In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: July 5, 2018

MARSHA DOUGHERTY,	*	No. 15-1333V
Petitioner,	*	Special Master Sanders
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Entitlement; Influenza ("flu") Vaccine; Narcolepsy; Cataplexy; *Althen* Causation; Failure to Satisfy *Althen* Prong One.
Respondent.	*	

David P. Murphy, Greenfield, IN, for Petitioner.
Voris E. Johnson, United States Department of Justice, Washington, DC, for Respondent.

DECISION ON ENTITLEMENT[1]

On November 6, 2015, Marsha Dougherty ("Petitioner") filed a petition pursuant to the National Vaccine Injury Compensation Program.[2] Petitioner alleged that she developed narcolepsy with cataplexy as a result of the influenza ("flu") vaccine she received on November 7, 2012. Pet., ECF No. 1.

The undersigned held an entitlement hearing in this matter on November 30 through December 1, 2017, in Boston, Massachusetts. After considering the record as a whole, and for the reasons explained below, the undersigned finds that Petitioner failed to show that her condition was caused by the flu vaccine, and is therefore not entitled to compensation under the Vaccine Act.

[1]This decision shall 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 note (2012) (Federal Management and Promotion of Electronic Government Services). In accordance with Vaccine Rule 18(b), a party has 14 days to identify and move to delete medical or other information that satisfies the criteria in § 300aa-12(d)(4)(B). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted decision. If, upon review, the undersigned agrees that the identified material fits within the requirements of that provision, such material will be deleted from public access.

[2] 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).

I. Procedural History

Petitioner filed her petition on November 6, 2015. Pet. Later that same day, the case was assigned to Special Master Hamilton-Fieldman. Not. Assignment, ECF No. 4. Petitioner filed her medical records over the subsequent several months. *See* ECF Nos. 6-19. On March 28, 2016, Respondent submitted his Rule 4(c) Report, arguing that Petitioner had failed to establish that the flu vaccine caused her narcolepsy with cataplexy. ECF No. 20 at 7-8. Petitioner submitted an expert report authored by Dr. Marcel Kinsbourne on October 13, 2016. Pet'r's Ex. 12, ECF No. 36.

The case was reassigned to the undersigned on January 12, 2017. ECF No. 45. On February 8, 2017, Respondent submitted responsive expert reports by Dr. Thomas Scammell and Dr. Andrew MacGinnitie. Resp't's Exs. A, C, ECF Nos. 47-1, -2. Petitioner then submitted a supplemental expert report by Dr. Kinsbourne on March 21, 2017. Pet'r's Ex. 16, ECF No. 54-1. Respondent replied on April 18, 2017 with a second report from Dr. MacGinnitie. Resp't's Ex. RR, ECF No. 58-1. On May 18, 2017, the undersigned scheduled a two-day entitlement hearing for September 21 and 22, 2017. Pre-Hearing Order, ECF No. 61. The parties submitted their pre-hearing briefs and outstanding medical literature over the ensuing months. ECF Nos. 66-82.

On September 18, 2017, Petitioner filed a Motion to Continue the Hearing for thirty days. Mot. Continuance, ECF No. 83. Petitioner requested this continuance in order to submit an expert report addressing an epidemiological study that examined "the occurrence of narcolepsy after the influenza vaccines used in the United States that contained the influenza A(H1N1)pdm09 virus strain" authored by Johnathan Duffy, MD, MPH, et alia. *See* Pet'r's Ex. 23; Jonathan Duffy et al., *Narcolepsy and influenza A(H1N1) pandemic 2009 vaccination in the United States*, 83 Neurology 1832 (2014) [hereinafter referred to as "Duffy"]. The study, Petitioner explained, was used by Special Master Corcoran in *McCollum*,[3] issued on September 15, 2017, to dismiss a case that also relied upon the theory of causation that Petitioner asserts here. *Id.* The undersigned granted the continuance and rescheduled the hearing to take place in Boston, Massachusetts from November 30 to December 1, 2017. Hearing Order, ECF No. 87. Petitioner submitted the expert report of Dr. Stanley Young and a supplemental report from Dr. Kinsbourne on October 24, 2017. Pet'r's Exs. 52, 53, ECF Nos. 89, 90. Respondent submitted a supplemental report from Dr. MacGinnitie on November 17, 2017. Resp't's Ex. WW, ECF No. 92. The undersigned held the entitlement hearing on the scheduled dates, and this matter is now ripe for a decision.

II. Factual Background

a. Medical Records

Petitioner's medical history prior to her receipt of the Fluzone vaccine includes complaints of abdominal pain, migraines, anxiety, hypertension, and neck pain. *See* Pet'r's Ex. 2 at 239-62. Petitioner was treated for these conditions by Dr. Cory Neumann, her primary care

[3] *McCollum v. Secretary of Health and Human Services*, No. 14-790V, 2017 WL 5386613 (Fed. Cl. Spec. Mstr. Sept. 15, 2017).

provider at Logansport Memorial Physicians' Office. *Id.* Petitioner also underwent neck and spine surgery following an accident while driving an all-terrain vehicle in October 2008. Pet'r's Ex. 2 at 24; Pet'r's Ex. 6 at 13, ECF No. 13-1. Following this accident, Petitioner suffered from chronic neck pain and was prescribed hydrocodone[4] for pain management. *See generally* Pet'r's Ex. 2. Petitioner was also prescribed metoprolol[5] and triamterene[6] for her hypertension and Zoloft for anxiety. Pet'r's Ex. 2 at 236-44. Petitioner began taking Imitrex[7] on March 29, 2010 to treat her migraines. Pet'r's Ex. 2 at 17.

Petitioner received the seasonal flu vaccine Fluzone on November 7, 2012. Pet'r's Ex. 2 at 118, 237; *see also* Pet'r's Ex. 7 at 6, ECF No. 16-1 (VAERS Report). On that date, Petitioner visited Dr. Neumann with complaints of neck pain, anxiety, and hypertension. Pet'r's Ex. 2 at 236. Petitioner stated that she needed stronger pain medicine for her neck pain. *Id.* Dr. Neumann recorded that Petitioner's anxiety waxed and waned, but that this change would be expected due to the multiple stressors in Petitioner's home. *Id.* Dr. Neumann increased Petitioner's hydrocodone prescription for her neck pain, and re-filled her Zoloft prescription. *Id.* at 237.

On December 4, 2012, Petitioner visited Dr. Neumann's office for "complaints of worsening fatigue." Pet'r's Ex. 2 at 232. Petitioner saw Tara Hughes, a nurse practitioner, and reported tiredness upon waking, despite sleeping for six to eight hours the previous night. *Id.* Petitioner noted to Ms. Hughes that she had to pull over on her way to work that day and sleep in the car because "[s]he feels like she can't keep her eyes open." *Id.* Petitioner also complained of some chest pain. *Id.* Ms. Hughes had Petitioner stop the metoprolol, and check back in two to three days. *Id.* at 234.

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[4] Petitioner was prescribed the brand-name medication Lortab, containing hydrocodone and acetaminophen, for her neck pain. *See generally* Pet'r's Ex. 2. Her medical records refer to both Lortab and Hydrocodone for this medication. *See id.* Unless specified in the record as "Lortab," the undersigned will refer to this medication as Hydrocodone.

[5] Metoprolol succinate, sold under the brand name Toprol XL, is used for the treatment of hypertension, chest pain, and heart failure. AstraZeneca LP, *Toprol-XL Medicine Label* (2014), https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=019962. Side effects of Metoprolol include dizziness/vertigo, bradycardia (abnormally slow heart action), and hypotension. *Id.* at 6.

[6] Triamterene and hydrochlorothiazide, sold under the brand name Dyazide, is used to treat hypertension and edema. GlaxoSmithKline, *Dyazide Medicine Label* (2011), https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=016042. Triamterene can be used in conjunction with other antihypertension medications for treatment, and pertinent side effects include hypersensitivity, postural hypotension, kidney stones, weakness, fatigue, dizziness, paresthesias, and vertigo. *See generally id.*

[7] Imitrex is a serotonin receptor agonist used to treat migraines in adults. GlaxoSmithKline, *Imitrex Medicine Label* (2017), https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=020132. Side effects of Imitrex include paresthesia, warm/cold sensations, sensations of pain/pressure/tightness/heaviness in the jaw or chest, vertigo and malaise/fatigue. *Id.* at 1.

On January 11, 2013, Petitioner returned to Dr. Neumann to follow up on her complaints of fatigue. Pet'r's Ex. 2 at 229. Petitioner reported that she wakes up "not rested" in the morning and has had to "pull over when she's driving because she's so drowsy." *Id.* Dr. Neumann wrote that a sleep study may be needed to determine the cause of Petitioner's drowsiness. *Id.* Dr. Neumann also reported that there is a "significant amount of stress in [Petitioner's] life which she may or may not recognize." *Id.* Dr. Neumann ordered a sleep study for Petitioner, advised her to stop taking Zoloft, and prescribed Lexapro for Petitioner's anxiety. *Id.* at 230. Dr. Theodore Nukes performed the sleep study at the Logansport Memorial Hospital on January 29, 2013. *Id.* at 144. Dr. Nukes noted that Petitioner's current medications included Zoloft, Lortab, triamterene, and a vitamin D supplement. *Id.* The study revealed "moderate mild to moderate obstructive sleep apnea ("OSA")." *Id.* at 144.

On April 17, 2013, Petitioner presented at Dr. Neumann's office for a two-month follow-up. Pet'r's Ex. 2 at 225. Petitioner requested to switch her migraine medication due to the cost, and Dr. Neumann noted that Petitioner's migraines "are really not any better." *Id.* Dr. Neumann also wrote that Petitioner "also has a lot of stress at home with both the mother and mother-in-law at home." *Id.*

On August 29, 2013, Petitioner saw Dr. Neumann to discuss her drowsiness "over the last couple days," and an "episode" that happened the day before. Pet'r's Ex. 2 at 220. Petitioner stated that she "passed out yesterday" while driving and "almost hit a telephone pole." *Id.* Petitioner also said that she has had "staring episodes." *Id.* Petitioner told Dr. Neumann that she has never had any seizures or "shaking activity." *Id.* Dr. Neumann recorded that Petitioner was supposed to see a neurologist six months ago, but "she seemed to improve" and did not visit a neurologist. *Id.* Under "Assessments," Dr. Neumann labeled Petitioner's diagnoses as syncope and seizure. *Id.* at 221. Dr. Neumann ordered labs, and referred Petitioner to Dr. Virginia Hemelt for neurology. *Id.*

Petitioner saw Dr. Virginia Hemelt on September 10, 2013 for "black outs." Pet'r's Ex. 6 at 13. Dr. Hemelt recorded that Petitioner's symptoms began "around January 2008 [when] she was falling asleep while driving." *Id.* Petitioner described an episode to Dr. Hemelt that occurred "[a] few months ago, [while Petitioner] was driving home around 4-5 [PM] from work." *Id.* Petitioner stated that she lost consciousness and realized when she awoke that the car was "still moving, and she was in the ditch moving toward a telephone pole." *Id.* Petitioner stated that she was able to avoid the pole, but that she had experienced staring episodes the next day. *Id.* Petitioner described vivid dreams and "episodes when her legs have given out." *Id.* Petitioner's husband described to Dr. Hemelt "periods of time when [Petitioner] acts differently." *Id.* He stated that these periods occurred "while golfing, shopping, and watching TV." *Id.* Petitioner's husband continued that "[t]here have been times when she is confused and cannot follow a football game[,] which is a passion for her." *Id.*

Dr. Hemelt recorded that Petitioner is a district manager for Frito-Lay and travels for her job. *Id.* Dr. Hemelt found that Petitioner's "[e]pisodes of altered awareness [are] likely due to disordered sleep and maybe medication effect from topiramate [Topamax]." *Id.* at 15. Dr. Hemelt also wrote in Petitioner's record that "[t]here is also [a] non-physiologic component of

her exam, which may be benign embellishment." *Id.* Dr. Hemelt did not rule out that Petitioner's sleep disorders could be due to snoring and mild OSA, "or a combination of those and narcolepsy." *Id.* Dr. Hemelt recommended for Petitioner to undergo a polysomnograph[8] and Multiple Sleep Latency Test[9] ("MSLT"), and recommended to taper off of Topamax. *Id.* Dr. Hemelt continued Petitioner's prescription for Lexapro. *Id.*

On September 12, 2013, Petitioner saw Dr. Kraft in the Logansport Memorial Hospital Emergency Department. Pet'r's Ex. 2 at 128. Petitioner went to the emergency room following "[two] trance-like seizures" she had earlier that day for approximately three minutes each. *Id.* Petitioner reported that her first "seizure" occurred two weeks prior. *Id.* Dr. Kraft ordered a CT scan of Petitioner's head, which returned normal. *Id.* at 129; Pet'r's Ex. 6 at 11. Dr. Kraft gave Petitioner a prescription for lorazepam,[10] increased her Topamax prescription, and advised Petitioner to call Dr. Hemelt's office tomorrow to "expedite the needed work-up for seizures." Pet'r's Ex. 2 at 129-30. Petitioner was discharged the same day. *Id.* at 129.

On September 13, 2013, Petitioner underwent a polysomnograph after a referral from Dr. Hemelt. Pet'r's Ex. 3 at 2; Pet'r's Ex. 6 at 4, ECF No. 13-1. The polysomnograph report noted that Petitioner was taking hydrocodone, Nasonex, Symbicort, Lexapro, Topamax, and lorazepam at the time. Pet'r's Ex. 3 at 2. The study revealed a diagnosis of mild sleep apnea and possible restless legs syndrome. *Id.* Nasal CPAP therapy was indicated, along with further evaluation "by means of a formal sleep medicine consultation . . . ." *Id.* Petitioner had a sleep onset latency of 7.8 minutes, with REM latency of 151 minutes. *Id.*

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[8] A polysomnograph is a sleep study used to monitor a patient's sleep throughout a night. *Mosby's Manual of Diagnostic and Laboratory Tests* 1124 (5th ed. 2014) [hereinafter "*Mosby's*"]. "This more simplified test includes the electrocardiogram (EKG), chest impedance, airflow monitor, and [oxygen] oximetry . . . . Under audiovisual monitoring the patient is placed in a comfortable room and sleeps." *Id.* During sleep, physicians gather data; "[t]he various stages of sleep architecture are determined by the EEG [electroencephalogram], and the physiologic changes during each stage are documented." *Id.*

[9] An MSLT takes place during the day after a polysomnograph. *Mosby's* 1124. "The MSLT is a measure of the patient's ability to sleep during a series of structured naps." *Id.* This test, along with the multiple wake test, is used "to diagnose narcolepsy that follows a night of inadequate sleep." *Id.* at 1125. During an MSLT, the patient is asked to nap "about every 2 hours throughout the testing period." *Id.* at 1126. Each nap is terminated after twenty minutes, and a diagnosis of narcolepsy can be made by measuring how quickly a patient enters rapid eye movement sleep during these naps. *Id.* at 1125-26.

[10] Lorazepam, sold under the brand name Ativan, is an antianxiety medication that "has a tranquilizing action on the central nervous system with no appreciable effect on the respiratory or cardiovascular systems." Valeant Pharms. North America LLC, *Ativan Medication Guide* (2016), https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=017794. Side effects include sedation, weakness, dizziness, and unsteadiness. *Id.* at 10.

The next day, Petitioner underwent an MSLT. Pet'r's Ex. 6 at 5. The test revealed that Petitioner "experienced a rapid sleep onset with each of the [five] [n]aps." *Id.* Additionally, Petitioner entered rapid eye movement ("REM") sleep in two of the five naps, and "[f]ocal [s]eizure-like activity was noted prior to the first [n]ap and prior to [n]ap 4." *Id.* The report also noted that Petitioner "took her lorazepam following the first [n]ap." *Id.* Ultimately, the "findings [from Petitioner's test] are consistent with narcolepsy," and "idiopathic CNS [central nervous system] hypersomnolence is less likely to explain the findings seen here." *Id.* The report also noted that "[c]hronic partial sleep deprivation by itself would be insufficient to explain these findings." *Id.*

On September 17, 2013, Petitioner underwent an electroencephalograph[11] ("EEG"), which showed no epileptiform activity. "In particular," the study emphasized, "there was no epileptiform correlation with the clinical event described by patient and husband." Pet'r's Ex. 2 at 141. On September 19, 2013, Dr. Hemelt prescribed ten milligrams ("mgs") of Ritalin[12] twice a day in light of Petitioner's narcolepsy diagnosis. Pet'r's Ex. 6 at 17.

Petitioner returned to Dr. Neumann on September 30, 2013. Pet'r's Ex. 2 at 218. Dr. Neumann recorded Petitioner's recent diagnosis of narcolepsy and that she "is doing a little better on the Ritalin." *Id.* Dr. Neumann wrote in his notes that Petitioner informed him that she "did some research and discovered that there is a link between the H1N1 flu vaccine and narcolepsy." *Id.* "It is not something I have heard or encountered before[,]" Dr. Neumann wrote, but "if that's the case we'll probably need to report her to the CDC." *Id.* Petitioner was not driving at the time of the appointment, and Dr. Neumann advised her to continue her medications. *Id.* at 218-19.

Petitioner returned to Dr. Hemelt on October 17, 2013. Pet'r's Ex. 6 at 17. Dr. Hemelt noted that Petitioner indicates "symptoms started after a flu immunization in the fall of 2012." *Id.* Petitioner also complained to Dr. Hemelt of recurring headaches, happening "almost everyday." *Id.* Dr. Hemelt wrote that her symptoms and sleep tests "are consistent with narcolepsy," but Dr. Hemelt was "unaware of an association with flu vaccine at this time." *Id.* at 19. Dr. Hemelt noted some improvement for Petitioner with "alerting medication," but added Xyrem[13] at bedtime and counseled for Petitioner to continue her other medications. *Id.*

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[11] EEGs are used to "identify and evaluate patients with seizures." *Mosby's* 549. During an EEG, "electrodes are placed on the scalp overlying multiple areas of the brain to detect and record electrical impulses within the brain." *Id.* at 550.

[12] Ritalin is a central nervous system stimulant used to treat attention deficit disorders and narcolepsy. Novartis Pharms. Co., *Ritalin Medication Guide* (2017), https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=010187. Common side effects include headache, stomach ache, trouble sleeping, nausea, decreased appetite, and nervousness. *Id.* at 13. More serious side effects include stroke, heart attack, hypertension, and elevated heart rate. *Id.* at 14.

[13] Xyrem is a "central nervous system depressant" used to treat cataplexy in narcolepsy and excessive daytime sleepiness in narcolepsy. Jazz Pharm., Inc., *Xyrem Medication Guide* (2015), https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=021196. The most common side effects include nausea, dizziness, vomiting, bedwetting, and

On November 11, 2013, Petitioner visited Dr. Neumann. Pet'r's Ex. 2 at 215. Petitioner "seem[ed] to be doing a little bit better[,] but is frustrated that she is not driving yet." *Id.* The next day, Petitioner returned to Dr. Hemelt for a follow-up. Pet'r's Ex. 6 at 21. During the November 11, 2013 appointment, Petitioner stated that the double vision had improved since the medication change and that her narcolepsy symptoms "are much better." *Id.* Dr. Hemelt released Petitioner to drive and advised her to continue her medication. *Id.*

Petitioner began treatment with neurologist Dr. Samiullah Kundi on February 27, 2014, with a review of medical history and current medication refill. Pet'r's Ex. 4 at 31, ECF No. 6-3. One month later, on March 20, 2014, Petitioner returned to Dr. Kundi's office, complaining "of worsening sleepiness and excessive daytime sleepiness" and "spells when she has loss of awareness for a few seconds." Pet'r's Ex. 4 at 29. Petitioner reported that she has had "three to four" of these "spells" since her last appointment with Dr. Kundi. *Id.* Dr. Kundi recommended to continue Petitioner's Xyrem and increased her Ritalin prescription to ten mgs. *Id.* at 31. Dr. Kundi also recommended an EEG test to "rule out epileptiform activity." *Id.* The EEG, performed on March 31, 2014, was negative for any indication of seizures. Pet'r's Ex. 4 at 3, ECF No. 6-3.

On May 29, 2014, Petitioner visited Dr. Kundi for a neurological follow-up. Pet'r's Ex. 4 at 23. Dr. Kundi reported that Petitioner was tolerating the higher doses of Ritalin and Xyrem prescribed at their last appointment. *Id.* Dr. Kundi, however, wrote that "[Petitioner] did have a spell when she was in the restroom," where "she [dozed] off and hit against [sic] the back of her neck." *Id.* Petitioner reported neck pain since the incident. *Id.* Dr. Kundi ordered a CT scan on Petitioner's neck and ordered refills for her prescriptions. *Id.* at 24-25. The CT scan revealed Petitioner's previous spinal surgeries, but otherwise found "a normal postoperative spine." Pet'r's Ex. 4 at 5.

On July 24, 2014, Petitioner visited Dr. Kundi to continue her treatment for narcolepsy. Pet'r's Ex. 4 at 21. Dr. Kundi recorded that Petitioner described "two small spells of sleep paralysis without associated loss of consciousness or loss of awareness." *Id.* Otherwise, Petitioner reported that her symptoms had improved on Xyrem and Ritalin. *Id.* at 22. Dr. Kundi recommended for Petitioner to continue her medication and follow up in three months. *Id.*

On September 22, 2014, Petitioner visited Dr. Neumann. Pet'r's Ex. 2 at 200. Dr. Neumann wrote that, "[Petitioner] does have narcolepsy which from a point in time seems to be right after she got her flu vaccine . . . ." *Id.* Dr. Neumann advised Petitioner to continue her medications for narcolepsy and high cholesterol. *Id.* at 200-01.

Petitioner returned to Dr. Kundi on October 23, 2014. Pet'r's Ex. 4 at 18. Dr. Kundi noted that Petitioner's "symptomatic improvement" with her current doses of Ritalin and Xyrem had continued since her last appointment. *Id.* at 19. Dr. Kundi recommended for Petitioner to have a second sleep study to investigate her "[a]pneic episodes along with snoring" to determine

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diarrhea. *Id.* at 24. Serious side effects include breathing problems, including sleep apnea, and mental health problems. *Id.*

whether she has "underlying sleep apnea." *Id.* Dr. Kundi also told Petitioner to continue her medications and follow up in one month. *Id.* at 19-20.

On November 20, 2014, Petitioner returned to Dr. Kundi. Pet'r's Ex. 4 at 15. Dr. Kundi recorded that Petitioner was stable on Xyrem and Ritalin. *Id.* Petitioner reported no recent episodes of cataplexy. *Id.* at 16. Dr. Kundi noted that he was waiting for Petitioner to complete the additional sleep study to determine whether she has sleep apnea, but found Petitioner capable of driving. *Id.* at 16-17. Dr. Kundi recommended for Petitioner to continue her current medications and follow up in two months. *Id.* at 17.

On November 25, 2014, Petitioner returned to Dr. Neumann's office after falling and hitting her head on the floor. Pet'r's Ex. 2 at 195. Petitioner recounted that "4-5 days ago," she was sitting at the table after taking her evening medication. *Id.* She then awoke on the floor with a bloody nose. *Id.* Petitioner denied any amnesia, confusion, or light sensitivity. *Id.* The nurse practitioner on staff ordered a CT scan of Petitioner's head to see whether she had any head or facial injury.[14] *Id.* at 196.

On December 1, 2014, Petitioner underwent another polysomnograph at the behest of Dr. Kundi. Pet'r's Ex. 3 at 3. Dr. Jatla Sridhar performed the study at the Howard Specialty Hospital and recorded Petitioner's medications as Xyrem, Ritalin, and hydrocodone. *Id.* The study revealed moderate sleep apnea, and Dr. Sridhar suggested CPAP therapy, "especially given the severity of OSA." *Id.* Dr. Sridhar did not note any signs of restless legs syndrome and Petitioner was recommended to practice "cognitive and behavioral techniques to improve sleep continuity" due to "reduced sleep efficiency." *Id.* Petitioner had a sleep onset latency of 4.1 minutes, and REM latency of 104 minutes. *Id.* Three days later, on December 4, 2013, Petitioner was seen by an ophthalmologist after a referral by Dr. Hemelt. Pet'r's Ex. 6 at 12. Petitioner was diagnosed with "decompensated congenital 4th nerve palsy of the left eye," but the physician wrote that "conservative management would likely be beneficial for [Petitioner]." *Id.*

On January 30, 2015, Petitioner visited the neurologist Dr. Hassan Arif after a referral from Dr. Kundi. Pet'r's Ex. 4 at 13. Dr. Arif recorded that Petitioner's symptoms are "about the same" as when she last saw Dr. Kundi in November of 2014. *Id.* Petitioner complained of "daytime headaches and sometimes sleepiness." *Id.* Dr. Arif noted that Petitioner was taking Valium as well as Ritalin at that time. *Id.* Dr. Arif recommended for Petitioner to see a pulmonologist to determine whether she has OSA, continue her Xyrem, and to have a follow-up in two months. *Id.* at 14.

