In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 15-085V
(to be published)

MYKELLE JIVON D'TIOLE,	*	Special Master Corcoran
Petitioner,	*	Filed: November 28, 2016
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Decision Without Hearing; Dismissal; Influenza ("Flu") Vaccine; Narcolepsy; Cataplexy.
Respondent.	*	

Marvin Firestone, Marvin Firestone, MD, JD, and Associates, San Mateo, CA, for Petitioner.

Lara Ann Englund, U.S. Dep't of Justice, Washington, DC, for Respondent.

DECISION GRANTING MOTION TO DISMISS CASE[1]

On January 27, 2015, Mykelle Jivon D'Tiole's parents filed a petition[2] seeking compensation under the National Vaccine Injury Compensation Program (the "Vaccine

[1] Because this decision contains a reasoned explanation for my actions in this case, I will post it on the United States Court of Federal Claims website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the published decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen 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 whole decision will be available to the public. *Id*.

[2] The matter was originally filed by Petitioner's parents on his behalf, due to his minor status. After Mr. D'Tiole attained majority while the case was pending, I ordered that he be identified as the petitioner in the caption. ECF No. 27.

Program").[3] In it, Petitioner alleged that the influenza ("flu") vaccine he received on December 13, 2011, caused him to develop narcolepsy with cataplexy.

After the parties filed expert reports, and based upon my initial review of the case record, I proposed that the matter be decided without holding an evidentiary hearing and invited briefing on the substantive merits of Petitioner's claim. Having completed my review of the evidentiary record and the parties' filings, I hereby **GRANT** Respondent's Motion for a Ruling on the Record Dismissing the Case, and therefore **DENY** Petitioner's request for compensation, for the reasons stated below.

I. FACTUAL BACKGROUND

Mr. D'Tiole was born on February 8, 1997. Pet'r's Ex. 3 at 1. His early pediatric history is not in contention in this case and therefore requires no discussion. On December 13, 2011, when he was 14 years old, he went to his pediatrician for a well teen visit. Pet'r's Ex. 4 at 10. At that time, Petitioner received FluMist,[4] a live attenuated influenza vaccine ("LAIV"). Pet'r's Ex. 9 at 1-2; Ex. 1 at 2; and Ex. 4 at 10. His parents had not given their consent for Mr. D'Tiole to receive the vaccine at that visit, and, after learning it had occurred, they were upset that it was administered without their advance approval. Pet'r's Ex. 1 at 2 ¶ 8. There are no records in the subsequent six weeks setting forth any reaction to this vaccine.

On February 1, 2012, Mr. D'Tiole hurt his wrist after a fall suffered while playing basketball and was taken for treatment at the John Muir Medical Center Emergency Department in Walnut Creek, California. Pet'r's Ex. 53 at 3-5. He was diagnosed with a wrist fracture and underwent a closed reduction with percutaneous pinning under general anesthesia. *Id.* at 18-22. He was otherwise deemed healthy at the time, with no mention in the relevant records of any sleep-related problems. *Id.* at 4, 16.

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

[4] As noted in *Agnew v. Sec'y of Health & Human Servs.,* No. 12-551V, 2016 WL 1612853, at *3 (Fed. Cl. Spec. Mstr. Mar. 30, 2016), FluMist is a cold-adapted vaccine received intranasally. It contains live, but attenuated (meaning reduced in virulence), strains of the wild flu virus. *See* FluMist Package Insert, filed on June 20, 2016, as Resp't's Ex. G (ECF No. 36-1), at 13-14. To achieve an immune response from the body's adaptive immune system, the viral strains contained in the vaccine replicate at a temperature consistent with that found in the nasal cavity, but not at the higher temperatures found elsewhere in the body. *Agnew,* 2016 WL 1612853, at *3. As a result, the flu strain can replicate sufficiently to produce the antibodies necessary to fight a wild infection, without itself replicating enough to cause infection if transmitted to others. *See* Resp't's Ex. G at 13 ("the attenuated vaccine virus replicates to induce protective immunity"). In this case, Petitioner received a trivalent version of the vaccine.

On February 10, 2012, Petitioner saw his pediatrician for a follow-up examination of his wrist fracture, and was referred to an orthopedist. Pet'r's Ex. 4 at 11. There was still no record of any sleep problems. Petitioner, however, has offered witness statements suggesting that his sleep-related symptoms began around this time. Thus, his mother, Ms. Sevela DePlush, states that she noticed Mr. D'Tiole behaving "differently" and "began noticing him exhibiting severe drowsiness" by February 2012, after his surgery. Pet'r's Ex. 1 at 2 ¶ 10. However, she attributed his symptoms to a normal post-surgery reaction or the medication he was taking for pain. *Id.* at 2 ¶¶ 10-11.

Over a month later, on March 26, 2012, Petitioner saw his pediatrician again, now complaining of ear pain and feeling tired all of the time, and the notes from the visit specifically state that he was falling asleep again at 11 a.m. after waking at 6 a.m. Pet'r's Ex. 54 at 18. This is the first medical record statement about the injury alleged in this case, but it is Ms. DePlush's assertion that Petitioner's symptoms continued to be evident in the period prior to this visit. *See, e.g.,* Pet'r's Ex. 1 at ¶ 11. Mr. D'Tiole was prescribed antibiotics for his ear pain and was instructed to engage in better sleeping hygiene (*e.g.,* limiting television time before sleep). *Id.*

There is subsequently a nearly four-month gap in the records, and thus no contemporaneous recording of any other sleep-related problems for Petitioner. But on July 18, 2012, Mr. D'Tiole was seen again by his pediatrician with complaints of "problem with equilibrium x three months/hard time focusing." Pet'r's Ex. 54 at 17.[5] The notes from this visit, however, are somewhat contradictory, and do not support the contention that Petitioner's sleep problems were progressing. Thus, this record includes statements by Mr. D'Tiole that he was playing videogames late into the night, sleeping until noon thereafter, and having trouble focusing (presumably in connection with his vision, since the record also mentions an eye doctor visit) – but also that he was not experiencing dizziness or balance problems, and otherwise was doing "great in school." *Id*.[6] Petitioner's treater assessed him with a dysfunctional sleep pattern that could be treated in the same manner recommended in March. *Id.*

On September 6, 2012, Petitioner saw his pediatrician again, reiterating prior complaints about focus problems and sleepiness. Pet'r's Ex. 54 at 16. The note in the medical record states, "feels tired a lot, trouble focusing – twice a day x 6 mo." *Id.* He also reported experiencing short "tremors" lasting a few seconds, involving his eyelids drooping and his eyes wandering. The impression was possible seizure activity, and he was referred to a neurologist at Children's Hospital in Oakland, California.

