In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 14-790V

(to be published)

* *		
MICHAEL McCOLLUM,	*	
	*	
	*	Filed: September 15, 2017
Petitioner,	*	
	*	
v.	*	Entitlement;
	*	Influenza ("Flu") vaccine;
	*	Narcolepsy; Cataplexy;
SECRETARY OF HEALTH AND	*	Preponderance Standard;
HUMAN SERVICES,	*	*Althen* Prong One; Relevance
	*	of Epidemiologic Evidence
Respondent.	*	
	*	
* *		

Richard Gage, Richard Gage P.C., Cheyenne, WY, for Petitioner.

Alexis B. Babcock, U.S. Dep't of Justice, Washington, DC, for Respondent.

DECISION DENYING ENTITLEMENT[1]

On August 29, 2014, Michael McCollum filed a petition seeking compensation under the National Vaccine Injury Compensation Program (the "Vaccine Program")[2], alleging that he developed narcolepsy with cataplexy due to his receipt of the influenza ("flu") vaccine in the fall of 2011. Petition ("Pet.") (ECF No. 1) at 1.

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

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

An entitlement hearing was held in this matter on April 4, 2017, in Washington, D.C. After considering the record as a whole, and for the reasons explained below, I find that Petitioner is not entitled to compensation, primarily due to his inability to establish a reliable causation theory.

I. Factual Background

A. *Pre-Vaccination Medical History*

Mr. McCollum's medical records are significant for several pre-existing health conditions, including obstructive sleep apnea ("OSA"),[3] smoking, attention deficit/hyperactivity disorder ("ADD"), obesity (having a body mass index score above 35), type II diabetes, severe hypertension[4], and chronic back problems. Ex. 1 at 4-5, 22-24; Ex. 2 at 4-5, 10, 25.[5] He was 51 years old at the time of his vaccination and subsequent sleep-related symptoms.

Throughout the records obtained from Petitioner's primary care physician, Dr. Joseph C. Petrini, there are several documented incidents of general sleep-related issues that predate the alleged flu vaccination. Ex. 1 at 4-5, 64-68. Those incidents vary in description and occur sporadically from October 2009 to July 2011. *Id.* at 64-68. Most were referred to in general terms, however - "sleep problems," "sleep disturbance," "sleepiness," "difficulty sleeping," and "still too fatigued to work." *Id.* at 64-68.

Mr. McCollum also experienced other health issues prior to vaccination that echo the symptoms complained of in this case. A year prior to the vaccination at issue, for example, Petitioner was hospitalized on July 10, 2010, at Salinas Valley Memorial Healthcare System ("Salinas Memorial") in Salinas, CA, for "an altered level of consciousness with difficulty expressing himself and bilateral shaking of his arms." Ex. 1 at 22. His blood pressure when he arrived at the emergency department was low (82/52), which eventually improved but remained low (108/66). *Id*. These symptoms lasted several hours before he was admitted at the hospital. *Id.* at 23. At this time, Mr. McCollum specifically reported that he fell asleep while riding in a car and had "developed speech disturbance" earlier in the day. Ex. 2 at 31. Consulting neurologist, Dr.

[3] OSA consists of periods in which one stops breathing during sleep. *Dorland's Illustrated Medical Dictionary* 117 (32d ed. 2012) (hereinafter "*Dorland's*"). Risk factors include obesity (a body mass index above 35), being male, hypertension, snoring, and daytime sleepiness. Transcript ("Tr.") at 144.

[4] Hypertension is otherwise known as high blood pressure. *Dorland's* at 896.

[5] Narcolepsy was also listed in an undated portion of the medical history section of the notes of Petitioner's primary care physician, Dr. Petrini. Ex. 1 at 5. This record is preceded by a page dated October 27, 2009 – suggesting that Mr. McCollum had been diagnosed prior to his vaccination with the condition - but that record is immediately followed by another record that indicates Petitioner was being treated at Stanford, which did not occur until 2012. Ex. 1 at 4-6. It is also unclear if the narcolepsy-referencing record was written by Dr. Petrini, or if it was Mr. McCollum describing his own medical history. Because of these factors, I cannot afford significant weight to this stray reference to narcolepsy possibly pre-dating Petitioner's vaccination.

Gerald Wahl, recommended an electroencephalogram ("EEG") and an echocardiogram;[6] both of which showed normal results. Ex. 1 at 23. Dr. Wahl concluded that Petitioner's clinical presentation was indicative of a transient ischemic attack[7] ("TIA"), but that the TIA could not account for the shaking of his arms. Ex. 2 at 32. Petitioner recovered at the hospital and was discharged on July 12, 2010. Ex. 1 at 22. On a follow-up visit, Dr. Petrini ultimately proposed that Petitioner's hypertension medications were a likely cause of his symptoms, stating "I feel that the patient's altered level of consciousness and hypotension was due to taking his antihypertensive medications as prescribed. They will be reduced." *Id.* at 23. The record does not reveal a similar occurrence until after Mr. McCollum received the flu vaccine over a year later.

B. Circumstances Relating to Mr. McCollum's 2011 Vaccination

Petitioner lacks direct proof establishing that he received the flu vaccine in October 2011 as alleged, but instead has sought to prove this via circumstantial evidence. Accordingly, certain facts involving third parties to this claim bear on resolution of that issue.

Linda McCollum, Petitioner's wife, was admitted to the Salinas Memorial emergency room on September 24, 2011, after experiencing a "near syncopal episode" likely due to hypotension.[8] Ex. 12 at 4-10. Upon discharge later that day, Mrs. McCollum received the flu vaccine, and was advised that the entire family should follow suit. *See* Affidavit of Linda McCollum, filed as Ex. 34 at 1; Transcript ("Tr.") at 7. Mrs. McCollum asserts that she specifically told Petitioner he also needed to receive the flu vaccination, which he claims to have accomplished a few weeks later. Tr. at 7-8.

Mr. McCollum has contended specifically that he received a flu vaccine from a Walgreens pharmacy near his home around October 5, 2011. *See* Affidavit of Michael McCollum, filed as Ex. 35. The Walgreens Company could not produce records regarding Petitioner's vaccination, however. *Id.* at 1-2. At best, Walgreens has confirmed that the H1N1 vaccine was being administered at its store locations across the U.S. in the fall of 2011, and that the cost for the vaccine was $31.99 for patients who were not insured. Ex. 38 at 1. Petitioner filed bank records for the relevant months in an attempt to show that he used a bank debit card at Walgreens numerous times in September or October of 2011. The bank records revealed that the only purchase dated

[6] An EEG is a test that detects electrical activity in your brain. *Dorland's* at 600. An echocardiogram uses sound waves to create an image of the subject's heart. *Dorland's* at 589.

[7] A TIA is caused by a clot blocking blood from reaching the brain. It is similar to a stroke, but much shorter in duration. *See Dorland's* at 1927, 1953, 961.

[8] A syncopal episode is a loss of consciousness due to "generalized cerebral ischemia." Hypotension is otherwise known as low blood pressure. *Dorland's* at 1818, 906.

after Mrs. McCollum's hospitalization that matched or surpassed the cost of a flu vaccine in 2011 occurred on October 18, 2011.[9] Ex. 36 at 5.

C. Post-Vaccination Medical History

Although the records from the months immediately after Mr. McCollum received the flu vaccine do not reference any possible early signs of narcolepsy, Petitioner contends that he was in fact beginning to experience such symptoms.[10] Mr. McCollum recalled at trial his first symptoms of narcolepsy beginning around December 2011, when he "would just drop [into sleep] like a stone." Tr. at 49. He remembered really noticing the symptoms shortly before he saw Dr. Petrini in January 2012, when he hallucinated while driving on the freeway. *Id.* at 64. During this time, he would sit in front of the television and would suddenly wake up and realize he had dropped the cup that was in his hand. *Id*. at 49. Mrs. McCollum specifically recalled that Petitioner's first incidence of cataplexy[11] was when they were watching football in late January. *Id*. at 18-19. She stated that Petitioner felt the cataplexy when he became animated by telling jokes, playing with his granddaughter, or when receiving praise. *Id*. 18-20.

On January 29, 2012 (three months after the alleged vaccination), Mr. McCollum reported to the Community Hospital of the Monterey Peninsula emergency room complaining about weakness in his left leg, tingling on the left side of his face, lightheadedness, and dizziness. Ex. 1 at 51. The attending physician, Dr. Samuel Melton, gave Petitioner a neurologic examination and a TIA workup, but both were normal. *Id*. Dr. Melton concluded that Petitioner's sedative medications, Soma and Norco, which had previously been prescribed for Petitioner's back pain, had likely contributed to his symptoms. *Id.* Petitioner went to see Dr. Petrini again on January 30, 2012, at which time Dr. Petrini noted that the cause of Petitioner's recent symptoms could be neurological. To that end, Dr. Petrini referred Petitioner to a neurologist, Dr. Wayne Shen. Ex. 1 at 69.

Petitioner visited Dr. Shen on February 7, 2012. Ex. 3 at 1. Mr. McCollum now reported (consistent with his trial testimony) that he had started to experience double vision, hallucinations, the sudden onset of sleep on long drives, weakness and numbness in his leg, and that he would get "a weird feeling on his face" when he laughed. *Id*. Petitioner also complained of constant sleepiness, increased sleeping generally, and sleep paralysis. *Id*. Mr. McCollum recalled that the

[9] These bank records did not itemize goods bought, but instead only denoted the total amount purchased -- $55.97. *See generally* Ex. 36.