On March 10, 2015, Petitioner visited Dr. Francois Abi Fadel for sleep apnea. Pet'r's Ex. 8 at 2, ECF No. 18-1. Dr. Fadel noted that this was Petitioner's first appointment for her diagnosis of OSA. *Id.* Dr. Fadel counseled Petitioner on the use of her CPAP machine and told her to follow up in four weeks. *Id.* at 3.

[14] It does not appear that this CT scan is in the records Petitioner submitted to the Court.

Petitioner returned to Dr. Arif on April 3, 2015. Pet'r's Ex. 4 at 10. Petitioner reported that her symptoms had improved after she began using her CPAP machine. *Id.* Dr. Arif noted that Petitioner went to the hospital after she began CPAP therapy due to two consecutive days of heart palpitations. *Id.* Dr. Arif advised her to stop taking Ritalin, as her heart palpitations may be a side effect of the drug. *Id.* Dr. Arif noted that Petitioner was doing fine without any other side effects and her "symptoms of tiredness and sleepiness are much improved with the start of CPAP for obstructive sleep apnea." *Id.* at 11. Dr. Arif agreed with Petitioner that she could stop Xyrem to see "if she needs that medicine." *Id.*

Petitioner returned to see Dr. Fadel on April 21, 2015. Pet'r's Ex. 8 at 5. Dr. Fadel recorded that Petitioner was "overall doing well." *Id.* Although Petitioner "still has intermittent daytime sleepiness," Dr. Fadel wrote, recently she has had "no significant sudden onset [of] sleep or narcolepsy." *Id.* Dr. Fadel noted that Petitioner had stopped taking her Ritalin and Xyrem, and Petitioner reported that "her daytime fatigue and sleepiness had markedly improved." *Id.* at 5-6. After observing that Petitioner had "excellent compliance" with her CPAP therapy, Dr. Fadel scheduled a follow-up in six months. *Id.* at 5-6.

On July 31, 2015, Petitioner returned to see Dr. Arif. Pet'r's Ex. 8 at 12. Dr. Arif noted Petitioner's new diagnosis of carpal tunnel syndrome and recommended surgery. *Id.* at 12, 13. Dr. Arif wrote that Petitioner denied any new medical problems other than carpal tunnel syndrome, but complained of "some sleepiness and tiredness during the day." *Id.* Dr. Arif noted that Petitioner had previously discontinued her Xyrem and Ritalin due to palpitations, but is back on Xyrem due to a recurrence of her symptoms. *Id.* at 13. Dr. Arif wrote that he would consider Ritalin if there were no improvements in her symptoms and advised her to continue her Xyrem. *Id.*

On September 25, 2015, Petitioner again saw Dr. Arif. Pet'r's Ex. 8 at 9. Dr. Arif observed that Petitioner's "symptoms are not bothering her much," and that she is on Xyrem "twice nightly." *Id.* Dr. Arif noted that Petitioner's symptoms have improved with CPAP use, but she still complained of daytime tiredness. *Id.* at 10. Dr. Arif started Petitioner on extended-release Ritalin in the morning, and advised her to continue her other medications, including hydrocodone and Lexapro. *Id.*

On September 28, 2015, Dr. Neumann authored a letter on behalf of Petitioner, presumably for this case. Pet'r's Ex. 5, ECF No. 6-4. Dr. Neumann wrote that Petitioner "started having extreme fatigue and drowsiness with falling asleep while she was driving" shortly after her November 7, 2012 flu vaccine. *Id.* "Within four weeks," Dr. Neumann wrote, "[Petitioner] called complaining of fatigue which was the start of her complaints that ultimately was diagnosed as narcolepsy." *Id.* It was Dr. Neumann's opinion that "there is a significant time correlation concerning the flu shot, i.e. H1N1[,] and the onset of her symptoms." *Id.*

On November 13, 2015, Petitioner saw Dr. Arif for a follow-up regarding her "narcolepsy and headaches." Pet'r's Ex. 8 at 7. Petitioner described her symptoms as "about the same" since her appointment with Dr. Arif in September of 2015. *Id.* Petitioner complained of morning sleepiness and no improvement overall with her symptoms. *Id.* Dr. Arif wrote that Petitioner's symptoms had improved with Xyrem and Ritalin, but she had discontinued them

because she believed her symptoms were due to sleep apnea. *Id.* at 8. Dr. Arif advised Petitioner to start Ritalin in the morning for sleepiness and to continue with her Xyrem. *Id.* Petitioner was not cleared to drive at this appointment. *Id.*

On February 8, 2016, Petitioner returned to visit Dr. Neumann. Pet'r's Ex. 10 at 6; Pet'r's Ex. 15 at 1, ECF No. 53-1. Dr. Neumann observed that Petitioner's narcolepsy and sleep apnea were stable, and that she was using her CPAP machine nightly. *Id.* Petitioner complained of chronic neck pain and pain in her shoulder. *Id.* Dr. Neumann noted that her neck pain was due to a past injury, but that Petitioner could "not remember any injury" to explain her shoulder pain. *Id.* Petitioner told Dr. Neumann that the pain "has been worsening over the last few weeks." *Id.* Dr. Neumann ordered a lipid profile to check on Petitioner's cholesterol and an x-ray of Petitioner's shoulder. *Id.* at 7-8. Dr. Neumann counseled Petitioner to continue her medication. *Id.* at 8.

Petitioner visited Dr. Neumann on April 1, 2016 to discuss "paperwork." Pet'r's Ex. 10 at 1, ECF No. 22-1; Pet'r's Ex. 15 at 5, ECF No. 53-1. Dr. Neumann wrote in his notes that "[Petitioner] has been fighting with the government concerning vaccine compensation." *Id.* "Apparently," Dr. Neumann continued, "they recognize idiopathic hypersomnia but don't recognize narcolepsy as being caused by the vaccine. There is a fine line between these two diagnoses." *Id.* Dr. Neumann believed that "[Petitioner's] symptomatology definitely has a time frame correlation to that vaccine. I don't see how anyone could prove anything more conclusive." *Id.* He noted that Petitioner has neck pain, "but I don't believe this has anything to do with her hypersomnia." *Id.* He also noted Petitioner's previous diagnoses of OSA and high cholesterol. *Id.* He advised her to continue Lipitor for her cholesterol and recorded her depression as stable. *Id.* He counseled her to continue her medications. *Id.* at 2-3.

On April 25, 2016, Dr. Neumann wrote another letter on behalf of Petitioner. Pet'r's Ex. 9, ECF No. 21-1. He briefly summarized her medical history, and wrote that "[i]t has come to my attention that apparently narcolepsy is not recognized as a vaccine-related injury." *Id.* "However," Dr. Neumann continued, "idiopathic hypersomnolence is." *Id.* Dr. Neumann wrote that these disorders are difficult to distinguish, and "are also treated with the exact[ly] similar regimen." *Id.* Dr. Neumann opined that "there is an overwhelming causality from a time frame standpoint that the H1N1 was responsible for [Petitioner's] onset of symptoms." *Id.* This time frame "is especially significant," Dr. Neumann continued, "as she was not having any of these symptoms and had a very productive career prior to this." *Id.* Dr. Neumann concluded that "the preponderance of the evidence points to a causality from the H1N1 vaccine." *Id.*

Petitioner saw Dr. Fadel on April 28, 2016 for a follow-up for her sleep apnea. Pet'r's Ex. 15 at 8. Dr. Fadel noted that Petitioner was "overall doing well from OSA standpoint; however, [Petitioner is] still having narcolepsy and cataplexy events." *Id.* Dr. Fadel wrote that Petitioner had "excellent compliance" with her sleep apnea treatment regimen and recommended Petitioner return again in six months. *Id.* at 9.

Petitioner reported to Dr. Neumann on May 9, 2016. Pet'r's Ex. 15 at 11. Dr. Neumann noted that Petitioner was "doing reasonably on her current regimen." *Id.* Petitioner complained of neck pain, due to "an old accident," but Dr. Neumann recorded that "[t]he biggest issue is her

hypersomnolence." *Id.* Her condition "[a]ffects her life and she is unable to work," Dr. Neumann continued, "but she is functioning decently at the present time." *Id.* Dr. Neumann also observed that Petitioner's sleep apnea was stable at the appointment and recommended for Petitioner to continue her medications. *Id.* at 11-13.

On November 3, 2016, Petitioner returned to Dr. Fadel. *Id.* at 18. Dr. Fadel noted that Petitioner was "overall doing better since her medications [have] been changed to Xyrem and Nuvigil." *Id.* Dr. Fadel diagnosed Petitioner with post-nasal drip, OSA, and narcolepsy with cataplexy and advised her to continue her medications and CPAP machine use. *Id.* at 19.

On December 14, 2016, a genetic test revealed that Petitioner possesses the gene associated with narcolepsy, HLA DQB1*06:02. Pet'r's Ex. 13 at 2, ECF No. 42-1; Pet'r's Ex. 14 at 1, ECF No. 43-1. Petitioner saw Dr. Neumann for a follow-up appointment on December 28, 2016. *Id.* at 21. Dr. Neumann noted Petitioner's history of narcolepsy with cataplexy, OSA, neck pain, and high cholesterol. *Id.* Petitioner will be temporarily moving to Wisconsin, Dr. Neumann wrote, but her conditions are stable. *Id.* at 21-22.

On June 13, 2017, Dr. Hemelt authored a letter, stating that Petitioner's diagnosis of narcolepsy with cataplexy was confirmed by an overnight polysomnogram in 2013. Pet'r's Ex. 17 at 2, ECF No. 67-1.

On August 29, 2017, Petitioner was granted Social Security disability benefits due to her previous diagnoses of narcolepsy with cataplexy. *See generally* Pet'r's Ex. 49, ECF No. 85-1.

III. Expert Reports

a. Petitioner's Expert, Dr. Marcel Kinsbourne

Dr. Kinsbourne received his medical degree at Oxford University in England and is board certified in pediatrics. Kinsbourne Curriculum Vitae ("Kinsbourne CV") 1-2, ECF 80-1. He first became licensed in 1955 in the United Kingdom and subsequently obtained medical licenses in North Carolina, Massachusetts, and Virginia. *Id.* at 2. From 1955 to 1964, Dr. Kinsbourne held a series of postdoctoral positions in pediatrics and neurology in hospitals in England, with one year of residency in pediatrics at Bellevue Hospital in New York. *Id.* at 1. His clinical experience includes a stint as a senior staff physician in the Hospital for Sick Children in Toronto, Ontario from 1974 to 1980, and as a clinical associate in neurology at Massachusetts General Hospital from 1981 to 1991. *Id.* at 2-3. Dr. Kinsbourne has also held a series of academic positions in pediatrics, neurology, and psychology in various universities throughout his years of practice. *Id.* at 2-3. Despite Dr. Kinsbourne's exceptional credentials, other cases in the Vaccine Program have noted that it has been many years since Dr. Kinsbourne has regularly seen patients. *See, e.g.*, *McCullom v. Sec'y of Health & Human Servs.*, No.14-790V, 2017 WL 5386613, at *6 (Fed. Cl. Spec. Mstr. Sept. 15, 2017) (citing *Pope v. Sec'y of Health & Human Servs.*, No. 14-078V, 2017 WL 2460503, at *8 (Fed. Cl. Spec. Mstr. May 1, 2017)). Dr. Kinsbourne is qualified to speak as an expert in neurology, although he does not have any specific expertise in narcolepsy besides his previous work in the Vaccine Program. *See*

generally id. Dr. Kinsbourne submitted one expert report and two supplemental reports in this case. Pet'r's Exs. 12, 16, 53.

In his first report, Dr. Kinsbourne proposed that Petitioner developed narcolepsy as a result of an autoimmune reaction to the flu vaccine Petitioner received on November 7, 2012. Pet'r's Ex. 12 at 7-8. Dr. Kinsbourne placed the onset of Petitioner's condition in early December of 2012, "less than four weeks" after her vaccination. *Id.* at 3. Dr. Kinsbourne explained that narcolepsy is a condition marked by a "deficient ability to maintain vigilan[t] states." *Id.* at 4. He wrote that narcoleptics "have daily periods of abnormal sleepiness, even when fully engaged in activities," and "the need to sleep is overwhelming and insurmountable." *Id.* Dr. Kinsbourne explained that, in normal sleep patterns, REM sleep begins "some one-and-a-half hours" after an individual falls asleep. *Id.* In narcoleptics, Dr. Kinsbourne continued, REM sleep can begin "within less than five minutes of sleep onset." *Id.*

Dr. Kinsbourne noted Petitioner's case also included a diagnosis of narcolepsy with cataplexy. *Id.* Cataplexy, Dr. Kinsbourne explained, "refers to the sudden onset of weakness of postural muscle tone, usually brought on by strong emotions, notably when expressed in laughter or anger." *Id.* These episodes are marked by a person's head dropping or a complete collapse "during which individuals are unable to move, speak, or keep their eyes open." *Id.* Dr. Kinsbourne wrote these periods "may last no longer than 30 seconds or up to 10 minutes." *Id.* Cataplectic episodes are differentiated from most seizure disorders, Dr. Kinsbourne wrote, because the individual suffering from a cataplectic attack remains fully conscious for the duration of the episode. *Id.*

Dr. Kinsbourne explained that the clinical diagnosis of narcolepsy can be verified by polysomnography or by "finding a low or undetectable level of neuropeptide [h]ypocretin in the cerebrospinal fluid." *Id.* Dr. Kinsbourne cited the criteria for narcolepsy with cataplexy as put forward by the International Classification of Sleep Disorders to confirm Petitioner's diagnosis. *Id.* at 4-5. Petitioner meets two diagnostic criteria for narcolepsy, Dr. Kinsbourne explained: 1) "The patient has daily periods of irrepressible needs to sleep or daytime lapses into sleep, occurring for at least 3 months, [and] 2) The presence of one or both of the following: cataplexy and a mean sleep latency of at most [eight] minutes and [two] or more sleep onset REM periods . . . or an MSLT (multiple sleep latency test) performed according to standard techniques."[15] *Id.* at 4-5.

Dr. Kinsbourne wrote that narcolepsy has a natural prevalence of two-five cases in 100,000 people. *Id.* at 5. However, Dr. Kinsbourne highlighted that several epidemiological studies show a "significant increase" in narcolepsy cases following both the 2009 H1N1 winter flu pandemic in China and the widespread administration of the pandemic H1N1 flu vaccine Pandemrix throughout Europe from 2008 to 2010. *Id.* at 5. An article published by Han et al., found it to be a "[three]-fold increase in narcolepsy onset following the 2009 . . . pandemic."

[15] Dr. Kinsbourne did not attest that Petitioner meets the second diagnostic criteria, as it requires a measurement of the subject's hypocretin-1 concentration in the spinal fluid, a test which is no longer done for diagnostic purposes in the United States. *See* Pet'r's Ex. 12 at 5; *see also* Tr. 270-71.

Pet'r's Ex. 24 at 1; Fang Han et al., *Narcolepsy Onset is Seasons and Increased following the 2009 H1N1 Pandemic in China*, 70 Annals Neurology 410, 410 (2011). Dr. Kinsbourne also discussed a study done in Sweden that found "within three months of Pandemrix vaccination, the incidence of new onset narcolepsy was 14.1/100,000, as compared to 1.3/100,000 [with no vaccination]." Pet'r's Ex. 12 at 5. Although Dr. Kinsbourne used these studies to support his theory relating Fluzone to narcolepsy, he conceded that "[t]here is no published formal epidemiological study of association of H1N1 vaccines and narcolepsy in the U.S." *Id.* at 6. Dr. Kinsbourne also discussed the Duffy study and characterized it as an "ecological study" that represented a "retrospective review of electronic healthcare databases of nine health maintenance organizations in the Vaccine Safety Link." *Id.* Dr. Kinsbourne found that "[t]he outcome of the safety review by Duffy et al. (2014) was not definitive." *Id.*

As for the mechanism behind narcolepsy, Dr. Kinsbourne explained that narcoleptics are deficient in the neuropeptide hypocretin (also known as orexin), which controls wakefulness. *Id.* at 6-7. He stated that hypocretin-secreting neurons project from the hypothalamus throughout the central nervous system "to neurons involved in the regulation of feeding, sleep-wakefulness, neuroendocrine homeostasis and autonomic regulation." *Id.* (citing Josh Mahlios et al., *The Autoimmune Basis of Narcolepsy*, 23 Current Op. Neurobiology 767, 767 (2013)). The excitatory action of hypocretin is counter-balanced, Dr. Kinsbourne continued, by other neurotransmitters released by the hypothalamus, GABA and galanin. *Id.* at 6-7. Thus, "[w]ake-promoting and sleep-promoting loci in separate regions of the hypothalamus inhibit each other" and the "inactivation of either system leaves the other in relative control, resulting either in insomnia or in narcolepsy." *Id.* at 6-7.

After describing what occurs when an individual suffers from narcolepsy, Dr. Kinsbourne opined that the loss of hypocretin in narcolepsy "appears to be a consequence of a destructive autoimmune attack." *Id.* at 7. Dr. Kinsbourne asserted that this autoimmune reaction is caused by the immune system's CD4+ T cells attacking hypocretin molecules. *Id.* He stated that there is a "double- or two-hit mechanism at work" that creates T cells that target hypocretin. *Id.* The first mechanism is a genetic susceptibility found in "almost all" narcoleptic patients with low hypocretin. *Id.* In this population, researchers found a specific, genetic immune system marker, the Human Leucocyte Antigen ("HLA") DR2/DQW1.[16] *Id.* The second mechanism that Dr. Kinsbourne described is "the provocative infection or vaccination that transforms [genetic susceptibility] into the clinical reality of a case of narcolepsy." *Id.* This infection or vaccination, Dr. Kinsbourne explained, causes HLA molecules to present antigens that cause T cells to recognize hypocretin as an "invader." *Id.*

Dr. Kinsbourne cited to an article by De La Herrán-Arita et al., for the proposition that the immune system targets hypocretin due to "molecular mimicry between epitopes of [h]ypocretin and the influenza hemagglutinin surface protein." *Id.* (citing to Alberto K. De la Herrán-Arita et al., *CD4+ T Cell Autoimmunity to Hypocretin/Orexin and Cross-Reactivity to a 2009 H1N1 Influenza A Epitope in Narcolepsy*, 5 Sci. Translational Med. 1 (2013) [hereinafter referred to as "De La Herrán-Arita"]). De La Herrán-Arita "reported the presence of CD4+ T cells that are reactive to [h]ypocretin in patients with narcolepsy." *Id.* at 8. Dr. Kinsbourne

[16] HLA alleles "present antigens to T cells." Pet'r's Ex. 12 at 7.

conceded that the exact component of the hypocretin neurons that cross-reacts with the influenza virus is unknown, and that "cross-reactivity between the hemagglutinin moiety of the H1N1 influenza . . . and a component peptide of the [h]ypocretin molecule has been suggested but not yet been conclusively demonstrated." *Id.*

Finally, Dr. Kinsbourne addressed several studies that contemplate whether the adjuvant present in the Pandemrix vaccine is the cause of some patients developing narcolepsy. *Id.* at 8. Dr. Kinsbourne argued that the AS03 adjuvant found in Pandemrix "maximizes existing population of CD4+ T cells," which then causes an enhanced immune reaction that "stimulates the production of hypocretin-specific CD4+ cells." *Id.* In this way, Dr. Kinsbourne argued, the adjuvants do not cause the autoimmune reaction by way of molecular mimicry, but instead enhances it. *Id.* Indeed, Dr. Kinsbourne wrote, "[t]his may explain why the incidence of post-vaccination onset of narcolepsy is more easily demonstrated in populations exposed to this variant of the H1N1 vaccine." *Id.* Dr. Kinsbourne concluded that the H1N1 virus itself triggers the autoimmune response that causes narcolepsy, rather than the vaccine's adjuvant. *Id.* He concedes that adjuvanted influenza vaccines have never been administered in the United States, and Petitioner did not receive an adjuvanted flu vaccine. *Id.*

b. Respondent's Expert, Dr. Thomas Scammell

Dr. Thomas Scammell submitted one expert report in this case. Resp't's Ex. A. Dr. Scammell is currently a Professor of Neurology at Beth Israel Deaconess Medical Center, Boston Children's Hospital, and Harvard Medical School. *Id.* at 1. He is board-certified in neurology, psychiatry, and sleep medicine. *Id.* For the last twenty years, he has practiced as a neurologist, a clinical and basic researcher in sleep medicine, and a lecturer on narcolepsy and the neurobiology of sleep and wakefulness. *Id.* He was a member of the International Classification of Sleep Disorders, and in that role, "helped develop the current consensus definitions of narcolepsy." *Id.* at 1-2. Dr. Scammell has also authored "over [one hundred] publications, mostly focused on narcolepsy and sleep disorders," and currently cares "for about [sixty] patients with narcolepsy." *Id.* at 1. Dr. Scammell estimates that he has treated over one hundred patients with narcolepsy over the course of his career. *Id.*

Dr. Scammell primarily raised concerns in his expert report regarding Petitioner's diagnosis. *Id.* at 5. Dr. Scammell also disputed Dr. Kinsbourne's contention that the Fluzone vaccine caused Petitioner's narcolepsy and argued that neither the medical literature, nor the clinical record, support Dr. Kinsbourne's argument. *Id.*

First, Dr. Scammell wrote that "[he] is not convinced" of Petitioner's diagnosis of narcolepsy with cataplexy. *Id.* Dr. Scammell explained that "one must consider" Petitioner's symptoms of cataplexy in order to determine whether Petitioner has narcolepsy type one ("NT1") or narcolepsy type two ("NT2"). *Id.* at 5. NT1 is defined as "symptoms of chronic sleepiness plus cataplexy, with a MSLT showing a sleep latency less than [eight] minutes and REM sleep in [two] or more of the daytime naps." *Id.* Alternatively, Dr. Scammell noted, "NT1 can be diagnosed by the combination of chronic sleepiness and low levels of hypocretin-1 in cerebrospinal fluid." *Id.*

Cataplexy, Dr. Scammell explained, consists of "brief periods of partial or complete muscle weakness, almost always triggered by strong, usually positive emotions." *Id.* Dr. Scammell described a typical cataplectic episode as the patient's speech becoming slurred, eyelids closing, and the head lolling forward. *Id.* In a severe attack, "the patient may develop widespread weakness, causing them to collapse to the ground." *Id.* Dr. Scammell wrote that a person suffering such an attack may be "unable to move for [one to two] minutes." *Id.* Dr. Scammell opined that Petitioner's episodes are "atypical" in both duration and character. *Id.* at 6.

Dr. Scammell indicated that Petitioner's self-described cataplectic episodes lasted up to twenty minutes, which is much longer than the typical cataplectic attack that lasts one-two minutes. *Id.* Additionally, Dr. Scammell explained that cataplexy is "almost always triggered by strong emotions;" however, the written record does not mention "any clear emotional triggers" for Petitioner. *Id.* Petitioner also stated that she stares during her episodes. *Id.* Dr. Scammell noted that staring is "quite unusual" for cataplexy, as an individual's eyes "are generally closed due to facial weakness." *Id.* Dr. Scammell commented on Petitioner's husband's testimony that someone always must be by Petitioner's side "to ensure her safety." *Id.* Dr. Scammell explained that throughout his practice treating narcolepsy, he has never "encountered this degree of dependence due simply to narcolepsy." *Id.* Dr. Scammell wrote that Petitioner's description of being tired and crying after an episode is also highly unusual, as in most cases "people usually regain full muscle power and resume their activities . . . ." *Id.* Dr. Scammell opined that Petitioner's episodes could be "pseudo-cataplexy[,] episodes of subjective weakness related to psychological factors." *Id.* Notwithstanding Dr. Scammell's written analysis contrasting Petitioner's symptoms with a more common manifestation of narcolepsy with cataplexy, ultimately the expert hesitated to confirm or reject her diagnosis without speaking with or examining Petitioner himself. *Id.*

If Petitioner does not have cataplexy, Dr. Scammell wrote, "one must consider the possibility of NT2." *Id.* at 7. NT2, Dr. Scammell explained, "is defined as chronic sleepiness with a MSLT showing a sleep latency less than [eight] minutes and REM sleep in [two] or more of the daytime naps." *Id.* A diagnosis of NT2 relies "strongly on the MSLT," but as Dr. Scammell explained, there is evidence in the medical record that Petitioner's MSLT was not performed per American Academy of Sleep Medicine guidelines. *Id.* These guidelines mandate that patients must be off "relevant psychoactive medications, . . . and concomitant sleep disorders . . . [and] must first be treated to minimize external factors that could produce a false-positive MSLT." *Id.* According to Petitioner's medical records, she was taking Lexapro, Topamax, and lorazepam during her MSLT performed on September 14, 2013. *Id.* Dr. Scammell explained that these medications are sedating and can affect REM sleep. *Id.* Dr. Scammell continued that Petitioner also had other medical issues that can cause sleepiness, including sleep apnea and depression. *Id.* In support that Petitioner's sleepiness may not be solely caused by narcolepsy, Dr. Scammell emphasized that Petitioner's sleepiness improved with the use of a CPAP machine that was prescribed for her sleep apnea. *Id.* Dr. Scammell further noted that Petitioner once "spent two weeks in bed," and such a lengthy stay in bed "is more consistent with depression." *Id.* at 8.

