Consensus Statement on the Diagnosis and Treatment of Postural Tachycardia Syndrome, Inappropriate Sinus Tachycardia, and Vasovagal Syncope*, 12 HEART RHYTHM at 3 (2017) (filed as Ex. 57) (hereinafter "Sheldon"). Sheldon goes on to note that "[t]he standing (or orthostatic) heart rate of individuals with POTS is often ≥120 bpm." *Id.*

1. Tilt Table Testing

Petitioner visited the Swedish Medical Center for tilt table testing on February 25, 2016. Ex. 23 at 18-25. Dr. Schofield contends that Petitioner was "officially diagnosed with POTS in February, 2016 by tilt table testing done at Swedish Medical Center in Denver." First Schofield Rep. at 4. However, Petitioner's treating neurologist, Dr. Moon, noted that Petitioner's tilt table test was "not conclusive". Ex. 16 at 13. In the assessment portion of the March 15, 2016 record, Dr. Moon further noted that "[a]t this point, we don't have definitive POTS." *Id.* Respondent's expert, Dr. Leist, provided an opinion consistent with that of Dr. Moon stating that "[t]he records do … not support a diagnosis of postural orthostatic tachycardia syndrome." First Leist Rep. at 14.

The results of Petitioner's tilt table test are documented in the following chart:

Time	B/P	Heart Rate	O_2 Sat	Symptoms
1300	120/75	68	100%	pre tilt table ØSymptoms laying down
1302	135/74	[illegible]	100%	few palpations first sitting up Sitting up
1305	132/90	94	100%	pre tilt table ØSymptoms standing
1335	128/88	102	100%	start tilt table ØSymptoms HOB↑
1340	126/88	89	100%	HOB↑ Ø symptoms 5min
1345	126/87	94	100%	HOB↑ ØSymptoms 10 min
1350	120/85	93	99%	HOB↑ ØSymptoms 15 min
1355	120/85	98	98%	HOB↑ ØSymptoms 20min
1400	119/85	101	96	HOB↑ ØSymptoms 25min
1405	120/85	107	97%	HOB↑ ØSymptoms 30 min
1410	122/85	108	96%	HOB↑ ØSymptoms 35min
1415	124/83	111	98%	HOB↑ ØSymptoms 40 min
1419	116/74	109	98%	HOB↓ ØSymptoms
1422	130/82	76	100%	pt Sitting up

Ex. 23 at 20. Dr. Leist noted that the first three entries were taken when Petitioner was laying down, sitting up, and standing, and that these entries took place prior to the start of the test. *See* First Leist Rep. at 13; Second Leist Rep. at 3. This interpretation is supported by the above chart which indicates "pre tilt table" when describing the entries at 1300 and 1305. Ex. 23 at 20.

According to Dr. Leist, the actual tilt table test was conducted between 1335 and 1415. Second Leist Rep. at 3. Once the test began at 1335, Petitioner's heart rate was recorded at 102 bpm. Ex. 23 at 20. At the conclusion of the test, her heart rate was 111 bpm. *Id.* This change in

heart rate does not meet the criterion outlined by Sheldon which requires an increase in heart rate of ≥30 beats per minute. Sheldon at 3. I also note that Petitioner's heart rate never exceeded 120 bpm, which is inconsistent with a POTS diagnosis; Sheldon noted that "[t]he standing (or orthostatic) heart rate of individuals with POTS is often ≥120 bpm." *Id.*

In addition, I note that Petitioner did not experience symptoms during the test, which further suggests that she does not have POTS. Dr. Schofield addressed this point in her second report. She stated,

> Dr. Leist also makes note that [L.P.] did not have any symptoms during the study. That portion of the report is usually done by a technician, many of whom do not even ask the patient if they have symptoms. All patients with POTS have numerous symptoms all the time and learn to not complain, so unless someone is specifically asking the patient if they are having symptoms, patients will almost never report them. In my experience, it is common for this to be the case on formal tilt table reports.

Second Schofield Rep. at 2. This point would be more compelling if there were an absence of symptom discussion by the technician during the test. The fact that "Ø symptoms" is repeatedly annotated in the records indicates that the technician asked whether Petitioner was experiencing symptoms and contemporaneously recorded that she was not.

Dr. Schofield contends that Petitioner's tilt table test was diagnostic of POTS and that she "very clearly … met the formal criteria for POTS." Second Schofield Rep. at 2. She stated, "A tilt table test demonstrated a rise in heart rate from 68 to the 100's without a drop in her blood pressure consistent with postural tachycardia syndrome." First Schofield Rep. at 5. Dr. Schofield combined the results from the pretest and the test to arrive at this conclusion. Although no literature was filed which directly addresses the point as to whether these initial readings should be considered in assessing the test results, several points indicate that they should not. First, the fact that the readings are classified as "pre tilt table" suggests that they are not to be used as part of the formal test. Second, Petitioner's treating neurologist, Dr. Moon, noted that "We did see that her heart rate did fluctuate significantly prior to the tilt table." Ex. 16 at 13. This statement also supports the distinction between the pre-test numbers and the rest of the testing. Finally, a second neurologist, Dr. Leist, has opined that the testing did not begin until 1335. Second Leist Rep. at 3. Ultimately, I credit the opinions of the two board certified neurologists over that of Dr. Schofield. In so doing, I find that Petitioner's tilt table test was not diagnostic of POTS.