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[5] The three-month onset reference in this July 2012 medical record would place onset in April – two months later than Ms. DePlush's recollection.

[6] Ms. DePlush's declaration directly contradicts this statement, and Petitioner has not offered any explanation for why she should be believed rather than the record itself. *See* Pet'r's Ex. 1 at 3 ¶ 12 ("[h]e was doing poorly in school").

There, on October 5, 2012, Mr. D'Tiole underwent an initial neurologic evaluation, at which time an electroencephalogram ("EEG") was performed. Pet'r's Ex. 5 at 1. The results were interpreted as normal, with no evidence of epileptiform discharges or focal abnormalities. *Id.* at 2. Nevertheless, Petitioner also obtained a consultation thereafter with Ali Mostajelean, M.D., of the hospital's epilepsy department. *Id.* at 3-5. Dr. Mostajelean concluded, based on the examination and EEG results, that there was no evidence that Petitioner was suffering from epilepsy. The notes from this examination reiterate concerns about Petitioner's dizzy spells and eye-fluttering episodes, but characterized them as only "recently experienced." *Id.* at 3. Some reference was also made in these notes to Mr. D'Tiole's sleep problems, but they were not identified as persistent; it was noted only that Petitioner often slept late on weekends, and poor sleep hygiene was again identified as the likely cause of such problems. *Id.* at 5.

In the months after, Mr. D'Tiole and his parents continued to investigate the source of his sleep problems, which were becoming more pronounced. On December 16, 2012, Petitioner was seen in the Emergency Department at John Muir Medical Center in Walnut Creek, CA, where he reported "he had 2 or 3 episodes at home where he felt weak and could not stand up and had some shaking of his extremities." Pet'r's Ex. 6 at 1. The chief complaint listed on the record was possible seizure. *Id.* The assessment section noted: "shaking episodes of uncertain cause," and a diagnosis of "altered consciousness" was given by Dan Buhler, M.D. *Id.* at 3; *see also* Pet'r's Ex. 1 at 3.

On February 1, 2013, Petitioner saw his pediatrician again, at which time concerns about both his purported seizure activity and previously-experienced sleep issues were reported. Pet'r's Ex. 4 at 14. Later that year, in August 2013, Mr. D'Tiole's parents took him for examination by the Stanford Hospital's Sleep Medicine Clinic in Redwood City, California. Pet'r's Ex. 7 at 1-12. Diagnoses provided after an initial examination were "hypersomnia due to medical condition classified elsewhere and narcolepsy with cataplexy[7]." *Id.* at 1. Notes contained in the record from the August 21, 2013, visit reflect statements by Ms. DePlush that "everything seemed to start after [Petitioner] broke his wrist and required anesthesia." *Id.* at 2. They also recorded progression in his symptoms over that year, with greater and greater daytime sleepiness. *Id.* at 3. The treater who examined Petitioner prescribed a trial of modafinil,[8] but also proposed consideration of medication aimed at addressing narcolepsy or cataplexy after more data on Petitioner (including a sleep study) had been obtained. *Id.* at 6.

[7] Cataplexy is a condition characterized by abrupt attacks of muscular weakness and hypotonia triggered by an emotional stimulus such as mirth, anger, fear, or surprise. *Dorland's Illustrated Medical Dictionary* (32d ed. 2012) at 303 (hereinafter, "*Dorland's*").

[8] Modafinil is a central nervous system stimulant, administered orally, used in the treatment of narcolepsy, obstructive sleep apnea, and sleep disorders associated with shift work. *Dorland's* at 1171.

By 2014 and thereafter, Petitioner received further treatment for his symptoms, and narcolepsy and cataplexy were no longer merely suspected but confirmed as the proper diagnoses for his condition. *See generally* Petitioner's Response to Respondent's Motion for Ruling on the Record, dated July 20, 2016 (ECF No. 37) ("Opp.") at 5-8. The confirmation was strengthened through tests (performed at Stanford Hospital's Sleep Medicine Clinic on January 15, 2014) revealing that Petitioner likely possessed the HLA allele associated with narcolepsy (HLA DQB1*0602). *See* Pet'r's Ex. 7 at 27-31. It was during treatment at the Sleep Medicine Clinic that Petitioner was seen by Dr. Emmanuel Mignot, a noted expert on the topic of narcolepsy. *Id*. In a follow up visit on April 16, 2014, it was confirmed that Mr. D'Tiole's test was positive for this HLA allele. *Id*. at 60. But Petitioner's parents were not made aware that he had received FluMist until the spring of 2014, and therefore did not bring this to the attention of the Sleep Clinic treaters. *See* Pet'r's Ex. 1 at 4; Pet'r's Ex. 9 at 1-2.

II. EXPERT REPORTS

A. Petitioner's Expert – Dr. Steinman

Dr. Lawrence Steinman is Petitioner's sole expert, although he submitted multiple reports in the case. He has opined that a viral component of the FluMist vaccine that Mr. D'Tiole received was causally responsible for his subsequent narcolepsy with cataplexy.

First Report

Dr. Steinman is a professor in Stanford University's Departments of Neurology, Pediatrics, and Genetics, and the chair of Stanford's Immunology Program. Pet'r's Ex. 62 at 1 (Dr. Steinman's curriculum vitae). He has been elected to the Institute of Medicine ("IOM") and has published more than 400 articles, including articles related to his research on autoimmune disease and molecular mimicry. *Id.* Dr. Steinman's primary focus is on multiple sclerosis, but he has conducted research, and authored papers, relevant to narcolepsy. *See id.* at 10, 35, 40. The core of Dr. Steinman's opinion is found in his first expert report, filed not long after the case's initiation. *See* January 30, 2015 Report, filed on February 19, 2015, as Pet'r's Ex. 11 (ECF No. 9-2) ("First Steinman Rep."). In it, Dr. Steinman reviews Mr. D'Tiole's medical history before turning to Petitioner's causal theory.