[10] For example, on November 16, 2011, Mr. McCollum visited Dr. Petrini complaining about a productive cough, and was diagnosed with bronchitis. Ex. 1 at 69.

[11] Cataplexy is a condition characterized by abrupt attacks of muscle weakness or hypotonia brought on by emotional stimuli (*e.g.* mirth, fear, surprise), and is often found in association with narcolepsy. *Dorland's* at 303.

symptoms started a week before his visit to Dr. Shen, although his wife relayed to Dr. Shen that she had noticed the symptoms weeks prior to the visit. *Id.*

In response, Dr. Shen proposed several differential diagnoses including narcolepsy, and ordered a Multiple Sleep Latency Test ("MSLT") to evaluate narcolepsy's likelihood. *Id.* at 3-4. Dr. Shen's notes from his examination of Mr. McCollum indicate the following:

> This is a very complicated patient with reports of hypersomnolence during the day and night with some symptoms of sleep paralysis and sensation of muscle weakness and laughing that raises the possibility of Narcolepsy. Other consideration is toxic encephalopathy from his medications with sedation but he has been on this regimen long term without these symptoms in the past. He has ADD which might cause difficulty with attention but the history does not suggest that his symptoms are due to distraction. He could also suffer daytime sleepiness from Obstructive Sleep Apnea Syndrome with the obesity and snoring but he reportedly already had a negative sleep study.[12] With the movements during dream sleep noted by the spouse we cannot rule out a REM state sleep disorder. Ex. 3 at 3.

D. Confirmation of Narcolepsy Diagnosis and Subsequent Treatment

By mid-February, about two months after his initial symptoms began, Petitioner started to experience cataplexy more often. He distinguished the symptoms from narcolepsy symptoms because with cataplexy he would drop straight to the ground, which frightened him before he knew what it was. Tr. at 50-51.

On March 1, 2012, Mr. McCollum returned to Dr. Shen reporting worsening symptoms that included "[s]leep dreaming and waking up." Ex. 3 at 5. During such an episode, Petitioner stated he "awoke from sleep and thought that he was carrying a leather pouch and wanted to give it to [his] son." *Id*. Dr. Shen also shared the results of the MSLT, which indicated sleep onset latency of five minutes, confirming for Dr. Shen the appropriateness of a diagnosis of narcolepsy along with "near cataplexy."[13] *Id.* at 6. At the same time, the other diagnostic tests returned negative results, helping Dr. Shen eliminate other potential causes such as a cord compression or abnormality. However, in an effort to further corroborate his diagnosis, Dr. Shen referred Petitioner to a neurologist/sleep specialist, Dr. June Seliber-Klein, at the June Klein Practice in Monterey, California, for additional evaluation. *Id.* at 5-7, Ex. 8 at 1.

[12] The records for this sleep study were never filed nor was there any other mention of such a sleep study being performed.

[13] Dr. Shen amended Mr. McCollum's diagnosis to formally include cataplexy on March 29, 2012. Ex. 3 at 10.

Petitioner saw Dr. Klein on April 16, 2012. *See generally* Ex. 8. As the notes from this visit indicate, because Mr. McCollum had by this time received from Dr. Shen a narcolepsy diagnosis that had some reliable clinical support, Dr. Klein felt it unnecessary to perform a second MSLT, even though the test had not generated evidence of sleep onset REM ("SOREM") - typically the hallmark diagnostic criteria of narcolepsy. Ex. 8 at 2; Tr. at 140. She further indicated that she wanted to rule out OSA because Mr. McCollum possessed the necessary risk factors. Ex. 8 at 2. Mr. McCollum, however, did not follow-up with Dr. Klein and the records from the visit are limited. Ex. 8 at 2. On April 30, 2012, Petitioner followed up with Dr. Shen reporting that his cataplexy was better, although he still experienced daily cataplectic attacks. Ex. 3 at 12. Dr. Shen referred him to a sleep clinic at the Stanford Sleep Medicine Center ("Stanford Clinic") in Redwood City, California. *Id.* at 13.

On June 20, 2012, Mr. McCollum visited the Stanford Clinic and was seen by Drs. Vikas Jain and Emmanuel Mignot.[14] Ex. 6 at 33. They conducted a diagnostic polysomnogram,[15] and after reviewing its results diagnosed Petitioner with "hypersomnia with sleep apnea (unspecified)"— a condition characterized by excessive day-time sleepiness but distinct from narcolepsy, as it is caused by the relaxation of muscles in the throat, which makes it difficult to breathe, leading a person's brain to wake them from nocturnal sleep. *Id* at 31; *Obstructive sleep apnea: Symptoms and causes*, Mayo Clinic, http://www.mayoclinic.org/diseases-conditions/obstructive-sleep-apnea/symptoms-causes/dxc-20205871 (last visited June 26, 2017). Although there is not extensive explanation of the doctors' evaluation of Mr. McCollum's condition, there is an indication at his first visit to Stanford of treater awareness of his prior MSLT and the flu shot. As Dr. Jain stated:

> "[Mr. McCollum] presents today for evaluation for narcolepsy/cataplexy…He only had an MSLT performed without PSG performed the night before. He was found to have a short sleep latency which raised concern for hypersomnia. He received the H1N1 vaccination in 2010. He also received flu shot this past year [2011] in September." *Id.* at 3.

The Stanford Sleep Clinic doctors took a blood sample from Petitioner in order to test for the presence of the gene that predisposes individuals to narcolepsy[16]—although it is also fairly

[14] Dr. Mignot is a recognized expert in the field of narcolepsy, and has published several research papers on the topic as well as running the Stanford Sleep Clinic. Dr. Mignot has also been recognized as an expert on the subject in the Program. *See, e.g., D'Tiole v. Sec'y of Health & Human Servs.,* No. 15-085, 2016 WL 7664475 (Fed. Cl. Spec. Mstr. Nov. 28, 2016) (denying entitlement on other grounds), *mot. for review den'd,* 2017 WL 2729570 (Fed. Cl. Mar. 2, 2017), *appeal docketed*, No. 2017-1982 (Fed. Cir. May 4, 2017); *Garrison v. Sec'y of Health & Human Servs*., No. 14-762V, 2015 WL 7424016 (Fed. Cl. Spec. Mstr. Oct. 29, 2015).

[15] A polysomnogram is the recording of multiple physiological variables during sleep. *Dorland's* at 1494.

[16] Human Leucocyte Antigen (HLA)-DQB1*06:02 is a genetic marker present in 12-38 percent of the general population. *See* Ex. 13 at 6. Narcoleptic patients with low hypocretin almost all express the genetic marker. *Id*.

common in the general population without narcolepsy— and found that Mr. McCollum possessed the gene. They did not, however, perform a spinal tap to look for the presence of hypocretin in his cerebral spinal fluid, a finding that constitutes strong diagnostic evidence of narcolepsy. Ex. 6 at 37; Tr. at 140, 154. Nevertheless, on July 13, 2012, the Stanford doctors revised Mr. McCollum's diagnosis to include narcolepsy and cataplexy after Petitioner took part in a sleep study at the Stanford Clinic, during which time he exhibited hypoventilation, low oxygen saturations, and OSA. Ex. 6 at 52-57.

Mr. McCollum visited the Stanford Clinic on numerous occasions between August 2012 and April 2013. He also took part in additional research conducted through the sleep clinic at Stanford. Ex. 5 at 7-10, 14-17, 30-34, 42-48; *see also* De la Herran-Arita *et al., CD4+T cell Autoimmunity to Hypocretin/Orexin and Cross Reactivity to a 2009 H1N1 Influenza A Epitope in Narcolepsy,* Science Transitional Med 5, 216ra176 (2014) (Retracted), filed as Ex. 19.[17] Despite the heavy medication he received to counteract his symptoms, Petitioner still reported "rather significant cataplexy." Ex. 5 at 7. Dr. Chad Ruoff suggested that Mr. McCollum might also have narcoleptic REM sleep behavior disorder ("RBD"). *Id*. at 9-10. Subsequently, Mr. McCollum reported that he had not experienced sleep paralysis in months, had decreased his napping to three times a week, and was able to drive for over two hours, although he continued to report cataplectic attacks and hallucinations. *Id.* at 25, 31. Petitioner's medication was eventually increased. *Id.* at 31, 34, 42-48. Mr. McCollum was finally able to return to work on May 10, 2013. Ex. 4 at 15.

On September 10, 2013, Mr. McCollum returned to the Stanford Clinic to ask for paperwork necessary to reinstate his driver's license. Ex. 5 at 55. Dr. Ruoff noted that Mr. McCollum had improved significantly. *Id*. In an e-mail message exchange between Petitioner and Dr. Ruoff in September 2013, Dr. Ruoff confirmed that Mr. McCollum possessed the HLA-DQB1*06:02 gene that may have predisposed him to narcolepsy. *Id.* at 65. Dr. Ruoff also stated "[q]uestionable reported history transient ischemic attacks - I do not know the details but could imagine a cataplectic attack being interpreted as a "TIA," although he acknowledged as well that he had not reviewed the prior records and was therefore speculating. *Id.* at 60.

II. Fact Witness Testimony

Petitioner presented three witness affidavits - two from Mrs. McCollum and one from himself. Exs. 34-35, 37. In addition, Mr. and Mrs. McCollum both testified at the hearing. Tr. at 4-73.

The McCollums's testimony focused on the attempt to establish that Mr. McCollum did in fact receive the flu vaccine in the fall of 2011. Neither of them could recall the specific day that

[17] This article was ultimately retracted, because its results could not be replicated. *D'Tiole*, 2016 WL 7664475, at *12 n.17.