2. Other Factors

Dr. Leist opined that other evidence in Petitioner's medical records also suggests that she does not have POTS. Dr. Leist pointed out that Petitioner wore an event recorder between November 6 and November 20, 2015. During this time, Petitioner's average heart rate was 63 bpm

and she was in sinus bradycardia[10] of less than 60 bpm for 24% of the time. Second Leist Rep. at 4. In addition, Petitioner's heart rate was greater than 100 bpm during only 2% of this time period. *Id.* Dr. Leist opined that these factors indicate that Petitioner does not have POTS.[11] *Id.* Dr. Leist further remarked about this time period as follows: "[L.P.] marked a total of 9 events when she felt symptoms between November 6 and November 12, 2015, 4 of these occurred before 6 am, and it could be argued that they occurred while she was in bed. She marked no events between November 13 and November 20." *Id.*

In addition to the November 6 through November 20 time period, Dr. Leist noted that "[c]ardiac monitor data obtained between about 39 and 59 days after [L.P.] had received influenza vaccine on September 25, 2015 are not supportive of a diagnosis of Postural Tachycardia Syndrome. The data do however support that [L.P.] has spontaneous, unprovoked fluctuations of the heart rate and that she is at times bradycardic." Second Leist Rep. at 4.

The tilt table test as well as the other evidence from Petitioner's medical records demonstrates that she does not meet the diagnostic criteria for POTS.

3. Treating Physicians

Petitioner visited Dr. Yeash (her PCP) on March 18, 2016 for dizziness, vertigo, poor concentration, tachycardia when standing up, extreme fatigue, and weakness. Ex. 18 at 5. Petitioner requested paperwork for short term disability. *Id.* In the HPI, Dr. Yeash's notes indicate that her neurologist had diagnosed her with dysautonomia and POTS. *Id.* In fact, during Petitioner's March 15, 2016 follow-up appointment with Dr Moon, he noted that "At this point we do not have definitive POTS." Ex. 16 at 13.

At each subsequent visit from March 18, 2016 through May 31, 2018, Dr. Yeash assessed Petitioner with POTS. *See* Ex. 18 at 1, 5; Ex. 54 at 14, 23. These assessments were based on inaccurate information; specifically, that Dr. Moon had assessed Petitioner with POTS. As such, I do not find it to be persuasive evidence that POTS is Petitioner's correct diagnosis.

None of Petitioner's other treating physicians (other than Dr. Schofield) diagnosed Petitioner with POTS or linked Petitioner's condition to her flu vaccine. Accordingly, based on the results of the tilt table test, the other factors described above, and the opinion of Petitioner's treating neurologist as well as the opinion of Dr. Leist, I conclude that there is not preponderant evidence that Petitioner suffers from POTS.

C. There is not Preponderant Evidence that Petitioner Suffers from APS

[10] Bradycardia is a slowness of the heartbeat, as evidenced by slowing of the pulse rate to less than 60. Dorland's, https://www.dorlandsonline.com/dorland/definition?id=6816&searchterm=bradycardia (last visited April 9, 2021).

[11] In *Balasco v. Sec'y of Health & Hum. Servs.*, 2020 WL 1240917, the special master noted that some of the medical literature filed in that case indicates that extended Holter monitors are not useful in detecting POTS. *See Balasco*, n32. The literature referenced in that decision was not filed in the present case.

Dr. Schofield repeatedly discussed APS in her expert reports. Although she did not definitively state that Petitioner had APS, she discussed the condition enough that it is appropriate to provide some background. I note that it is unclear whether Dr. Schofield is contending that Petitioner developed APS as a result of her flu vaccine. Certainly, Dr. Leist believed that to be her contention. ("Dr. Schofield's theory appears to be that influenza vaccine induced antiphospholipid syndrome which in turn induced an inner ear condition [L.P.'s] case.") Second Leist Rep. at 1. Based on this ambiguity, I have included a brief analysis concerning whether there is preponderant evidence that Petitioner suffers from APS and whether the flu vaccine can cause APS.

Cruz-Tapias described APS as

> an autoimmune multisystemic disease associated with recurrent fetal loss, thromboembolic phenomena, thrombocytopenia as well as neurological, cardiac and dermatological involvement. APS is characterized by the presence of antiphospholipid antibodies which bind negatively charged phospholipids, mainly through b2-glycoprotein I (b2-GPI). The factors causing production of anti-b2-GPI antibodies remain undefined, but there is evidence that molecular mimicry is one of the mechanisms by which experimental APS can occur in association with pathogens.

Cruz-Tapias at 390.

Throughout her two reports, Dr. Schofield noted that a number of Petitioner's clinical signs and symptoms were consistent with APS. She described these consistencies without ever giving Petitioner an APS diagnosis. *See e.g.*, First Schofield Rep. at 4 ("Autonomic dysfunction, migraine headaches, cognitive issues, sensorineural hearing loss and Meniere's like syndrome may all [occur] in association with APS"); First Schofield Rep. at 8 ("In addition, all the clinical manifestations she experienced have been well described in association with the antiphospholipid syndrome, including migraines and cognitive dysfunction, hearing and vestibular issues and autonomic nervous system dysfunction."); Second Schofield Rep. at 4. ("Anticardiolipin antibodies are often present in individuals with the antiphospholipid antibody syndrome").