As Dr. Steinman's first report notes, scientific and medical research in the past 20 to 30 years has resulted in a number of discoveries highly relevant herein. Narcolepsy (which Dr. Steinman characterized as "a chronic sleep disorder presenting with excessive day-time sleepiness and often cataplexy") (First Steinman Rep. at 13)) has been associated (based upon tests of cerebral spinal fluid) with a deficiency in the protein hypocretin (also called orexin) – a neuropeptide that regulates arousal, wakefulness, and appetite. *See Dorland's* at 901, 1333; C. Peyron et al., *A Mutation in a Case of Early Onset Narcolepsy and a Generalized Absence of*

Hypocretin Peptides in Human Narcoleptic Brains, 6 Nature Medicine 9:991 (2000) (Pet'r's Ex. 26) ("Peyron"). This deficiency, in turn, has been shown to be the result of the loss of hypothalamic cells in the brain. *See, e.g.*, S. Nishino et al., *Hypocretin (Orexin) Deficiency in Human Narcolepsy*, Lancet 355, at 39 (2000) (Pet'r's Ex. 25) (ECF No. 10-7); Peyron at 5.

Although the precise mechanism responsible for impairment of hypocretin-mediated neurotransmission is not yet fully understood, Dr. Steinman has proposed (for purposes of the present claim) an autoimmune process triggered by viral components of flu vaccines such as FluMist. His reports opine that components from the wild flu virus contained in FluMist cross-react with certain self-proteins in the brain responsible for sleep regulation, via the mechanism of molecular mimicry (a topic upon which Dr. Steinman possesses considerable expertise, and one he has opined upon in numerous other Program cases).[9] Specifically, nucleoproteins contained in the H1N1 strains found in FluMist would share "molecular similarities" with certain amino acid peptides on the surface of the hypocretin receptors in the brain. First Steinman Rep. at 13-14. After receipt of the vaccine, in the course of the human body's adaptive immune response the host's immune system is "tricked" into attacking the receptors, thereby interfering with the hypocretin-mediated neurotransmission process that would, if functioning properly, prevent daytime sleepiness. *Id.* at 16-17.

Besides his expertise in studying the causes of other autoimmune illnesses, Dr. Steinman's opinion in this case is rooted in studies involving the relationship between narcolepsy and a different version of the flu vaccine than FluMist. Thus, he noted that Pandemrix – an inactivated[10] form of the flu vaccine containing the H1N1 viral strain also found in FluMist – had been determined by several reputable studies to be closely associated with the development of narcolepsy in European children, after a 2010 outbreak of narcolepsy in Finland. First Steinman Rep. at 20-21; M. Partinen et al., *Increased Incidence and Clinical Picture of Childhood Narcolepsy Following the 2009 H1N1 Pandemic Vaccination Campaign in Finland*, 7 PLoSone 3:1-8 (2012) (Pet'r's Ex. 44) ("Partinen"). Much of the literature that focused on the outbreak, such as Partinen, had speculated as to whether the cause of the narcolepsy was attributable to adjuvants in the vaccine, or some genetic predisposition unique to Finns. Partinen at 7-8. Such

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[9] *See generally* First Steinman Rep. at 7-13. Molecular mimicry has been defined to be a "sequence and/or conformational homology between an exogenous agent (foreign antigen) and self-antigen leading to the development of tissue damage and clinical disease from antibodies and T cells directed initially against the exogenous agent that also react against self-antigen." Institute of Medicine, *Adverse Effects of Vaccines: Evidence and Causality* at 70 (K. Stratton et al., eds. 2011) [hereinafter "Adverse Effects of Vaccines"]; *see also* L. Steinman, *Autoimmune Disease*, 269 Scientific American 106-14 (Sept. 1993) (Pet'r's Ex. 13). In essence, in the course of the immunologic process begun after vaccination, antigens comprised of protein sequences from the H1N1 strain erroneously interact with the hypocretin receptors in the brain, targeting them because of shared structural homologies between the components of the antigen and the receptors. First Steinman Rep. at 13.

[10] 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.

literature also stressed the fact that the Pandemrix flu vaccine was the *only* form of the vaccine associated with an increased incidence of narcolepsy. *Id.* at 7 ("there is no evidence of an increased risk of narcolepsy with any other vaccine than the As03 adjuvanted Pandemrix").

Two pieces of literature co-authored by Dr. Steinman took steps toward explaining why Pandemrix may have caused narcolepsy, and they play a key role in the opinion he offers herein. *See* S. 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. of Autoimmunity 1-11 (2014) (Pet'r's Ex. 12) ("Ahmed I"); S. Ahmed et al., *Antibodies to Influenza Nucleoprotein Cross-React with Human Hypocretin Receptor 2*, 7 Sci. Translational Med. 294 (S2015) (Pet'r's Ex. 63) ("Ahmed II"). Although they were not both addressed in Dr. Steinman's first report,[11] they have since been filed in the action. They are important to understanding the foundation of Petitioner's theory, and so I am addressing them together.

Ahmed I was a review article proposing that the relationship between Pandemrix and narcolepsy was most likely attributable to "how the specific influenza antigen component" in Pandemrix was prepared. Ahmed I at 1. The article considered Partinen and other epidemiologic or laboratory studies involving Pandemrix. It specifically suggested that narcolepsy was properly considered an autoimmune disease, and detailed the process by which antibodies (produced as a result of molecular mimicry) would attack the hypocretin receptors. *Id.* at 3-4. Ahmed I evaluated the possibility (previewed in literature such as Partinen) that adjuvants specific to Pandemrix might have played a role in causing narcolepsy, but noted that "no similar association has been reported to date with the [similarly-adjuvanted] pandemic vaccine made using the Canadian inactivation/purification protocol," suggesting that the adjuvant itself may not have played a causal role. *Id.* at 8. Indeed, Ahmed I acknowledged that the fact that the Canadian version of Pandemrix was not associated with narcolepsy suggested that the vaccine's flu virus component (which was the same for both) was not itself to blame for the causal association with the disease. *Id.* at 6.