Dr. Scammell observed that "[s]ome other [of Petitioner's] clinical features are consistent with narcolepsy but not of much help diagnostically." *Id.* These include Petitioner's positive test for the narcolepsy genetic marker, HLA DQB1*06:02. *Id.* Dr. Scammell cautioned that although the gene is found in 90% of patients with NT1 and about 50% of patients with NT2, "it is also found in 12-25% of the general population . . . ." *Id.* This occurrence in the general population, Dr. Scammell wrote, makes a positive test "of little diagnostic usefulness." *Id.*

Dr. Scammell then addressed Dr. Kinsbourne's opinion that Petitioner's narcolepsy was caused by her Fluzone vaccination. *Id.* at 9. Dr. Scammell agreed with Dr. Kinsbourne that there was an associated increase in narcolepsy cases following the use of the Pandemrix vaccination. *Id.* However, Dr. Scammell emphasized, "the great majority of patients who developed narcolepsy were under the age of [twenty] years, the increased risk in adults was only [two to four] fold, and even with this vaccine, there was no increase in narcolepsy among adults over age [forty]." *Id.* In addition, the increased rate of narcolepsy was associated with Pandemrix, but not the two other flu vaccines used in the same year, Arepanrix and Focetria. *Id.* Dr. Scammell concluded that the increased rate with respect to Pandemrix is a result of "brand-specific differences in vaccine production." *Id.*

Dr. Scammell highlighted that the increase in new cases of narcolepsy was limited to the 2009-2010 flu season, and noted there were "no reports of narcolepsy associated with influenza vaccine in subsequent years." *Id.* at 10. Indeed, Dr. Scammell wrote that "[m]oderate evidence suggests that . . . infection with H1N1 influenza (not vaccination) was associated with an increase in new cases of narcolepsy in China" in the winter of 2009-2010, but "narcolepsy rates then returned to typical levels in subsequent years." *Id.* This "return to baseline" suggested to Dr. Scammell that "some factor specific to 2009-2010 H1N1 strain contributed to the development of narcolepsy." *Id.* Thus, for Dr. Scammell, the Fluzone vaccination Petitioner received for the 2012-2013 flu season, "should not trigger the development of narcolepsy." *Id.* Dr. Scammell then emphasized that Pandemrix was never used in the United States, and "there is no evidence that influenza vaccines used in the U.S. were associated with narcolepsy." *Id.*

Finally, Dr. Scammel emphasized that "[t]here is no direct evidence for a mechanism of molecular mimicry." *Id.* He noted Petitioner's expert discussed the De la Herrán-Arita article that suggests an autoimmune response could "harm the hypocretin neurons through a mechanism of molecular mimicry." *Id.* at 11. Dr. Scammell then immediately pointed out that Dr. Kinsbourne "failed to mention that the findings were retracted soon after publication." *Id.* As further evidence against vaccine causation, Dr. Scammell applied De la Herrán-Arita's finding to Petitioner and noted that "[e]ven with Pandemrix, there was no increase in narcolepsy among adults over age [forty]." *Id.* Therefore, "even if [Petitioner] had received Pandemrix," she was forty-four at the time of her vaccination and "her risk of developing narcolepsy would not be increased." *Id.* Dr. Scammell did concede that the interval between vaccination and onset of her condition "seems reasonable" given the onset of narcolepsy in European patients after Pandemrix vaccination. *Id.* Dr. Scammell concluded that, assuming Petitioner has narcolepsy, "the simplest explanation" was that her condition was caused by "factors other than Fluzone," such as a "common infection." *Id.*

c. Respondent's Expert, Dr. Andrew MacGinnitie

Dr. Andrew MacGinnitie submitted a total of three expert reports in this case. Respondent filed Dr. MacGinnitie's first report on February 8, 2017. Resp't's Ex. C. Dr. MacGinnitie is an attending physician and the Clinical Director for the Division of Immunology at Boston Children's Hospital, and a Professor of Pediatrics at Harvard Medical School. *Id.* at 1. Dr. MacGinnitie graduated from the University of Chicago Pritzker School of Medicine with an M.D. and a Ph.D. from the Department of Pathology. *Id.* Dr. MacGinnitie then completed a residency in pediatrics "primarily" at Boston Children's Hospital and Boston Medical Center. *Id.* at 1-2. He is board-certified in both allergy/immunology and pediatrics, and has been practicing as an allergist/immunologist for fifteen years. *Id.* at 2. He states that he sees "more than 1,500 patients annually" for a "variety of immunologic diseases[,] including reactions to vaccines." *Id.* He has provided expert testimony in the Vaccine Program since 2015 and wrote that this is the sixth case in which he has opined. *Id.*

Dr. MacGinnitie focused on Dr. Kinsbourne's argument that Petitioner's Fluzone vaccine caused her narcolepsy with cataplexy and asserted three main points in rebuttal. *Id.* at 3. First, he argued that there is no evidence linking seasonal influenza vaccinations to narcolepsy, and the 2009 increase in post-vaccination narcolepsy patients was most likely caused by the adjuvant present in that specific vaccine. *Id.* at 1. Second, Dr. MacGinnitie posited that there is strong epidemiological evidence showing "no increased risk with seasonal vaccination," and finally, he noted that Dr. Kinsbourne's theory of causation "relies primarily on an article that has been **retracted** and is therefore not reliable." *Id.* (emphasis in original).

Dr. MacGinnitie first explained that "all references cited by Dr. Kinsbourne [to show a connection between an influenza vaccination and narcolepsy] report on an association between adjuvanted influenza vaccines and narcolepsy." *Id.* at 8. An adjuvant, Dr. MacGinnitie continued, is a substance added to a vaccine in order to amplify the immune response, such as the "formulation of oil mixed in water" that was added to Pandemrix by the manufacturers. *Id.* Dr. MacGinnitie explains that adding an adjuvant can "elicit[] a response [measured by antibody titers] 3.5 to 10 times greater than non-adjuvanted vaccines." *Id.* at 8. Dr. MacGinnitie emphasized that the Fluzone vaccine received by Petitioner does not contain adjuvants and went on to state that no seasonal influenza vaccines used in the United States contain adjuvants. *Id.* at 5, 8. Therefore, the "most logical interpretation of the data on influenza vaccination and [narcolepsy] is that the increased risk is limited to adjuvanted subunit vaccines such as Pandemrix . . . . Other vaccines, including non-adjuvanted subunit vaccines such as Fluzone, are not associated with development of narcolepsy." *Id.* at 9.

In fact, Dr. MacGinnitie wrote, there exists "direct epidemiologic evidence [that] demonstrates no association between season influenza vaccination and narcolepsy." *Id.* at 8. Dr. MacGinnitie then cited to three studies that show this lack of an association. The first, Lee et al., did not find any link between non-adjuvanted pandemic and seasonal flu vaccines and narcolepsy through a database search containing over four million reports of adverse events. *Id.* (citing Resp't's Ex. PP; Grace M. Lee et al., *H1N1 Seasonal Influenza Vaccine Safety in the Vaccine Safety Datalink Project*, 41 Am. J. Preventative Med. 121 (2011)). Second, Choe et al., examined new diagnoses of narcolepsy in South Korea following an epidemic H1N1 vaccination

program wherein both adjuvanted and non-adjuvanted vaccines were used. *Id.* (citing Resp't's Ex. HH; Young June Choe et al., *No Association Between Influenza A(H1N1)pdm09 Vaccination and Narcolepsy in South Korea: An Ecological Study*, 30 Vaccine 7439 (2012)). Dr. MacGinnitie wrote that the study found no increases in narcolepsy rates, "and rates were actually higher prior to the vaccination program." *Id.* Last, Dr. MacGinnitie cited to the Duffy study to show that non-adjuvanted influenza vaccines are not associated with an increase in narcolepsy. *Id.* In their study, Duffy, "conducted a careful examination of new cases of narcolepsy utilizing the Vaccine Safety Datalink . . . for patient who received a pandemic H1N1 vaccine in 2009 and seasonal influenza vaccine during the 2010-2011 season." *Id.* Dr. MacGinnitie highlighted that forty-three percent of the patients who received the vaccine during the 2010-2011 season received the Fluzone vaccine. *Id.* Out of an expected rate of 4.35 new cases of narcolepsy (estimated as the underlying rate of new cases in the population), Duffy found no new cases of narcolepsy out of more than 439,000 patients. *Id.* Relatedly, out of "almost 741,000 vaccinated individuals receiving H1N1-containing seasonal influenza vaccine[s] in 2010-2011 there were [two] cases of narcolepsy, compared to an expected incidence of more than 7.5 cases." *Id.* "In summary," Dr. MacGinnitie wrote, "narcolepsy has been associated with adjuvanted influenza vaccines[,] which are known to produce very strong immune responses, but not with non-adjuvanted vaccines such as Fluzone." *Id.*

Dr. MacGinnitie concluded by finding that Dr. Kinsbourne's reliance upon the De la Herrán-Arita article for a theory of causation is misplaced, as the article was retracted by the authors. *Id.* at 1. Dr. Kinsbourne relied upon the De la Herrán-Arita study "as evidence that individual T cells can recognize both the hemagglutinin of H1N1 influenza and hypocretin." *Id.* at 4. The data produced by De la Herrán-Arita purported to support this hypothesis, but "certain experiments could not be reproduced and the paper was retracted." *Id.* at 6. Dr. MacGinnitie explained that in fact, copies of the data produced by the study "suggest[] that the paper was fraudulent a[nd] in several instances[,] duplicate images are shown as coming from different patients." *Id.* Although the official retraction "states that the authors were unable to replicate key findings," Dr. MacGinnitie continued, "presenting the same image as from different patients is fraud and indicates that the findings were almost certainly never accurate." *Id.* at 7. Dr. MacGinnitie does note, however, that the Ahmed study (2015),[17] suggests a link between Pandemrix and development of antibodies between hypocretin receptors, but added the caveat that the "article is quite limited in numbers and reports that a number of healthy controls also have such antibodies." *Id.*

d. Dr. Kinsbourne's Second Expert Report

Dr. Kinsbourne's second report was written largely in response to Dr. Scammell's report. Pet'r's Ex. 16. Dr. Kinsbourne raised three points in response to Dr. Scammell. *Id.* First, Dr. Kinsbourne wrote that he relies on Petitioner's treating physicians for Petitioner's diagnosis of narcolepsy with cataplexy and "the timing of its onset." *Id.* Second, Dr. Kinsbourne agreed with Dr. Scammell that narcolepsy was not the only cause of Petitioner's sleepiness. *Id.* Dr.

[17] Resp't's Ex. LL; Syed Sohail Ahmed et al., *Antibodies to Influenza Nucleoprotein Cross-React with Human Hypocretin Receptor 2*, 7 Sci. Translational Med. 1 (2015) [hereinafter referred to as Ahmed (2015)].

Kinsbourne noted that Petitioner also has sleep apnea. *Id.* Third, Dr. Kinsbourne put forward a new, "medically-reasonable mechanism by which a non-adjuvanted H1N1 containing vaccine, and specifically Fluzone, could have caused [Petitioner's] narcolepsy with cataplexy." *Id.* Although Dr. Kinsbourne did not address Dr. MacGinnitie's report and more specifically Dr. MacGinnitie's observation that the De la Herrán-Arita article was retracted due to fraud, Dr. Kinsbourne's new causation theory did not rely upon the De la Herrán-Arita article. *Id.* Instead, Dr. Kinsbourne explicated a mechanism by which the nucleoprotein in the influenza vaccine is the primary agent that causes an autoimmune reaction to induce narcolepsy.

Dr. Kinsbourne discussed Dr. Scammell's opinion that Pandemrix is associated with an increase in narcolepsy cases due to "brand specific differences in vaccine production." *Id.* at 1. These "brand specific" differences, Dr. Kinsbourne argued, include adjuvants and the amount of influenza nucleoprotein found within the vaccine. *Id.* at 1-2.

Dr. Kinsbourne first argued that it is the virus itself, not adjuvants, that causes narcolepsy following an influenza vaccination. *Id.* at 2. He posited that adjuvants "potentiate the adaptive immune response but they do not initiate it." *Id.* Dr. Kinsbourne argued that adjuvants "can also participate in instigating the autoimmune response[,] . . . [but] the higher risk of narcolepsy onset . . . is related to the viral component of vaccine." *Id.* (citing Pet'r's Ex. 41; Ji Hyun Song et al., *Narcolepsy: Association with H1N1 Infection and Vaccination*, 7 Sleep Med. Res. 43 (2016)). For Dr. Kinsbourne, the "ability to cause narcolepsy resides in the viral component of the vaccine, whereas the adjuvant . . . could lead to an increase in the size of the affected population." *Id.* This explanation shows why an adjuvanted vaccine like Pandemrix resulted in a larger increase in narcolepsy cases compared to the non-adjuvanted vaccines used in the United States. *Id.*

Dr. Kinsbourne argued that the component within the vaccine itself that causes narcolepsy is influenza nucleoprotein. *Id.* at 2. Dr. Kinsbourne argued that there is cross-reactivity between "a comparable peptide in the influenza vaccine and hypocretin receptor 2." *Id.* Dr. Kinsbourne cited to Ahmed (2015) for the proposition that "antibodies from vaccine-associated narcolepsy sera cross-reacted with both influenza nucleoprotein and hypocretin receptor 2 [("HCRTR2")]." *Id.*

Ahmed (2015) surveyed several groups to judge the prevalence of antibodies against hypocretin receptor-2, primarily comparing groups of individuals vaccinated with Pandemrix and Focetria, a vaccine similarly adjuvanted to Pandemrix. Pet'r's Ex. 38 at 1, Ahmed (2015). The study found that there were increased levels of this antibody in people with narcolepsy after Pandemrix vaccination, compared to the groups who had been exposed to the wild-type influenza virus and who had been vaccinated with Focetria. *Id.* The authors then theorized that this difference could be explained by the level of influenza nucleoprotein in the different vaccines. *Id.*

Dr. Kinsbourne explained that hypocretin receptors are part of a positive feedback loop, wherein hypocretin stimulates hypocretin neurons through excitation of hypocretin receptors to produce more hypocretin. *Id.* at 3-4. Inactivation of the hypocretin receptors, Dr. Kinsbourne wrote, "would diminish their output of hypocretin," leading to "a hallmark dwindling away of

hypocretin levels as observed in cerebrospinal fluid in people with narcolepsy." *Id.* at 4. Indeed, Dr. Kinsbourne continued, studies show that inactivation or damage to hypocretin receptors result in narcolepsy in animals. *Id.* at 2 (citing Pet'r's Ex. 26, Ling Lin et al., *The Sleep Disorder Canine Narcolepsy Is Caused by a Mutation in the* Hypocretin (Orexin) Receptor 2 *Gene*, 98 Cell 365 (1999) (inactivation caused by mutation); Pet'r's Ex. 43, Jon T. Willie et al., *Distinct Narcolepsy Syndromes in* Orexin Receptor-2 *and* Orexin *Null Mice: Molecular Genetic Dissection of Non-REM and REM Sleep Regulatory Processes*, 38 Neuron 715 (2003) (inactivation caused by genetic manipulation)). One study, Dr. Kinsbourne continued, found that "the loss of hypocretin function in narcolepsy results from a cytotoxic or immunologically mediated attack focused on hypocretin receptor 2 or an antigen anatomically linked to hypocretin receptor 2." *Id.* at 3. (citing Pet'r's Ex. 42, Thomas C. Thannickal et al., *Pattern of Hypocretin (Orexin) Soma and Axon Loss, and Gliosis, in Human Narcolepsy*, 13 Brain Pathology 340 (2003)).

This immunological attack on hypocretin receptors, Dr. Kinsbourne theorized, is caused by cross-reactivity between influenza nucleoprotein found in the flu vaccine and hypocretin receptors. *Id.* at 2. Dr. Kinsbourne cited to Ahmed (2015) to show that "the amount of nucleoprotein [in brands of H1N1 flu vaccines] correlates with the expected differential frequency of narcolepsy arising in reaction to the individual vaccines." *Id.* at 4. He stated that Ahmed (2015) found that Fluzone, the vaccine at issue in this case, has "one of the highest nucleoprotein contents among the available seasonal influenza vaccines, falling short only of the even higher nucleoprotein contents of Pandemrix . . . ." *Id.* Dr. Kinsbourne concluded that "a medically reasonable mechanism for the action of vaccines in causing narcolepsy is necessarily incomplete;" however, his theory "derives from respected sources and is a sufficient basis for proposing a mechanism of injury at a level of reasonable medical probability." *Id.*

e. Dr. MacGinnitie's Second Report

Dr. MacGinnitie's second report primarily disputed the significance of Ahmed (2015), which Dr. Kinsbourne relied upon to elucidate his theory of causation. Resp't's Ex. RR. Dr. MacGinnitie wrote that Dr. Kinsbourne "has abandoned his original theory that cross-reactivity between hemagglutinin component of the H1N1 influenza vaccine and neurons producing hypocretin-1 in the hypothalamus caused [Petitioner's] narcolepsy." *Id.* at 1. Instead, Dr. MacGinnitie continued, Dr. Kinsbourne "now proposes that [Petitioner's] illness was caused by cross-reactivity between a distinct influenza protein, nucleoprotein, and neurons expressing the receptor for hypocretin," as proposed by Ahmed (2015). *Id.*

Dr. MacGinnitie summarized that Ahmed (2015) found hypocretin receptor antibodies in seventeen out of twenty patients with narcolepsy after receiving Pandemrix. Resp't's Ex. RR at 1. Dr. MacGinnitie then argued that the significance of these antibodies is unclear, as numerous control groups in the study also had these antibodies. *Id.* For example, the study found the antibodies in five out of twenty patients without narcolepsy who had been exposed to wild-type influenza. *Id.* In addition, the study found the antibodies in eleven out of twenty historical control sera, but these control patients did not present with any evidence of narcolepsy. *Id.*

Dr. MacGinnitie then presented four issues with the study. *Id.* First, Dr. MacGinnitie highlighted the small sample size of the Ahmed (2015) study. *Id.* He noted that the study was "a single report on [twenty] patients with post-vaccination narcolepsy and [sixty] poorly matched controls [that] represents the sum total of published data suggesting" a causal link between influenza nucleoprotein and manifestation of narcolepsy. *Id.* at 2. Second, Dr. MacGinnitie emphasized that "there is [no] good explanation for the fact that cross-reactive hypocretin receptor/nucleoprotein antibodies are present in a number of patients without narcolepsy." *Id.* "This includes," Dr. MacGinnitie continued, "**greater than 50% of children serving as historical controls and without narcolepsy** . . . ." *Id.* (emphasis in original). Additionally, the levels of the antibodies in the control group without narcolepsy, Dr. MacGinnitie wrote, "are not statistically significantly different from those found in the Pandemrix[-]vaccinated patients with narcolepsy." *Id.* Patients with influenza infections, but not narcolepsy, Dr. MacGinnitie wrote, also have the antibodies; "[t]his fact casts considerable doubt on the importance of these antibodies." *Id.*

Third, Dr. MacGinnitie argued that "no evidence is provided that T[]cells specific for the proposed cross-reactive nucleoprotein exist." *Id.* at 3. Dr. MacGinnitie explained that narcolepsy is "almost exclusively seen in patients who carry the HLA DQB 1*0602 allele." *Id.* at 1. He continued that HLA proteins "present peptides (protein fragments) on the surface of cells," and the exclusivity between this allele and narcolepsy "indicates the obligate involvement of T cells that recognize this HLA type as the pathogenesis of narcolepsy." *Id.* However, Dr. MacGinnitie wrote, "no data is presented that these [T] cells exist." *Id.* at 3. In addition, Dr. MacGinnitie continued, "no evidence is presented that the cross-reactive antibodies cause narcolepsy." *Id.* "Correlation does not imply causation," Dr. MacGinnitie wrote of the anti-hypocretin receptor antibodies, "and it is possible that the identified antibodies are as result, not a cause of narcolepsy." *Id.* Fourth, Dr. MacGinnitie wrote that the Ahmed (2015) study "lacks appropriate controls, particularly antibody data from individuals immunized with Pandemrix but not developing narcolepsy." *Id.* Dr. MacGinnitie quoted the Ahmed (2015) study to emphasize that "[t]he findings reported in this study should be viewed as a step in understanding the mechanism of vaccine-associated narcolepsy and will benefit from additional confirmatory studies." *Id.* at 4 (citing Ahmed (2015) at 8). Dr. MacGinnitie concluded his report by citing again to the Duffy study to show "there is **not an association between non-adjuvanted influenza vaccines, such as the Fluzone that [Petitioner] received, and development of narcolepsy, regardless of nucleoprotein content**." *Id.* (emphasis in original).

f. Petitioner's Expert, Dr. S. Stanley Young

Dr. S. Stanley Young's expert report was filed by Petitioner after the undersigned granted Petitioner's motion to continue the hearing. *See* Docket Rep. Dr. Young's expert report was submitted to address the Duffy study and "provide the Court with a detailed report of the study's methods and conclusion." Order, ECF No. 86. Dr. Young is the CEO of CGStat, LLC, a consulting firm located in Raleigh, North Carolina.[18] Pet'r's Ex. 50 at 1, ECF No. 89-1. Dr.

[18] Dr. Young's CV is silent on the work his company undertakes. *See* Pet'r's Ex. 50 at 1. His CV also does not specify the specialty in which Dr. Young received his degrees, although he presumably studied statistics based upon his academic and professional career. *Id.*

Young received his BS, MES, and Ph.D. from North Carolina State University in 1966, 1968, and 1974, respectively. *Id.* Dr. Young is also an Adjunct Professor of Statistics and Biostatistics and has published a book and numerous academic papers on these subjects. *Id.* at 1-7.

Dr. Young first presented a summary of Petitioner's causation theory based upon the Ahmed article. Pet'r's Ex. 52 at 1, ECF No. 89-3. Dr. Young then wrote that Duffy presents "two important claims." *Id.* First, Dr. Young wrote, Duffy asserts that "the vaccine by itself will not cause narcolepsy," and second, "ASO3 [the adjuvant in Pandemrix] is not the causative agent." *Id.* (emphasis in original). Dr. Young argued that Ahmed (2015) correctly identified nucleoprotein as the causative agent Duffy was looking for. *Id.* at 5-6. Dr. Young cited to the Ahmed article to show that there was "a lower association" between new narcolepsy cases following vaccination with Arepanrix in Canada, even though it shares the same adjuvant, ASO3, with Pandemrix. *Id.* at 3. Instead, Dr. Young wrote, "[t]here is very good evidence that the causative agent is high levels of antibodies to NP [, and] [**t**]**here was no way for Duffy in 2014 to know about the future Ahmed hypothesis**." *Id.* at 6 (emphasis in original).