As discussed later in this Decision, Petitioner had three tests for antiphospholipid antibodies, none of which were positive. Dr. Leist opined that "…low levels of antiphospholipid IgM antibodies are not diagnostic antiphospholipid syndrome. Negative antiphospholipid IgM, IgG, and IgA antibody tests are not consistent with the diagnosis of antiphospholipid syndrome…" First Leist Rep. at 14. In Schofield-1, Dr. Schofield stated:

> The diagnosis of APS was determined by the presence of at least one antiphospholipid antibody (lupus anticoagulant, anticardiolipin immunoglobulin IgG or IgM, or beta 2 microglobulin I IgG or IgM) on more than one occasion at least 12 weeks apart as well as one or more clinical manifestations of the syndrome. Not all patients met the revised Sapporo classification criteria for definite APS, which requires thrombosis or specific pregnancy morbidity and medium to high titer antibody levels. The classification criteria were designed for rigorous clinical research studies not for diagnosis, and patients with low titer antibody positivity

> were included as were patients without a history of thrombosis who had well-described nonthrombotic manifestations of the syndrome.

Schofield-1 at 698. Additionally, in Schofield-2, Dr. Schofield noted, "The diagnosis of APS was determined by the presence of one or more antiphospholipid antibodies on more than one occasion at least 12 weeks apart as well as one or more clinical manifestations of the syndrome." Schofield-2 at 3. Although Petitioner did not file the diagnostic criteria for APS, I note that she did not test positive for antiphospholipid antibodies on more than one occasion at least 12 weeks apart. Based on Dr. Leist's opinion, and Dr. Schofield's lack of a clear diagnosis, I conclude that Petitioner has not presented preponderant evidence that she suffered from APS.

Based upon the findings that Petitioner has not established through preponderant evidence that she suffered from either POTS or APS, Petitioner may not receive compensation. *Lombardi v. Sec'y of Health & Hum. Servs.*, 656 F.3d 1343 (Fed. Cir. 2011). However, for the sake of completeness, I will review the other elements of her claim.

D. Petitioner Has Not Carried Her Burden of Proof regarding Causation

1. *Althen* Prong 1

In the context of the Program, "to establish causation, the standard of proof is preponderance of evidence, not scientific certainty." *Langland v. Sec'y of Health & Hum. Serv.*, 109 Fed. Cl. 421, 441 (2013). Petitioner's burden under *Althen*'s first prong is to provide a medical theory causally connecting the vaccination and the injury. *Id.* This theory must be sound and reliable. *Boatmon*, 941 F.3d at 1359.

Before discussing Petitioner's prong one theory in this case, I will briefly address whether Petitioner has presented preponderant evidence that the flu vaccine can cause APS.

a. Antiphospholipid Syndrome

In her first report, Dr. Schofield opined that "It is well recognized that APS may be triggered by vaccination and infection." First Schofield Rep. at 4. Dr. Schofield cited to Cruz-Tapias in support of this proposition. Cruz-Tapias noted that the infections most frequently associated with APS include parvovirus B19, cytomegalovirus (CMV), toxoplasma, rubella virus, varicella-zoster virus, HIV, streptococcal and staphylococcal infections, gram-negative bacteria and Mycoplasma pneumoniae. Cruz-Tapias at 389. With respect to vaccination, Cruz-Tapias discussed an association between APS and tetanus toxoid vaccines and noted that individuals immunized with tetanus toxoid vaccines developed anti-b2-GPI/antitetanus toxoid cross-reactive antibodies via molecular mimicry. *Id.* at 390. While this article provides some support for a connection between APS and tetanus toxoid vaccines, it does not discuss the flu vaccine.

In Schofield-1, Dr. Schofield noted that "[o]ne patient (#13) developed APS, POTS, and NCS two months after human papillomavirus (HPV) vaccination…" Schofield-1 at 698. The article did not elaborate on how the HPV vaccine caused APS (or POTS). The article did not discuss the flu vaccine.

Dr. Leist opined that "Dr. Schofield's claim that influenza vaccine caused antiphospholipid syndrome as root cause for a host of symptoms in L.P.'s case is not supported by the records." First Leist Rep. at 12.

Two articles which discuss APS following different vaccines (not the vaccine at issue in this case) along with Dr. Schofield's opinion that "It is well recognized that APS may be triggered by vaccination..." is not sufficient for Petitioner to preponderantly establish that the flu vaccine can cause APS.

b. POTS

Petitioner's prong one theory is that the influenza vaccination caused Petitioner to develop a transient upregulation of antiphospholipid antibodies which in turn caused damage to Petitioner's inner ear and vestibular system and resulted in Petitioner developing POTS. This theory can be broken down into two discrete questions: 1) Can the influenza vaccine cause the development of transient antiphospholipid antibodies; and 2) can a transient upregulation in antiphospholipid antibodies cause POTS.

i. Can the Influenza Vaccine Induce Transient Upregulation in Antiphospholipid Antibodies?