In a section titled "Vaccine types and related immune responses" (Ahmed I at 4), there appears a discussion about the difference between the formulation of the Pandemrix vaccine and an LAIV like FluMist, a portion of which warrants complete reproduction herein:

> While it may be possible for the live vaccine virus or bacteria to rarely revert to its disease-causing form and thus be transmitted to other non-immune subjects, most live vaccines do not. Due to their similarity in structure with the natural virus or bacteria, live

[11] At the time Dr. Steinman's first expert report was filed in this case, Ahmed II had not yet been published, and thus Dr. Steinman could only tangentially refer to its findings. First Steinman Rep. at 16. His subsequent reports specifically relied upon it, however.

> vaccines could induce molecular mimicry similar to that associated with the natural infection. However, during development of a live vaccine, *this concern for molecular mimicry is carefully considered and vaccine candidates demonstrating these attributes are screened for and excluded.*

Ahmed I at 5 (emphasis added).

In Ahmed II, Dr. Steinman and his co-authors conducted a series of tests aimed at answering some of the many questions raised in Ahmed I. This study examined the sera of 20 Pandemrix-vaccinated narcoleptic patients. Ahmed II at 10. The article began by observing that another adjuvanted inactive pandemic flu vaccine similar to Pandemrix containing the same H1N1 viral strain – Focetria – was not associated with an increased risk for narcolepsy, further suggesting that there was something unique to Pandemrix that made it more pathologic. *Id.* at 1. Ahmed II's authors performed a study aimed at identifying the specific mimic between protein sequences from the flu strain contained in Pandemrix and the hypocretin receptors, finding that there was a homologous flu nucleoprotein peptide. *Id.* at 2-3. Based on this determination, they next identified hypocretin receptor antibodies produced from the cross-reaction between the mimic and the receptors, thereby interfering with the orexin production and resulting in narcolepsy. *Id.* at 3. Those antibodies were detected in the blood sera of higher numbers of Pandemrix-vaccinated individuals with narcolepsy than individuals who did not have the disease. *Id.*

After that step, Ahmed II's authors reached the heart of their discovery with respect to Pandemrix. They compared the nucleoprotein antibody content found in individuals who had received eight different inactivated flu vaccines plus three monovalent A(H1N1) pdm09 vaccines (a group that included Pandemrix). Ahmed II at 4.[12] Of the latter three, Focetria had 72.7 percent fewer nucleoproteins than Pandemrix – "suggesting the possibility that lower [nucleoproteins] concentrations in Focetria could have attenuated both the immune response . . . and the subsequent generation of [nucleoprotein] antibodies capable of cross-reactivity." *Id.* Ahmed II's authors do not formally propose an explanation for this difference, but they did note that Focetria was "differently manufactured" (Ahmed II at 1). For its part, Ahmed I contained a longer discussion of the different manufacturing processes for these Pandemrix-like vaccines (specifically, the purification procedures for the viral antigens they contained). Ahmed I at 7.

Dr. Steinman's first report went on to opine that (in addition to his causation theory) the other prongs of the Federal Circuit's test for vaccine causation claims in *Althen v. Sec'y of Health & Human Servs.,* 418 F.3d 1274, 1278 (Fed. Cir. 2005) had been met. With respect to the second, "did cause" prong, he proposed that, consistent with the science of immunology and the

[12] FluMist was not included in any of the Ahmed II tests.

theory of molecular mimicry, Mr. D'Tiole's medical records evidenced a response to the flu vaccine. First Steinman Rep. at 22. Regarding the third prong, Dr. Steinman maintained that the timing of onset of Petitioner's first symptoms, in February 2012, was consistent with his understanding of how long the process for an immunologic response of this sort would take, based on scientific studies like Schonberger et al., *Guillain-Barre Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976-1977*, 110 Am. J. of Epidemiology 2:105 (1979) (Pet'r's Ex. 38); First Steinman Rep. at 17-18.

Supplemental Reports

Dr. Steinman also filed two supplemental expert reports, responding at length to points made by both of Respondent's experts. *See* September 28, 2015 Report, filed on September 28, 2015, as Pet'r's Ex. 61 (ECF No. 25-2) ("Second Steinman Rep."); January 10, 2016 Report, filed on January 19, 2016, as Pet'r's Ex. 66 (ECF No. 31-2) ("Third Steinman Rep.").

Dr. Steinman's second report attempted to rebut the assertion of Respondent's first expert, Dr. Michael Kohrman, that there is no demonstrated link between FluMist and narcolepsy. Dr. Steinman insisted that there is in fact a link, as the promotional materials for FluMist reveal that it contains the same nucleoprotein that Dr. Steinman's research demonstrated cross-reacts with hypocretin receptors in the brain. Second Steinman Rep. at 2, 7. While he admitted that the research he had participated in (as reflected by Ahmed I and II) did not involve FluMist specifically (or even a comparable LAIV), it had studied the nucleoproteins derived from the same viral strain as that contained in FluMist. *Id.* at 7. He further acknowledged the absence of epidemiologic studies connecting narcolepsy with FluMist, but disagreed that the primary epidemiologic evidence cited by Dr. Kohrman (Duffy et al., *Narcolepsy and Influenza A (H1N1) Pandemic 2009 Vaccination in the United States*, 83 Neurology 1827 (Oct. 15, 2014) (Resp't's Ex. D-13) ("Duffy")) was persuasive or reliable evidence disproving his theory. *Id*. at 3. Dr. Steinman asserted that the Duffy results (which are discussed in greater detail below) were not relevant to Mr. D'Tiole's case, because the study did not cover the form of flu vaccine from the 2011-12 season in which Mr. D'Tiole was vaccinated, and thus did not involve the same viral strain. *Id.*