In terms of the study itself, Dr. Young commented that the "Duffy study is sensible in terms of data set and analysis." *Id.* at 6. The Duffy study, Dr. Young observed, found a higher incidence of narcolepsy in people age nineteen or younger in Europe, although in the United States it tends older, aged twenty or above. *Id.* Dr. Young concluded that the Duffy study suggested "that it is not the H1N1 vaccine itself or ASO3 adjuvant (a false lead) which causes narcolepsy." *Id.* Dr. Young asked, "What, then, is the causative agent?" *Id.* Dr. Young answered, "The Ahmed hypothesis, antibodies to the nuclear protein [sic], is the current last man standing." *Id.*

g. Dr. Kinsbourne's Third Report

Dr. Kinsbourne's third report was also submitted along with Dr. Young's to address the Duffy study. *See* Docket Rep. Dr. Kinsbourne began his report by reiterating the argument he presented previously, specifically that "the adjuvant does not by itself cause narcolepsy but that it expands the number of affected individuals when it is combined with a vaccine that can cause narcolepsy." Pet'r's Ex. 53 at 1. This fact, Dr. Kinsbourne wrote, explains how the H1N1 vaccine used in the United States "would be expected to cause far fewer cases of narcolepsy" due to its lack of adjuvants. *Id.*

Dr. Kinsbourne then explained the Duffy study in depth. *Id.* In Duffy, Dr. Kinsbourne wrote, "[t]he investigators identified [sixteen] narcoleptics within the chosen six-month period of interest . . . following H1N1 vaccine (pandemic or seasonal)." *Id.* In lieu of a control group, Dr. Kinsbourne wrote, Duffy "compared the number of narcoleptics they identified with an estimated expected number of cases of narcolepsy which they derived from Silber et al." *Id.* (citing Pet'r's Ex. 53B, Michael H. Silber et al., *The Epidemiology of Narcolepsy in Olmsted County, Minnesota: A Population-Based Study*, 25 Sleep 197 (2002)). The Silber study, Dr. Kinsbourne continued, "found an incidence rate of narcolepsy of 1.37 per 100,000 (1.05 for women)." *Id.* Dr. Kinsbourne also cited to "[t]he only other study of whether H1N1 vaccinations impact the incidence of narcolepsy[,]" Montplaisir et al. *Id.* (citing Pet'r's Ex. 33, Jacques Montplaisir et al., *Risk of Narcolepsy Associated with Inactivated Adjuvanted (ASO3)*

A/H1N1 (2009) Pandemic Influenza Vaccine in Quebec, 9 PLoS ONE 1 (2014)). This study, performed in Canada, found an "excess risk of narcolepsy of approximately one case per million vaccine doses" of Arepanrix. *Id.* Duffy "uncovered six patients with narcolepsy and cataplexy . . . within the study period," with only one patient showing "onset of narcolepsy within six months of an H1N1 vaccination." *Id.* In total, Duffy found one patient with narcolepsy and cataplexy out of "some one-and-one-half-million subjects." *Id.* at 2. Dr. Kinsbourne conceded that Duffy's data are consistent "with the Montplaisir estimate of one additional case per million vaccine doses." *Id.*

Dr. Kinsbourne argued "there would be a serious limitation to applying the results of the Duffy study to the case of [Petitioner]." *Id.* The primary impediment, Dr. Kinsbourne noted, is that the Duffy study did not even consider the incidence of narcolepsy in someone Petitioner's age. *Id.* Duffy limited their study to subjects below the age of thirty, whereas Petitioner was forty-four years old when she developed narcolepsy. *Id.* According to Silber, "[t]he incidence rate [of narcolepsy] was highest in the second decade, followed in descending order by the third, fourth, and first decade," with zero in the fifth decade of life (age 40-49). *Id.* Consequently, in the study used a baseline for Duffy, the incidence of narcolepsy in Petitioner's age range is zero. *Id.* This is because "physicians tend not to consider narcolepsy in the differential diagnosis of sleep disorders in older adults." *Id.* Duffy's data, Dr. Kinsbourne noted, is therefore inapposite, as "an appropriate expected value for [Petitioner], aged [forty-four] years, in a Duffy-type study would be zero, rather than the expected rate that the investigators based on [the Silber study's] data for much younger people." *Id.* "As is frequently the case with rare event[s]," Dr. Kinsbourne concluded, "decisions as to causation in [Petitioner's] case cannot be based on the outcomes of epidemiological research." *Id.*

h. Dr. MacGinnitie's Third Report

Dr. MacGinnitie's third expert report addresses both the reports of Dr. Kinsbourne and Dr. Young, specifically their use of the Ahmed and Duffy studies. Resp't's Ex. WW.

With respect to the Ahmed study, Dr. MacGinnitie wrote that "[t]here is no data linking the anti-hypocretin receptor antibodies observed in Ahmed . . . to the destruction of hypocretin-producing neurons." *Id.* at 1. Dr. MacGinnitie cited to a comment on Ahmed (2015) that the mechanism by which the anti-hypocretin receptor antibodies actually cause narcolepsy is "a major unanswered question . . . ." *Id.* (citing Anne Vassalli, Sha Li, & Mehdi Tafti, *Comment on "Antibodies to Influenza Nucleoprotein Cross-React with Human Hypocretin Receptor 2,"* 7 Sci. Translational Med. 314 (2015)). Dr. MacGinnitie agreed with Vassalli et al., that "the hypothesis advanced by Ahmed (that the antibodies cross the blood-brain barrier and destroy cells expressing this receptor) is 'unlikely,' as '[hypocretin receptors] [are] expressed in numerous brain cell types, including some with critical functions.'" *Id.* And, Dr. MacGinnitie continued, "[t]here is no evidence that these antibodies are harmful or perform any of the functions attributed to them by Dr. Young or Ahmed 2015." *Id.* Dr. MacGinnitie wrote "[t]he fact that the rate of narcolepsy varied among different adjuvanted vaccines does not prove the adjuvant is not responsible." *Id.* Instead, Dr. MacGinnitie argued, "[w]hile this data may indicate adjuvant is not **sufficient by itself** to cause narcolepsy, it does not change the fact that adjuvant is **required**." *Id.* (emphasis in original).

"Duffy," Dr. MacGinnitie wrote, "remains convincing evidence against a relationship between non-adjuvanted H1N1 vaccine and narcolepsy . . . ." *Id.* at 2. Dr. MacGinnitie addressed Dr. Young's argument that the Duffy authors were unaware of the possible causation mechanism asserted in Ahmed (2015). *Id.* Dr. MacGinnitie wrote that "it is irrelevant if the authors [of Duffy] were aware" of the Ahmed (2015) hypothesis, because Duffy "undertook their study to determine" whether there was any association between non-adjuvanted flu vaccines and narcolepsy. *Id.* Dr. MacGinnitie reasoned that the knowledge of any specific mechanism would not have affected the statistical findings and "Ahmed et al. simply propose[d] one mechanism by which non-adjuvanted vaccines could be associated with narcolepsy." *Id.* Dr. MacGinnitie also concluded that "Dr. Kinsbourne is mistaken when he asserts that" Duffy did not have a control group. *Id.* Duffy, Dr. MacGinnitie explained, "used as a control group patients who developed narcolepsy before the H1N1 pandemic started" and compared the rate found therein with the data from Silber et al. *Id.* Duffy, Dr. MacGinnitie continued, further "consider[ed] the fact that this baseline rate [found in Silber] could be wrong, but still would not change their analysis," as "'the zero cases [Duffy] observed in [their] 2009 pandemic vaccinated cohort would still be less than the 0.652 cases expected.'" *Id.* Dr. MacGinnitie then highlighted that the Montplaisir study relied upon by Dr. Kinsbourne concerned an adjuvanted vaccine, and Dr. MacGinnitie dismissed Dr. Kinsbourne's argument concerning the age restriction found in Duffy. *Id.* Dr. MacGinnitie wrote that "it is true that Duffy was restricted to patients under [thirty] years of age," but found "this is reasonable given the increased incidence in younger patients." *Id.* "In fact," Dr. MacGinnitie continued, "[Duffy] did not observe a single patient in the 20-29 age group who developed narcolepsy within 180 days of vaccination." *Id.*

Dr. MacGinnitie concluded that "little if any new information is added by" the supplemental reports of Dr. Young and Dr. Kinsbourne. *Id.* The Ahmed hypothesis is "speculative," and "Duffy remains strong evidence against a relation between non-adjuvanted vaccination and narcolepsy." *Id.*

IV. Testimony[19]

The undersigned held an entitlement hearing in this case from November 30, 2017 to December 1, 2017. Petitioner's counsel called eight witnesses to testify, with five of the witnesses appearing via video teleconferencing. ECF No. 94. Petitioner, her husband, and Dr. Marcel Kinsbourne testified in person. The witnesses called by video teleconferencing included: Ms. Walters, Petitioner's mother-in-law; Ms. Burdette, Petitioner's mother; Mr. Ritchey, Petitioner's son; Ms. Sanders, Petitioner's friend; and Ms. Gilmore, Petitioner's neighbor. *Id.* Respondent's experts, Dr. Thomas Scammell and Dr. Andrew MacGinnitie, testified in person. ECF No. 93.

[19] All grammatical and other errors contained within quotations in this decision are as they appear in the original documents of the parties or as recorded by the court reporter.

a. Fact Testimony

i. Petitioner's Mother-in-Law

Ms. Walters first met Petitioner in 2008 when Petitioner and Ms. Walters' son began dating. Tr. 14-15. Ms. Walters lived with Petitioner and Mr. Dougherty from 2012 to 2016. *Id.* at 15. Ms. Walters testified that prior to receiving the flu vaccine Petitioner was "very active" and "very involved" with her family. *Id.* at 16. Ms. Walters stated that Petitioner traveled for her job as a regional manager with Frito-Lay and visited cities across central Indiana while working up to sixty hours per week. *Id.* at 16-18. Additionally, Petitioner was active in her free time, enjoying boating, swimming, and fishing. *Id.* at 19.

Ms. Walters testified that she was "fairly certain" Petitioner's behavior began to change around September of 2013, approximately ten months after her Fluzone vaccination. *Id.* at 19-20. At that time, Petitioner's "episodes of cataplexy" began to have an effect on Petitioner. *Id.* at 20. Ms. Walters described Petitioner's cataplectic attacks as "terrifying." *Id.* She stated that Petitioner "would go down . . . into a state where you couldn't wake her up." *Id.* at 21. Ms. Walters testified that these attacks would occur once or twice a day. *Id.* Ms. Walters described one instance where Petitioner had a cataplectic episode during one Fourth of July cookout at Petitioner's house. *Id.* Ms. Walters testified that Petitioner entered the garage and "went down." *Id.* at 21-22. Ms. Walters explained that she had to call for Petitioner's son to help Petitioner to her bed. *Id.* at 21-22. Ms. Walters could not say "if it's sadness or joy or what could bring these incidences on." *Id.* at 22. Ms. Walters recounted Petitioner telling her that Petitioner could hear her family during these attacks, but "it was obvious [during these episodes that Petitioner] couldn't move her body." *Id.* at 23. Ms. Walters also recalled two more incidents. *Id.* at 24. Ms. Walters said that once in March of 2014, Mr. Dougherty had to pick up Petitioner "a half a mile from our house" because Petitioner "had [gone] off the road . . . and almost hit[] a telephone pole." *Id.* at 24. There was another incident, Ms. Walters continued, where Petitioner's son Jake discovered Petitioner in their barn "out of it, in her car and the car door was locked." *Id.* at 24. Ms. Walters said that Petitioner became "a totally different person" after the vaccination; Petitioner was unable to participate in her favorite outdoor activities or even cook for herself. *Id.* at 24-25. Ms. Walters finished her direct testimony by stating how emotionally and financially difficult it has been "to have to go through this on a daily basis, it's hard, very hard." *Id.* at 25-26. "Because I see what it's doing not only to [Petitioner]," Ms. Walters continued, "but to . . . her family that love her." *Id.* at 26.

Respondent questioned Ms. Walters on the circumstances surrounding Petitioner's cataplectic episodes and her daytime sleepiness. *Id.* at 26-27. Concerning the Fourth of July incident, Ms. Walters stated that Petitioner's mood was "very happy . . . . I know she was having a good time." *Id.* at 27. Ms. Walters further testified that Petitioner has an exaggerated mood when she has a cataplectic attack. *Id.* at 27-28. Ms. Walters explained that there were occasions when Petitioner "goes down" during an episode and is down for "at least [ten] minutes[,] . . . if not longer sometimes." *Id.* at 28. Ms. Walters further explained that Petitioner can "just fall asleep . . . several times a day," and this sleepiness could affect Petitioner while watching television or mid-conversation. *Id.* at 29.

ii. Petitioner's Mother

Petitioner's mother described Petitioner as a "strong willed, hard-working person" before she received the Fluzone vaccination. *Id.* at 33. Ms. Burdette stated that Petitioner was a district manager for Frito-Lay prior to her vaccination, and in that role, Petitioner had to drive across central Indiana to oversee her sales district. *Id.* at 34-35. Ms. Burdette estimated that it took her daughter an hour to drive from her house to her "bin" or warehouse for work. *Id.* at 35-36.

Ms. Burdette described Petitioner as "[not] exactly herself" beginning "about three or four months after" Petitioner received her Fluzone vaccination on November 7, 2012. *Id.* at 36. Ms. Burdette described one instance where Petitioner and the family were sitting in the living room and watching television. *Id.* at 36. Petitioner could not respond to Ms. Burdette's questions and began "staring off into space but still looking at the TV with no response." *Id.* at 36-38. Ms. Burdette "poked [Petitioner] and talked to her," but Petitioner did not respond for "probably about [five] to [ten] minutes." *Id.* at 38. When Petitioner came out of her episode, she "was very, very emotional because she did not know what had happened, and she just started crying." *Id.* These episodes happened "numerous times." *Id.* Ms. Burdette said that the first time Petitioner had an episode was during the Fourth of July picnic also described by Ms. Walters. *Id.* at 39. Ms. Burdette said that Petitioner "just dropped to the ground" and had to be helped to bed by her husband. *Id.* During these episodes, Ms. Burdette continued, it was like Petitioner "wasn't there." *Id.* at 40. Ms. Burdette also described several times when Petitioner called her on the side of the road, "because [Petitioner] just couldn't go, and she thought she was going to pass out . . . ." *Id.* at 41. Ms. Burdette noted that Petitioner would sometimes be on the side of the road for fifteen to twenty minutes "because she couldn't drive any further." *Id.* Ms. Burdette testified that Petitioner had to stop driving because of these episodes and eventually had to stop working. *Id.* at 42-43.

Ms. Burdette testified that Petitioner never had any of "these kinds of spells or events" before her vaccination, and she was a very "independent" and "self-sufficient person" prior to her illness. *Id.* at 44. "I would say," Ms. Burdette stated, "six months after [Petitioner] had that vaccination she was a totally different person, totally." *Id.* Now, Ms. Burdette continued, Petitioner was almost entirely reliant on other people. *Id.* at 45.

During cross-examination, Ms. Burdette explained that she had lived with Petitioner from 2012, when Ms. Burdette's house burned down, until Petitioner and her family moved to Minnesota in 2016. *Id.* at 46-47. Respondent asked if, during that time, Ms. Burdette had seen her daughter ever "experience episodes that you would describe as sleepiness?" *Id.* at 47. Ms. Burdette denied that she could characterize the episodes as "sleepiness." *Id.* Instead, Ms. Burdette said there would be times when Petitioner would be busy with a task; then "she could not function any further, and she just had to sit down or lay down or whatever." *Id.* at 47-48. Petitioner would then "sit in the recliner for maybe [twenty] [or] [thirty] minutes, and then she would be fine when she became aware again." *Id.* at 48. Ms. Burdette stated that, at the beginning of Petitioner's condition, "she would just be sitting up and participating in a conversation, and she would be gone." *Id.* "[Y]ou'd say something to her," Ms. Burdette continued, "and she wouldn't answer you." *Id.* at 49. During these episodes, Ms. Burdette described Petitioner has having a blank, open stare and "looking like she was watching TV but

unaware." *Id.* Ms. Burdette was asked what the nature of the conversation was like when Petitioner became unresponsive while watching television. *Id.* at 50. She stated that she did not "think that made any difference." *Id.* at 50-51. "There wasn't any anxiety or anything going on," Ms. Burdette noted. *Id.* at 51.

Ms. Burdette recalled an instance when Petitioner fell off a toilet and hit the wall opposite. *Id.* at 52. Ms. Burdette explained that Petitioner's husband heard a "big thump," and found Petitioner on the floor in the bathroom. *Id.* Ms. Burdette described a three- to four-inch diameter hole from Petitioner's head making contact with the wall.[20] *Id.* Ms. Burdette then recalled that immediately prior to Petitioner's cataplectic events, Petitioner would seem to experience "extreme excitement, or high anxiety, or sadness." *Id.* at 54. Ms. Burdette described one incident where a box of Petitioner's father's football memorabilia "caused her to have an emotional moment," but Ms. Burdette "[did not] know if something like that would bring it on or not . . . ." *Id.* at 54-55. When asked about how quickly an episode would occur after Petitioner became emotional, Ms. Burdette answered that Petitioner "was more emotional after the incident than she was prior to the incident . . . ." *Id.* at 55.

iii. Petitioner's Son

Petitioner's son has been living with his mother since she moved to Minnesota in 2016. *Id.* at 58-59. Mr. Ritchey stated that he saw his mother weekly prior to her Fluzone vaccination, and lived with her on the day of her vaccination, November 7, 2012. *Id.* at 59. He described his mother as outgoing and hard-working, and stated that she "worked three times harder than she should have" to provide the best for her son. *Id.* After her vaccination, Mr. Ritchey said that "it started slow," but she would "space[] out in a blank stare . . . [;] when she finally [comes to], she [says], I heard you. I was trapped." *Id.* at 60-61. Mr. Ritchey described his mother's spells as "the creepiest thing I've ever seen my mom do in my life," and very frightening. *Id.* at 61.

Mr. Ritchey first saw his mother have one of these attacks one day when she pulled into the barn after work. *Id.* Mr. Ritchey stated that his mother fell asleep in her vehicle, but Mr. Ritchey could not help her because "all [of] the windows [and] doors were locked . . . ." *Id.* Mr. Ritchey "thought [his] mom had an accident, like a heart attack . . . . It was a very scary experience." *Id.* He stated that when his mother came to, "she didn't know what happened." *Id.* at 62. Mr. Ritchey recalled that his mother "just remembered pulling into the . . . barn and [she was] out." *Id.* Mr. Ritchey testified that Petitioner was out for "a good [ten], [twelve] minutes." *Id.* Mr. Ritchey said that he has seen "many" of these attacks. *Id.* at 63. When Petitioner takes "medicine so she falls asleep at night," Mr. Ritchey has "had to move her so she could get her breathing machine on . . . ." *Id.* Mr. Ritchey testified that his mother "felt like a dead corpse because she couldn't wake up because of how that medicine puts her to sleep now." *Id.* Petitioner has also, Mr. Ritchey continued, "fall[en] asleep in [Mr. Ritchey's] chair and just . . . stare[d] at things." *Id.* He noted that "she does that a lot." *Id.* During these episodes, Petitioner's eyes would be open, and "[i]t's scary." *Id.* at 64. It has been difficult for Mr. Ritchey to see his mother become so incapacitated; "[i]t's heartbreaking," Mr. Ritchey said. *Id.*

[20] Petitioner filed photographs of the damage to the wall. Pet'r's Exs. 46, 47, ECF Nos. 77-1, 77-2.

Mr. Ritchey testified that these episodes occur "if something emotional comes up." *Id.* at 65. These episodes occur "once a day[,] [m]aybe more," Mr. Ritchey said. *Id.* Mr. Ritchey recalled the incident where Petitioner fell off of the toilet, damaging the wall. *Id.* at 66. He remembered that he was asleep in his bed when he heard "a large boom." *Id.* He then ran into his mother's room, where Petitioner's husband was tending to her. *Id.* Mr. Ritchey testified that his mother was "in a mixed state" after the fall. *Id.* Mr. Ritchey also recalled how Petitioner would enter into these staring episodes while Mr. Ritchey drove her from Minnesota to Indiana. *Id.* Mr. Ritchey could not remember if any specific events precipitated these staring spells. *Id.* at 66-67. Mr. Ritchey also stated that his mother has some "bad days," where she is not "able to function." *Id.* at 68.

On cross-examination, Mr. Ritchey detailed the difference between Petitioner's episodes. *Id.* at 69. When Petitioner is "trapped in her body," Mr. Ritchey explained, "her eyes are wide open." *Id.* When Petitioner is tired, "she'll go close her eyes and sleep and try to sleep it off." *Id.* Mr. Ritchey said that Petitioner would have an episode "seconds to minutes" after an emotional moment occurred. *Id.* at 70.

iv. Petitioner's Friend

Ms. Sanders first met Petitioner in kindergarten, and they were "inseparable" until Ms. Sanders moved to Indianapolis during their middle school years. *Id.* at 73. Petitioner and Ms. Sanders reunited in 2009, and "picked up where [they] left off." *Id.* at 74. Ms. Sanders still resides in Kokomo, a city in Indiana fifteen minutes away from Petitioner's former residence. *Id.* at 73. Ms. Sanders testified that prior to Petitioner's flu vaccination, the two would often see each other and talk on the phone in the mornings when Petitioner was on the way to work. *Id.* at 75. Ms. Sanders said that she knew Petitioner was very busy as a manager for Frito-Lay, and was very healthy prior to the onset of her narcolepsy. *Id.* at 75-76.

It was "much later," after Petitioner's vaccination, that Ms. Sanders noticed a change in Petitioner. *Id.* at 76. Ms. Sanders remembered that Petitioner was in bed "for two weeks straight." *Id.* Ms. Sanders stated that Petitioner was also "tired all the time" and "would have a rough time staying awake while she was at work." *Id.* at 76-77. Petitioner would call Ms. Sanders while driving "on [Petitioner's] way home just to help her stay awake, . . . because she was afraid she was going to fall asleep." *Id.* at 77. Ms. Sanders also remembered one instance where Petitioner "blacked out for just a second and went off the road." *Id.* Petitioner came to, Ms. Sanders recalled, as she was "c[oming] to a stop before she hit [a telephone pole]." *Id.*

Ms. Sanders recalled the first time she witnessed Petitioner have an attack. *Id.* at 78. Ms. Sanders testified that she was at a bonfire with Petitioner's family when she "noticed [Petitioner] was kind of staring off into the distance." *Id.* Ms. Sanders said that Petitioner's mother "told [Ms. Sanders] that's what [Petitioner] does[;] she said [Petitioner] is having one of her episodes." *Id.* Petitioner was "just staring off into space," and Ms. Sanders went to hold Petitioner's hand to talk to her during the episode. *Id.* When Petitioner came to, Ms. Sanders "noticed [Petitioner] had a single tear come down her eye," and "it scared [Ms. Sanders] to death." *Id.* After this episode, Petitioner's husband helped put Petitioner to bed, and Petitioner "was so emotionally

drained that she'd just cry." *Id.* at 79. When asked what kind of conversation they were having prior to the episode, Ms. Sanders answered that "it was probably something that was . . . comical, like lighthearted . . . ." *Id.* at 80. Petitioner's staring episode lasted "at least five minutes, maybe longer," Ms. Sanders explained. *Id.* Ms. Sanders recalled another time that Petitioner had a staring episode while Ms. Sanders and Petitioner were "sitting on the steps in her house." *Id.* at 81. In this instance, Petitioner "just got to a blank stare" for "a couple minutes." *Id.* After these episodes, Petitioner told Ms. Sanders that Petitioner could hear her, but not react. *Id.* Ms. Sanders testified about one instance after Petitioner had to stop driving and Ms. Sanders had to drive Petitioner to work. *Id.* at 82. It "was around the holidays," and Ms. Sanders said that Petitioner's work was "pretty busy" due to the time of year. *Id.* Ms. Sanders drove Petitioner to her warehouse where "they were doing inventory." *Id.* Ms. Sanders testified that when they arrived, Petitioner felt that "she was going to . . . fall out." *Id.* Petitioner then retreated to her office, Ms. Sanders recalled, and "sat there for a while and just laid her head down." *Id.*

Ms. Sanders testified that Petitioner would "stumble a little bit" and told Ms. Sanders of one instance where Petitioner fell down and broke her glasses. *Id.* at 82-83. Petitioner told Ms. Sanders that Petitioner went downstairs "to get some ice cream or something," and broke her glasses while falling. *Id.* at 83. Ms. Sanders said that she was "always worried about [Petitioner] being by herself," and described how Petitioner had lost her independence since the onset of her narcolepsy with cataplexy. *Id.* Ms. Sanders also testified that she has telephone conversation with Petitioner "once or twice, three times a week" now that Petitioner lives in Minnesota. *Id.* at 84. Ms. Sanders explained that Petitioner sometimes has an episode during these calls, "because we'll be talking and all of a sudden she's not there." *Id.* Respondent did not cross-examine Ms. Sanders. *Id.* at 85.

v. Petitioner's Neighbor

Ms. Gilmore is Petitioner's friend and neighbor, and has known Petitioner since March of 2017. *Id.* at 90. Ms. Gilmore sees Petitioner "almost daily." *Id.* Ms. Gilmore described four instances where Petitioner experienced a cataplectic episode. *Id.* at 90-91. Ms. Gilmore recalled an instance wherein a car pulled out in front of Ms. Gilmore's car while Petitioner was in the passenger seat. *Id.* at 91. Ms. Gilmore stated that Petitioner had a "startled look," said "'I need a minute,' and then all of a sudden [Petitioner] was out," Ms. Gilmore said. *Id.* Petitioner's episode lasted "four, five minutes," and she could not respond to Ms. Gilmore. *Id.* Ms. Gilmore said that she pulled over when Petitioner had her attack, "because [Ms. Gilmore] was kind of shocked." *Id.* at 92.

Ms. Gilmore also recalled another time she witnessed Petitioner have a cataplectic episode. *Id.* at 93. Ms. Gilmore and Petitioner were leaving "Minnesota's largest candy store," in Ms. Gilmore's car and entered traffic. *Id.* Ms. Gilmore "didn't know if [Petitioner] just got overwhelmed[,] . . . [but] [Ms. Gilmore] looked back over at [Petitioner] and she was out." *Id.* Ms. Gilmore said that Petitioner's eyes were closed during both of these attacks, and Petitioner was out for "probably four, five minutes" during the second attack. *Id.* Ms. Gilmore spoke of another instance where she saw Petitioner have a cataplectic attack. *Id.* at 94. Ms. Gilmore said that she and Petitioner were shopping at Walmart in Arnold's Park, Iowa. *Id.* As they both entered Ms. Gilmore's car, Ms. Gilmore turned and saw Petitioner asleep in the passenger seat.