Petitioner received the vaccine, but they both testified that the vaccination occurred at their local Walgreens shortly after Mrs. McCollum's hospitalization in late September 2011. Tr. at 7, 41-42. Although Petitioner could not remember in which arm he received the vaccine, he specifically recalled that it was an injection administered in his arm, noting the big knot he got in his arm following vaccination. *Id.* at 8, 42, 61. The McCollums also verified that due to the proximity of the Walgreens to their home, they—more frequently Mr. McCollum—dropped by the location quite often, making it difficult to pinpoint in their billing records which charge could have been the vaccination. *Id.* at 29.

Mr. and Mrs. McCollum addressed in their testimony the issue of Petitioner's documented sleep problems predating the fall 2011 vaccination. Both admitted that they could not completely explain such prior sleep issues. Tr. at 10, 44. However, the McCollums did propose that Mr. McCollum's earlier two back surgeries had made it uncomfortable for him to sleep. *Id*. They also suggested that Petitioner had sleep apnea at the time but it was undiagnosed. *Id*.

Both Mr. and Mrs. McCollum also noted in their testimony that during Mr. McCollum's treatment at the Stanford sleep clinic, his physicians requested (contrary to the theory proposed herein relating the vaccine to the claimed illness) that he receive an *additional* flu shot, and that he did so in October 2012, although (like the vaccination at issue in this case) there is no formal record of it. Tr. at 56-57. Mr. McCollum recalled that Mrs. McCollum was hesitant for Petitioner to receive the vaccine, but he was convinced to go ahead with vaccination because he wanted to help others with the condition by assisting the clinic in evaluating whether the vaccine was in fact related. *Id.* at 56. Petitioner stated that this vaccine was received at a local CVS, not at the Stanford Clinic. Tr. at 39. He and Mrs. McCollum also reported that his vivid dreams became more severe for about a week after receipt of his second flu shot, but did not otherwise report any other related symptoms stemming from the second vaccination. Tr. at 22-23.

III. Expert Testimony

One expert witness was presented by each party. Petitioner offered Dr. Marcel Kinsbourne, a neurologist. Respondent presented Dr. Maryanne Deak, whose specialty is sleep disorders. The opinions and testimony of the relevant experts are set forth below.

A. Dr. Marcel Kinsbourne

Dr. Kinsbourne testified at hearing, and offered two expert reports opining that the flu vaccine caused Petitioner to develop narcolepsy and cataplexy. Tr. at 74-128; Expert Report, filed on Sept. 15, 2015 as Ex. 13 (ECF No. 21) ("Kinsbourne First Rep."); Supplemental Expert Report, filed on Feb. 22, 2017, as Ex.41 (ECF No. 40) (Kinsbourne Second Rep.").

As his CV indicates, Dr. Kinsbourne is board certified in pediatrics. *See* Dr. Kinsbourne Curriculum Vitae, filed on Sep. 15, 2015 as Ex. 14 (ECF No. 21) ("Kinsbourne CV"), at 1. He received his medical degree in England, and he has been licensed to practice medicine in North Carolina since 1967. *Id*. From 1967 to 1974, Dr. Kinsbourne served as an associate professor in pediatrics and neurology and a senior research associate at Duke University Medical Center before holding a series of academic positions, including professorships in pediatrics, neurology, and psychology. *Id*. at 2. His clinical experience includes serving as a senior staff physician in Ontario from 1974-1980, and a clinical associate in neurology at Massachusetts General Hospital from 1981-1991, although (as noted in other cases) many years have passed since he regularly saw patients. *Pope v. Sec'y of Health & Human Servs.,* No. 14-078V, 2017 WL 2460503, at *8 (Fed. Cl. Spec. Mstr. May 1, 2017). He does not have any specific expertise in narcolepsy, nor has he studied or researched the immunologic issues raised by theories claiming vaccine causation (although his general neurologic expertise made him competent to discuss such matters).

Dr. Kinsbourne proposed that by way of the mechanism of molecular mimicry, the H1N1-containing flu vaccine that Petitioner received in October 2011, was the cause of his narcolepsy and cataplexy. *See* Kinsbourne First Rep. at 10. As Dr. Kinsbourne explained, narcolepsy is a condition characterized by a "disturbance of the wake/sleep cycle such that the sleep aspect of the wake/sleep cycle is exaggerated." Tr. at 76, 80. Narcolepsy is very often associated with a deficiency of hypocretin, a neuropeptide found in the brain that helps regulates sleep. *Id.* at 80. Hypocretin is secreted throughout the day and when it is signaled by another neuron in the brain, it is projected to other areas of the brain and activates those areas, which has the effect of stimulating neurotransmitters that control the activation level in the brain sufficient to maintain a person's wakeful state. *Id*. In patients with narcolepsy, by contrast, the receptors responsible for the release of the hypocretin are blocked or destroyed. *Id*. at 79. Today, narcolepsy is understood to be an autoimmune condition, based on its association with an immune system marker— human leukocyte antigen—as well as the fact that certain autoantibodies are believed likely to cause the hypocretin receptor interference that results in the condition's sleep-related clinical symptoms. *Id.* at 78.

In support of his statements about how narcolepsy is believed to occur, Dr. Kinsbourne referenced animal studies. *See, e.g.*, Ying Li, et al., *Hypocretin/Orexin Excites Hypocretin Neurons via a Local Glutamate Neuron - A Potential Mechanism for Orchestrating the Hypothalamic Arousal System*, 36 Neuron 1169, 1169-81 (2002), filed as Ex. 43 (ECF No. 43-2); Ming-Fing Wu, et al., *Role of the Hypocretin (orexin) Receptor 2 (Hcrt-r2) in the Regulation of Hypocretin Level and Cataplexy*, 31 J. Neuroscience 6305, 6305-10 (2011), filed as Ex. 44 (ECF No. 43-3); Akihiro Yamanaka, et al., *Orexin Directly Excites Orexin Neurons Through Orexin 2 Receptors*, 30 J. Neuroscience 12642, 12642-52 (2010) filed as Ex. 45 (ECF No. 43-4). These studies focused on the idea of positive feedback within hypocretin neurons, ultimately showing that hypocretin neurons produce "hypocretin which then stimulates the neuron's own hypocretin receptor further

to activate the neuron." Tr. at 83. But if the hypocretin receptor is blocked from sending feedback, then less hypocretin will be produced because the neuron is dramatically less activated. *Id*. Dr. Kinsbourne opined that if that positive feedback theory is accurate, it explains why hypocretin levels fade away in patients with narcolepsy – some biologic process blocks the receptors. *Id*. at 84.

With that context in mind, Dr. Kinsbourne opined specifically how the flu vaccine could have a causal relationship to narcolepsy, by relying on epidemiologic evidence involving a different form of flu vaccine. Pandemrix is an inactivated, adjuvanted monovalent H1N1 flu vaccine[18] administered in Europe and associated with a high rate of narcolepsy in a number of countries, such as Finland. *See* Elizabeth Miller et al., *Risk of Narcolepsy in Children and Young People Receiving AS03 Adjuvanted Pandemic A/H1N1 Influenza Vaccine: Retrospective Analysis,* Brit. Med. J. 346, 794 (2014), filed as Ex. 29 (ECF No. 23); Jacques Montplaisir, et al., *Risk of Narcolepsy Associated with Inactivated Adjuvanted (AS03) A/H1N1 (2009) Pandemic Influenza Vaccine in Quebec*, 9 PLOS One, no. 9, 2014, at 1-9, filed as Ex. 30 (ECF No. 23); D. O'Flanagan, et al., *Investigation of an Association Between the Onset of Narcolepsy with Pandemic Influenza Vaccine, Ireland April 2009-2010*, 19 Euro Surveillance 5, 5-15 (2014), filed as Ex. 32 (ECF No. 23) ("O'Flanagan"); Markku Partinen, et al., *Increased Incidence and Clinical Picture of Childhood Narcolepsy Following the 2009 H1N1 Pandemic Vaccination Campaign in Finland*, 7 PLOS One, no. 3, 2012, at 1-8 ("Partinen").[19]

Recent research in the United States has attempted to determine what lies beneath the generally observed association between Pandemrix and narcolepsy. Dr. Kinsbourne relied specifically upon a series of related articles: S. Sohail Ahmed, et al., *Narcolepsy, 2009 A(H1N1) Pandemic Influenza, and Pandemic Influenza Vaccinations: What is Known and Unknown About the Neurological Disorder, the Role for Autoimmunity, and Vaccine Adjuvants*, 50 J. Autoimmunity 1, 7 (2014), filed as Ex. 40 (ECF No. 39) ("Ahmed I"), and S. Sohail Ahmed, et al., *Antibodies to Influenza Nucleoprotein Cross-React with Human Hypocretin Receptor 2*, 7 Sci. Translational Med. 294 (2015) , filed as Ex. 15 (ECF No. 22) ("Ahmed II").

Researchers had initially opined that an adjuvant Pandemrix contained, as opposed to the inactivated H1N1 virus itself, was responsible for the high association with narcolepsy. Ahmed I, however, observed that "no similar association has been reported to date with the [similarly-adjuvanted] pandemic vaccine made using the Canadian inactivation/purification protocol [Arepanix]," and widely administered in Canada, suggesting that the adjuvant itself may *not* have

[18] A vaccine is rendered inactive through the process of destroying the biological activity of the virus in the vaccine, by the action of heat or other physical or chemical means. *Dorland's* at 925. In a vaccine, the adjuvant serves to increase the adaptive immune response created by the antigen—in this case the antigen for the flu. Tr. at 86.