Additionally, Dr. Steinman reiterated his view that there was a strong correlation between the wild H1N1 virus and narcolepsy – something addressed in Ahmed I and II. Second Steinman Rep. at 5; Ahmed I at 7-8; Ahmed II at 6. In so arguing, he relied on F. Han et al., *Narcolepsy Onset is Seasonal and Increased Following the 2009 H1N1 Pandemic in China*, 70 Am. Neurological Ass'n 410 (2011) (Resp't's Ex. A-3) ("Han"). Han was a retrospective study of narcolepsy onset in patients diagnosed in Beijing, China from 1998-2010. *Id.* at 1. In Dr. Steinman's reading, Han showed 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. Second Steinman Rep. at 5-6; Han at 5-6. Dr. Steinman noted that Han could be interpreted to mean that the wild H1N1 influenza virus itself, along with other upper airway infections, was highly correlated to narcolepsy. Second Steinman Rep. at 6. However, weaknesses in these arguments were anticipated in some of Dr. Steinman's own earlier work. Thus, as Ahmed II notes, studies outside China have not shown an increase in narcolepsy cases in unvaccinated patients, and Beijing's dense population (coupled with low vaccination numbers) was deemed to have possibly contributed to the increased narcolepsy cases rather than the prevalence of the wild virus. Ahmed II at 6.

Dr. Steinman also rejected the significance of points made by Dr. Kohrman that none of Mr. D'Tiole's treating doctors linked the vaccination to the narcolepsy in the records, observing that the science linking narcolepsy and influenza vaccines is currently the subject of advanced research of which they were likely unaware. Second Steinman Rep. at 7-8. He also noted that Mr. D'Tiole's vaccination history had not been made clear to all of his treaters – but that if it had, and if they had been aware that he had received the flu vaccine before his narcolepsy symptoms began, they would likely have considered it a potential causal factor. *Id.* at 8.

Dr. Steinman's third report addressed both Dr. Kohrman and the arguments of Respondent's other expert, Dr. Andrew MacGinnitie. This final report was much longer than the second, and nearly as long as the first, given the number of topics Dr. Steinman chose to address and points he hoped to rebut. In it, Dr. Steinman asserted that Ahmed II was far more important than Respondent allowed, given its scope and the large number of scientists involved in all aspects of the studies it conducted. Third Steinman Rep. at 6. However, he did candidly discuss its limitations, noting that neither he nor Ahmed II's other authors denied their existence. Third Steinman Rep. at 12-14. Thus, while Dr. Steinman would have liked to test more than 20 clinical sera samples from patients with post-vaccination narcolepsy to lend more certainty to the results, additional samples were not available due to local health authorities' regulations regarding ethical informed consent. *Id*. at 13. He echoed this sentiment regarding the inability to obtain more appropriate controls. *Id.* at 17. However, Dr. Steinman asserted that Ahmed II's findings were still reliable and sufficient to form the basis of a medically plausible theory. *Id.*

Dr. Steinman also repeated his arguments about the reliability of the Duffy epidemiologic evidence (showing zero cases of narcolepsy associated with FluMist vaccination), asserting that its findings were not meaningful because the incidence rate (the expected cases of narcolepsy absent vaccination) was too low in the first place. Third Steinman Rep. at 9. If, he reasoned, the background incidence rate is less than one case in the investigated groups, there is no way to actually draw any meaningful conclusions from the study. *Id.* He also noted that the Duffy authors were unsure of the expected incidence rate of narcolepsy by a factor of 10, which Dr. Steinman understood to mean that the authors did not even know the true baseline rate. *Id.* Because of these limitations, Dr. Steinman argued that Duffy should not be given much weight.

Dr. Steinman next addressed the various scientific evidence showing that the cross-reactive nucleoprotein antibodies were present in patients without narcolepsy (a matter Ahmed II explicitly acknowledged). Third Steinman Rep. at 14; Ahmed II at 8-9. He offered a possible explanation, proposing that the presence of the autoantibodies could simply reflect a subacute infection, and thus signal the first steps of disease development – especially when found in individuals that also likely carry the narcolepsy susceptibility allele (HLA DQB1*0602). Third Steinman Rep. at 15. He noted that several studies show that up to 20 percent or more of otherwise healthy individuals could have antinuclear antibodies associated with other autoimmune diseases, such as systemic lupus erythematosus, Hashimoto's thyroiditis, and multiple sclerosis. *Id.* at 15 (citing Ahmed II at 8-9). Dr. Steinman thus did not find this a significant detracting point from his theory relating the nucleoprotein antibodies to narcolepsy.

Dr. Steinman also reacted to Dr. Kohrman's reliance on an article written in response to Ahmed II. *See* A. Vassalli et al., *Comment on "Antibodies to Influenza Nucleoprotein Cross-React with Human Hypocretin Receptor 2*, 7 Science Translational Medicine 314 (2015), filed as Resp't's Ex. C-1 ("Vassalli"); Third Steinman Rep. at 19. Vassalli included data from narcolepsy studies involving dogs and mice, and argued that although the mechanism causing destruction of the hypocretin receptors in narcoleptic patients remained unclear, there was no evidence in these studies that antibodies against the hypocretin receptors were the cause of narcolepsy. Vassalli at 1. In Dr. Steinman's own rebuttal article[13] to the Vassalli comment, he had discussed the study's failure to provide additional data regarding the influenza virus. Third Steinman Rep. at 19. Dr. Steinman concluded that because the Vassalli data contained no studies related to influenza or cross-reactivity specifically, the conclusions reached in the study were preliminary, and it would be premature to determine the relevancy of such conclusions. *Id*.

Finally, Dr. Steinman reiterated his prior assertion (set forth in his first report) that the nucleoprotein in FluMist has the same protein sequence as the hypocretin receptors in the brain, and hence sufficient homology for an autoimmune cross-reactive process to occur, at least in theory. Third Steinman Rep. at 20-21. Because of this matching sequence, Dr. Steinman expressed confidence that molecular mimicry was the mechanism linking the FluMist vaccine to Petitioner's narcolepsy, especially given the relevant legal causation standard applicable in Vaccine Program cases. *See id.* at 21-22.