Id. Ms. Gilmore testified that Petitioner's attack lasted "six, seven minutes" in the parking lot. *Id.* at 95. The other time Ms. Gilmore saw Petitioner suffer an episode involved Petitioner's dogs' barking. *Id.* Ms. Gilmore stated that "the dogs started barking," and "then all of a sudden . . . [Petitioner] went down." *Id.* Petitioner fell in the grass with her eyes closed. *Id.* Ms. Gilmore speculated that the dogs' barking "[m]aybe raised her anxiety level," but she was "not sure." *Id.* at 95-96. Petitioner damaged her glasses falling in the grass, and Ms. Gilmore took Petitioner to have her glasses repaired a few days later. *Id.* at 96. Respondent did not ask any questions of Ms. Gilmore. *Id.* at 97.

vi. Petitioner's Husband

Mr. Dougherty first met Petitioner in 2008 when they started dating, and in 2009, Petitioner moved in with Mr. Dougherty. *Id.* at 100. They married in 2012. *Id.* at 99. Mr. Dougherty said this about Petitioner's work area: "She covered two districts . . . . [S]he pretty much had two jobs, doing the work of two district managers." *Id.* at 100. Mr. Dougherty stated that the development of her condition has "been gradual" following her Fluzone vaccine. *Id.* at 102. In the beginning, "once a week, [Petitioner would] say she had to pull over, just exhausted, [and] not knowing what's going on." *Id.* at 103. Her symptoms then increased, Mr. Dougherty said, "to where she had the blackout episode behind the wheel." *Id.*

Mr. Dougherty testified that Petitioner's episodes "were probably first noticeable March, April 2013." *Id.* The first episode Mr. Dougherty saw was during a family cookout at his and Petitioner's house to watch an Ultimate Fighting Championship ("UFC") fight. *Id.* Mr. Dougherty stated that it appeared like "Petitioner was in a coma with her eyes wide open[;] [she] would not move, lift her arm, nothing . . . ." *Id.* Mr. Dougherty said that Petitioner "understands what's going on around her, but she cannot react." *Id.* This incident occurred "probably right around the Fourth of July episode," Mr. Dougherty estimated. *Id.* at 104. Mr. Dougherty eventually clarified that Petitioner had two episodes on the Fourth of July, one in the garage and one in the kitchen. *Id.* Mr. Dougherty recalled that the second incident occurred "late, probably eleven o'clock," and Petitioner had a cataplectic episode at the kitchen table. *Id.* at 105. Petitioner went limp, and her eyes remained open. *Id.* Mr. Dougherty testified that there is a pattern to Petitioner's episodes. *Id.* at 106. "[I]t all seems to do with emotions," Mr. Dougherty stated, "I've seen it to where if she's upset, she gets sleepy or disordered." *Id.* Petitioner's husband also mentioned episodes following "over excitement and she just completely collapses, whether it be a scared reaction, a loud yell." *Id.* Mr. Dougherty described one instance where he "was joking around with [Petitioner]," and tapped the brakes while driving. *Id.* He said that "it was like turning an on and off button on her." *Id.* Petitioner began to react, but "[then] she was just out," Mr. Dougherty stated. *Id.*

Mr. Dougherty also described an incident, "as little as a month ago," where Mr. Dougherty's son "came up behind [Petitioner] and scared her and just grabbed her and said, 'Hey.'" *Id.* at 106-07. Mr. Dougherty explained that his son had recently moved to the area and had not been around Petitioner. *Id.* at 107. Mr. Dougherty said that he was "a hundred yards away . . . , and then I see this going on . . . ." *Id.* Mr. Dougherty stated that he yelled "'[g]rab her,' and she just collapsed." *Id.* After Petitioner fell, Mr. Dougherty and his son carried her to

Mr. Dougherty's truck. *Id.* Mr. Dougherty said that during the first year of Petitioner's incidences, her eyes would remain open while she was cataplectic. *Id.*

That has changed, according to Mr. Dougherty, and whether it's her medication or something else, "it just puts [Petitioner] into sleep mode." *Id.* Mr. Dougherty testified that Petitioner had four such episodes in court that day. *Id.* During these episodes, Petitioner "just closes her eyes and you can't get any reaction out of her, for two to three minutes, and it's emotions." *Id.* at 108. Mr. Dougherty noted that earlier that day, Petitioner had an episode after she and Mr. Dougherty were delayed in reaching the courthouse. *Id.* Mr. Dougherty reiterated that Petitioner's episodes are "all tied to emotions." *Id.* For instance, Mr. Dougherty described how Petitioner saw several small children walking together in the courthouse, and "then she came down to the bench and she's out." *Id.* Mr. Dougherty also mentioned that the stressors of their financial situation, their mothers living with them, and their moves seem to contribute to Petitioner's episodes. *Id.* at 109. Mr. Dougherty testified that Petitioner's sickness has made their income level drop from $260,000 a year to "probably" $120,000 a year. *Id.* at 110. Consequently both their cars were repossessed and their house entered foreclosure. *Id.* Mr. Dougherty testified that the family moved to Minnesota because he "had the opportunity to financially make things better for [them,]" and Petitioner's condition had made it impossible for her to continue her job at Frito-Lay. *Id.* at 111.

Mr. Dougherty said that Petitioner was just awarded social security disability benefits, but otherwise has no current sources of income. *Id.* Prior to Petitioner's condition, she and Mr. Dougherty would work "sometimes [seventy] hours a week" but would "have a good time" on their days off. *Id.* at 112. As a result of her condition, Mr. Dougherty testified that Petitioner can no longer participate in the activities that she used to enjoy. *Id.* Mr. Dougherty spoke of one incident in a pool, where Petitioner had an episode "on a floaty by herself." *Id.* Mr. Dougherty jumped into the pool "and stayed with [Petitioner] until she came out of it, which was four, five minutes." *Id.* at 113. Mr. Dougherty testified that Petitioner's episodes can vary in length "from [two] to [three] minutes to [ten] to [fifteen] minutes." *Id.* Initially, Petitioner's episodes were "with her eyes open," and would last "two to three minutes." *Id.* Over time, Mr. Dougherty noted a pattern stating, "this seems like the more emotional that it is, the longer that it takes her to come out." *Id.* For the more emotional episodes, Mr. Dougherty stated that, it can take fifteen to twenty minutes before Petitioner returns to her normal state. *Id.* at 114.

Mr. Dougherty testified that he has been with Petitioner during her medical appointments, and detailed one instance where Petitioner had an episode in a doctor's office. *Id.* at 114-15. Mr. Dougherty stated that Dr. Hemelt witnessed a cataplectic attack and had never seen anything like Petitioner's symptoms. *Id.* at 115. Mr. Dougherty ended his direct testimony by noting that Petitioner takes Xyrem at night, and Effexor and Nuvigil during the day. *Id.* at 115-16.

On cross-examination, Mr. Dougherty further distinguished Petitioner's types of episodes. *Id.* at 117. "Emotional is more a blackout," Mr. Dougherty explained. *Id.* Other times, "[w]e can argue, whether it be over bills or insurance or something like that, and it's more of a sleepiness." *Id.* Mr. Dougherty stated that during the latter episodes, Petitioner can feel a sleepiness coming on. *Id.* at 118. At that point, "she'll say, 'Hey, I need to go lay down,' or get away." *Id.* "[B]ut the extreme emotions," Mr. Dougherty said, "I mean, that's—somebody

turned the switch off." *Id.* Mr. Dougherty explained that when Petitioner has a sudden attack, "she goes blank . . . . [S]he just collapses." *Id.* Respondent questioned Mr. Dougherty's knowledge about Petitioner's stressors, including her stepson. *Id.* at 119. Mr. Dougherty's son's tendency to get in and out of trouble is documented on Petitioner's medical record as a stressor. *Id.* Mr. Dougherty responded that Dr. Neumann "kind of understood my son [was] in and out of trouble with school and things like that." *Id.* at 120.

On re-direct examination, Mr. Dougherty described the incident where Petitioner fell off of the toilet. *Id.* at 121. Mr. Dougherty testified that Petitioner "got up to go to the restroom, and I hear a big thump, and . . . she's laying on the ground from the toilet with a hole in the wall." *Id.* at 121-22. Mr. Dougherty said Petitioner was unconscious when he found her. *Id.* at 122. Mr. Dougherty testified that this incident happened "probably [in] 2015" after "one of the UFC fights, [around] one o'clock in the morning." *Id.* at 123. In response to a question from the undersigned, Mr. Dougherty said that Petitioner had collapsed, "kind of like the overexcitement of when she just collapsed." *Id.* Mr. Dougherty also stated that Petitioner told him she could remember collapsing, but not hitting the wall. *Id.* at 124.

vii. Ms. Marsha Dougherty, Petitioner

Petitioner began her testimony detailing her former job with Frito-Lay. *Id.*at 125-26. In 2008, she was transferred to Indiana to work a district "that did $8 million a year in potato chips." *Id.* at 126. She held her job as a district sales leader until she "left in March of 2014." *Id.* at 127. Petitioner testified that she and her husband were on the same career track at their respective employers and purchased a house in Galveston in 2009. *Id.* at 127-30. Petitioner stated that her mother moved in after her house burned down in 2012. *Id.* at 130. At that time, Mr. Dougherty's mother, Petitioner's mother, Petitioner's children, and Mr. Dougherty's children all lived in the same house. *Id.* at 130-31. During this time, Petitioner recalled working "probably [sixty], [seventy]" hours a week. *Id.* at 131. Petitioner testified that "four to five weeks" after her vaccination on November 7, 2012, she "could not understand why [she] could not get out of bed." *Id.* at 133-34. Petitioner testified that she never had issues getting up in the morning previously, but following her vaccination, "[she] couldn't stay awake." *Id.* at 134. Petitioner "tried everything" to wake up, but she found herself only rising out of bed to eat "for two weeks." *Id.* at 135. Due to this two-week period of sleepiness, Petitioner recalled that she missed a large company meeting hosted by Frito-Lay, "when all the new products come out," known as "the Blue Chip." *Id.* Petitioner expressed disappointment that she missed the meeting, and "all of the new mission states for that year[,] what our goals are[,] . . . and a lot of team building." *Id.*

After she missed the meeting, Petitioner recalled that she was able to return to work; however, she was still tired. *Id.* at 136. At this time, Petitioner began to drink several caffeinated beverages a day, but "it didn't make a difference." *Id.* During the first week after her return, Petitioner testified that she would pull over "at least once a day" due to her sleepiness. *Id.* at 137. Petitioner remembered that she had three stops on the way to work that she could pull into in order to rest. *Id.* at 137-140. Petitioner testified that she "never went to sleep" after pulling over. *Id.* at 138. Instead, she stated that she would "just lay there[,] . . . like I knew what was going on." *Id.* Petitioner would then "come back up, . . . and go on [her] way." *Id.* at 138.

This process of stopping to rest lengthened Petitioner's commute to work from fifty minutes to "[a]bout an hour and a half." *Id.* at 140. Throughout 2013, Petitioner continued to make her sales goals, but began to slow down "when [she] . . . hit the telephone pole." *Id.* at 140-41. Petitioner described the episode "right before Labor Day" in 2013 when she stopped at a stop sign. *Id.* at 141. She testified that "the next thing I know I look up and there's a telephone pole right there in front of me and I just winged the wheel." *Id.* at 141-42. Petitioner avoided striking the telephone pole, but could not recall that she crossed into on-coming traffic and veered off of the road. *Id.* at 142. Petitioner recalled "too many times" where she "came close to . . . colliding with something." *Id.* at 144. Petitioner stated that after the telephone pole incident, Dr. Neumann advised her against driving "'until we figure out what's going on.'" *Id.* at 145-46. Petitioner recalled that she told Dr. Neumann in September of 2013 that the flu vaccine had caused her narcolepsy. *Id.* at 146. Petitioner believed this "[b]ecause there's nothing else that could. I didn't do anything different." *Id.* Petitioner remembered that Dr. Neumann said that "she had not heard anything" regarding a connection between the flu vaccine and narcolepsy. *Id.* at 146-47.

Petitioner testified that she was first diagnosed with narcolepsy in September of 2013. *Id.* at 147. Petitioner said that they started her on Ritalin then; however, she could not sleep on the drug. *Id.* Petitioner and her physicians then started to experiment with other pharmaceuticals in order to determine the best treatment regimen. *Id.* at 148. In November of 2013, Petitioner returned to work after she began her narcolepsy treatment. *Id.* Petitioner explained that it was during this time that she began to experience cataplectic episodes. *Id.* at 149. Petitioner recalled one instance where she began staring at the television during a Green Bay Packers game. *Id.* The Packers scored a touchdown, Petitioner said, and "[t]hat was what put me out." *Id.* Petitioner described that she can "feel [the attacks] coming on," and her "body just gets tired." *Id.* at 150. Petitioner said that her eyes were open during this episode, allowing her to see the television, but "[she] couldn't move [her] eyes. [She] was like what the hell is going on?" *Id.* This instance was the first of Petitioner's cataplectic episodes. *Id.* at 151. Petitioner also stated that she does not know how long her attacks last; "when you're on the inside, . . . you don't know how long it is." *Id.* "[I]f you're in there for a couple minutes," Petitioner said, "it could seem like hours." *Id.*

Her second cataplectic attack occurred in April of 2014. *Id.* at 152. Petitioner stated that she was out with her husband and his father on Mississinewa, a reservoir in east Indiana, when the motor on their boat failed. *Id.* Petitioner began to feel anxious and said that before they reached the dock, "I was just out." *Id.* at 152-53. Mr. Dougherty and his father "had to sit there and wait until it was over." *Id.* Petitioner realized that she "[has] no control over" when these cataplectic episodes occur. *Id.* at 154. The unpredictability of the attacks forces Petitioner to remain "stuck at home," either in her house or on her family's farm. *Id.*

Petitioner testified that she worked from November of 2013 to February of 2014, "[a]nd during all these times I'm . . . better, but I'm not a hundred percent." *Id.* at 148. But, in March of 2014, Petitioner went on short-term disability "and never returned [to work]." *Id.* at 154. "It wasn't that I didn't have the will," Petitioner recounted. *Id.* Petitioner clarified, "I know I have the will, but my body would not let me." *Id.* Petitioner then discussed the treatment she received for her narcolepsy, and how she was prescribed Effexor XR and Nuvigil. *Id.* at 154-56.

Although it was originally helpful, Petitioner, stated that the Effexor XR was no longer controlling her emotions or her cataplexy. *Id.* at 156. Petitioner stated that she was currently on Effexor XR, Nuvigil, and Xyrem for her narcolepsy with cataplexy, and Claritin "every day." *Id.* at 157. Petitioner attested that she does not have high blood pressure. *Id.*

Petitioner then described the incidents that occurred during the hearing. *Id.* She stated that the first incident occurred during her mother-in-law's testimony because "I had not seen . . . how it hurts them or how it affects them." *Id.* Petitioner was aware of her husband's efforts to wake her, but she remembers thinking at that time, "You're just going to have to wait." *Id.* at 158. Petitioner's counsel apologized, and Petitioner responded that she has "dealt with this since . . . I got that shot." *Id.* She said that she "know[s] when they're coming," except for "when I get scared, [] I get excited real fast, or some loud thing happens." *Id.* Petitioner described one instance when Ms. Gilmore set off fireworks next door, and she "just collapsed . . . [d]own in the middle of the live room floor, just because of fireworks." *Id.* at 158-59. When Petitioner can feel an attack happening, she has an emotion, and "then all of a sudden I start to yawn, and I'll yawn and yawn, and I have to go sit down." *Id.* at 159-60. Petitioner stated that she is aware of her surroundings during these attacks, and she has become "used to it." *Id.* at 160. "I've lived with it for so long" that during attacks, she said she can think, "oh, you're only [three and a half] minutes in, you're fine, no problem." *Id.* Petitioner testified that there was no possibility that she could return to work, and said that she has been awarded Social Security Disability benefits. *Id.* at 160-61. Petitioner stated that, if she could, she would return to work "in a New York second." *Id.* at 161. She attested that she loved her work and "my people." *Id.*

During cross-examination, Petitioner described a usual day. *Id.* at 163. She wakes "anywhere between 7:00 and 9:00," makes a protein shake, and then waits for her Nuvigil and Claritin "to kick in, get going . . . ." *Id.* Petitioner stated that she may start cleaning in the kitchen at that point, but "might get halfway through doing some of it, and I end up back in the chair or laying in my bed." *Id.* Petitioner stated that she does not sleep once she lies back down, noting that "the only time that I fall asleep is if I lay down in the afternoon, . . . and then I'll take about an hour and a half nap." *Id.* at 164. Petitioner has been on this schedule "probably for about the last three months, and it's probably close to every other day or every day." *Id.* Petitioner explained that her naps are "not really sleep." *Id.* She is still aware what is happening in her surrounding, "but it's deeper than just like a regular attack . . . ." *Id.* Petitioner continued that her afternoon naps are similar to when "you hand falls asleep, [a]nd you can't move." *Id.* at 165. "But," Petitioner said, "in the hour and a half in the afternoon, that is extremely intense." *Id.* Petitioner is in this state until her eyes open, "and then it starts from here down, to come out of it." *Id.* The process to come out of her cataplexy takes "30 to 45 seconds." *Id.* Petitioner stated that she sometimes feels refreshed after her episodes, "[b]ecause it's almost like . . . my body is [] regenerating itself." *Id.* Petitioner explained that the short attacks, lasting five to ten minutes, are similar to the longer episodes in that she can hear what is happening around her, and she is "frozen solid." *Id.* at 166. Petitioner also stated that she enters a "deep state . . . almost immediately" upon lying down. *Id.*

Petitioner stated that she tries to accomplish some things around the house after her afternoon naps and tries to go to bed from 10 to 11 PM. *Id.* at 167. At bedtime, Petitioner stated that she takes two doses of Xyrem and uses her CPAP machine. *Id.* at 167-69. Petitioner also

clarified that the incident where she fell off of the toilet occurred in 2015, but "[she] do[esn't] remember a lot about that." *Id.* at 170. Petitioner stated that she is not able to organize things as well as she used to due to her condition. *Id.* at 171. Petitioner also explained the medical record notation from her October 17, 2013 visit with Dr. Hemelt that she thought her narcolepsy was due to the flu vaccine. *Id.* Petitioner stated that her mother found "that there's a connection" between narcolepsy and the flu vaccine on Facebook. *Id.* at 171-72. Petitioner said that her mother found information on the connection between Pandemrix and narcolepsy around three to four months after her vaccination. *Id.* at 172.

b. Expert Testimony

i. Petitioner's Expert, Dr. Marcel Kinsbourne

Dr. Marcel Kinsbourne identified himself a "pediatric and behavioral neurologist" with "an unlimited license to practice medicine." *Id.* at 177. He first began his association with the Vaccine Injury Compensation Program in 1988, with a "workshop for [prospective special masters]" and a "lecture on neurology." *Id.* at 177-78. After reviewing the medical records in this case, Dr. Kinsbourne testified that he concluded Petitioner's narcolepsy "was caused or triggered by the influenza vaccination [] she [received] on November 7th, 2012." *Id.* at 179-80. Dr. Kinsbourne posited that "the most likely mechanism is an autoimmune attack on certain neurons in the brain, and the influenza vaccine triggered that attack." *Id.* at 180.

Dr. Kinsbourne explained that the hypothalamus emits hypocretin, or orexin, during the day to allow people to stay awake. *Id.* at 180-81. Dr. Kinsbourne stated that about 70,000 neurons secret this substance, which is then "picked up by so-called hypocretin receptors on other neurons and stimulates them to activate various processes [to] keep the person awake." *Id.* at 181. Dr. Kinsbourne then explained that in narcolepsy, the "amount of hypocretin secreted . . . is almost absent in many cases." *Id.* This absence "appear[s]" to cause the "hypocretin neurons . . . to die or disappear, gradually." *Id.* Dr. Kinsbourne then said that he is "going to present one theory as being medically reasonable but not as being proven." *Id.*

Dr. Kinsbourne cited the Ahmed and Steinman studies he relied on in his written report. *Id.* at 182. He stated that both authors found antibodies to hypocretin receptors and postulated that these antibodies are caused by a cross-reaction to protein present in both the vaccine and in hypocretin receptors. *Id.* at 182-83. Damage to hypocretin receptors, Dr. Kinsbourne explained, reduces the effect of hypocretin, because the process is "a feedback of excitation." *Id.* at 182. Dr. Kinsbourne testified that Ahmed and Steinman have "put into evidence that a nuclear protein is present in varying amounts in different vaccines used for each H1N1 pandemic influenza vaccination." *Id.* at 183. "[W]hat [Ahmed and Steinman] claim in their publication is that the more nuclear proteins there are in a particular vaccine," Dr. Kinsbourne continued, "the more likely that vaccine is to trigger narcolepsy, keeping in mind that's still a very rare event." *Id.* Dr. Kinsbourne noted that, because narcolepsy is so rare, "it might not show up in epidemiology." *Id.* He went on to state that the vaccine with the highest amount of nucleoprotein is the Pandemrix vaccination, "which clearly, indubitably caused narcolepsy in a number of European countries." *Id.* Dr. Kinsbourne explained that the Fluzone vaccine

Petitioner received does not have as much nucleoprotein as Pandemrix, but "still a [] large amount compared to other vaccines." *Id.* at 185.

The other difference between Pandemrix and Fluzone, Dr. Kinsbourne stated, is that Pandemrix is adjuvanted. *Id.* An adjuvant is "a substance which helps magnify the effects of the vaccine." *Id.* Dr. Kinsbourne opined that adjuvants are "used by manufacturers basically to save money." *Id.* at 186. "Instead of having a bigger dose of the virus [in the] vaccine itself, which is expensive," Dr. Kinsbourne continued, "an adjuvant enables you to get as a good or a better effect with a smaller dose, somewhat smaller." *Id.* Dr. Kinsbourne added that contrary to some people, he does not believe that the adjuvant itself causes narcolepsy. *Id.* at 186-87. Dr. Kinsbourne explained that the adjuvant "is also [present in] other vaccines that are not known to cause narcolepsy," such as the DTaP, HPV, pneumococcal, and HIV vaccines. *Id.* at 187. "So," Dr. Kinsbourne stated, "I don't think anybody would argue the mere adjuvant is . . . the cause of the narcolepsy regardless of which particular vaccine is being given." *Id.* "It's argued," however, "that something about the Pandemrix [vaccine] makes it unique in [causing] narcolepsy." *Id.* at 187-88. Dr. Kinsbourne then pointed out that "the very same adjuvant has been given to a second vaccine, Arepanrix, . . . which does cause narcolepsy but very rarely [compared to] Pandemrix." *Id.* at 187-88. Additionally, Dr. Kinsbourne stated, Focetria, another vaccine, is "adjuvanted and doesn't cause . . . narcolepsy at all." *Id.* at 188.

Dr. Kinsbourne reiterated that he believes the nucleoprotein present in the Fluzone vaccine causes narcolepsy, and that this nucleoprotein is also present in the wild H1N1 virus. *Id.* at 188. Dr. Kinsbourne noted that "a well-known study in China shows that the . . . infectious, H1N1 influenza virus can cause narcolepsy even in the absence of vaccination." *Id.* at 189. Dr. Kinsbourne clarified that adjuvanted flu vaccines are not used in the United States. *Id.*

Dr. Kinsbourne then turned his attention to the Duffy study and noted that Dr. Jonathan Duffy works for the Centers for Disease Control and Prevention. *Id.* at 190. Dr. Kinsbourne referred to the study as "observational" and explained that the authors "ascertained a number of cases called narcolepsy across two years, 2009 [and] 2010, and compared the number before introduction of the [seasonal flu] vaccine and after." *Id.* at 191 "And also, and in a way more importantly," Dr. Kinsbourne said, "they took the control data from a totally different study, mainly one with the Mayo Clinic, in an area where the Mayo Clinic is located, called Olmsted County." *Id.* at 191-92. This Mayo Clinic study, Dr. Kinsbourne explained, was used to "ascertain the . . . background rate, roughly per year, of what to expect in terms of numbers of narcolepsy cases . . . ." *Id.* at 192. Dr. Kinsbourne then summarized that Duffy "had 870,000 people who were vaccinated that they picked up and did the study. And then they found, among those people, [sixteen] cases that were chart[-]confirmed into the diagnosis of narcolepsy." *Id.* Focusing on "the key sentence," Dr. Kinsbourne continued, "'none have their symptoms onset during the [one-hundred-and-eighty] days of the receipt of a 2009 pandemic vaccine compared with 6.5 expected.'" *Id.* at 192-93. The Duffy study researchers "decided that they were looking for narcolepsy cases that had begun within six months of their vaccination," and the background rate they were expecting from the Mayo Clinic study was 6.52. *Id.* at 193. Dr. Kinsbourne noted that despite this expectation, "the number they found, amazingly, was zero." *Id.* Dr. Kinsbourne opined that "it's beyond belief that in this period of six months after an influenza vaccination,

nobody had narcolepsy, and yet a bunch of people did have narcolepsy within that two-year period." *Id.* at 194.