[19] Petitioner's expert, Dr. Kinsbourne, referenced the Partinen article in his first expert report; however, the article was never filed. The article is now filed as Court's Exhibit 1.

played a causal role. *See* Ahmed I at 8. Rather, the Ahmed I authors proposed that autoantibodies generated in response to a cross reaction with the H1N1 components (via a molecular mimicry process) contained in Pandemrix likely blocked hypocretin receptors sufficient to trigger narcolepsy in those individuals susceptible to it (mainly because they possess the genetic haplotype HLA-DQB1*0602). Kinsbourne First Rep. at 7; Ahmed I at 8.

There still remained the question of what specific aspect or feature of the H1N1 components in the flu vaccines studied could be implicated in the autoimmune process that resulted in blocking of the hypocretin receptors. Ahmed II's authors began to suspect that that the nucleoprotein ("NP") antibody content of the H1N1-based flu vaccines was a more likely causal factor for narcolepsy than the adjuvant. Ahmed II at 1-2. To evaluate why different forms of the same adjuvanted flu vaccine could have different associations with narcolepsy, they measured the amounts of NP in different versions, finding in fact that Pandemrix was high in NP due to the process used to inactivate its H1N1 viral components – while other versions had less NP. *Id.* at 4. Thus, *any* vaccine containing similar H1N1 viral strain components could have the same effect, depending on the NP amounts contained therein. Kinsbourne First Rep. at 7-8.

There is an immediate facial limitation, however, to the application of such literature to this case. Pandemrix is not a form of the flu vaccine administered in the U.S. Tr. at 86; *see also Narcolepsy Following Pandemrix Influenza Vaccination in Europe*, CDC, https://www.cdc.gov/vaccinesafety/concerns/history/narcolepsy-flu.html (last visited September 5, 2017). It is also undisputed in this case that Petitioner did not receive Pandemrix. Indeed, if he had, his claim would have been promptly dismissed, since the 2009 monovalent H1N1 vaccine is not a covered Program vaccine. *Morris Sabin v. Sec'y of Health & Human Servs.*, No. 13-624V, 2014 WL 2979385, at *2 (Fed. Cl. Spec. Mstr. Feb. 7, 2014) (citations omitted).

In order to apply the Pandemrix-associated findings to the likely form of the vaccine administered herein, Dr. Kinsbourne made several contentions. First, he noted literature associating the wild H1N1 virus with narcolepsy. Kinsbourne Rep. at 4; Fang Han, et al., *Narcolepsy Onset is Seasonal and Increased Following the 2009 H1N1 Pandemic in China*, 70 Am. Neurological Ass'n 410, 410-17 (2011), filed as Ex. 22 (ECF No. 22) ("Han"). Han was a retrospective study of narcolepsy onset in patients diagnosed in Beijing, China from 1998-2010. Han at 1. Han purported to show that the occurrence of narcolepsy onset was seasonal, based upon a reported increase in the condition's onset following the 2009 H1N1 winter influenza pandemic. Accordingly, the wild H1N1 influenza virus itself, along with other upper airway infections, was highly correlated to narcolepsy. Han at 1. However, Han's authors acknowledged that the sample of patients in the study was not representative of China as a whole. *Id.* at 7. The Ahmed articles also conceded that Han's findings were far from definitive in establishing a wild virus-narcolepsy link. *See, e.g.*, Ahmed II at 6 (observing that "studies outside China have not reported an increase

in narcolepsy cases in unvaccinated subjects," and proposing that the high residential density of Beijing might simply have made the studied residents more susceptible to flu infection).

Second, Dr. Kinsbourne pointed to certain findings in the literature on Pandemrix and NP levels that pertained to other forms of the vaccine akin to what has been administered in the United States. A chart presented in Ahmed II compared the levels of NP in different flu vaccines, including some actually administered in the United States, such as Fluvirin and Fluzone. Ahmed II at 8, Table 2; Kinsbourne Second Rep. at 5; Tr. at 123-26. The NP levels for certain non-Pandemrix forms of the trivalent flu vaccine that are administered in the U.S. were in fact comparable to Pandemrix. *Id.* Dr. Kinsbourne allowed for the fact that "it makes sense that Pandemrix had the strongest effect because it had the most nucleoprotein in it," thereby making the risk of narcolepsy lower for different forms – but (as the Ahmed II Chart established) that did not mean the other forms could not also have the same cross-reactive impact, given their similar NP levels. Tr. at 102.

Dr. Kinsbourne also addressed in his opinion an observational epidemiologic study[20] filed by both sides that undermines the proposed connection between non-Pandemrix forms of the vaccine and narcolepsy. *See* Jonathan Duffy et al., *Narcolepsy and Influenza A (H1N1) Pandemic 2009 Vaccination in the United States*, 83 Neurology 1823, 1823-30 (2014), filed as Ex. 20 (ECF No. 22) ("Duffy"). Duffy's authors studied the association between narcolepsy and the unadjuvanted version of the H1N1 vaccine utilized in the United States, retrospectively surveying 650,995 individuals vaccinated with an H1N1 strain flu vaccine in 2009, but failed to find an increase in narcolepsy. *Id*. at 1823. Of these patients, zero developed symptoms during the 180 days following receipt, despite an expected incidence of 6.52. *Id.* In the 2010-11 seasonal flu vaccine study, 870,530 individuals received some form of the vaccine, but only two had onset of narcolepsy symptoms during the defined time period, compared to 8.83 expected. *Id.* at 1827. The Duffy authors hypothesized that the H1N1 antigens in these versions of the vaccine were themselves not sufficient to increase narcolepsy incidence. *Id*. Dr. Kinsbourne argued, however, that Duffy's reliability was limited by the fact that it was not a controlled study, and that its authors admitted that because of the inherent limits to the study, its conclusions "must be interpreted with caution." *Id*. at 1828; Kinsbourne First Rep. at 5; Tr. at 116.

In his testimony, Dr. Kinsbourne was also asked to address Mr. McCollum's prior TIA diagnoses, along with his pre-vaccine history of sleepiness. Dr. Kinsbourne characterized such instances as distinguishable from Petitioner's post-vaccination symptoms, attributing some to a

[20] Dr. Kinsbourne's report flatly denies the existence of any "published formal epidemiological study of the association of H1N1 vaccines and narcolepsy." First Kinsbourne Rep. at 4. He nevertheless discussed Duffy at trial and in his report, but denied that it constituted epidemiologic evidence, characterizing it instead as either an "ecological study" or merely an "observational" but "uncontrolled" study that was therefore inherently less reliable. Kinsbourne First Rep. at 4; Tr. at 116. But (as discussed in greater detail below) Dr. Kinsbourne's attempts to make category distinctions between Duffy and a "true" epidemiologic study were not persuasive.

failure to get enough sleep rather than as evidence of narcolepsy, which he proposed would more likely present as sleeping too much or being unable to resist day sleep urges. Tr. at 110. He acknowledged that one of Mr. McCollum's Stanford doctors, Dr. Ruoff, had speculated that the incidents of TIA could have reflected undiagnosed cataplexy, but expressed adamant disagreement, arguing that the TIA incident had lasted far too long to be so considered. *Id*. at 112. TIA, he maintained, is a mini stroke and would therefore only effect one side of the body, where a cataplectic attack affects a person's entire body. *Id*.

Dr. Kinsbourne finally addressed appropriate timelines for the onset of narcolepsy. He recognized that "typical" onset is difficult to determine because narcolepsy's symptoms can go undiagnosed for a long period, or be confused with other conditions. Nonetheless, based on a chart in O'Flanagan setting forth time periods between vaccination with Pandemrix and discovery of narcolepsy, Dr. Kinsbourne opined that he would expect onset to occur between six weeks and six months after vaccination. Kinsbourne First Rep. at 9-10, O'Flanagan at 6, Table 3. O'Flanagan listed the percentage of 32 patients who developed narcolepsy after vaccination, starting at 4.6 percent at 0-6 days and ending at 100 percent after 12 months had passed since vaccination. *Id.* As a result, Dr. Kinsbourne felt that Petitioner's development of narcolepsy in two to three months after vaccination was temporally appropriate, especially in light of its "subtle" and "underdiagnosed" character. Kinsbourne First Rep. at 10.

B. Dr. Maryanne Deak

Dr. Deak testified at hearing, and offered one expert report. Ex. A, dated June 13, 2016 (ECF No. 32) ("Deak Expert Rep."); Tr. at 128-57. She opined not only that the evidence linking the flu vaccine to narcolepsy was weak, but also that Mr. McCollum's symptoms had not been shown to fit the proper clinical criteria for a narcolepsy diagnosis, and that his prior symptoms ruled out vaccine causation in any event.

Dr. Deak is a board-certified neurologist and sleep specialist currently employed at eviCore healthcare, where she works on guideline development and clinical case review for sleep medicine or neurology cases. *See generally* Ex. B (ECF No. 32) ("Deak CV"); Tr. at 130-32. She graduated from Georgetown University School of Medicine in 2004 after completing her bachelor's degree there in 2000. Deak CV at 1. Dr. Deak completed residencies in neurology at New York University and University of Massachusetts. *Id*. She then served as a clinical and research fellow in sleep medicine at Brigham and Women's Hospital at Harvard Medical School before becoming an instructor there in the Division of Sleep Medicine in the Department of Internal Medicine. *Id*. As part of this work, she worked in the sleep clinic, which meant that she saw a fairly large patient population all with sleep related issues. Tr. at 133. She stated that she had often seen patients being evaluated for narcolepsy, although many were ultimately diagnosed with a different sleep disorder. *Id*. Dr. Deak has also helped develop a stimulant medicine for patients with narcolepsy and central

hypersomnia. *Id*. at 8. Her CV also indicates that she has written or coauthored several peer reviewed articles and book chapters in the area of sleep disorders. *Id*. at 8-10.