B. Respondent's Experts

1. Dr. Michael Kohrman

[13] L. Steinman et al., *Response to Comment on "Antibodies to Influenza Nucleoprotein Cross-React with Human Hypocretin Receptor 2*, 7 Sci. Translational Med. 314 (Nov. 2015), filed as Pet'r's Ex. 74 (ECF No. 31-10).

Respondent's first expert report was authored by Dr. Michael Kohrman, who primarily opined that the relevant medical and scientific literature reveals no evidence that a live H1N1-containing influenza vaccination is associated with narcolepsy. *See* June 29, 2015 Report, filed on July 13, 2015, as Resp't's Ex. A (ECF No. 22-1) ("First Kohrman Rep."). Further, he interpreted Mr. D'Tiole's history of delayed sleep phase, poor sleep hygiene, and obstructive sleep apnea as making it highly difficult to pinpoint an onset date for Mr. D'Tiole's narcolepsy. First Kohrman Rep. at 2-8.

As of the date of his first expert report,[14] Dr. Kohrman was a Professor of Pediatrics, Neurology, and Surgery at the University of Chicago. First Kohrman Rep. at 1; Resp't's Ex. B at 1. The majority of his practice is clinical work, while approximately 20 percent of his time is devoted to research. First Kohrman Rep. at 1. He is board certified in Child Neurology and Psychiatry, with a special focus in Child Neurology. *Id.* Additionally, he has qualifications in clinical neurophysiology, sleep medicine, and epilepsy, and is board certified by the American Board of Sleep Medicine, among other certifications. Resp't's Ex. B at 2-4. His clinical practice focuses on treating refractory epilepsy, with an underlying interest in sleep medicine. *Id.* at 1. He treats child patients with epilepsy and sleep problems on a daily basis. *Id.* at 2. His opinion arose from review of Mr. D'Tiole's medical records and his medical history. *Id.*

Dr. Kohrman first addressed Dr. Steinman's theory that FluMist could be linked to narcolepsy. He began by noting that Dr. Steinman's own research had nothing to do with FluMist, but rather had proposed (at least before the publication of Ahmed II)[15] that the adjuvant in the Pandemrix vaccine (a different form of flu vaccine, moreover) could be the possible cause of narcolepsy in the European studies. First Kohrman Rep. at 9. FluMist is a non-adjuvanted vaccine, meaning that the adjuvant suggested to cause narcolepsy would not have been present in Mr. D'Tiole's vaccine. Ahmed I also hypothesized that the antigens in the various vaccines studied were possibly different, leading Dr. Kohrman to conclude that Dr. Steinman's research was not supportive of cross-reactivity between FluMist and the hypocretin receptors. *Id*. At bottom, all of the reported vaccine-related cases of narcolepsy were linked to vaccines produced in a single antigen extraction method, and then administered with an adjuvant. *Id.* at 11. There was thus no evidence that a live influenza vaccine is also associated with narcolepsy.

Dr. Kohrman relied on the Duffy epidemiologic study to bulwark his opinion. Duffy's authors studied the association between narcolepsy and the H1N1 vaccine in its various

[14] Dr. Kohrman is now the Director of Pediatric Neurology at Akron Children's Hospital in Akron, Ohio. *See* Akron Children's Hospital, https://www.akronchildrens.org/cms/doctors/michael-kohrman-md (last visited Nov. 21, 2016).

[15] As noted above, Dr. Steinman's first report did not include specific reference to Ahmed II, which had not yet been published, and therefore Dr. Kohrman's response to the initial report in this respect addressed an issue (the adjuvant's role in causing narcolepsy) that Ahmed II ruled out. Respondent's experts thereafter modified their responses to Petitioner's expert's opinion in light of Ahmed II's findings.

permutations, surveying 650,995 individuals in the United States vaccinated with the 2009 pandemic vaccine. Duffy at 1823. Both the inactivated form of the vaccine and LAIVs were included. Of the patients included in the observed sample, 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. Out of the 45,246 individuals between the ages of 10 and 19 who received an LAIV, none developed narcolepsy despite an incidence rate of 3.84 per 100,000 individuals (meaning .83 cases of narcolepsy would have been expected). *Id.* The authors concluded that the forms of influenza vaccines in the United States containing the A(H1N1) virus strain could not be associated with an increased risk of narcolepsy. *Id.* at 1823. Further, the Duffy authors hypothesized that the antigens in this particular H1N1 vaccine strain were themselves not sufficient to increase narcolepsy incidences. *Id*.

Dr. Kohrman also presented literature to support his assertion that the flu wild virus is not linked to narcolepsy. He cited an article by Partinen – the same scientist whose research on the Pandemrix vaccine's link to narcolepsy in Finland was discussed by Dr. Steinman in his various reports. M. Partinen et al., *No Serological Evidence of Influenza A H1N1pdm09 Virus Infection as a Contributing Factor in Childhood Narcolepsy after Pandemrix Vaccination Campaign in Finland*, 8 PLOSone 1:7 (2013) (filed as Resp't's Ex. A-2) ("Partinen II"). Partinen II found that it was unlikely the wild H1N1 virus had contributed to the increase in childhood narcolepsy in Finland after receipt of the adjuvanted Pandemrix vaccine. Partinen II at 7. Even the Han article relied on by Dr. Steinman did not support a link between the wild H1N1 virus and narcolepsy, Dr. Kohrman maintained. First Kohrman Rep. at 10. Han's authors had acknowledged that the sample of patients in the study was not representative of China as a whole. Han at 7. Thus, Dr. Kohrman argued, because the article did not constitute a reliable epidemiological study of narcolepsy in China, no direct link between the wild H1N1 virus and narcolepsy could be inferred. First Kohrman Rep. at 10.

Dr. Kohrman further proposed that Petitioner's own medical history did not support his claim about the causal role of the FluMist vaccine. Mr. D'Tiole had a documented history of poor sleep habits and obstructive sleep apnea months before the diagnosis of narcolepsy was confirmed, making it difficult to identify when the actual onset of his symptoms might have occurred. *Id*. at 11. Dr. Kohrman also noted that no acute symptoms were reported after Mr. D'Tiole's FluMist vaccination. *Id.* at 8.