"[I]n a normal epi[demiological] study," Dr. Kinsbourne said, "you have a background rate and then you see whether, in the period you're examining, they're significantly more than the background rate." *Id.* at 194-95. Instead, Dr. Kinsbourne elaborated, the Duffy researchers saw "the background itself going away." *Id.* at 195. Dr. Kinsbourne challenged the study, stating, "[w]hat happened to the background, is the question." *Id.* at 195. Dr. Kinsbourne's other objection to Duffy was that Petitioner was over forty when she had her onset of narcolepsy, and Duffy did not have a background rate for her age group; in fact "[t]hey didn't even consider that narcolepsy would [at] all appear at that time." *Id.* at 195-96. "So," Dr. Kinsbourne said, "I don't think it really examines [Petitioner's] case in this study." *Id.* at 196. "[H]aving said this," Dr. Kinsbourne noted, "I think my confidence [in Duffy] [is] undermine[d] by this curious . . . effect of zero versus a loss of background rate, relative to vaccination." *Id.*

Dr. Kinsbourne noted two other studies, one "by a Japanese researcher" that found narcolepsy in all age groups though a study of autopsies, and Montplaisir, which found "one in a million people had narcolepsy." *Id.* at 196-97. Dr. Kinsbourne said that such a small number would not concern epidemiology because that discipline is "concerned with public health," not "individuals." *Id.* at 197. Dr. Kinsbourne continued that in Montplaisir, the researchers also were blind to whether the narcoleptic had been vaccinated. *Id.* at 200. He contrasted this methodology to the Duffy study where they were not blind as to vaccination. *Id.* This is significant for Dr. Kinsbourne because "people have sometimes very emotional reactions for or against vaccine risks and that complicates a person's review, even unconsciously." *Id.*

Dr. Kinsbourne also noted that Petitioner tested positive for the genetic marker that "makes her more susceptible to develop narcolepsy." *Id.* at 202. People who have the HLA-DQB1*0602 allele, Dr. Kinsbourne said, "pretty much exclusively . . . only get narcolepsy." *Id.* But, Dr. Kinsbourne conceded that "it is also a fact that many, many who, in fact, don't get narcolepsy also have it." *Id.* at 203. He explained that this association is "compatible with our theory, but it doesn't necessarily make our theory that much stronger." *Id.* Petitioner's counsel quoted Dr. Scammell's assertion that "an immune stimulus, such as [an] infection" could trigger "in genetically susceptible persons" an inflammatory reaction that could disrupt hypocretin production "through a process of molecular mimicry." *Id.* at 203. Dr. Kinsbourne agreed, but emphasized that there is no evidence in the record that Petitioner had an infection "at a relevant time" that could have caused her narcolepsy. *Id.* at 203-04. Dr. Kinsbourne concluded that "there is no direct proof" that H1N1 causes narcolepsy, but based upon his research he concluded "to a reasonable medical probability" that Petitioner's flu vaccine caused her narcolepsy. *Id.* at 204-05.

On cross-examination, Dr. Kinsbourne conceded that he has not had a formal clinical practice since the "early 1990s." *Id.* at 206-07. He stated that he "see[s] patients from time to time, . . . in [his] home" for a condition he "discovered years ago." *Id.* at 207. Dr. Kinsbourne stated that, although he described himself as a pediatric neurologist, he has "held appointments as [a] professor assistant [sic], [a] social professor of pediatrics, and an associate professor of neurology." *Id.* at 209. Dr. Kinsbourne also stated that "although [he] was chief of the pediatric

section [of neurology], [he] worked in both [adult and pediatric neurology]." *Id.* His practice does not involve "the treatment or diagnosis of sleep disorders," and the last person he treated for narcolepsy was "quite a while ago," in the late 1980s or 1990. *Id.* at 209-10. Dr. Kinsbourne stated that he diagnosed people with narcolepsy as a student, resident, and in his neurological practice with children. *Id.* at 210. Dr. Kinsbourne conceded that his knowledge of the issues in this case derives from the research he did for this case. *Id.* at 211. Dr. Kinsbourne agreed that he does not have any "formal specialized education, training, or experience" in sleep disorders, and he stated that he relied upon Petitioner's tests to determine her diagnosis. *Id.* at 212. "I don't have to rely on somebody's opinion here," he said. *Id.*

Respondent turned to Dr. Kinsbourne's first report, based upon the De la Herrán-Arita article. *Id.* at 213. Dr. Kinsbourne did not know if he had discussed the retraction of the article in his report and explained that they failed to "find homology between the vaccine and the hypocretin neurons in the hypothalamus." *Id.* Dr. Kinsbourne claimed that "it is not essential when proving an autoimmune attack by a vaccine or any substance, actually, to have found the homology." *Id.* Dr. Kinsbourne said that he "[had] no idea why [he] didn't discuss the retraction." *Id.* He continued to champion the De la Herrán-Arita study, despite its retraction, and stated that "it still seemed, to me, overwhelmingly likely that narcolepsy was caused by an autoimmune process, even if we don't know the homology that's involved." *Id.* at 215. Respondent asked Dr. Kinsbourne if his first report was based upon an article that was retracted, and Dr. Kinsbourne responded that, "No. there are numerous articles which state the opinion or come to the conclusion that it is likely to be an autoimmune attack on . . . the hypocretin neurons." *Id.*

Respondent then asked, "Can you point me towards the page or reference in your [first] report . . . where you offer a theory other than the one based on the De la Herrán-Arita article?" *Id.* at 215-26. Dr. Kinsbourne answered, "It's the same theory, whether it's based on the article or not." *Id.* at 216. Dr. Kinsbourne cited to the De la Herrán-Arita study to "give at least more medical opinion" and noted that Dr. Scammell also thinks that "it's an autoimmune process that's involved in causing narcolepsy." *Id.* Dr. Kinsbourne stated that the retraction of the De la Herrán-Arita study "doesn't change my opinion." *Id.* Dr. Kinsbourne clarified that he is not relying upon the De la Herrán-Arita article to support his opinion that Petitioner's flu vaccine caused her narcolepsy and emphasized that the Ahmed and Steinman article, "which wasn't around when I did my first report," provides the best support. *Id.* at 217-18. When questioned about the timing of the Ahmed studies, Dr. Kinsbourne reversed course and agreed that "the Ahmed studies that [he is] now relying on were already published at the time [he] wrote [his] initial report in this case . . . ." *Id.* at 220. Dr. Kinsbourne added that he "could have presumably, yes," relied upon the Ahmed and Steinman study to base his opinion, but conceded that "I can't remember the logical contortions I went through to decide or to notice any of this." *Id.* at 220-21. "[O]n further consideration," Dr. Kinsbourne then stated, "and particularly since the retraction[,] it seemed to that [the Ahmed and Steinman study] will be the more reasonable theoretical approach to offer – to show that indeed the H1N1 vaccine can cause narcolepsy." *Id.* at 221. Under Respondent's questioning, Dr. Kinsbourne agreed with a quote from the Vassalli letter that "'until the pathogenicity of the reported anti-HCRTR2 antibodies is established, the findings of Ahmed and colleagues should be considered as preliminary and not as evidence for

molecular mimicry between H1N1 nuclear protein and HCRTR2, resulting in hypocretin deficiency.'" *Id.* at 221-22.

Returning to the Duffy study, Dr. Kinsbourne explained that he did not criticize Duffy for being an observational study; "[i]t was a statement." *Id.* at 222. Dr. Kinsbourne noted that an observational study, "when done appropriately," could "still provide some reliable evidence of associations." *Id.* Dr. Kinsbourne explained that "[i]t would have been . . . probably preferable to have controls from the actual Duffy study than to have control from another part of the country, but still acceptable." *Id.* at 223-24. Dr. Kinsbourne added upon further reflection that he didn't "have an issue with [Duffy] using [the Mayo study] as a reference point." *Id.* at 224. Correspondingly, Dr. Kinsbourne stated that he did not have an issue with the Montplaisir study also using the Mayo Clinic study as a reference. *Id.* at 225. Dr. Kinsbourne clarified that his objection to Duffy was that they "report zero for what they actually find in a period for which there must have been a base rate." *Id.* A study should find a number that's "comparable to the base rate," Dr. Kinsbourne explained, "[b]ut you wouldn't expect suddenly nothing." *Id.* at 226. Dr. Kinsbourne found it unlikely "that just after a vaccination, there aren't any cases [of narcolepsy], and yet without a vaccination, there are a certain number, six cases, for a period." *Id.* at 227. Dr. Kinsbourne stated that he is not an epidemiologist, nor did he perform any statistical analysis on Duffy. *Id.* Dr. Kinsbourne also clarified his prior criticism that, because Duffy did not include any analysis of subjects within Petitioner's age range, "[i]t's not as informative to this case . . . ." *Id.* at 228. Respondent highlighted that the Pandemrix studies also did not investigate narcolepsy onset cases in subjects in Petitioner's age range. *Id.* at 230. Dr. Kinsbourne responded that Petitioner's case "is a rare case," and "[f]or something not to be a signal in epidemiology, is not evidence against the existence of a rare case." *Id.* Respondent then asked what kind of study would be required to demonstrate a connection between Fluzone and narcolepsy, if Duffy is unreliable. *Id.* at 231. Dr. Kinsbourne responded that a study showing "a homology" would be required. *Id.* at 232. "If you have a homology," Dr. Kinsbourne said, "you don't care about the epidemiology, because you have direct proof." *Id.* "We don't have direct proof in this issue," Dr. Kinsbourne stated. *Id.* at 232. He continued, "There is no direct proof of anybody's theory." *Id.* "I'm offering a theory which was published in peer-reviewed articles, and is one way of explaining what happened to [Petitioner]." *Id.* at 232. "I'm not asserting that it's necessarily the case," he continued, "[i]t's not scientifically certain." *Id.*

The undersigned asked Dr. Kinsbourne if he was relying upon an autoimmune reaction based on homology, or on "the plausibility of molecular mimicry in this case?" *Id.* at 233. Dr. Kinsbourne answered that he is relying upon the hypothesis put forward by Drs. Ahmed and Steinman. *Id.* Dr. Kinsbourne also answered that he believed this hypothesis is specific enough to apply to the Fluzone vaccine. *Id.* He explained that "in vaccines, you rarely have all the parts [of a causation theory]." *Id.* at 234. Dr. Kinsbourne noted that has "some of the parts[,] . . . enough parts to say that it's more likely than not." *Id.* at 234. The undersigned asked Dr. Kinsbourne if he believed "it would ever be possible to develop a population-based study to prove" his theory. *Id.* Dr. Kinsbourne believed that it would be cost-prohibitive to assemble "[ten] million people or whatever it is you need statistically to show an effect." *Id.* Dr. Kinsbourne concluded his testimony by stating that he believes his causation theory meets the *Althen* criteria. *Id.* at 236.

ii. Respondent's Expert, Dr. Scammell

Dr. Thomas Scammell is a Professor of Neurology at Beth Israel Deaconess Medical Center and has "a 10 percent appointment at Boston Children's Hospital." *Id.* at 244. He is also the division chief for sleep medicine in the neurology department and undertakes research in narcolepsy and other sleep disorders. *Id.* Dr. Scammell stated that he conducts research three days a week and the rest of his time is spent in a clinical setting. *Id.* Dr. Scammell also noted that he was involved in drafting the International Classification of Sleep Disorders by the American Academy of Sleep Medicine. *Id.* at 245. In his clinical practice, Dr. Scammell currently cares for "about [sixty]" patients with sleep disorders. *Id.* at 246.

Dr. Scammell testified that he and his colleagues take narcolepsy very seriously, "because, as best we understand it, narcolepsy is a lifelong diagnosis." *Id.* Due to the permanent aspect of the diagnosis, he explained that "you want to be sure that you're calling it right." *Id.* For himself and other doctors settling on that diagnosis, "we really want to get a very careful medical history, we want to do a careful physical exam, and we want to have really high-quality sleep lab tests to be confident that we're making the right diagnosis." *Id.* Dr. Scammell stated that "a lot of the diagnosis is in the history [and] listening to the patient's story . . . ." *Id.* Dr. Scammell continued that once he and his colleagues have the patient's medical history, "we do a physical exam, which is usually normal, and the sleep studies." *Id.* at 247. Dr. Scammell explained that there are "very precise rules about how to do a good set of sleep studies[,] and then you also have to acknowledge that the tests have some limitations too." *Id.* Dr. Scammell explained that "we do an overnight sleep study [to diagnose narcolepsy], also called a polysomnogram, where we record brain activity, muscle activity, and so forth." *Id.* at 249. Dr. Scammell continued that the next day, they perform the multiple sleep latency test, "and it's the combination of these two tests together that really is diagnostically useful." *Id.* The first test is "probably the most important role . . . [in] that it helps us look for other sleep disorders . . . ." *Id.* Dr. Scammell noted as an example that Petitioner's polysomnogram showed that Petitioner has sleep apnea. *Id.*

Dr. Scammell then noted that the "only other symptom that's really specific to narcolepsy is cataplexy." *Id.* It is similarly important to listen to the patient's history in making a diagnosis, because "we end up putting a lot of weight on the sleepiness itself and the cataplexy" due to the occurrence of other symptoms in the general population. *Id.* at 248. In overnight sleep studies of people who have narcolepsy with cataplexy, Dr. Scammell stated that "a third of the time it shows that the patient goes into REM sleep very quickly." *Id.* at 249-50. People with narcolepsy also fall sleep "very, very quickly at night on the polysomnogram." *Id.* at 250. "So," Dr. Scammell said, "if somebody has an essentially normal polysomnogram, [the physicians have] dealt with other sleep problems, and [the patient is] on no psychoactive medications, then we can really trust the results of [the] multiple sleep latency test." *Id.* This test involves asking the individual "to try to fall asleep about every two hours, five times across the day," Dr. Scammell stated. *Id.* Dr. Scammell continued that physicians look for "how quickly does the person fall asleep, and do they go into REM sleep during those daytime naps." *Id.* It is "very unusual for a person to have REM sleep during the daytime," unless they are on certain psychoactive medication or have narcolepsy, Dr. Scammell explained. *Id.* at 250-51. If physicians see a patient, across all five naps, "fall[] asleep, on average, in less than eight minutes, and if at least

two of the naps contain REM sleep, then we consider that supportive evidence for narcolepsy." *Id.* at 251. But, Dr. Scammell cautioned that the multiple sleep latency test "is not proof in itself that a person has narcolepsy, because we know that the test can be falsely positive sometimes or falsely negative." *Id.*

Prior to the multiple sleep latency test, Dr. Scammell continued, "we try our best to ask patients to discontinue" certain medication that can alter the effects of the tests. *Id.* at 251-52. These medications include "pretty much any medicine that affects the brain," including any sedating medicines or stimulants, and any antidepressants. *Id.* at 252. Dr. Scammell said that his office instructs patients to "stop antidepressants about three weeks before the [multiple sleep latency] test, stop stimulants and sedatives a week before, and at least for the week running into the test" to try to get seven-and-a-half to eight hours of sleep every night. *Id.*

Turning to Petitioner's case specifically, Dr. Scammell explained that her symptoms were predominantly, from her medical records, "sleepiness and these episodes of staring, unresponsiveness." *Id.* at 253. Narcolepsy type one, narcolepsy type two, and other sleep disorders were thus considered by Dr. Scammell in analyzing Petitioner's case. *Id.* Dr. Scammell explained that he approached Petitioner's diagnosis of narcolepsy with some skepticism, but he ultimately stated that narcolepsy would be on the list of differential diagnoses he would make for Petitioner. *Id.* at 254, 260.

Dr. Scammell also expressed his skepticism towards Petitioner's diagnosis of cataplexy. *Id.* at 254. Because cataplexy occurs "in almost no other medical disorders [than narcolepsy]," Dr. Scammell reasoned that it is important to have an understanding whether a patient has it in order to make a firm diagnosis of narcolepsy. *Id.* at 254-55. Dr. Scammell defined cataplexy as "emotionally triggered episodes of muscle weakness." *Id.* at 255. In fact, "many patients," Dr. Scammell continued, "can identify specific emotions that trigger" cataplexy. *Id.* What Dr. Scammell gleaned from Petitioner was that she was triggered "where something unexpected and really positive happens." *Id.* Dr. Scammell stated that this "is a very typical thing to cause an event of cataplexy." *Id.* But, Dr. Scammell continued, Petitioner's cataplexy is atypical. *Id.* at 256. Dr. Scammell explained that normal cataplexy first presents with "partial weakness . . . . It's pretty rare for people to suddenly fall to the ground." *Id.* During a typical cataplectic episode, Dr. Scammell continued, a person can't respond, but "after a minute or two, sometimes three at most, the cataplexy resolves, and they're able to give a good explanation of what happened during that." *Id.* In Petitioner's case, Dr. Scammell stated there was not a consistent trigger for her events, and it's very unusual for someone's eyes to remain open during a cataplectic episode. *Id.* at 256-57. One of the first things usually affected with cataplexy, Dr. Scammell noted, are the eyelids, and "people sort of look sleepy because the face becomes slack and the head bobs forward." *Id.* at 257. In fact, Dr. Scammell noted, "almost everybody has this facial weakness as part of [their cataplexy]," but "[t]here are rare patients where they may have other parts of the body affected . . . ." *Id.* Additionally, Dr. Scammell stated that Petitioner has unusually long cataplectic episodes, as most cataplectic spells last "for a few seconds, to, you know, a handful of minutes, two, three minutes at most." *Id.* at 258. The last atypical aspect of Petitioner's condition is that, after she recovers from her spells, she is tearful and upset, where normally, "over the course of a few seconds [after a cataplectic incident], they're better." *Id.* at 258-59.

Dr. Scammell acknowledged that "in clinical medicine, everybody is different and people have different triggers, people have different symptoms, and there certainly is a spectrum." *Id.* at 259. After hearing witness testimony in this case, Dr. Scammell stated that, "I'm still not fully convinced that [Petitioner] has narcolepsy, but I think it's . . . on the list." *Id.* at 260. Dr. Scammell noted that there are some other disorders that could explain Petitioner's sleepiness, "[a]nd it's possible that some of these factors or some combination of them is accounting for the overall picture." *Id.* Dr. Scammell explained that the incident where Petitioner was on the toilet and fell into the opposite wall could be explained by her taking Xyrem, but he did not have enough information to know for certain. *Id.* at 261-62.

Respondent then asked Dr. Scammell whether Petitioner's sleep apnea could contribute to her symptoms. *Id.* at 262. Dr. Scammell noted that there "was this honeymoon period after starting the CPAP when it sounded like, from the description in the notes, that her sleepiness got better, to the point where her doctor stopped some of her narcolepsy medicines." *Id.* CPAP "doesn't do anything for narcolepsy," Dr. Scammell said, so this period of improvement "would suggest that at least some of the sleepiness could be due to sleep apnea." *Id.* at 263. It is, in fact, "very common," for narcoleptics to have other sleep disorders, Dr. Scammell attested, and he and his practice "try to look for those alternative causes and really try to fix them as best we can" because narcolepsy is incurable. *Id.* at 263-64.

Dr. Scammell then noted that Petitioner tested positive for the HLA-DQB1*0602 allele connected with narcolepsy. *Id.* at 265. Dr. Scammell explained that this allele appears in ninety percent of people with narcolepsy type one and in about fifty percent of people with narcolepsy type two, narcolepsy without cataplexy. *Id.* Unfortunately, Dr. Scammell continued, the allele itself is not that helpful diagnostically because it also appears in twenty-five percent of the general population. *Id.* "However," Dr. Scammell explained, "if somebody has a story that's consistent with narcolepsy, their sleep tests are consistent with narcolepsy, and they carry the gene, well, these things collectively help build a case and it makes the probability of that being a diagnosis stronger." *Id.*

Dr. Scammell highlighted the issues with the diagnostic tests performed on Petitioner. *Id.* at 266. On September 13, 2013, Petitioner had an overnight polysomnogram and a multiple sleep latency test the next day, but both "had some issues which make them a little bit hard to interpret[;] actually, in this case, more than a little hard. I would say difficult to interpret." *Id.* First, Dr. Scammell stated, Petitioner only slept six hours during her polysomnogram, which is "just on the edge of what we consider an adequate amount of sleep." *Id.* at 267. This lack of sleep, Dr. Scammell continued, would make it easier for a patient to fall asleep during the nap test on the following day. *Id.* Dr. Scammell also explained that Petitioner had "less than the usual amount of rapid eye movement sleep on that overnight test." *Id.* This is common, Dr. Scammell explained, "but it . . . raises a question of [whether] some medications were interfering with REM sleep . . . ." *Id.* In fact, Dr. Scammell continued, Petitioner was taking escitalopram at that time, "which we know alters REM sleep." *Id.* at 267-68. Petitioner additionally did not go into REM sleep within fifteen minutes of sleep onset, which is not "indicative of narcolepsy." *Id.* at 268. Dr. Scammell again raised the issue that Petitioner was on medication during the day-time naps that is known to interfere with REM sleep and also noted that Petitioner was

additionally taking two sedating medications at the time of her test, topiramate and lorazepam. *Id.* at 268-69. Dr. Scammell explained that these issues complicate Petitioner's sleep study and "make[] [the study] hard to interpret." *Id.* at 260.

Dr. Scammell stated that in narcolepsy with cataplexy, patients have "very little or no detectable hypocretin or orexin in their spinal fluid." *Id.* at 270-71. He noted that in Europe, physicians "quite frequently now" will measure hypocretin levels in spinal fluid as a way to diagnose narcolepsy. *Id.* at 271. In fact, in about ninety percent of people suffering from narcolepsy with cataplexy, "the hypocretin levels are low or just plain undetectable." *Id.* Petitioner would benefit from such a test, Dr. Scammell said; however, there is no commercial lab that runs the test in the United States. *Id.* at 272. Dr. Scammell noted that it would be helpful, however, for Petitioner to undergo a "clean sleep study" where she has been off of any psychoactive medication prior to the study, or to undergo a lumbar puncture to have a clear picture of her diagnosis. *Id.* at 273-74. Dr. Scammell ultimately stated that "there's about a 50/50 chance . . . that indeed there's narcolepsy with cataplexy" in Petitioner's case. *Id.* at 275. Dr. Scammell highlighted the mediating factors to make him question Petitioner's diagnosis, including her descriptions of her cataplexy and the irregularities in her sleep study; but, "everybody is different, and in the clinical world, we see a spectrum of symptoms." *Id.* at 274-75. If Dr. Scammell were caring for Petitioner, he would "like to see more objective evidence . . . because, as I said before, it's a lifelong diagnosis." *Id.* at 275.

Turning to Petitioner's causation theory, Dr. Scammell began by referencing his article, "Narcolepsy" from the New England Journal of Medicine. *Id.* at 276-77; Pet'r's Ex. J. He stated that "around 1998," researchers made the connection between narcolepsy and the HLA gene, and hypothesized that narcolepsy was an autoimmune condition. *Id.* at 277. "That was a long time ago," Dr. Scammell said, "and in the last, you know, 30-plus years, research have not found any convincing evidence that really proves [the autoimmune hypothesis]." *Id.* Dr. Scammell continued that the idea that an "inflammatory reaction damages the orexin-producing neurons, perhaps through a process of molecular mimicry" is countered by the fact that "no signs of inflammation are detected in cerebrospinal fluid or seen on magnetic resonance imaging." *Id.* In addition, Dr. Scammell noted, "[T]here's no strong evidence of an increased prevalence of other autoimmune disorders among people with narcolepsy." *Id.* Lastly, Dr. Scammell added that immune system-altering drugs have been used on narcoleptics and "have not been helpful." *Id.* Dr. Scammell commented that the idea that an autoimmune reaction causes narcolepsy "is an interesting idea," but added, "it's a hypothesis." *Id.* at 279.

Dr. Scammell then explained how hypocretin works in the brain. *Id.* He began that "there are a cluster of neurons, brain cells that produce hypocretin, also called orexin." *Id.* at 280. "These cells send connections to lots and lots of places in the brain, pretty much all of the brain," Dr. Scammell continued. *Id.* When those hypocretin neurons are stimulated, Dr. Scammell said, "they release hypocretin, which has excitatory effects on those [target] neurons, and it makes them fire more and wake up." *Id.* In narcolepsy, when the hypocretin neurons die, "those signals that help turn on lots of great regions are absent and people consequently end up with chronic sleepiness and REM sleep is no longer properly controlled." *Id.*

The Ahmed paper, Dr. Scammell said, "hypothesizes that there's some autoimmune process that acting upon hypocretin-2 receptors," one type of hypocretin receptor that allows for excitation of the target neurons. *Id.* at 280-81. "The fundamental problem with this idea," Dr. Scammell said, "is that those receptors are found in a tremendous amount of the brain." *Id.* at 281. Dr. Scammell estimated that those receptors are found in thirty to fifty percent of brain neurons. *Id.* If narcolepsy caused an autoimmune attack on these receptors, Dr. Scammell reasoned, "you would have widespread damage across the brain." *Id.* But, in narcoleptics, "we see only a loss of the hypocretin neurons without damage to all these other brain regions." *Id.* Dr. Scammell explained that additional research would be needed to prove Ahmed's hypothesis. *Id.* at 282. Dr. Scammell noted that this is a "very active area of research[, with] [ten] or a dozen research groups around the world that are now trying to find that evidence that there is an autoimmune process that could cause narcolepsy." *Id.* Dr. Scammell emphasized that "there's been dozens of papers written on this, but none of them really provide conclusive proof." *Id.*

Dr. Scammell then clarified that "it depends on which study you're looking at" whether it is ninety or ninety-eight percent of type one narcolepsy patients have the HLA gene. *Id.* at 283. Dr. Scammell also attested that this fact does not have any relevance to the question of whether the flu vaccine causes narcolepsy. *Id.*

Respondent then turned Dr. Scammell's attention to the Duffy study. *Id.* at 284. Before addressing the study, Dr. Scammell clarified that the "general feeling is that narcolepsy affected one in 2,000 people[,] and narcolepsy usually begins in children, typically in the teen years, between ages [ten] and [twenty]." *Id.* at 285. Referencing the one in 2,000 number, Dr. Scammell said that these cases occur without an understanding of "what the usual trigger and factor is." *Id.* at 285-86. Dr. Scammell reiterated the fact that it is unusual for someone to have an onset of narcolepsy after the age of forty, like Petitioner; however, Dr. Scammell also noted that "I've seen patients myself who have developed narcolepsy in their adults years, but generally it occurs in children." *Id.* at 286. Dr. Kinsbourne, Dr. Scammell said, relied upon the Montplaisir study to say that there is a one-in-a-million chance of developing narcolepsy after flu vaccination, and, when you consider that one in 2,000 people will develop narcolepsy normally, "it's hard to envision even designing and paying for a study that would actually be able to detect an event of such rarity." *Id.* at 286-87. Comparing these probabilities, Dr. Scammell concluded, "it certainly seems like just getting narcolepsy for the usual reasons, whatever they might be, is a much more likely event." *Id.* at 287.