The initial focus of Dr. Deak's testimony and expert report was the overall propriety of Mr. McCollum's narcolepsy diagnosis. In her view, Petitioner's clinical symptoms and test results did not meet the objective criteria for diagnosis for narcolepsy established by the American Academy of Sleep Medicine—an organization in which Dr. Deak previously served as a committee member. Tr. at 140-41. Although Mr. McCollum underwent an MSLT sleep study when he was first diagnosed by Dr. Shen, Dr. Deak did not consider the study to have been performed under the proper conditions to reliably diagnose narcolepsy because Mr. McCollum had not tracked his sleep patterns in advance of the test, an overnight polysomnography was not performed the night before the MSLT, nor did the study consider the medications he had been taking at the time. *Id*. at 142-43. She therefore felt that the Stanford sleep specialists may have over-relied on the MSLT results without double-checking. *Id.* at 154-55. However, literature Dr. Deak filed suggests that the MSLT testing might not be all that conclusive for older individuals believed to possibly suffer from narcolepsy like Mr. McCollum. *See* Christian Guilleminault, et al., *Narcolepsy: Diagnosis and Management, in* Principles and Practice of Sleep Medicine 957-67 (5th ed. 2011), filed as Ex. C (ECF No. 32) ("Guilleminault") at 960 (MSLT too stringent to apply to older patients).

Dr. Deak further maintained that Mr. McCollum possessed several co-morbidities that could have contributed to some form of sleep disorder. Deak Expert Rep. at 4. For example, she suggested that Mr. McCollum might suffer from daytime sleepiness due to his use of sedating medications, and because of his apnea-related trouble breathing while he slept. Tr. at 144. And she noted the absence of any lab results confirming that Mr. McCollum possessed the lesser levels of hypocretin in his CSF associated with narcolepsy (a well-known strong link with the condition), although such testing appears never to have been performed on Mr. McCollum in the first place. *Id.* at 154; Guilleminault at 960.

Dr. Deak addressed the difficulty of determining the onset of narcolepsy due to its insidious nature – a fact that in her view undercut the conclusion that Mr. McCollum's symptoms likely post-dated his vaccination. Deak Expert Rep. at 5. As she noted, narcolepsy can go undiagnosed for as long as decades, especially when it is not also seen in the presence of cataplexy. *Id*. The diagnostic criteria she filed as part of her medical literature, however, limited that time frame, stating "[c]ataplexy most often occurs within one year of onset but in rare cases, may precede the onset of sleepiness or commence up to 40 years later." *See* American Academy of Sleep Medicine, *International Classification of Sleep Disorders* 12 (3d ed. 2014), filed as Ex. D (ECF No. 32) ("AASM").

Finally, Dr. Deak discussed the pathogenesis of narcolepsy in connection with vaccines. While she recognized that Pandemrix has been associated with higher incidence of narcolepsy abroad, she rejected the idea that vaccines in the United States, made without adjuvants, could be

equally associated with narcolepsy due to the lack of confirming research in the area. Tr. at 145-46.

Dr. Deak's report relied on some literature evaluating the relative role of the H1N1 components in a flu vaccine versus the adjuvant in triggering narcolepsy. In particular, her report cited a review article authored in part by one of the individuals most associated with first observing the relationship between Pandemrix and narcolepsy. *See* Markku Partinen, et al., *Narcolepsy as an Autoimmune Disease: the Role of H1N1 Infection and Vaccination,* 13 Lancet Neurol. 600, 600-13 (2014), filed as Ex. G (ECF No. 32-7) ("Partinen II"). Partinen II embraces the consensus in the medical and scientific community that narcolepsy is autoimmune in nature, and that "an H1N1 virus-derived antigen might be the trigger" for the condition. Partinen II at 600, 605-06. But (even while underscoring the reliable evidence linking Pandemrix to narcolepsy), Partinen II also notes that it could not be concluded that adjuvants contained in Pandemrix and similar H1N1 flu vaccines played no contributory role, and therefore the two factors (NP content plus adjuvant) might have a "dual effect." *Id.* at 608; *see also* Outi Vaarala, et al., *Antigenic Differences Between AS03 Adjuvanted Influenza A (h1n1) Pandemic Vaccines: Implications for Pandemrix-Associated Narcolepsy Risk*, 9 PLOS, no. 10, 2014, at 20, filed as Ex. I (ECF No. 32) ("[t]he role of [the adjuvant] may have been indispensable as a booster of the immune response triggering narcolepsy"). Partinen II's authors proposed that this relationship should be further investigated, "because *no reports exist of narcolepsy in association with other non-adjuvanted H1N1 virus-containing vaccines"* – thus suggesting that it could not be assumed that the NPs derived from the H1N1 components of the vaccine were alone enough to cause narcolepsy, even if they were a more significant factor than the adjuvant. *Id.* (emphasis added).

IV. Procedural History

Mr. McCollum filed his Petition on August 29, 2014. ECF No. 1. Petitioner thereafter began to file medical records, although the glaring lack of documented proof of vaccination – a central matter in any Vaccine Program case - became apparent soon after the case was filed. Despite this, Respondent filed his Rule 4(c) Report on April 20, 2015. ECF No. 13. Throughout the remainder of 2015, Petitioner continued filing medical records and the first expert report from Dr. Kinsbourne, while also attempting to gather evidence of proof of vaccination from Walgreens and through the affidavits of Mr. and Mrs. McCollum.

Those efforts produced some results, including a letter from Walgreens stating the type of flu vaccine offered during the relevant time period, plus its cost and formulation for the 2011 season. *See e.g.*, Exs. 38-39. However, by December 2016, Petitioner was still unable to provide direct proof of vaccination. After a status conference, I scheduled the case for hearing in April 2017, noting that it would provide the parties the opportunity at trial to address the proof of

vaccination question along with the greater issue of entitlement. The hearing was held as scheduled on April 4, 2017, and this case in now ripe for a decision.

V. Applicable Legal Standards

A. Petitioner's Overall Burden in Vaccine Program Cases

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury" – *i.e.*, an injury falling within the Vaccine Injury Table – corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & 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).[21] In this case, Petitioner does not assert a Table claim.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Human Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

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

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

and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury." *Althen*, 418 F.3d at 1278.

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

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Human Servs.*, 121 Fed. Cl. 230, 245 (2015) ("[p]lausibility . . . in many cases *may* be enough to satisfy *Althen* prong one" (emphasis in original)), *vacated on other grounds*, 844 F.3d 1363 (Fed. Cir. 2017). But this does not negate or reduce a petitioner's ultimate burden to establish his overall entitlement to damages by preponderant evidence. *W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted).[22]

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

[22] Although decisions like *Contreras* suggest that the burden of proof required to satisfy the first *Althen* prong is less than the other two, there is ample contrary authority for the more straightforward proposition that the first *Althen* prong (as a component of the overall test) simply requires application of a preponderance evidentiary standard when evaluating if a reliable and plausible causation theory has been established. *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339, 1350 (Fed. Cir. 2010).

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

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

B. Law Governing Analysis of Fact Evidence

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then

required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Human Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

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

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Human Servs*., No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony – especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Human Servs*., 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

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

those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Human Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

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

C. Analysis of Expert Testimony

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

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial for a (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health*

& Human Servs., 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742-45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts of her own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 91997)); *see also Isaac v. Sec'y of Health & Human Servs*., No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review den'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 Fed. App'x 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325-26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Human Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. Consideration of Medical Literature

Both parties filed medical and scientific literature in this case, but not all such items factor into the outcome of this decision. While I have reviewed all of the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to this Decision – just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Human Servs.*, No. 2015-5072, 2016 WL 1358616, at *5 (Fed. Cir. Apr. 6, 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Human Servs.,* 527 F. App'x 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to – and likely undermines – the conclusion that it was not considered").

ANALYSIS

A. *Althen Prong One*

I have recently had the occasion to consider the scientific reliability and evidentiary persuasiveness of the theory that flu vaccines administered in the U.S. and containing the H1N1 influenza strain can provoke an autoimmune process that (via molecular mimicry) results in blockage of the hypocretin receptors in the brain responsible for sleep regulation, thereby producing narcolepsy. *See, e.g., D'Toile v. Sec'y of Health & Human Servs.,* No. 15-085, 2016 WL 7664475 (Fed. Cl. Spec. Mstr. Nov. 28, 2016) (denying entitlement), *mot. for review den'd,* 2017 WL 2729570 (Fed. Cl. Mar. 2, 2017), *appeal docketed*, No. 17-1982 (Fed. Cir. May 4, 2017).

I denied entitlement in *D'Toile* because I determined that the version of the flu vaccine at issue – Flumist, a nasally-administered live attenuated influenza vaccine – could not (based upon the evidence presented) be reliably shown to cause narcolepsy as opposed to other, more well-studied forms such as Pandemrix. Not only was Flumist manufactured differently (and therefore contained fewer of the NPs proposed by some of the reliable literature to be the trigger for the autoimmune process leading to narcolepsy), but the expert testimony and literature offered in that case acknowledged (directly and indirectly) that the theory could not be reliably extended to cover the relevant form of the vaccine for other reasons. *D'Tiole*, 2016 WL 7664475, at *20-28.