Respondent filed a supplemental report from Dr. Kohrman as well, reacting to Dr. Steinman's second report. *See* December 23, 2015 Report, filed on January 8, 2016, as Resp't's Ex. C (ECF No. 28-1) ("Second Kohrman Rep."). In it, Dr. Kohrman examined Dr. Steinman's hypothesis (supported now by Ahmed II) that the nucleoprotein antigens in FluMist cross-react

with hypocretin receptors, causing narcolepsy. Second Kohrman Rep. at 2. Although such nucleoproteins might be present in killed vaccines like Pandemrix, Dr. Kohrman pointed out that the vaccine at issue here, FluMist, is a *live* attenuated vaccine that involves a different master donor virus as well. *Id.* He further examined the development process for FluMist, finding that the nucleoprotein present in FluMist is derived from the Master Donor Virus A/AA/6/60, rather than the Influenza A(H1N1) 2009 virus. *Id.* at 3-5; B. Zhou et al., *Engineering Temperature Sensitive Live Attenuated Influenza Vaccines From Emerging Viruses*, 30 Vaccine 3691:3691-92 (2012) (Resp't's Ex. C-2) (ECF No. 28-3). Thus, it could not be assumed that the nucleoproteins derived from H1N1 and present in Pandemrix were equally present in FluMist. *Id.* at 5. Dr. Steinman's third report, however, attempted to diminish the strength of this point by observing that the protein sequences for the nucleoproteins that he alleged were cross-reacting with the hypocretin receptors were the same for FluMist and Pandemrix. Third Steinman Rep. at 19-21.

Dr. Kohrman's supplemental report also highlighted the uniqueness of Pandemrix and its antigens. He thus noted that in Ahmed II, 85 percent of patients had antibodies to the hypocretin-2 receptor, but 35 percent of vaccinated patients who did not develop narcolepsy also exhibited these antibodies. Second Kohrman Rep. at 2, *citing* Ahmed II at 7. Meanwhile, those patients vaccinated with Focetria had no antibodies against this hypocretin receptor. *Id.* Dr. Kohrman relied on these findings to conclude that Pandemrix's formula and make-up made it difficult to extrapolate conclusions about its association with narcolepsy to other forms of the flu vaccine – even ones more similar to Pandemrix than FluMist.

Dr. Kohrman ultimately maintained that there is no clear understanding yet for what causes the lack of hypocretin in narcolepsy patients, and this, plus the lack of scientific evidence and/or medical literature supporting a link between narcolepsy and FluMist, made him unable to conclude that Mr. D'Tiole's narcolepsy was likely vaccine-related. Second Kohrman Rep. at 5.

2. Dr. Andrew MacGinnitie

Dr. MacGinnitie also submitted two expert reports on behalf of Respondent. His first report set forth the opinion that while there might be reliable epidemiologic evidence linking an increased rate of narcolepsy to the Pandemrix vaccine, as well as some tentative evidence of a link to the H1N1 wild type variant, there was no such evidence linking the FluMist vaccine, given its distinct formulation. *See* December 21, 2015 Report, filed on January 8, 2016, as Resp't's Ex. D (ECF No. 29-1) ("First MacGinnitie Rep.").

Dr. MacGinnitie is an attending physician and the clinical director for the Division of Immunology at Boston Children's Hospital. First MacGinnitie Rep. at 1; Resp't's Ex. E. He is also an Assistant Professor of Pediatrics at Harvard Medical School. First MacGinnitie Rep. at 1. He is board certified in Allergy/Immunology and Pediatrics, and has been in practice as an

allergist/immunologist for 15 years. *Id.* Further, he has seen patients with various immunologic diseases, including reactions to vaccines. *Id*.

Dr. MacGinnitie explained the differences in production and administration between Pandemrix and FluMist, as well as the different and distinct mechanistic ways the vaccines stimulate an immune response. *Id*. at 9. Subunit inactive vaccines (like Pandemrix) are produced by growing several influenza strains in chicken egg cells, which are then inactivated to kill the potentially infectious virus. *Id.*; R.J. Cox et al., *Influenza Virus: Immunity and Vaccination Strategies*, Scandinavian J. of Immunology 59:6 (2004) (Resp't's Ex. D-11) (ECF No. 30-2). Some of these subunit vaccines also include an adjuvant to increase the immune response. *Id.* LAIVs such as FluMist, by contrast, are cold-adapted, delivered into the nose where they replicate in the nasal epithelium, rather than in the lower respiratory tract (i.e., the lungs). *Id.* at 8-11. FluMist was, by design, intended to result in more limited viral replication in the same region of the body where the wild flu virus might attack (the mucosal membranes of the respiratory tract), but would also generate antibody titers lower than that of a subunit vaccine like Pandemrix. First MacGinnitie Rep. at 9.[16] It is those antibodies that would, under Dr. Steinman's theory, produce the autoimmune reaction, via molecular mimicry, necessary to inhibit the hypocretin receptors.

Further, narcolepsy has been linked to only one of these specific vaccine types – adjuvanted subunit vaccines. First MacGinnitie Rep. at 9. Adjuvanted vaccines were shown in data to elicit a greater response than non-adjuvanted vaccines. *Id.*; C. Waddington et al., *Safety and Immunogenicity of ASO3B Adjuvanted Split Virion Versus Non-Adjuvanted Whole Virion H1N1 Influenza Vaccine in UK Children Aged 6 Months-12 Years*, BMJ 340, at *8 (2010) (Resp't's Ex. D-12) (ECF No. 30-3). Pandemrix is an adjuvanted vaccine, while FluMist is an LAIV and is non-adjuvanted. First MacGinnitie Rep. at 9-10. Looking at the differences in the production of the two vaccines, the immune responses they cause, and the difference between adjuvanted and non-adjuvanted vaccines, Dr. MacGinnitie could not conclude that any demonstrated link between Pandemrix and narcolepsy applied to a non-adjuvanted vaccine like FluMist.