Dr. Schofield stated that "Transient production of anticardiolipin antibodies and clinical manifestations of APS (including stroke) as occurred in [L.P.'s] case has been reported in more than one publication … in association with the influenza vaccine." First Schofield Rep. at 8. As support for this proposition, Dr. Schofield cited to several articles. *See* Perdan-Pirkmajer, et al., *Autoimmune response following influenza vaccination in patients with autoimmune inflammatory rheumatic disease*, 21 LUPUS 175-83 (2012) (filed as Ex. 34) (hereinafter "Perdan-Pirkmajer"); Agmon-Levin; and Toplak.

Perdan-Pirkmajer studied 218 patients with autoimmune inflammatory rheumatic disease (AIRD). In this study, 50 patients were vaccinated against seasonal influenza, six against H1N1, 104 against both, and there were 58 non-vaccinated controls. Perdan-Pirkmajer at 175. Blood samples were taken and screened for autoantibodies before vaccination, one month after vaccination, and six months after vaccination. *Id.* The study concluded that "Although no convincing differences between the seasonal and H1N1 vaccines were observed, our results imply that there might be a slight tendency of the H1N1 vaccine towards aCL [anticardiolipin antibodies] induction." *Id.* The authors noted "the potential of both vaccines to induce de novo aCL IgG/IgM in susceptible subjects. Nevertheless, although a transient increase in aCL IgG after either vaccination was often observed, the long-term effect of vaccination resulted in lower aCL IgG in most patients." *Id.* at 181. This study seems to tell us that patients with AIRD may experience a transient increase in anticardiolipin antibodies after vaccination with seasonal influenza/H1N1. Because Petitioner does not have AIRD, it is unclear how this study is relevant to her case.

Dr. Schofield cited to the Toplak paper as support for her theory that flu vaccination can cause an increase in anticardiolipin antibodies and/or APS. Toplak evaluated the possibility of

autoimmune responses following flu vaccination by measuring specific autoantibodies in 92 healthy adults before vaccination, one month after vaccination, and six months after vaccination. Toplak at 134. Toplak found that "There were no statistically significant differences in the percentage of positive ANA, aCL, anti-β2-GPI, LA and anti-ENA before,1 month and 6 months after the vaccination." *Id.* However, while the study found that influenza vaccination did not alter the percentage of healthy adults with positive autoantibodies, an "[i]ncreased level of autoantibodies or appearance of new autoantibodies was observed 1 month after the vaccination in 15% and 6 months after the vaccination in 13% of participants, suggesting de novo induction of autoantibodies after the influenza vaccination in selected individuals." *Id.* at 137. Toplak did note changes in anticardiolipin antibodies in some study participants. Topak at 138. Ultimately, Topak provides some support for the proposition that flu vaccine can result in an increase in anticardiolipin antibodies.[12] Of note, the Topak paper specifically found that no participant developed clinical signs of autoimmune disease within six months of vaccination. *Id.* at 136.

The Agmon-Levin article is an opinion piece that presents a broad discussion of vaccines and autoimmunity. The authors note that "the latency period between vaccination and autoimmunity ranges from days to years." Agmon-Levin at 648. They cite to Toplak as one study that supports this proposition (noting that "Toplak et al. reported the production of autoantibodies (such as antinuclear and antiphospholipid antibodies) in 92 healthy medical workers up to 6 months after influenza vaccination."). This article provides no further discussion of anticardiolipin antibodies or APS.

In summary, the above-mentioned literature, specifically the Toplak article does provide some evidence that the flu vaccine can result in the transient upregulation of anticardiolipin antibodies.

ii. Can the Transient Upregulation of Antiphospholipid Antibodies Cause POTS?

Petitioner filed a one-page abstract which described patients with hearing loss. *See* Mouadeb & Ruckstein. The abstract described a study cohort which included 168 patients referred for diagnosis and treatment of progressive hearing loss. Mouadeb & Ruckstein at 879. All patients had blood tests for autoimmune and infectious diseases, including testing for anticardiolipin antibodies, anti-B2 glycoprotein, and lupus anticoagulant. *Id.* The results of the study indicated that 42 patients (25%) had at least one elevated antiphospholipid antibody marker. *Id.* The study concluded that "These data support the hypothesis that antiphospholipid antibodies are involved in the pathogenesis of some forms of inner ear dysfunction, presumably by causing microthrombus formation in the labyrinthine vasculature." *Id.* The abstract went on to note that "Basic science studies are required to better understand the mechanisms by which antiphospholipid antibodies mediate inner ear dysfunction. Clinical studies to evaluate the efficacy of anticoagulation in this group of patients are also required." *Id.*

[12] This point does not necessarily support the proposition that flu vaccine can cause APS. The fact that anticardiolipin antibodies are often present in individuals with APS does not mean that an increase in anticardiolipin antibodies leads to APS.

Dr. Leist did not find the one page abstract persuasive and remarked that the Mouadeb & Ruckstein article "does not go beyond the description that 42 of a series of 168 patients with sensorineural hearing [loss] had a least one antiphospholipid marker." Second Leist Rep. at 5. He further stated that "the authors speculate how anticardiolipin antibodies could potentially cause hearing issues." *Id.*

This one-page abstract provides some *minimal* evidence that hearing loss can be associated with antiphospholipid antibodies. However, it does not provide any connection to POTS. Dr. Schofield stated that "Autonomic dysfunction, migraine headaches, cognitive issues, sensorineural hearing loss and Meniere's like syndrome may all occur in association with APS." First Schofield Rep. at 4. Similar to the one page abstract, this statement does not include any analysis of whether or how a "Ménière's like syndrome" can lead to POTS.