The undersigned then questioned Dr. Scammell. *Id.* at 288. Dr. Scammell was first asked whether Petitioner's diagnosis of type one or type two narcolepsy has any bearing on whether it is an autoimmune reaction. *Id.* Dr. Scammell stated that the influx in narcolepsy cases following the use of Pandemrix "led many of us to think that narcolepsy is caused by a combination of" genetics and an immune stimulus. *Id.* at 289. Importantly, Dr. Scammell said, all of the patients who had narcolepsy following Pandemrix had very clear cases of narcolepsy type one, or narcolepsy with cataplexy. *Id.* "I don't believe that there's any epidemiological evidence, from other papers or other events, that suggest any increase with vaccines causing narcolepsy type [two]," said Dr. Scammell. *Id.* at 289-90. Dr. Scammell explained that this difference is why it is important to consider whether Petitioner has cataplexy, especially when Petitioner has many atypical aspects of cataplexy. *Id.* at 290-91. Dr. Scammell also noted that

Petitioner's stories of having a cataplectic attack after being frightened are atypical, as "when people are startled, they generally have an increase in muscle tone, not a decrease in muscle tone." *Id.* at 292. But, Dr. Scammell admitted that the touchdown story Petitioner told is "a really classic trigger[,]" and he repeated his estimate that it was a 50/50 chance whether Petitioner has narcolepsy with cataplexy. *Id.* at 290, 294.

iii. Respondent's Expert, Dr. MacGinnitie

Dr. Andrew MacGinnitie is the Clinical Director for the Division of Immunology at Harvard Medical School, where he is also an associate professor. *Id.* at 195. He is also an attending physician at Boston Children's Hospital, where he sees patients two days a week. *Id.* at 295-96. He manages the clinical and business operations of the Division of Immunology, and conducts research, "particularly into food allergy and [a] rare illness called hereditary angioedema." *Id.* at 296. In his clinical practice, Dr. MacGinnitie primarily sees children with a typical diagnosis of "dermatitis, food allergy, asthma, allergic rhinitis." *Id.* Dr. MacGinnitie also sees adult patients in five to ten percent of his practice, "particularly with immunologic disorders." *Id.*

Dr. MacGinnitie first addressed Dr. Kinsbourne's causation theory relying upon the Ahmed hypothesis. *Id.* at 297. Dr. MacGinnitie stated that he does not think the Ahmed paper provides "a coherent explanation that links the flu vaccine and specifically Fluzone to narcolepsy." *Id.* He reiterated Dr. Scammell's point that hypocretin-2 receptors are found throughout the brain, and the theory does not detail why researchers do not find widespread damage due to the antibody if it were the cause. *Id.* Dr. MacGinnitie also noted that "there's no data [from studies] from patients who are vaccinated with nonadjuvanted vaccine[s] [who develop narcolepsy]." *Id.* at 297-98. Dr. MacGinnitie explained that adjuvants "are a substance that are added to a vaccine to increase the immune response . . . ." *Id.* at 298. Dr. MacGinnitie stated that he doesn't "have any particular knowledge" whether adjuvants are added to vaccines to save money, as Dr. Kinsbourne attested. *Id.* at 299. But, Dr. MacGinnitie continued, "I know that in particular, for younger children[,] the immune system is much weaker." *Id.* Dr. MacGinnitie continued, "So if you use nonadjuvanted vaccines in infants, you see a very weak immune response, and so adding an adjuvant particularly in that age group will increase the strength of the immune response." *Id.*

Returning to the Ahmed (2015) study, Dr. MacGinnitie explained that the existence of the hypocretin-2 receptor antigens "could be a marker of the disease rather than a cause of disease." *Id.* at 300. In other diseases, "as an autoimmune attack occurs and the cells that are being attacked die, they release other proteins that are often not exposed to the immune system . . . ." *Id.* "[A]nd then," Dr. MacGinnitie continued, "you can actually see antibodies against [the other proteins] that aren't causative of the disease but are just a marker of it." *Id.* Dr. MacGinnitie referenced the Kawashima, Bergman, and Saariaho articles as evidence that researchers have found "a total of four . . . potential antibodies in [narcolepsy] and so whether these are actually causative of disease or they're just a marker is not clear." *Id.* at 301 (citing Resp't's Ex. TT, Minae Kawashima et al., *Anti-Tribbles Homolog 1 (TRIB2) Autoantibodies in Narcolepsy are Associated with Recent Onset of Cataplexy*, 33 Sleep 869 (2010); Resp't's Ex. UU, Peter Bergman et al., *Narcolepsy patients have antibodies that stain distinct cell populations*

in rat brain and influence sleep patterns, PNAS Plus (Aug. 18, 2014), http://www.pnas.org/cgi/doi/10.1073/pnas.1412189111; Resp't's Ex. VV, Anna-Helena Saariaho et al., *Autoantibodies against ganglioside GM3 are associated with narcolepsy-cataplexy developing after Pandemrix vaccination against 2009 pandemic H1N1 type influenza virus*, 63 J. Autoimmunity 68 (2015)).

Dr. MacGinnitie then provided background and explained that there are two "major parts of what's called the adaptive immune [system]." *Id.* at 302. These two parts are the B cell mediated antibody system, and the T cell system. *Id.* B cells, Dr. MacGinnitie illustrated, "make antibodies that are proteins in the blood" that bind to "whatever their target is, and if that was a bacteria or a virus, it would either prevent infection or cause the infectious agent to be cleared." *Id.* "T cells," Dr. MacGinnitie said, "are a little more complex." *Id.* Dr. MacGinnitie continued that the HLA antigens that are associated with the HLA gene "are expressed on all cells of the body[,] and they pick up fragments of a protein called peptides." *Id.* These HLA antigens bind with peptides, and T cells "float around and look for the specific peptide in that specific HLA type." *Id.* Dr. MacGinnitie explained that narcolepsy type one is "almost entirely present in patients who have a specific HLA type." *Id.* The association between narcolepsy and a specific HLA type "provides very strong evidence that T[]cells must be involved in the pathogenesis if it truly is an autoimmune disease . . . ." *Id.* at 302-03. There is "a high degree of variability in which HLA proteins people express, . . . [s]o we refer to this as a disease being HLA restricted." *Id.* at 303. Narcolepsy is thus "dependent on specific HLA types, . . . and that indicates an obligate role for T[]cells in the disease." *Id.* Dr. MacGinnitie explained that the De la Herrán-Arita was appealing because "it really purported to demonstrate that these T[]cells were present[,] and they were directed against hypocretin." *Id.* Dr. MacGinnitie stated that because we know hypocretin is HLA restricted, "[w]e have . . . T[]cells that we know must exist," and De la Herrán-Arita provided an explanation how these T cells target hypocretin. *Id.* at 303-04. This hypothesis would have provided "a great explanation" of the mechanism behind narcolepsy if the data therein were legitimate. *Id.* at 303.

Dr. MacGinnitie explained that the Ahmed article does not provide any of the certainty the De la Herrán-Arita article would have provided were it found to be reliable. *Id.* at 304. The autoantibodies that Ahmed proposes are "less specific" than HLA-associated T cells, and the Ahmed article does not provide "any evidence for T[]cell[]" involvement. *Id.* at 303-04. In fact, Dr. MacGinnitie said, the Ahmed authors acknowledge that their inability to identify any T cells is a "weakness of their paper." *Id.*

Dr. MacGinnitie explained that the "real weakness" of Ahmed is that their control groups without narcolepsy have the antibodies Ahmed posits as causative. *Id.* at 305. For instance, Dr. MacGinnitie commented, the authors of Ahmed found seventeen out of twenty people vaccinated with Pandemrix had the hypocretin-2 receptor antibody, "which, right, that sounds pretty impressive." *Id.* The authors also had twelve people vaccinated with Focetria, a vaccine adjuvanted similarly to Pandemrix, who did not have narcolepsy and did not have antibodies against hypocretin-2 receptors. *Id.* But, Dr. MacGinnitie said, "roughly four or five" out of twenty people who had narcolepsy not following vaccination also had antibodies, and, more importantly, over half of the control group of eleven Finnish children "had antibodies against the hypocretin receptor." *Id.* "[I]t's a little hard to square [Ahmed's] findings of over half of normal

children expressing antibodies against this receptor with [the antibodies] being causative." *Id.* at 306. Dr. MacGinnitie also mentioned that the study was published in 2015, "and there's been no data since then." *Id.* Dr. MacGinnitie quoted the Ahmed article's noted limitations, "that the findings reported in this study should be viewed as a step of understanding the mechanism of vaccine-associated narcolepsy and will benefit from additional confirmatory studies . . . ." *Id.* at 308.

Dr. MacGinnitie then addressed Dr. Kinsbourne's argument that adjuvants could not be the cause of narcolepsy because adjuvants are present in other vaccines. *Id.* at 309. Dr. MacGinnitie said, "I think it's a little bit misleading to say that many vaccines contain adjuvants, [as] adjuvant is just really a term that we could define as a substance that's not immunogenic in itself," meaning that it "does not cause [an immune] response to itself but increases the body's response to whatever it's mixed with." *Id.* "[T]here are a wide variety of substances that have been used as adjuvants," Dr. MacGinnitie continued, "for example, Pandemrix, and Arepanrix, have a specific adjuvant that's called ASO3, [which] is best described as oil and water, . . . an emulsion . . . that's added to [] these influenza vaccines." *Id.* at 309-10. "[I]n DTaP and HPV[,]" Dr. MacGinnitie explained, "[t]he adjuvant . . . is completely different." *Id.* at 310. It is a "salt of aluminum." *Id.* Dr. MacGinnitie concluded, "And so I don't think the fact that DTaP or HPV vaccines have not shown an increased risk of narcolepsy really provides any evidence that adjuvants couldn't be involved . . . ." *Id.* It is very important "to realize that really the only evidence for an increased risk of narcolepsy after influenza vaccine is with adjuvanted vaccines," Dr. MacGinnitie stressed. *Id.* Dr. MacGinnitie stated that he did not think "we could know the answer" whether the adjuvant by itself is sufficient to cause narcolepsy." *Id.* "[B]ut," Dr. MacGinnitie said, "it seems to me to be clear that the adjuvant is required." *Id.* Dr. MacGinnitie noted that adjuvanted vaccines have also never been used in the United States. *Id.* at 311.

Dr. MacGinnitie then explained how differing manufacturing processes for vaccines can affect how the vaccine triggers and immune response. *Id.* at 312. He stated that "early in the year," what experts believe will be the most prevalent flu strains are selected, "produced in mass, and then isolated into vaccines." *Id.* In Europe, they then add adjuvants to these vaccines, but in the United States some additives are used. *Id.* Dr. MacGinnitie explained that "studies have shown some differences among different preparations of vaccines even containing the same strands, in terms of protein content and the amount of immune stimulus that's given." *Id.* These differences can result from how "the proteins were isolated, which cell lines were used, etc.," Dr. MacGinnitie continued. *Id.* at 312-13. Dr. MacGinnitie then explained that it is unclear if the wild-type virus can cause narcolepsy in itself. *Id.* at 313. He commented that inflammation can be a trigger in other autoimmune diseases and that an influenza illness can cause inflammation and a "very strong" immune stimulus. *Id.* 313-14. This strong stimulus could "break[] tolerance" and cause an autoimmune reaction. *Id.* at 313-14. Dr. MacGinnitie then explained that a wild-type infection would provide the strongest immune stimulus, followed by the adjuvanted flu vaccine. *Id.* at 314. The unadjuvanted flu vaccine would then provoke the least stimulating immune response of the three. *Id.*

Addressing Duffy, Dr. MacGinnitie stated that "I thought it was a very strong study." *Id.* at 314. Dr. MacGinnitie said that he understood Dr. Kinsbourne's criticism that they found zero cases of narcolepsy compared to a background rate of "six or eight cases of narcolepsy." *Id.* at

315. To begin, Dr. MacGinnitie stated, the researchers found sixteen cases of narcolepsy, including two that had onset within one-hundred-and-eighty days of the 2010 to 2011 seasonal vaccine. *Id.* Dr. MacGinnitie said that Dr. Kinsbourne critique that they "didn't have the ability to pick up narcolepsy cases" is unfounded, "because they did pick up narcolepsy cases. They just saw less than expected." *Id.* Dr. MacGinnitie also noted that he had not performed a statistical analysis, but with any rare event, "there can be more variation than you might expect than when you have a large population." *Id.* Furthermore, with something as rare as one in a million, "you could see significant variation in the actual count." *Id.* That is why it is possible that zero cases "was within the range of what could be not statistically significant for [the] condition." *Id.* at 316. Dr. MacGinnitie stated that Dr. Young's inability "to identify or flag [the found rate of zero as compared to the background rate] as a flaw in this study . . . confirmed [Dr. MacGinnitie's] belief that it's a very strong study." *Id.*

Dr. MacGinnitie then addressed Dr. Kinsbourne's use of the Montplaisir study. *Id.* at 317. Dr. MacGinnitie first stressed that Montplaisir concerns an adjuvanted form of the flu vaccine, Arepanrix, and not the type of vaccine Petitioner received. *Id.* Then, Dr. MacGinnitie emphasized that Arepanrix has more nucleoprotein than Pandemrix, which, according to Petitioner's causation theory, should make it more likely to cause narcolepsy. *Id.* But, Dr. MacGinnitie continued, the level of risk "can only be detected at a level of one in a million, and I think that really calls into question this idea that it's the nuclear protein that is causative." *Id.*

Dr. MacGinnitie then turned to the Han study and noted its weaknesses, the failure to separate the patients who developed narcolepsy into groups corresponding to vaccination and to account for any other virus that was circulating in China at that time. *Id.* at 318-19. Dr. MacGinnitie also cited to two other studies, one is the Choe study that "showed no increased rate of narcolepsy" following both an adjuvanted and non-adjuvanted vaccination program in South Korea. *Id.* at 320. In the Lee study, Dr. MacGinnitie noted that researchers found no specific increase in any autoimmune or neurological disease following vaccination. *Id.* at 320-21.

Dr. MacGinnitie concluded that there are two main weaknesses with Petitioner's theory of causation. *Id.* at 321. First, "it's not a coherent story," because the presence of hypocretin receptor antibodies does not provide "a really good explanation" without some "evidence of involved T[]cells . . . ." *Id.* Second, Dr. MacGinnitie continued, "there's strong epidemiological evidence against such an occurrence." *Id.*

The undersigned asked Dr. MacGinnitie whether there "is a potential autoimmune pathogenesis for narcolepsy." *Id.* at 323. Dr. MacGinnitie responded in the affirmative, but clarified that Petitioner's specific theory that "antibodies are generated against the hypocretin receptor" is problematic. *Id.* Dr. MacGinnitie also explained that the immune responses to both the wild-type virus and adjuvanted vaccines are different compared to non-adjuvanted vaccines, "apples to oranges." *Id.* at 324.

iv. Dr. Kinsbourne's Rebuttal

Dr. Kinsbourne retook the stand to clarify his criticism of the Duffy study. *Id.* at 325. He explained that Duffy looked at two six-month periods of a year to see if any narcolepsy cases

developed during that time. *Id.* at 325-26. Duffy found that no narcolepsy cases occurred during that year following vaccination, even though they proposed a background rate of six cases. *Id.* at 326-27. Dr. Kinsbourne commented that Duffy's failure to find any narcolepsy cases "just doesn't sound right . . . ." *Id.* at 327. Dr. Kinsbourne said, "I don't think one can just say, oh, well, things vary." *Id.* "I think it's simply not believable that every one of the narcolepsy cases in that year [were skipped] when it was only a year," Dr. Kinsbourne continued. *Id.* Dr. Kinsbourne concluded that "the Ahmed proposal" was a "medically reasonable mechanism," and that science was not able to give "a definitive answer; we don't have that." *Id.* at 331. The "Ahmed proposal is science in the making," Dr. Kinsbourne concluded, and "it does show what [the *Althen*] criterion asks for, which is that to relate an H1N1 influenza vaccination to the outcome of narcolepsy with cataplexy is biologically plausible." *Id.*

V. The Applicable Legal Standard

To receive compensation under the Vaccine Act, Petitioner must demonstrate either that: (1) Petitioner suffered a "Table injury" by receiving a covered vaccine and subsequently developing a listed injury within the time frame prescribed by the Vaccine Injury Table set forth at § 14, as amended by 42 C.F.R. § 100.3; or (2) that she suffered an "off-Table Injury," one not listed on the Table, as a result of her receipt of a covered vaccine. *See* § 11(c)(1)(C); *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006). Petitioner's claim that her flu vaccine caused her to develop narcolepsy with cataplexy does not fall within the Vaccine Table. Thus, she must prove that her injury was caused-in-fact by the flu vaccine.

To establish causation-in-fact, Petitioner must demonstrate by a preponderance of the evidence that the vaccine was the cause of the injury. § 13(a)(1)(A). Petitioner is required to prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321-22 (Fed. Cir. 2010) (quoting *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)).

In *Althen v. Secretary of the Department of Health and Human Services*, the Federal Circuit set forth a three-pronged test used to determine whether a petitioner has established a causal link between a vaccine and the claimed injury. *See* 418 F.3d 1274, 1278-79 (Fed. Cir. 2005). The *Althen* test requires the petitioner to set forth: "(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.* To establish entitlement to compensation under the Program, Petitioner is required to establish each of the three prongs of *Althen* by a preponderance of the evidence. *See id.*

Specifically, under the first prong of *Althen*, Petitioner must offer a scientific or medical theory that answers in the affirmative the question "can [the] vaccine(s) at issue cause the type of injury alleged?" *See Pafford v. Sec'y of Health & Human Servs.*, No. 01-0165V, 2004 WL 1717359, at *16 (Fed. Cl. Spec. Mstr. July 16, 2004). This may be accomplished in a number of ways. "Reliability and plausibility of [] pathogenesis can be bolstered by providing evidence

that at least a sufficient minority in the medical community has accepted the theory, so as to render it credible." *Id.* at *16-17. In addition, "epidemiological studies and an expert's experience are not dispositive, but lend credence to a claim of plausibility." *Id.* at *17. Medical literature published in respected medical journals is also persuasive. *Id.* "However, publication 'does not necessarily correlate with reliability,' because 'in some instances well-grounded but innovative theories will not have been published.'" *Id.* (quoting *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 593-94 (1993)).

In addition to showing that the vaccine at issue can cause a particular injury, a petitioner must also, under *Althen's* second prong, prove that the vaccine actually did cause the alleged injury in a particular case. *See Pafford*, 2004 WL 1717359 at *16; *Althen*, 418 F.3d at 1279. A petitioner does not meet this obligation by showing only a temporal association between the vaccination and the injury; the petitioner must explain "how and why the injury occurred." *Pafford*, 2004 WL 1717359 at *16.

Although a temporal association alone is insufficient to establish causation, under the third prong of *Althen*, a petitioner must show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d at 1278. The special master cannot infer causation from temporal proximity alone. *See Thibaudeau v. Sec'y of Health & Human Servs.*, 24 Cl. Ct. 400, 403-04 (Fed. Cl. Oct. 23, 1991); *see also Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992) ("The inoculation is not the cause of every event that occurs within the ten[-]day period . . . . Without more, this proximate temporal relationship will not support a finding of causation." (quoting *Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1983))).

A petitioner who demonstrates by a preponderance of the evidence that he or she suffered an injury caused by vaccination is entitled to compensation, unless Respondent can demonstrate by a preponderance of the evidence that the injury was caused by factors unrelated to the vaccination. *See Althen*, 418 F.3d at 1278; *Paluck v. Sec'y of Health & Human Servs.*, 786 F.3d 1373, 1386 (Fed. Cir. 2015) (citing *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008) (holding that it is not a petitioner's burden "to rule out every other potential cause of his injury"); *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 547 (Fed. Cir. 1994).

VI. Discussion[21]

a. Diagnosis

Petitioner's causation theory begins with a diagnosis of narcolepsy type one with cataplexy. Petitioner's treating physician described her symptoms as consistent with narcolepsy,

[21] The undersigned has reviewed all of the medical literature provided by the parties, but will only discuss the literature relevant to this decision. *See Moriarty v. Sec'y of Health & Human Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though [she] does not explicitly reference such evidence in [her] decision.") (citation omitted).

as well as sleep apnea, side effects from medication, stress and anxiety, and/or seizures. *See generally* Pet'r's Exs. 2, 4. Petitioner's expert, Dr. Kinsbourne, conceded that he does not have the formalized training or clinical experience to diagnose sleep disorders generally or narcolepsy specifically. Tr. at 212. He then acknowledged that he relied on the results from the sleep tests as the basis for the diagnosis underlying his causation theory. *Id.* At the time of Petitioner's testing, she was taking several medications that can significantly alter sleep patterns, cause drowsiness, and insomnia; including, but not limited to, hydrocodone, lorazepam, and topiramate. *See id.* Petitioner's test results, while within the range consistent with narcolepsy, are less persuasive given all of the other factors that could have materially affected the integrity of the tests. Additionally Dr. Kinsbourne's admitted lack of clinical experience with narcolepsy undercuts his opinion as probative evidence with regard to Petitioner's diagnosis.

Alternatively, Respondent's expert Dr. Scammell noted that he currently treats patients for sleep disorders, including narcolepsy. Tr. at 244-46. Both in his written expert reports and testimony, Dr. Scammell questioned the accuracy of Petitioner's diagnosis through a discussion of Petitioner's symptoms and a comparison to what a clinician would see in a common narcolepsy with cataplexy case. *Id.* at 254-59. The sleep tests were particularly troublesome for Dr. Scammell, because of the lack of precision and control exerted by the administrators. *Id.* at 267-69. Petitioner was not taken off of the medications that could negatively impact her ability to stay and fall asleep or awaken. The record revealed that Petitioner was unable to get the ideal number of sleep hours in the nights immediately prior to the test, or during the polysomnogram. *Id.* at 267. Dr. Scammell also noted that additional testing and treatment for Petitioner's sleep apnea could have better established Petitioner's baseline for comparison to her testing for narcolepsy. *Id.* at 263-64. Although Dr. Scammell was not convinced that Petitioner suffered from narcolepsy, ultimately he could not say it was more likely than not that Petitioner did not have narcolepsy. *Id.* at 275.