As I recognized in *D'Toile*, the general theory that *certain formulations* of H1N1-containing flu vaccines can cause narcolepsy due to their NP content has several reliable components.[23] For example, the proposition that narcolepsy is an immune-mediated condition is fairly well-established. Tr. at 78, 139. In addition, as Dr. Kinsbourne opined, the decrease in, or complete disappearance of, hypocretin caused by autoantibodies produced via the mechanism of molecular mimicry likely results in a disruption in a person's wake cycle leading to narcolepsy. These deficiencies in the hypocretin-mediated neurotransmission process have been studied and persuasively linked to narcolepsy. Ahmed II at 2. And there is extensive literature associating narcolepsy with Pandemrix, and persuasive studies suggesting that the NP content of Pandemrix-like versions of the flu vaccine may be an important causal factor (although such studies do not

[23] Petitioner's pretrial brief maintains that "the fact that the H1N1 influenza vaccine *can cause* narcolepsy in a susceptible individual (Althen Step I) cannot seriously be disputed" (perhaps intending to suggest that any failure by the Petitioner to offer adequate evidence in support of causation herein is attributable to the obviousness of the question). Pre-Hearing Statement, dated February 23, 2017 (ECF No. 41) at 1 (emphasis in original). But this vastly overstates what the reliable scientific evidence offered in this case establishes. Such literature limits the "can cause" association upon which Petitioner relies to a form of the flu vaccine that has never been administered in the U.S. and is not involved in this case. And it is not a defense to the failure to offer sufficient evidence in support of a causal theory at the appropriate time to argue that the question presented was so obviously in one's favor that there was no need to even try. Program claimants may not reserve their real evidentiary "fire power" for only after their initial showing has been found inadequate.

completely rule out the previous conventional wisdom in the scientific community that the adjuvants also play a contributory role in encouraging an autoimmune process).

But can science regarding a *different* form of flu vaccine be applied to the version Mr. McCollum allegedly received, allowing the determination that the latter could cause narcolepsy? I conclude that Petitioner has not so established.

Based upon unrebutted evidence, Petitioner most likely received an H1N1-containing inactive, unadjuvanted version of the flu vaccine, as that was the predominant form being administered in the fall of 2011. *See* Exs. 38-39. Petitioner offered no direct evidence, however, suggesting that such a version has been tested in connection with narcolepsy to the degree his other evidence associates narcolepsy with the Pandemrix version. Instead, Petitioner sought to leverage what is known about Pandemrix to the facts of this case.

To do so, he relies on two points. First, Petitioner notes that H1N1 flu vaccines administered in the U.S. in the relevant time period contained levels of NP almost comparable to that of Pandemrix, allowing for the conclusion that the vaccine he received could have the same cross-reactive capacity. Tr. at 96; Ahmed II at 8. This argument in turn relies on the concept that it is the NP levels that trigger narcolepsy. Ahmed II provides somewhat reliable support for this contention. Indeed, studies of similar adjuvanted H1N1 vaccines less associated with narcolepsy than Pandemrix, such as Arepanix, corroborate the importance of the manner in which the H1N1 components were inactivated as determinant of NP levels.[24]

As I noted in *D'Toile*, however, there are limits to the conclusiveness of the Ahmed II findings about NP content. Not only are its own experiments insufficiently powered enough in terms of numeric sample to be fully reliable in establishing causation, but Ahmed II's authors admit that the interplay between NP content and genetic susceptibility impact whether any form of an H1N1 vaccine can be associated with the condition. *D'Toile*, 2016 WL 7664475, at *21, 23 n.22; Ahmed II at 10. More importantly, as discussed above, while Ahmed II shifts the focus on the likely primary cause of narcolepsy away from the adjuvants contained in the Pandemrix-like vaccines, it does not wholly eliminate the adjuvant as possibly playing an important role (thus reducing the applicability of its findings to the proposed causal effects of unadjuvanted vaccines). Partinen II at 608.

Second, Petitioner proposed that there was reliable evidence suggesting that the wild H1N1 virus can cause narcolepsy, offering two articles discussing that link. *See, e.g.*, Han I; Fang Han, et al., *Genome-Wide Analysis of Narcolepsy in China Implicates Novel Immune Loci and Reveals*

[24] *See* T. Harris et al., *Did Narcolepsy Occur Following Administration of AS03 Adjuvanted Pandemic Vaccine in Ontario, Canada? A Review of Post-Marketing Safety Surveillance Data*, 19 Euro Surveillance 1, 1-5 (2014), filed as Ex. 23 (ECF No. 22).

Change in Association Prior to Versus after the 2009 H1N1 Influenza Pandemic, 9 PLOS Genetics, no. 10, 2013, filed as Ex. 21 (ECF No. 22). While Respondent did not rebut the findings in these items of literature, I note (as I also observed in *D'Toile*) that such studies have been inconsistent in their findings, and even (as the Ahmed authors agree) that circumstances unique to the relevant countries may play more of a role in the findings than the virus itself. Ahmed, et al., *Mechanistic Insights into Influenza Vaccine-Associated Narcolepsy*, in Human Vaccines and Immunotherapies 12 (2016).[25] The findings in Han and similar articles may also only establish that the development of narcolepsy requires a confluence of factors (an H1N1 vaccine containing an adjuvant, coupled with an ongoing pandemic involving the wild virus) – strengthening the conclusion that the capacity of the vaccine's NP content to spark narcolepsy still requires other boosting factors if it is to occur.

All of the above 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 Petitioner's contentions about a causal link. Petitioners are of course not obligated to offer epidemiologic evidence supporting their causation theory, and cannot be required by special masters to produce it. *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). Thus, the fact that Mr. McCollum could offer no such evidence establishing an association between unadjuvanted versions of the H1N1 vaccine and narcolepsy does not mean he could not still prevail. But both sides filed Duffy, and it is reasonable to consider whether it negatively impacts Petitioner's evidentiary showing. *Taylor v. Sec'y of Health & Human Servs.*, 108 Fed. Cl. 807, 819–21 (Fed. Cl. 2013) (special master did not err in considering epidemiological evidence); *Andreu*, 569 F.3d at 1379 (a special master may assess epidemiological evidence in "reaching an informed judgment as to whether a particular vaccination likely caused a particular injury.").[26]

In a recent decision, *Crutchfield v. Sec'y of Health & Human Servs.,* No. 09-0039V, 2014 WL 1665227 (Fed. Cl. Spec. Mstr. Apr. 7, 2014), former Special Master Hastings provided a cogent explanation of the evidentiary purpose served by reliable epidemiologic evidence, and the proper manner in which it is to be evaluated under the Vaccine Program's lenient evidentiary standards. The petitioner in *Crutchfield* sought to establish that the measles-mumps-rubella ("MMR") vaccine caused her to develop Type I diabetes. To rebut that contention, Respondent's experts relied in part on epidemiologic studies that demonstrated no association between the two. *Crutchfield*, 2014 WL 1665227, at *13. Special Master Hastings (observing the fact that Program

[25] This piece of medical literature was referenced in Dr. Kinsbourne's supplemental report (Ex. 41) but was not filed as an exhibit in the case.

[26] I also note that the Petitioner has offered several items of epidemiologic evidence involving Pandemrix intended to support his theory, offering studies that persuasively linked it to narcolepsy. *See, e.g.,* Exs. 29-30, O'Flanagan. Arguments that epidemiologic evidence cannot in fairness be marshalled against a Program petitioner lose much of their limited effectiveness when the claimant relies on evidence of the same category.

case law permits consideration of epidemiologic evidence even though it simultaneously does not mandate that claimants offer it in their prima facie case) evaluated it and found it tended to negate Petitioner's claim. *Id.* at *13-15.

The Petitioner's expert in *Crutchfield* attempted to distinguish the epidemiologic studies offered by Respondent by arguing that the very rarity of a vaccine-caused injury rendered such studies incapable of detecting the possibility of the injury (except where the study was large enough to be considered adequately powered in a statistical sense). *Crutchfield*, 2014 WL 1665227, at *15. This argument arises from the oft-cited proposition (noted above) that epidemiologic evidence need not be offered by petitioners at all – and Special Master Hastings credited its logic. Yet he rejected it nonetheless:

> It is, in fact, *always* true that epidemiologic studies can *never* prove definitively that Factor A *never* causes Condition B. Even when large studies fail to identify an association between Factor A and Condition B, it is *always theoretically possible* that Factor A causes Condition B in a very small number of cases, an effect too rare for the study to detect. But it is not the Respondent's burden in this case to prove that it is *impossible* that [the relevant vaccine] can cause [the alleged injury]. It is, rather, the *Petitioner's burden* to [show the vaccine can cause the injury] . . . And, therefore, the epidemiologic studies cited in this case . . . clearly do *not* help Petitioner carry her burden.

Id. at *15 (emphasis in original). Special Master Hastings's reasoning in *Crutchfield* is highly persuasive and I shall apply it to this case weighing Duffy.