Further, in Schofield-1, the authors wrote: "we do not know what the frequency of autonomic dysfunction may be in the overall APS patient population, nor how often antiphospholipid antibodies may be present in patients with various autonomic disorders." Schofield-1 at 700-01. The fact that it is unclear to Dr. Schofield whether antiphospholipid antibodies are even present in patients with autonomic disorders suggests that there is not preponderant evidence that the upregulation of antiphospholipid antibodies can cause POTS.

Ultimately, for the reasons discussed above, I find that Petitioner has not presented preponderant evidence in the form of a reputable medical theory which demonstrates that the flu vaccine can cause either APS or POTS.

2. *Althen* Prong 2

Under *Althen's* second prong, a petitioner must "prove a logical sequence of cause and effect showing that the vaccination was the reason for the injury." *Althen*, 418 F.3d at 1278. The sequence of cause and effect must be "'logical' and legally probable, not medically or scientifically certain." *Id.* A petitioner is not required to show "epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." *Id.* (omitting internal citations). *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1325 (Fed. Cir. 2006). Instead, circumstantial evidence and reliable medical opinions may be sufficient to satisfy the second *Althen* prong. *Isaac v. Sec'y of Health & Hum. Servs.*, No. 08-601V, 2012 U.S. Claims LEXIS 1023 at *75 (Fed. Cl. Spec. Mstr. July 30, 2012), *aff'd* 108 Fed. Cl. 743 (Fed. Cl. 2013).

a. Petitioner's Pre-Existing Symptoms

A petitioner cannot succeed on a claim of causation-in-fact where the alleged condition preexisted the vaccination. *See W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1354–55 (Fed. Cir. 2013) (affirming the special master's denial of compensation on claim of causation-in-fact because "[i]f a petitioner has a disorder before being vaccinated, the vaccine logically cannot have caused the disorder"). In this case, the medical records demonstrate that Petitioner was suffering from a host of symptoms prior to her flu vaccination that were similar to her symptoms post vaccination. For at least two years prior to September 25, 2015, Petitioner frequently

complained of a number of symptoms that she reported to Dr. Moon as "fluctuating since October 2015."

Symptoms Alleged by Petitioner prior to Vaccination

Symptoms alleged as "fluctuating since Oct 2015"	Prior report of symptom in the medical records	Reference
Increased Heartrate/Palpitations/ Pounding Heartbeat/Tachycardia	02-27-13: palpitations, sometimes at night 03-20-13: palpitations mostly when sleeping or sitting still 03-20-13: pulse increases when P gets up in the middle of the night 05-06-14: palpitations 04-08-15: irregular heartbeat 04-17-15: cardiologist diagnosed her with PACs due to "hormones" 04-22-13: symptomatic PACs & short atrial runs up to 5 beats in length 08-03-15: palpitations	Ex. 18 at 28 Ex. 5 at 8 Ex. 5 at 8 Ex. 18 at Ex. 11 at 12 Ex. 21 at 5 Ex. 5 at 2 Ex. 15 at 1
Can't regulate body temp	03-20-13: palpitations accompanied by feeling flushed and clammy	Ex. 5 at 8
Gastrointestinal constipation/Loose stool/ GERD	05-06-13: constipation 12-03-14: constipation as a result of taking iron supplement 04-08-15: constipation 04-17-15: cyclical constipation and diarrhea 07-08-15: constipation 06-16-15: umbilical hernia due to straining from constipation 08-03-15: constipation	Ex. 18 at 23 Ex. 21 at 5 Ex. 11 at Ex. 21 at Ex. 11 at 19 Ex. 21 at 3 Ex. 15 at 1
Nervousness/Anxiety	02-27-13: palpitations and anxiety 04-08-15: taking Xanax - PT noted she appeared anxious at every appt. 04-14-14: Petitioner reported having some anxiety 04-15-15: Therapist noted that she seemed anxious 04-17-15: anxiety, "I am losing my mind" 06-16-15: Citalopram made her more anxious and jittery	Ex. 18 at 28 Ex. 11 at 2 Ex. 13 at 1 Ex. 11 at 10 Ex. 21 at 5 Ex. 21 at 3
Dizzy/Lightheaded	03-20-13: palpitations make her lightheaded	Ex. 5 at 8
Endolymphatic Hydrops/ Hearing Loss/ Tinnitus	11-18-13: tinnitus 03-26-14: eustachian tube dysfunction 10-15-14: ear discomfort	Ex. 18 at 21 Ex. 10 at 11 Ex. 10 at 23
Insomnia/Interrupted Sleep	11-18-13: having trouble sleeping 04-24-14: PMS-related insomnia, heavy bleeding gets her up at night 04-17-15: Petitioner reports that "she feels like she has sleep issues"	Ex. 18 at 21 Ex. 21 at 7 Ex. 21 at 5
Loss of Menstrual Cycle for 3 mos.	04-08-15: concerned about pre-menopausal symptoms 04-17-15: PMDD symptoms 06-16-15: PMDD symptoms	Ex. 11 at 1 Ex. 21 at 5 Ex. 21 at 3
Left Hip/Back Pain	09-13-12: left lower back pain/x-ray reveals scoliosis 02-11-15: left side dull ache 04-08-15: pain left lumbar and lumbopelvic region 04-10-15: sharp stabbing left lower quadrant abdominal pain 04-2015 to 10-2105: sharp burning stabbing pain left buttock 04-2015 to July 2015: left side low back pain 07-15-15: low back pain 07-28-15: MRI shows scoliosis and degeneration at L4-5 08-05-15: back pain	Ex. 18 at 55 Ex. 21 at 6 Ex. 21 at 6 Ex. 25 at 5 Ex. 13 at1 Ex. 11 at 1 Ex. 22 at 1 Ex. 13 at 1 Ex. 11 at 10
Loss of Sex Drive	04-24-14: loss of libido	Ex. 21 at 7
Hay fever/Grass-Pollen Allergy	03-25-03: allergic rhinitis 04-25-03: allergic rhinitis 04-15-13: allergic rhinitis 03-26-14: allergic rhinitis	Ex. 10 at 17 Ex. 10 at 19 Ex. 18 at 26 Ex. 10 at 11
Post-Nasal/Non-Allergic Rhinitis	04-12-14: chronic rhinitis/non-allergic rhinitis in the winter	Ex. 10 at 14