Accordingly, the evidence supports by a preponderant standard that Petitioner did meet the minimum requirements for a narcolepsy diagnosis based on her polysomnogram and MSLT. Her cataplexy symptoms, however, were more dubious. Dr. Scammell described typical cataplexy episodes as brief and emotion-triggered. *Id.* at 255. He went on to describe how the facial muscles relax, the eyes are rarely open, and other common characteristics of cataplexy episodes. *Id.* at 257. Once the episode is over, Dr. Scammell noted that the person suffering from the episode quickly returns to normal. *Id.* The witness testimony describing Petitioner's cataplexy episodes were inconsistent with each other and Dr. Scammell's description. Additionally, there were only a few incidents of emotional triggers for Petitioner's episodes. Petitioner was often reduced to a catatonic state for several minutes or hours with her eyes wide open in a fixed, blank stare. *Id.* After Petitioner regained consciousness and muscle control, she was often upset and inconsolable for an additional period of time. *Id.* at 258-59. Dr. Scammell noted that Petitioner's description of her episodes were extremely unusual, but he would not rule out narcolepsy with cataplexy and neither will I. Based off the polysomnogram and MSLT results, the symptoms insofar as they are consistent with narcolepsy, the therapeutic effects of treatments used for narcolepsy, the presence of the HLA-DQB1*0602 genetic marker common in those with narcolepsy, and the expert opinions, Petitioner has established that she more likely than not suffered from narcolepsy with cataplexy.

b. *Althen* Prong One

Petitioner's Theory

Petitioner's contends that narcolepsy sometimes develops following a flu vaccination because the body produces antibodies in response to the vaccine, and those antibodies cross-react (improperly) with hypocretin receptors and damage them. Pet'r's Ex. 16 at 2-5. These receptors are then unable to properly regulate the excitation feedback necessary for the brain to awaken and stay awake, and narcolepsy is the result. *Id.* at 4. This theory, based on molecular mimicry, has been asserted previously in the Program. *See D'Tiole v. Sec'y of Health & Human Servs.*, No. 15-085V, 2016 WL 7664475 (Fed. Cl. Spec. Mstr. Nov. 28, 2016), *mot. for review denied*, 123 Fed.Cl. 421 (2017), *aff'd*, No. 2017-1982, 2018 WL 1750619 (Fed. Cir. 2018) (finding petitioner failed to establish a reliable causation theory). It is unsuccessful here as it has been previously, for many of the same reasons. Petitioner's theory analogizes two very different flu vaccines, Pandemrix to Fluzone, in an attempt to illustrate a cross-reaction between the immune system and an unknown protein within Fluzone. These vaccines are not analogous, however, because they differ in manufacturing, viral strains, and the presence of an adjuvant. Pandemrix is an adjuvanted, influenza vaccine that was administered in Europe in 2009 to combat an H1N1 pandemic. *See* Resp't's Ex. C at 9. Fluzone is a non-adjuvanted trivalent vaccine currently used in the United States and at issue here. One cannot be substituted for the other in a simple cut and paste to establish a causality that contradicts epidemiological findings.

Other Narcolepsy Cases in the Program

A comparison between this case and two recent flu-narcolepsy decisions will help illustrate Petitioner's failure to meet her burden under *Althen*. *D'Tiole* was the first of two cases wherein Special Master Corcoran considered whether a flu vaccine could cause narcolepsy with cataplexy. *D'Tiole*, 2016 WL 7664475 (Fed. Cl. Spec. Mstr. Nov. 28, 2016). In *D'Tiole*, the petitioner received the FluMist vaccine, a live attenuated flu vaccine, on December 13, 2011. *Id.* at *1. The petitioner's narcolepsy symptoms did not arise for several months, and he was ultimately diagnosed with narcolepsy with cataplexy in August of 2013. *Id.* at *3. This diagnosis was confirmed in 2014, and testing revealed that the petitioner possessed the HLA gene associated with narcolepsy. *Id.*

The petitioner's expert, Dr. Steinman, argued that the petitioner's narcolepsy was caused by an autoimmune reaction brought about through molecular mimicry between nucleoprotein found in the flu vaccine and hypocretin receptors. *Id.* Dr. Steinman referred to the Pandemrix studies to support his theory with respect to FluMist. *Id.* at *5.

Respondent put forward two experts, Dr. Michael Kohrman and Dr. Andrew MacGinnitie. *Id.* at *10, *11. Dr. Kohrman argued that there is no evidence that a live H1N1-containing flu vaccine is associated with narcolepsy and relied upon the Duffy study as support of his argument. *Id.* at *10. Dr. Kohrman found this result as evidence that whatever caused Pandemrix to be associated with narcolepsy was unique in its manufacturing, and therefore its connection is non-transferrable to vaccines not produced in a similar way. *Id.*

Dr. Andrew MacGinnitie primarily focused on how the flu vaccine administered in the case differs from Pandemrix. *Id.* at *11. Dr. MacGinnitie also cited Duffy as evidence against a connection between unadjuvanted vaccines and narcolepsy. *Id.* at *12. Dr. MacGinnitie concluded that the petitioner in fact received a vaccine that was "functionally the same" as the one studied in Duffy, further evidence against the petitioner's causation theory. *Id.* at *13.

In response, Dr. Steinman attacked the Duffy study much in the same way Dr. Kinsbourne did in the present case. *Id.* at *7. Special Master Corcoran then explained that, although petitioners are not expected or required to produce epidemiological studies to prove their theory, "this does not mean that epidemiological evidence relevant to a vaccine at issue in a case has no place in evaluating a claim – especially when the evidence is particularly on point and persuasive." *Id.* The petitioner "unconvincingly quibble[d] with aspects of Duffy," wrote Special Master Corcoran. *Id.*

Special Master Corcoran did not find reliable the petitioner's attempt to apply the evidence surrounding Pandemrix to FluMist, a completely different formulation of the flu vaccine.[22] "[The] [p]etitioner has, in effect, attempted to leverage a theory that is reliable with respect to one form of the flu vaccine into a case involving a different form, but without showing that the theory is similarly reliable in the different setting." *Id.* at *20. Special Master Corcoran ultimately dismissed the petitioner's claim. *Id.* at *28.

In *McCollum*, Special Master Corcoran was again asked to determine whether a flu vaccine could cause narcolepsy. *McCollum v. Sec'y of Health & Human Servs.*, No. 14-790V, 2017 WL 5386613 (Fed. Cl. Spec. Mstr. Sept. 15, 2017), *motion for reconsideration denied*, 135 Fed. Cl. 735 (2018), *appeal docketed*, No. 18-1623 (Fed. Cir. Feb. 28, 2018). The petitioner's medical history was replete with a host of pre-existing health conditions, including OSA, smoking, ADHD, obesity, type II diabetes, severe hypertension, and chronic back pain. *Id.* at *1. The petitioner reportedly received his flu vaccine on September 24, 2011, and his medical records do not show any narcoleptic symptoms until February 2, 2012. *Id.* at *3. In March of 2012, the petitioner's physician diagnosed him with narcolepsy with "near cataplexy." *Id.*

The petitioner called one expert in *McCullom*, Dr. Marcel Kinsbourne. *Id.* at *6. Dr. Kinsbourne put forward the same causation theory as the one argued in the current case. In summarizing the petitioner's theory, Special Master Corcoran noted that "[t]here is an immediate facial limitation . . . to the application of such literature in this case," because Pandemrix was never used in the United States. *Id.* at *8. Special Master Corcoran wrote that the petitioner attempted to get around this issue by arguing that the wild-type virus can cause narcolepsy and by claiming that Pandemrix has comparable nucleoprotein levels as vaccines used in the United States. *Id.* Dr. Kinsbourne also addressed the Duffy study the same way as he does in the case at hand. *Id.*

[22] Special Master Corcoran further made legal findings regarding why the Court did not need a hearing in *D'Tiole*. 2016 WL 7664475 at *25-28. Because these findings are irrelevant to the undersigned's analysis, they are omitted.

Special Master Corcoran wrote, "[a]ll of [the petitioner's causation theory] must be evaluated in a context in which Duffy, the sole relevant epidemiologic evidence regarding the impact of the version of the H1N1 flu vaccine administered in the U.S., contradicts [the petitioner's] contentions about a causal link." *Id.* at *17. Although epidemiological studies are not required of petitioners in the Vaccine Program, Special Master Corcoran credited Duffy as "highly persuasive" and summarized his past findings of the study as reliable. *Id.* "[I]t is not enough to respond by arguing [as Dr. Kinsbourne proposed in that case and the present case] that the rare nature of a vaccine injury renders all epidemiologic evidence effectively useless." *Id.* Special Master Corcoran concluded by stating that although the petitioner's theory does not meet *Althen* prong one, it "remains intriguing despite [his] determination." *Id.* at *19. The petitioner's claim was accordingly dismissed. *Id.* at *23.

In both of these cases, Special Master Corcoran outlined why the application of the science pertaining to the development of narcolepsy following an adjuvanted flu vaccine does not translate to an unadjuvanted vaccine alleged to cause narcolepsy with cataplexy. *D'Tiole*, 2016 WL 7664475 at *20-28; *McCullom*, 2017 WL 5386613 at *17-19. These cases are apposite to the case at hand, and ultimately Petitioner, like the petitioners in *D'Tiole* and *McCullom*, failed to meet her burden.

In *D'Tiole*, Respondent put forward Dr. MacGinnitie as an expert. 2016 WL 766475 at *10-13. MacGinnitie is the same expert used by Respondent in this case, and in that case as he did here, he opined that the flu vaccine administered to the petitioner is sufficiently different from Pandemrix to make the comparison unpersuasive. *Id.* at *11. He also effectively explained why the Duffy study is strong evidence against the petitioner's theory. *Id.* at *12. Dr. MacGinnitie is qualified to opine on vaccine injuries and narcolepsy and that is apparent in his testimony and written reports.

McCullom is also illustrative in comparison to this case. Both the petitioner in *McCullom* and Petitioner in this case suffered from other sleep-related conditions that made the diagnosis an issue that required in-depth, expert analysis. 2017 WL 5386613 at *1. Most importantly, the petitioner in *McCullom* put forward the same expert with the same causation theory. *Id.* at *6. Special Master Corcoran ultimately found that the petitioner's theory cannot overcome the evidence presented in Duffy, and consequently, the petitioner did not meet his burden in the face of compelling medical literature that conflicts with his theory. *Id.* at *17-19. Despite Petitioner's request to have more time to address the Duffy study in this case and the potentially damaging arguments against Dr. Kinsbourne's theory that it presents, Petitioner was unsuccessful in presenting a theory that meets the preponderant standard.

Medical Literature Provides Probative Evidence that Undercuts Petitioner's Theory

Petitioner's expert, Dr. Kinsbourne, discussed an unidentified influenza protein that he suggested is present in both vaccines and cross-reacts with "the same protein in the receptor for the hypocretin." Tr. at 182-83. This theory is an overbroad extension of the widely accepted theory that a relationship exists between Pandemrix and narcolepsy. Epidemiologist have tried, without success, to identify similar relationships between narcolepsy and other influenza vaccines, including Fluzone. Some studies have focused on adjuvanted vaccines to determine if

the presence of an adjuvant is a necessary condition to establish a causal link between a flu vaccine and a subsequent narcolepsy diagnosis. *See* Pet'r's Ex. 19 at 9, Yves Dauvilliers et al., *Increased Risk of Narcolepsy in Children and Adults after Pandemic H1N1 Vaccination in France*, 136 Brain 2486, 2494 (2013) ("The mechanisms underlying such an association [between Pandemrix and narcolepsy] remain unclear . . . ."); Pet'r's Ex. 33 at 5-8, Jacques Montplaisir et al., *Risk of Narcolepsy Associated with Inactivated Adjuvanted (AS03) A/H1N1 (2009) Pandemic Influenza Vaccine in Quebec*, 9 PLoS ONE 1, 5-8 (2014) (discussing narcolepsy rate and risk of narcolepsy); *see also* Pet'r's Ex. 52F at 2, S. Sohail Ahmed, MD et al., *The Safety of Adjuvanted Vaccines Revisited: Vaccine-Induced Narcolepsy*, 18 Isr. Med. Ass'n J. 216, 217 (2016) (finding that previous research "support[s] the concept that vaccine-associated narcolepsy is not due solely to the characteristics of the adjuvant"). Dr. Kinsbourne mentioned those studies during his testimony and counts himself among those that do not believe that the adjuvant within any given vaccine is the cause or significant contributing factor to the development of narcolepsy. Tr. at 186-87. Specifically, he discussed studies of two other adjuvanted vaccines, Arepanrix and Focetria, and noted that the medical literature does not reflect as significant an increase in the incidence of narcolepsy in individuals following these vaccinations as with Pandemrix. *Id.* at 187-88.

Other studies have focused on non-adjuvanted vaccines (like the one Petitioner received) and concluded that there does not appear to be any relationship between these vaccines and narcolepsy. *See* Duffy. Despite these results that appear to be more conclusive than the studies Dr. Kinsbourne relies on to discount the possible role of adjuvants, Dr. Kinsbourne opined that a nucleoprotein within the vaccine Fluzone is the causal agent for the development of narcolepsy. Tr. at 182-83. Dr. Kinsbourne did not identify the specific protein, but stated the protein is present in the Fluzone vaccine, the Pandemrix vaccine, and also the wild H1N1 influenza virus.[23] *Id.* at 183-85, 188-89. He also did not provide any evidence to support his premise that this particular protein is found in both vaccines and the wild virus. Dr. Kinsbourne did discuss a study that found an increase in narcolepsy following an H1N1 epidemic in China. *Id.* at 189. The cases in China were not related to vaccination, but Dr. Kinsbourne asserted that the nucleoprotein in the H1N1 wild virus that likely triggered the increase in narcolepsy is also present in Fluzone. *See* Pet'r's Ex. 16 at 4-5. This study did not identify the relevant protein, but Dr. Kinsbourne reasoned that the H1N1 protein is so similar to the neuropeptide hypocretin that cross-reaction occurs once the immune system is triggered by the vaccine. *Id.* at 4-5. Consequently, the body begins to destroy the hypocretin neurons in addition to the H1N1 proteins. *Id.* at 3-5.

[23] Medical literature, epidemiological studies, general acceptance of an asserted medical theory, nor demonstration of a specific mechanism are requirements to satisfy a petitioner's burden pursuant to the first prong of *Althen*. *Andreu v. Sec'y of Health & Human Servs.,* 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano,* 440 F.3d at 1325-26). Accordingly, special masters must take care not to increase the burden placed on petitioners that are offering a scientific theory linking vaccine to injury. Ultimately, petitioners must prove their cases by satisfying a preponderance of the evidence burden of proof that is applied to every aspect of their claim, including the reliable and plausible causal theory pursuant to *Althen's* first prong.

Dr. Kinsbourne relied on the De la Herrán-Arita study in support of his theory, but ultimately conceded that the study had been retracted due to fraudulent results prior to the filing of Petitioner's initial expert report. *See* De la Herrán-Arita; Tr. at 214. Additionally, both of Respondent's experts effectively explained why the 'results' in the De la Herrán- Arita study are not probative here. Dr. Scammell admitted that he originally thought it "probable that an immune stimulus such as influenza . . . triggers a T[]cell response and that in genetically susceptible persons [with the HLA-DBQ1*0602 gene] this inflammatory reaction damages the orexin-producing neurons . . . ." *Id.* at 278. Dr. Scammell stated that he ultimately discounted this hypothesis when presented with "the facts that no signs of inflammation are detected in . . . cerebrospinal fluid or seen on magnetic resonance imaging," in these narcoleptic patients. *Id.* He also noted that treatments designed to target immune system malfunctions, "like steroids . . . have not been helpful" to treat these cases. *Id.*

Dr. MacGinnitie also discussed his initial belief in this theory, which he stated sought to confirm that in genetically susceptible narcoleptics "T[]cells were present and they were directed against hypocretin[,] [thereby providing]… a great explanation" for the autoimmune pathogenesis of narcolepsy. *Id.* at 302-03. Dr. MacGinnitie explained the peptide-specific nature of a T cell response compared to the more generalized role of B cell antibodies. *Id.* Dr. MacGinnitie then noted that the Ahmed study produced findings opposite to De La Herrán-Arita and, "shows antibodies, which are not so specific[;] it has no evidence for T cells, and the antibodies are directing it against an antigen that probably can't be the cause of the disease because otherwise it would cause such widespread neurological problems." Ahmed (2015); Tr. at 304.

Dr. Kinsbourne was asked if the Herrán-Arita study "is still a reliable piece of scientific evidence," and he replied, "[n]o . . . [b]ut it still seemed to me, overwhelmingly likely . . . [,] even though we don't know the homology that's involved." Tr. at 215. He went on to note, "[i]t's the same theory, whether it's based on the article or not." *Id.* Dr. Kinsbourne ultimately concluded that the Herrán-Arita article's theory was correct even though the results could not be replicated, and stated, "[the retraction] doesn't change my opinion." *Id.* at 216.

The Role the Immune System Plays under Petitioner's Theory Does Not Withstand Scrutiny

Respondent's experts enumerated three problems with Petitioner's reliance on this theory in addition to the article's retraction. Resp't's Ex. A at 11; Resp't's Ex. C at 3-4, 6-7. After a full consideration of the evidence, Petitioner is unable to adequately respond to the critiques her causation theory welcomes. Therefore, it cannot survive under the preponderance standard. First, Dr. Scammell noted that Dr. Kinsbourne pointed to the autoimmune system's destruction of hypocretin receptors as the cause of vaccine-induced narcolepsy. Dr. Scammell countered that there is no explanation as to how or why the antibodies produced in response to the vaccine only damage these receptors if they are located in this limited region on the brain, despite their widespread presence in other regions. Tr. at 281. Dr. MacGinnitie agreed, testifying that "this idea that antibodies against the hypocretin-2 receptor would be causative [i]s problematic because the receptor is so widely distributed." Tr. at 297.

Dr. MacGinnitie also pointed out that "the fact that antibodies against hypocretin receptor exists, could be a marker of the disease, rather than the cause of the disease." *Id.* at 300. Dr. MacGinnitie further explained this, stating that "as an autoimmune attack occurs and the cells that are being attacked die, they release other proteins that often are not exposed to the immune system, and then you can actually see antibodies against them that aren't causative of the disease but are just a marker of it." *Id.* Dr. Kinsbourne was unable to explain why his proposed immune response was so localized, or counter Dr. MacGinnitie's statement that the antibodies could just as easily be catalysts as markers. His continued reliance on the largely unknown state of vaccine-induced injuries is particularly weak in this case, where so much research has been done to understand the relationship between flu vaccines and narcolepsy.

Finally, Dr. MacGinnitie noted that the there are no studies that apply the type of causal relationship seen with the adjuvanted Pandemrix to a non-adjuvanted vaccine like Fluzone. *Id.* at 297-98. "The simplest [possibility] is that it's something about the adjuvant that actually triggered the narcolepsy." *Id.* at 298. Dr. MacGinnitie clarified that it is not clear if the adjuvant is sufficient to cause narcolepsy, but he does believe that it is clear that the adjuvant is necessary. *Id.* at 310.

Dr. MacGinnitie concluded his testimony by discussing several epidemiological studies that support his conclusion that there is no relationship between nonadjuvanted vaccines and narcolepsy. *Id.* at 314-22. Dr. MacGinnitie acknowledged that vaccines can cause injury and even went as far as to agree that "there is a potential autoimmune pathogenesis for narcolepsy." *Id.* at 323. Dr. MacGinnitie's problem with Petitioner's theory is specific to the causation mechanism, "the idea that antibodies are generated against the hypocretin receptor" in response to any flu vaccination or exposure to the H1N1 wild virus. *Id.*

Petitioner does not present any convincing evidence to undercut the findings from the Duffy study. Furthermore, Dr. Kinsbourne's unofficial reliance on science offered in a retracted study is not persuasive. The mechanism that Petitioner is relying on is vague and what little specificity his expert does articulate runs contrary to documented epidemiology. Studies that provide insight into rare medical events are often impossible to create. They are therefore not necessary for a successful claim in the Program. However, when there are relevant studies such as those that have been discussed by the experts in this case, they are valuable evidence to support or rebut a vaccine's role in the causation of an alleged medical condition. Dr. Kinsbourne's criticism of the Duffy study and further explanation of the De La Herrán-Arita study does not provide sufficient corroboration for his causation theory. Petitioner fails to satisfy his burden under prong one of *Althen*.

c. *Althen* Prong Two

It is impossible to do any meaningful analysis for prong two without a developed theory to apply to Petitioner's circumstances. Furthermore, an attempt to apply the theory asserted by Dr. Kinsbourne to Petitioner's history reveals that there is no evidence in the record to explain how Petitioner's vaccination triggered an immune response that resulted in narcolepsy. There is no evidence that supports an autoimmune reaction in Petitioner's case. There was no attempt to rule out autoimmune disease based on any of her symptoms. There was no evidence of

inflammation or an acute reaction at the time of the vaccination. *See* Pet'r's Ex. 2 at 118, 237. Petitioner was being treated for neck pain and migraine with hydrocodone. *Id.* Petitioner was also prescribed Zoloft for anxiety, which can cause insomnia. Pfizer, Inc., *Zoloft Medication Guide* 8 (2016), https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=020844; Pet'r's Ex. 2 at 236-44. Dr. Kinsbourne made it clear during his testimony that the theory he presented is "one way of explaining what happened to [Petitioner,]" and that he is "not asserting that [his theory is] necessary [sic] the case" for her. Tr. at 232. He cautioned that the theory "[is] not scientifically certain" but opined that it is more likely than not what happened to Petitioner. *Id.* Unequivocally, Petitioner does not have to prove any aspect of her causation theory with scientific certainty. The assurances of an expert without supporting evidence, is not, however, enough to meet the preponderant standard in the face of relevant and credible epidemiological studies, well-versed opposing experts, and Petitioner's reliance on a retracted article.

d. *Althen* Prong Three

I will complete the *Althen* analysis and address the evidence of a temporal relationship between the onset of Petitioner's narcolepsy with cataplexy and the date of her vaccination. Petitioner's medical records and witness testimony describe Petitioner's sixty-hour work weeks and long stretches of work-related driving. Petitioner's witnesses stated that she "was up very early in the morning and gone, and then she would not come home until very late at night." Tr. at 18-19. Petitioner's son described her as "busy with her job" and stated that she "worked three times harder than she should have – she was always tired after a long day at work . . . ." *Id.* at 60. This is clear evidence in the record that Petitioner suffered from tiredness and fatigue prior to her vaccination. There is also, however, witness testimony that approximately four to five weeks following vaccination, Petitioner began to fall asleep driving and was unable to stay awake without drinking multiple caffeinated drinks throughout the day or taking a nap. Tr. at 133-34, 136-37. Witnesses describe post-vaccination episodes of 'cataplexy' wherein Petitioner would "go down" for ten minutes at a time or longer or stare "off into space but still looking at the TV with no response" for several minutes. *Id.* at 28, 37-38. These episodes were characterized by Dr. Scammell as "atypical" and "unusual[,] but" he ultimately conceded that "everyone is different" and there is "a spectrum of [cataplexy] symptoms." *Id.* at 275.

Dr. Scammell noted that individuals with narcolepsy often have other sleep disorders "[a]nd it's possible that some of these factors or some combination of them is accounting for the overall picture." *Id.* at 260. Petitioner was also diagnosed with sleep apnea, another sleep disorder similar to narcolepsy in symptoms, but she does not assert that the vaccine is responsible for this condition. The similarities between the symptoms for sleep apnea and narcolepsy, coupled with the unusual nature of Petitioner's cataplexy episodes, make it difficult to determine onset for Petitioner's narcolepsy. However, Petitioner's account of the development of her narcolepsy was consistent with her medical records and Respondent's experts did not contest her timeline. Therefore, I find that the four week temporal relationship between the development of Petitioner's symptoms and the administration of the vaccine would be appropriate based on what is known and widely accepted with respect to molecular mimicry reactions to vaccination that result in injury. This temporal relationship, however, does not take the place of a cogent causation theory necessary to meet the burden for prongs one and two. A

temporal relationship alone is insufficient to establish causation under prong three, and I find that the one established here is of no consequence without a causation theory that explains the development of Petitioner's narcolepsy within the timeframe described.

Dr. Kinsbourne relied largely on the timing between Petitioner's vaccination and diagnosis of narcolepsy to conclude a causal relationship. In his first expert report, Dr. Kinsbourne's conclusion began with the fact that Petitioner's "narcolepsy became clinically apparent within one month after vaccination." Pet'r's Ex. 12 at 10. Finding that Petitioner's condition developed "within a medically reasonable temporal interval of a trivalent influenza vaccine," and in the absence of "reliable evidence for any alternative cause," Dr. Kinsbourne opined that "the influenza vaccination did cause [Petitioner's] narcolepsy." *Id.* This conflation of the factors necessary to show entitlement under *Althen* has been soundly rejected by the program, including a prior flu vaccine - narcolepsy claim that asserted the same theory Dr. Kinsbourne espouses here. *See D'Tiole*, 2016 WL 7664475; *see, e.g.*, *Moberly*, 592 F.3d at 1323 (quoting *Althen*, 418 F.3d at 1278) ("[N]either a mere showing of a proximate temporal relationship between vaccination and injury, nor a simplistic elimination of other potential causes of the injury suffices, without more, to meet the burden of showing actual causation."); *Grant*, 956 F.2d at 1148.

e. Alternative Cause

Petitioner has not provided a causation theory that meets Petitioner's burden of proof under *Althen* prongs one and two. Respondent never offered an alternative cause to Petitioner's condition, and as the prima facie case has not been met, Respondent was never under obligation to do so.

VII. Conclusion

It is undeniable that Petitioner suffers from one or more sleep disorders that have disrupted her way of life. However, Petitioner has failed to prove by a preponderance of the evidence that she suffered from narcolepsy with cataplexy as a result of her Fluzone vaccination. The causation theory presented by Petitioner is vague and incomplete, preventing any meaningful application to the onset and character of Petitioner's symptoms. Therefore, she is not entitled to compensation under the Program.

In the absence of a timely-filed motion for review filed pursuant to Vaccine Rule 23, **the Clerk of Court is directed to ENTER JUDGMENT** consistent with this decision.

IT IS SO ORDERED.

s/Herbrina D. Sanders
Herbrina D. Sanders
Special Master