Duffy involved forms of the flu vaccine that are administered in the U.S. (unadjuvanted H1N1 flu vaccines), yet observed no increase in the occurrence of narcolepsy after receipt by thousands of individuals. I have previously found Duffy to be a reliable and persuasive piece of evidence. *See D'Toile*, 2016 WL 7664475, at *22-23. It is true that Duffy studied versions of the H1N1 vaccine produced in different years than the precisely relevant year herein, but because Petitioner's theory focuses on antigens contained in the H1N1 strain as the primary cause of the hypocretin receptor blockage resulting in narcolepsy, I do not find such distinctions reduce its evidentiary value. Duffy stands as the only evidence directly relevant to the propensity of the version of the H1N1 flu vaccine administered in the U.S. to cause narcolepsy – but does not support Petitioner's theory at all.

Dr. Kinsbourne attempted to belittle Duffy as not a "true" epidemiologic study, but was unpersuasive in so doing (putting aside the fact that opining on the trustworthiness of this kind of evidence is somewhat outside of his primary area of expertise). Contrary to Dr. Kinsbourne's suggestion, an observational study like Duffy is not distinguishable from an epidemiologic study, but is instead a *kind* of epidemiologic study. Michael D. Green et al., *Reference Guide on*

Epidemiology, *in* Reference Manual on Sci. Evidence 549, 555-56 (3d ed. 2011) (hereinafter "Green") (in an observational epidemiologic study, researchers analyze groups of individuals who were exposed to a test agent, comparing them with groups not so exposed).[27] He also attacked Duffy as lacking the greater trustworthiness of a controlled experiment or case-controlled observational study, which would more precisely establish, or rebut, an association between vaccine and illness. I acknowledge the validity of Petitioner's general objections that such a study has limitations. *Dwyer v. Sec'y of Health & Human Servs.*, No. 03-1202V, 2010 WL 892250, at *64 (Fed. Cl. Spec. Mstr. Mar. 12, 2010) ("[e]very observational epidemiological study has some weaknesses because such studies examine the world as it is"). But Duffy still stands as reasonable evidence that calls into doubt Petitioner's theory – and it is not enough to respond by arguing (as Dr. Kinsbourne proposed) that the rare nature of a vaccine injury renders all epidemiologic evidence effectively useless. Kinsbourne First Rep. at 8; *Crutchfield,* 2014 WL 1665227, at *15.

Weighing all of the above together, I find that Petitioner has not offered preponderant reliable medical and scientific evidence sufficient to satisfy the first *Althen* prong. The concept that an adjuvanted version of the H1N1 vaccine comparable to Pandemrix could cause narcolepsy finds support in the Ahmed articles plus other literature offered by Dr. Kinsbourne. If Pandemrix were the version of the vaccine at issue, none of the foregoing analysis would be necessary. But the contention that the NP content of an unadjuvanted H1N1 vaccine administered in the U.S. is enough by itself to cause narcolepsy is far weaker, and rebutted by reliable and relevant epidemiologic evidence.

Petitioner's theory remains intriguing despite my determination. It may not be long before reliable evidence sufficient to establish the causal propensity of the relevant version of the flu vaccine administered in the U.S. will exist to fill in the evidentiary holes. But special masters have frequently observed that an evidentiary gap in a causal theory can be fatal to the overall claim – even if it is foreseeable that the gap may be filled sometime in the future. *Isaac v. Sec'y of Health & Human Servs*., No. 08-601V, 2012 WL 3609993, at *18 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review denied,* 108 Fed. Cl. 743 (2013), *aff'd,* 540 F. App'x 999 (Fed. Cir. 2013) ("[i]n most cases, there are no definitive answers to the question of vaccine causation. The answers will come in the future, as medical science progresses"); *Browning v. Sec'y of Health & Human Servs.,* No. 02-929V, 2010 WL 3943556, at *3 n.8 (Fed. Cl. Spec. Mstr. Sept. 27, 2010)("[s]pecial masters cannot delay indefinitely making decisions in vaccine cases to find out what the future holds"). I thus do not find the first *Althen* prong has been satisfied.

[27] Dr. Kinsbourne similarly erred in classifying Duffy as an "ecological" study. First Kinsbourne Rep. at 4. An ecological study is a kind of observational study in which broader data about a group as a whole is gathered, instead of individualized data. Green at 561. Duffy, by contrast, is properly considered a "cohort" observational study, in which a group classified based on exposure to the "agent of interest" (here, the flu vaccine) is "constructed retrospectively" and "followed over historical time toward the present" in order to observe the proportion of individuals who develop the relevant disease in comparison to individuals not exposed to the agent in question. *Id.* at 557. Indeed, Duffy itself acknowledges its cohort observational design. Duffy at 1824.

B. *Althen Prong Two*

Before addressing Petitioner's overall "did cause" showing, I will consider two fact issues raised in the case, both of which I resolve in his favor.

1. Petitioner Likely Received the Flu Vaccine in October 2011 - The most immediate factual obstacle facing Petitioner in this case was the lack of documented proof of vaccination. A Vaccine Act petitioner must, as a threshold matter in advancing a claim for damages, establish by a preponderance of the evidence receipt of "a vaccine set forth in the Vaccine Injury Table." § 300aa–11(c)(1)(A). The preponderance of the evidence standard means that an allegation is established to be "more likely than not." *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010).

Although contemporaneous documentation of vaccination from a healthcare provider is the best evidence that a vaccination occurred, it is not absolutely required in all cases. *Centmehaiey v. Sec'y of Health & Human Servs.*, 32 Fed. Cl. 612, 621 (1995) ("[t]he lack of contemporaneous documentary proof of a vaccination . . . does not necessarily bar recovery"). Indeed, as Vaccine Rule 2 states, "[i]f the required medical records are not submitted, the petitioner must include an affidavit detailing the efforts made to obtain such records and the reasons for their unavailability." Vaccine Rule 2(c)(2)(B)(i). Furthermore, if a petitioner's claim is "based in any part on the observations or testimony of any person, the petitioner should include the substance of each person's proposed testimony in a detailed affidavit(s) supporting all elements of the allegations made in the petition." Vaccine Rule 2(c)(2)(B)(ii).

Special masters have found that vaccine administration occurred even in the absence of direct documentation. In such cases, preponderant evidence was provided in the form of other medical records and/or witness testimony. For example, corroborative, though backward-looking, medical notations have been found to tip the evidentiary scale in favor of vaccine receipt. *Lamberti v. Sec'y of Health & Human Servs*., No. 99–507V, 2007 WL 1772058, at *7 (Fed. Cl. Spec. Mstr. May 31, 2007) (finding multiple medical record references to vaccine receipt constituted adequate evidence of administration); *Groht v. Sec'y of Health & Human Servs*., No. 00–287V, 2006 WL 3342222, at *2 (Fed. Cl. Spec. Mstr. Oct. 30, 2006) (finding a treating physician's note—"4/30/97—Hep B. inj. # 1 (not given here) (pt. wanted this to be charted)"—to be sufficient proof of vaccination); *Wonish v. Sec'y of Health & Human Servs.*, No. 90–667V, 1991 WL 83959, at *4 (Cl. Ct. Spec. Mstr. May 6, 1991) (finding parental testimony "corroborated strongly by medical records [referring] back to the [vaccination]" to be sufficient to establish vaccine administration).

In addition to corroborative medical records, witness testimony can also help establish a sufficient basis for a finding that a vaccine was administered as alleged. *Alger v. Sec'y of Health &*

Human Servs., No. 89–31V, 1990 WL 293408, at *2, 7 (Fed. Cl. Spec. Mstr. Mar. 14, 1990) (oral testimony from a parent and the doctor who administered the vaccine was "more than adequate to support a finding that the vaccine was administered"). The Court of Federal Claims has recognized that special masters may base a finding of vaccination on lay testimony. *Epstein v. Sec'y of Health & Human Servs.*, 35 Fed. Cl. 467, 478 (Fed. Cl. 1996); *see also Brown v. Sec'y of Health & Human Servs.*, 18 Cl. Ct. 834, 839–40 (1989) (proof of vaccination in the absence of contemporaneous medical records established via testimony of petitioner's parent, her personal calendar, and evidence of a charge for the vaccine on the physician's billing statement), *rev'd on other grounds*, 920 F.2d 918 (Fed. Cir. 1990).

In the present case, Petitioner has marshaled enough circumstantial evidence for me to find that he more likely than not received an unadjuvanted trivalent H1N1 flu vaccine (administered by injection rather than in intranasal fashion like Flumist) in October 2011. Although Mr. McCollum was not able to produce documentary proof from Walgreens providing direct evidence of his vaccination, he did establish that he made a purchase at Walgreens for the appropriate amount and during the relevant time period. Ex. 36 at 5. Walgreens also confirmed the types of flu vaccines being administered at the time (which included the H1N1 version) and their general costs. Ex. 7. In addition, Petitioner established a specific reason to obtain the flu vaccine —his wife's hospitalization. Tr. at 41-42. I also credit his testimony recalling the administration of the vaccine, as well as his wife's recollection of the circumstances in which she encouraged him to obtain it. Tr. at 7.

Based on Petitioner's bank statements, the only charge from Walgreens that could have included the vaccine is one from October 18, 2011, and I will therefore adopt that as the date of vaccination in this case.

2. Petitioner's Prior Symptoms Are Likely Unrelated to his Narcolepsy - Fundamentally, a Vaccine Act claim must establish that the injury in question did not precede the relevant vaccine's administration. *See, e.g., Shalala v. Whitecotton*, 514 U.S. 268, 273-74 (1995). Thus, onset of an injury must be shown to have occurred *after* the date of vaccination (for, except where a significant aggravation claim is pled, only under those circumstances can the vaccine possibly be said to have caused the alleged injury).