Polymorphous Light Eruption/ Rash due to Sun Exposure	10-15-14: ENT history of pruritic erythema, possible photosensitivity 06-10-15: possible polymorphous light eruption	Ex. 10 at 24 Ex. 10 at 27
Hypermobility	04-14-14: Petitioner reported feeling "hypermobile at times"	Ex. 13 at 1

Petitioner's medical records demonstrate that she had a number of medical concerns prior to September 25, 2015 that were similar in nature to her symptoms after vaccination. Petitioner contends that her symptoms after vaccination were different in both their nature and severity.

Although Petitioner states that "there is not a single pre-vaccination record of dysautonomia or POTS" (Pet'r's Reply at 3), this contention is not supported by the medical records cited above, which demonstrate that Petitioner repeatedly complained of heart palpitations in the years before she received her flu vaccination.

Petitioner additionally differentiated between a low frequency "thumping" sound that she experienced after vaccination (Ex. 3 at 1) and her tinnitus documented pre-vaccination. In her affidavit, Petitioner stated that "[a]lthough I had experienced a high-pitched tinnitus in both ears before, this sensation was different, as I began to experience a low hum, vibrating noise in my left ear that would not go away." Ex. 1, ¶ 3. Dr. Leist opined that that Petitioner had a history of Eustachian tube dysfunction and tinnitus. He remarked in his report "Dr. Kreutzer recorded an at least 10-year history of tinnitus, intermittent ear pressure, and fullness of the left ear (Exhibit 4 at 1; Exhibit 13 at 2)." First Leist Rep. at 14. He further opined that "[L.P.] had tinnitus and pressure and fullness before and after administration of influenza vaccine on September 25, 2015." *Id.* While the specific symptoms that Petitioner experienced after vaccination are somewhat different than her pre-vaccination complaints, they appear to be substantially similar. Ultimately, the medical records establish that Petitioner experienced symptoms of dysautonomia and tinnitus prior to her September 25, 2015 vaccination.

In her second expert report, Dr. Schofield stated, "many patients who develop severe autoimmune dysautonomia have much milder underlying symptoms suggesting mild orthostatic intolerance and/or immune dysregulation just as [L.P.'s] history suggests." Second Schofield Rep. at 3. Dr. Schofield did not provide any further discussion concerning this point. She did not elaborate as to how Petitioner's pre-existing symptoms supported her theory that the flu vaccine did cause Petitioner's condition.

b. Anticardiolipin Antibodies

Aside from a temporal correlation between Petitioner's symptoms and her vaccination, Dr. Schofield points to two main tests in support of her position that the flu vaccine did cause Petitioner's illness: Petitioner's aCL IgM and her low C4 level. I will address each of these in turn.

Dr. Schofield ordered tests for anticardiolipin antibodies on June 8, 2016. These results are depicted below:

Resulted: 06/14/16 1344, Result status: Final result

Anti-Cardiolipin IgG Antibody [273418214] (Normal)

Filed by: Chavez, Toshia 06/14/16 1344 | Resulting lab: RHEUMATOLOGY LABORATORY, AURORA CO

Narrative: Units: 2

Acknowledged by: Schofield, Jill R, MD on 06/14/16 2031

Specimen Collection

Source	Collected On
Blood	06/08/16 1410

Components

	Value	Reference Range	Flag	Lab
Cardiolipin IgG Antibody	<20	Negative (<20) Units		UCD RHEUM

Resulted: 06/14/16 1344, Result status: Final result

Anti-Cardiolipin IgM Antibody [273418215] (Normal)

Filed by: Chavez, Toshia 06/14/16 1344 | Resulting lab: RHEUMATOLOGY LABORATORY, AURORA CO

Narrative: Units: 18

Acknowledged by: Schofield, Jill R, MD on 06/14/16 2031

Specimen Collection

Source	Collected On
Blood	06/08/16 1410

Components

	Value	Reference Range	Flag	Lab
Anti-Cardiolipin IgM Antibody [273418215] (Normal) (continued)				result
Cardiolipin IgM Antibody	<20	Negative (<20) Units		UCD RHEUM

Ex. 24 at 66-67. The lab assessed both tests as negative. In her first expert report, Dr. Schofield described the test results as follows: "I ordered serological testing for autoimmune and non-autoimmune causes for her POTS which was notable for a positive anticardiolipin IgM antibody--one of the antibodies associated with the autoimmune clotting disorder antiphospholipid syndrome (APS)." First Schofield Rep. at 4. In her second report, Dr. Schofield clarified this point and noted that Petitioner's anticardiolipin antibody test came back as "indeterminate" or "low positive."

> Her anticardiolipin IgM level during my initial evaluation (one full year after the vaccination) was actually indeterminate or low positive at 18 MPL (indeterminate or low positive is 12.5 to 20 MPL), not negative. The University of Colorado Rheumatology laboratory has elected not to report the low positive/indeterminate anticardiolipin antibody results based on the formal 2006 revised Sapporo Criteria for a diagnosis of antiphospholipid syndrome (APS). … The University of Colorado laboratory is the only laboratory I know of that does this and when I was practicing there, I met with the head of the Rheumatology laboratory requesting they report the low/indeterminate positive results as they were clearly clinically important in some of my patients. They preferred to report the low/indeterminate titer results to me directly rather than reporting them in the chart.

Second Schofield Rep. at 3. Dr. Schofield pasted an example of the way other laboratories report anticardiolipin antibodies into her report.

Reference Interval

- Negative: <13 MPL
- Indeterminate: 13–20 MPL
- Low-medium positive: >20–80 MPL
- Positive: >80 MPL

1 MPL unit = cardiolipin-binding activity of purified IgM anticardiolipin (at 1 U/mL) from an international reference standard.

Second Schofield Rep. at 4. While Dr. Schofield classified Petitioner's results as "indeterminate or low positive", indeterminate is the more applicable descriptor, as "low/medium positive" falls in a range from >20-80 MPL.

Petitioner was tested for anticardiolipin antibodies again on September 28, 2016 and on October 14, 2016. The results of both tests were negative. The September 28, 2016 test was performed by the University of Colorado Hospital.

Resulted: 10/04/16 1208, Result status: Final result

Anti-Cardiolipin IgM Antibody [273418278] (Normal)

Filed by: Parish, Mark 10/04/16 1208 — Resulting lab: RHEUMATOLOGY LABORATORY, AURORA CO

Acknowledged by: Machala, Maria Caruso, NP on 10/07/16 0909

Specimen Collection

Source	Collected On
Blood	09/28/16 1056

Components

	Value	Reference Range	Flag	Lab
Cardiolipin IgM Antibody	<20	Negative (<20) Units		UCD RHEUM

Resulted: 10/04/16 1208, Result status: Final result

Anti-Cardiolipin IgG Antibody [291453404] (Normal)

Filed by: Parish, Mark 10/04/16 1208 — Resulting lab: RHEUMATOLOGY LABORATORY, AURORA CO

Acknowledged by: Machala, Maria Caruso, NP on 10/07/16 0909

Specimen Collection

Source	Collected On
Blood	09/28/16 1056

Components

	Value	Reference Range	Flag	Lab
Cardiolipin IgG Antibody	<20	Negative (<20) Units		UCD RHEUM

Ex. 29 at 16. Unlike with the June 8, 2016 test, Dr. Schofield did not provide any additional information about this particular test in her report which indicated whether the test was indeterminate or negative.

The October 14, 2016 result as reported by LabCorp of America is depicted below:

Anticardiolipin Ab, IgG [L-3181-5]	<10	GPL	F
Reference Range: Negative: <15 Indeterminate: 15 - 20 Low to medium positive: >20 - 80 High positive: >80			
Anticardiolipin Ab, IgM [L-3182-3]	<10	MPL	F
Reference Range: Negative: <13 Indeterminate: 13 - 20 Low to medium positive: >20 - 80 High positive: >80			

Ex. 28 at 8. It is not clear why Dr. Schofield sent these results to a different lab. With respect to this testing, she stated, "Repeat testing for antiphospholipid antibodies … many months later showed this testing had normalized, suggesting the autoimmunity was transient…" First Schofield Rep. at 7.

Dr. Leist opined as follows: "Absence of anticardiolipin antibodies renders anticardiolipin syndrome or for that matter an anticardiolipin antibody related condition unlikely." Second Leist Rep. at 1. He further stated that "Laboratory tests in [L.P.] do not fulfill laboratory criteria of the "The International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS)" [antiphospholipid antibodies include anticardiolipin, beta-2 glycoprotein I, and lupus anticoagulant antibodies]." *Id.* at 2.

It is unclear how an indeterminate level aCL taken more than eight months after vaccination demonstrates that Petitioner's flu vaccination did cause her condition. Although Dr. Schofield stated, "I suspect it would have been higher if it were tested closer to the time of the illness onset" (Second Schofield Rep. at 7), this statement is entirely speculative. Further, it is also unclear how Petitioner's negative test from June 2016 compares with her negative test from the same lab in September 2016, as Dr. Schofield included the indeterminate test value of 18 in her report, but did not indicate what the value was for the September test. In short, I do not find Dr. Schofield's opinion concerning this matter to be persuasive.

c. Complement Component 4 (C4)

Dr. Schofield also opined that Petitioner's low C4 is indicative of autoimmunity and thus supports her position that the flu vaccine did cause Petitioner's condition. Dr. Schofield stated: "There was also a persistently low C4 level on three serial occasions (the first being done Sept 2016) suggestive of either active autoimmunity or a genetic predisposition to autoimmunity. Repeat testing in January 2018 showed this level had normalized consistent with active autoimmunity rather than a genetically low level." Second Schofield Rep. at 7.