As Respondent argued, the medical record revealed several instances suggesting that Mr. McCollum had a pre-vaccination history of sleepiness or sleep disturbances. *See, e.g.*, Ex. 1 at 4-5, 64-68. Arguably, these instances establish that his narcolepsy (only diagnosed in 2012) predated vaccination. Given the literature discussing the fact that formal diagnosis of narcolepsy often comes long after symptoms first began, this interpretation of the medical record is entirely plausible.

Nevertheless, I find that the evidence offered by Petitioner is sufficient to conclude that his symptoms prior to vaccination were either related to his back problems or undiagnosed OSA – and therefore not evidence of pre-vaccination onset. While it is now understood that Petitioner has OSA, he had many, if not all of the risk factors for OSA before vaccination—excess weight, hypertension, nasal congestion, smoking, male gender, family history of OSA, etc. *Obstructive Sleep Apnea: Symptoms and Causes*, Mayo Clinic, http://www.mayoclinic.org/diseases-conditions/obstructive-sleep-apnea/symptoms-causes/dxc-20205871 (last visited June 26, 2017). OSA can lead to daytime fatigue and sleepiness, which are very similar to what Mr. McCollum reported experiencing, but the causal mechanisms for OSA are unrelated to those of narcolepsy. Rather than being a result of depletion of hypocretin in the brain, OSA occurs when the muscles of the throat relax too much and do not allow for a normal breathing rhythm. *Id*.

Other prior instances of sleep-related problems are also distinguishable. Thus, the instance in 2010 when Mr. McCollum reported "an altered level of consciousness with difficulty expressing himself and bilateral shaking of his arms" and was briefly hospitalized appeared to provide evidence of a day sleepiness/altered consciousness occurrence that looks more like a narcolepsy symptom than his OSA symptoms, although it was at the time diagnosed as TIA. Ex. 2 at 32. However, the instance was interpreted by Dr. Petrini to be the result of a change in hypertension medication, resulting in low blood pressure. Ex. 1 at 23. Once the medication balances were altered, Petitioner did not again experience anything similar until the late fall of 2011 (after he had received the flu vaccine). Dr. Ruoff's speculation, as set forth in the medical records, that Petitioner's TIA might have actually been a misdiagnosed instance of cataplexy is self-limited by his admission that he pondered this possibility without the benefit of review of the actual record. Respondent otherwise did not establish strong grounds that would permit me to conclude that these occurrences, despite the degree to which they suggest narcolepsy, were in fact evidence of it.

Petitioner's overall medical picture makes it difficult to assign significance to these prior sleep-related incidents. Petitioner has suffered from a variety of interrelated illnesses and medical problems, making it difficult to tell where one ends and the next begins. But given the ambiguity of the evidence purportedly showing related sleep problems, I cannot conclude that Mr. McCollum's narcolepsy more likely than not predated his receipt of the flu vaccine.

3. Conclusions with Respect to Second *Althen* Prong – Despite my determinations above, I find that preponderant evidence does not support the conclusion that the flu vaccine more likely than not caused Mr. McCollum's narcolepsy. Admittedly, the evidence largely supports the diagnosis, and Dr. Deak's efforts to rebut it were not persuasive.[28] Petitioner

[28] Dr. Deak argued that narcolepsy was an incorrect diagnosis, but undercut that opinion with admissions at trial that the diagnosis actually had medical plausibility. Tr. at 151. Moreover, her opinion must be weighed against the equally-qualified sleep specialist treaters at Stanford who opined as to Petitioner's condition. Indeed, Mr. McCollum took part in a research sleep study at Stanford that published results indicating that the doctors had confirmed that Mr. McCollum had met the diagnostic criteria for narcolepsy. In addition, Dr. Shen's notes from his evaluation of Mr.

has also proposed a logical sequential explanation consistent with his causation theory – although he has not established (beyond evidence of the genetic haplotype associated with narcolepsy) that Mr. McCollum possessed biomarkers for the condition, such as low hypocretin, and largely relies on the existence of post-vaccination symptoms rather than offering other circumstantial evidence.[29] But Petitioner's failure to establish a persuasive causal theory ultimately dooms his *Althen* two showing. Because the unadjuvanted H1N1 vaccine Mr. McCollum likely received has not been shown to cause narcolepsy, it does not matter how consistent Petitioner's arguments are with the causation theory proposed but rejected.

C. *Althen Prong Three*

As Petitioner has argued, the nature of narcolepsy as a condition makes it difficult to establish a clear timeframe in which it would develop after the autoimmune process leading to it (whatever its cause) began, thus allowing for a wide range of ostensibly medically appropriate onset timeframes. Tr. at 109. Here, and based upon my determination that Mr. McCollum received the vaccine on October 19, 2011, approximately four to six weeks passed before his first symptoms manifested. Petitioner primarily relied on O'Flanagan to conclude that this was a medically acceptable timeframe – although that article unquestionably did not involve the relevant formulation of the vaccine, and had other weaknesses that make it difficult to give it the weight urged by Petitioner.[30] Respondent's expert, however, devoted more energy to attempting to rebut the first two prongs, thus largely not contesting this showing.[31]

McCollum indicate that he performed a thorough review of Mr. McCollum's symptoms and eliminated other potential causes before diagnosing Petitioner with narcolepsy. Ex. 3 at 3. Similarly, Dr. Klein indicated that she recognized that the MSLT needed be repeated but did not do so because of Mr. McCollum's convincing clinical presentation of narcolepsy. Ex. 8 at 2. Due to such evidence, I do not find that Respondent persuasively established that the narcolepsy diagnosis was in error.

[29] I also note the testimony of the McCollums that Petitioner received a *second* flu vaccine sometime during his treatment at the Stanford Sleep Clinic as somewhat suggestive of the uncertainty surrounding the link between vaccination and his condition (since it is not likely his treaters would have been cavalier about exacerbating his condition had they been certain of a causal connection), although this evidence on this matter is fairly vague in the record.

[30] O'Flanagan's limitations go beyond the fact that, like most of Petitioner's scientific or medical proof, it involved Pandemrix. It (like the criticized Duffy study) was a retrospective cohort study – again underscoring the extent to which Petitioner and his experts were inconsistent in their views as to the reliability of such epidemiologic evidence, embracing it when invoked in favor of the claim, while criticizing it where it assisted Respondent. O'Flanagan at 1. In addition, O'Flanagan involved a sample of only 32 individuals diagnosed with narcolepsy, and relied on an individual's first contact with a treater as the best evidence of onset given the difficulties in diagnosing the condition – something that Program case law rejects as proper evidence of onset. *Id.* at 3-4. Moreover, of that sample only *three* individuals were adults like Mr. McCollum; O'Flanagan's authors were forthright in admitting how little could be reliably concluded based on so few observed cases. *Id.* at 7, 10.

[31] Dr. Deak endeavored to rebut the very possibility that the vaccine could cause narcolepsy, rather than attacking the timeframe in which it might be expected to do so. She only briefly discussed onset of narcolepsy, which she allowed could fall within an extremely broad timeframe, extending from one to 15 years. Tr. at 142.

Nevertheless, the deficiencies in Petitioner's causation theory make it impossible for him to establish that onset of his narcolepsy was temporally reasonable. It therefore does not matter that onset of Mr. McCollum's narcolepsy post-dated his vaccination by a month or two consistent with ranges proposed for Pandemrix in a single piece of literature. *Caves v. Sec'y of Health & Human Servs.*, No. 07-443V, 2010 WL 5557542, at *22 (Fed. Cl. Spec. Mstr. Nov. 29, 2010) (a finding of an appropriate temporal relationship is insufficient to show causation-in-fact, as the other two prongs must *also* be met). Absent more compelling proof that the version of the H1N1 vaccine in question administered in the U.S. *can cause* narcolepsy, I cannot conclude that the proposed timeframe herein has preponderant support.

Indeed – even if Petitioner had more successfully established the first prong, the amorphous, somewhat open-ended nature of the proposed timeframe for the onset of narcolepsy would make it difficult to conclude (based on present science) that the timeframe in question is medically acceptable. This Court has in the past noted that arguments about the acceptability of widely varied time periods between receipt of a vaccination and onset of an autoimmune illness or condition run the risk of rendering "*Althen's* first and third prongs essentially meaningless." *Hennessey v. Sec'y of Dep't of Health & Human Servs.*, 91 Fed. Cl. 126, 135 (2010) (rejecting argument of claimant's expert that an almost unlimited time period was possible for onset of autoimmune-induced diabetes). O'Flanagan itself observed "onset" (defined therein as treater contact – *not* first symptom, as is mandated by relevant case law) of anywhere from a few days to an entire year. O'Flanagan at 6, Table 3. Such a wide range is very difficult to square with the Program's requirements of establishing a proximate, medically acceptable timeframe as a matter of law.

CONCLUSION

This case presented numerous reasonably-disputed questions regarding onset, proof of vaccination, and prior evidence of similar symptoms. While I have found that Petitioner was successful in establishing some of these matters in his favor, he could not provide preponderant evidence on a key component of his claim, for the evidence supporting the proposed causal theory with respect to the version of the flu vaccine in question was too thin: there simply is not enough reliable scientific evidence at this point in time to conclude that the unadjuvanted version of the flu vaccine administered in the United States is associated with narcolepsy. Accordingly, Petitioner is not entitled to compensation under the Vaccine Program.

In the absence of a timely-filed motion for review (see Appendix B to the Rules of the Court), the Clerk shall enter judgment in accord with this decision.[32]

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

IT IS SO ORDERED.

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