Petitioner's testing does indicate that her C4 level was low on three occasions. On June 8, 2016, Petitioner's C4 level was 13.7 (reference range 19.0-52.0 mg/dL). Ex. 24 at 56. On September 28, 2016, Petitioner's C4 was 13.3 (reference range 19.0-52.0 mg/dL). Ex. 29 at 16. On October 14, 2016, Petitioner's C4 was 12 (reference range 14-44). Ex. 28 at 6. Dr. Schofield did not spend time in her reports discussing the meaning of C4 levels. Other than to state that these

levels are indicative of persistent autoimmunity, Dr. Schofield did not explain or describe how a low C4 level eight plus months after vaccination is significant to this case. Further, it is unclear why Petitioner's aCL level normalized and her C4 did not and how this supports Petitioner's theory that her flu vaccine did cause her condition. Dr. Leist did not discuss Petitioner's C4 levels in his report. Ultimately, while Petitioner's C4 level was low on three occasions, the significance of these levels has not been explained in any meaningful way that connects these results to vaccination, which occurred between eight and twelve plus months prior.

d. Petitioner's Treating Physicians

In weighing evidence, special masters are expected to consider the views of treating doctors. *Cappizano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1326 (Fed. Cir. 2006). The views of treating doctors about the appropriate diagnosis are often persuasive because the doctors have direct experience with the patient whom they are diagnosing. *See McCulloch v. Sec'y of Health & Human Servs.*, No. 09-293V, 2015 WL 3640610, at *20 (Fed. Cl. Spec. Mstr. May 22, 2015).

I have considered the fact that Dr. Schofield was one of Petitioner's treating physicians in arriving at my determination in this case. I also note that none of Petitioner's other treating doctors connected any of her symptoms with her flu vaccination.

For the reasons articulated above, I find that Petitioner has failed to preponderantly demonstrate that her flu vaccination "did cause" any of her medical problems and has thus not established the second prong of *Althen*.

3. *Althen* Prong 3

The timing prong contains two parts. First, a petitioner must establish the "timeframe for which it is medically acceptable to infer causation" and second, she must demonstrate that the onset of the disease occurred in this period. *Shapiro v. Sec'y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542-43 (2011), *recons. denied after remand on other grounds*, 105 Fed. Cl. 353 (2012), *aff'd without op.,* 503 F. App'x 952 (Fed. Cir. 2013).

Petitioner failed to establish a timeframe for which it is medically acceptable to infer causation. In Dr. Schofield's first report, she stated that "The mean time to post-vaccination symptom onset is two weeks, but it may range from a few days to a few months." In her second report, Dr. Schofield claimed that "it is generally accepted by most experts in the field of autoimmune disease that vaccinations are one of the environmental triggers of autoimmune disease and a period of 30 days has been usually used to define temporal association." Second Schofield Rep. at 6. Dr. Schofield did not provide a specific opinion on the appropriate window between flu vaccine and onset of POTS or APS. Further, she did not cite to any medical literature specifically establishing a temporal association between the flu vaccine and POTS or APS. Painting with such a broad brush in discussing the appropriate onset interval between vaccinations generally and autoimmune diseases generally is not persuasive.

Additionally, even assuming 30 days is an acceptable timeframe to infer causation, Petitioner failed to establish that the onset of her alleged injury occurred during this window. Dr. Schofield reported that there was "a clear temporal relationship to the onset of [Petitioner's] symptoms and the influenza vaccine she received and [Dr. Schofield] was suspicious of an immune-mediated mechanism for her dysautonomia triggered by the vaccination." First Schofield Rep. at 4. However, in drafting her first report, Dr. Schofield failed to review Petitioner's prior medical history and instead chose to rely on Petitioner's statement that she "was completely healthy" prior to her vaccination. Second Schofield Rep. at 2. Dr. Schofield failed to distinguish Petitioner's pre-vaccination symptoms from her post-vaccination symptoms, and thus failed establish the onset of Petitioner's alleged injury.[13] Petitioner has not presented preponderant proof with respect to the third *Althen* prong.

VII. Conclusion

Upon careful evaluation of all the evidence submitted in this matter, including the medical records, the affidavit, as well as the experts' opinions and medical literature, I conclude that Petitioner has not shown by preponderant evidence that she is entitled to compensation under the Vaccine Act. **Her petition is therefore DISMISSED. The clerk shall enter judgment accordingly.**[14]

IT IS SO ORDERED.

s/ Katherine E. Oler
Katherine E. Oler
Special Master

[13] In her second report, Dr. Schofield pivoted from her position that Petitioner was completely healthy before vaccination and opined that "many patients who develop severe autoimmune dysautonomia have much milder underlying symptoms suggesting mild orthostatic intolerance and/or immune dysregulation just as [L.P.'s] history suggests." Second Schofield Rep. at 3. Dr. Schofield did not elucidate how vaccination as a trigger for Petitioner's underlying symptoms fits into the 30-day temporal window discussed above.

[14] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by each filing (either jointly or separately) a notice renouncing their right to seek review.