Dr. MacGinnitie also emphasized that reliable epidemiologic evidence (in particular, Duffy) demonstrated that there was in fact no connection between FluMist and narcolepsy. First MacGinnitie Rep. at 10. Duffy observed zero cases of narcolepsy out of thousands of patients who received FluMist. Duffy at 1. This result was the same for non-adjuvanted subunit vaccines during the 2009 influenza season. *Id.* at 5. The study was also extended to the 2010 influenza season, but again, no cases were found in nearly 130,000 studied individuals. *Id.* If there were a

[16] As previously noted, Dr. Steinman agreed with this proposition in his own literature, such as the Ahmed articles (although he did not acknowledge the point in the expert reports filed in this case). *See, e.g.,* Ahmed I at 5.

link between FluMist and narcolepsy, at least one case would have been seen in such a large test group of patients, Dr. MacGinnitie proposed.

Dr. MacGinnitie raised another point that he maintained undercut Petitioner's theory. Narcolepsy is almost always seen in patients, like Mr. D'Tiole, who have the HLA DQB1*0602 allele. First MacGinnitie Rep. at 3. This HLA protein produces protein fragments on the cells' surfaces, and T-cells (that would be generated in an immune response, whether brought on by infection or immunization) recognize this combination. *Id.* When the T-cells are activated, they kill infected cells and help B-cells to generate antibodies. *Id.* Dr. MacGinnitie stressed that because most patients with narcolepsy carry this allele, T-cells specific to it would be essential to develop narcolepsy. *Id.* Yet there is to date insufficient scientific evidence that these T-cells exist. Indeed, the only literature suggesting T-cell involvement in the development of narcolepsy was a paper written by Dr. Mignot, one of Petitioner's treaters at Stanford's Sleep Center. E. Mignot et al., *CD4+ T Cell AutoImmunity to Hypocretin/Orexin and Cross-Reactivity to a 2009 H1N1 Influenza A Epitope in Narcolepsy*, 5 Sci. Translational Med. 216 (2013) (filed as Resp't's Ex. D-4) ("Mignot"). Mignot showed that a fragment of the influenza hemagglutinin protein was cross-reactive with hypocretin, and activated T-cells were identified in narcolepsy patients that recognized both hypocretin and the hemagluttinin protein, thus supporting the hypothesis that the immune response to the hemagluttinin protein could also damage the cells that produce hypocretin. Mignot at 7, 9. But the Mignot paper was ultimately retracted because its results could not be replicated, and therefore a critical component needed to confirm Petitioner's theory was missing.[17]

Dr. MacGinnitie devoted some time in his first report to attacking the bases for Dr. Steinman's theory about cross-reactivity between proteins in the flu vaccine and hypocretin receptors. He first noted that the evidence supporting this theory was limited to Ahmed II – a single report written by Ahmed and Dr. Steinman based on a very small sample of 20 patients. First MacGinnitie Rep. at 6. He also argued that Ahmed II lacked specific controls, because it failed to include data on antibodies in individuals who received the Pandemrix vaccine but did not develop narcolepsy, or in patients who developed narcolepsy unrelated to vaccination. *Id.* at 7. According to Dr. MacGinnitie, this lack of appropriate controls reduced the reliability of findings made about the importance of these antibodies. In sum, Dr. MacGinnitie did not believe that a single peer-reviewed report without appropriate controls was sufficient support for

[17] Dr. Steinman also acknowledged that Mignot had been retracted, but emphasized that this was not due merely to an inability to replicate results, but rather due to fraud in misrepresenting its findings. Third Steinman Rep. at 1-5. For purposes of the present case, this is a distinction without a difference – the point remains that an element of proof that would corroborate the more general framework of Petitioner's theory about the autoimmune nature of narcolepsy is missing. But, because I find that Petitioner's theory is deficient for reasons outside of the broader argument about the causes or nature of narcolepsy, the inability of researchers to date to provide this critical probative link that would add scientific reliability to the overall theory is somewhat of a tangential matter, for purposes of determining entitlement.

Petitioner's theory, nor did it constitute evidence that the discussed antibodies are actually involved in the development of narcolepsy in patients.

Dr. MacGinnitie additionally took issue with Dr. Steinman's alleged failure to explain why the nucleoprotein antibodies upon which he relied in his theory were also present in patients without narcolepsy. More than 50 percent of children in Ahmed II possessed the same cross-reactive antibodies, but did not suffer from narcolepsy. *Id.* at 6-7. Because of this, Dr. MacGinnitie did not believe that these antibodies were as critical to causing narcolepsy as Dr. Steinman's theory suggested.

Respondent submitted a supplemental report from Dr. MacGinnitie as well. *See* January 31, 2016 Report, filed on February 3, 2016, as Resp't's Ex. F (ECF No. 33-1) ("Second MacGinnitie Rep."). The supplemental report responded to several points made by Dr. Steinman in his January 2016 third report, but otherwise presented little new argument or evidence. Thus, Dr. MacGinnitie reaffirmed his view that Duffy was reliable evidence that there was no connection between FluMist and narcolepsy. Second MacGinnitie Rep. at 2. Though Dr. Steinman criticized the low baseline rate in the study, Dr. MacGinnitie asserted that a low background rate is epidemiologically desirable, since it renders even the slightest increase in observed cases easier to note. *Id.* at 1-2. He also stressed that, out of over 300,000 individuals receiving LAIV flu shots in the Duffy study, not a single identified case of narcolepsy occurred. *Id.* In Dr. MacGinnitie's view, there would have to have been some cases of narcolepsy observed if a link truly existed.

Dr. MacGinnitie objected to Dr. Steinman's hypothesis that the lack of observed cases of narcolepsy related to inactivated influenza vaccines in the United States was attributable to the lack of individuals with the HLA DQB1*0602 allele in the United States (as compared to Finland and Sweden). Second MacGinnitie Rep. at 2. He admitted that the number of cases would potentially be affected by the prevalence of the allele in a population, but noted that the number would also be affected by the population size. *Id.* The United States is more than 20 times larger than Finland and Sweden combined, meaning that any link between the allele and narcolepsy would have to be evident – but was not in the sample considered in Duffy. *Id.*

Finally, Dr. MacGinnitie expressed some additional thoughts about the competing flu vaccine formulations in this case and their relationship to Petitioner's theory. Thus, and in reaction to Dr. Steinman's assertions that Respondent could not show that Duffy studied the same formulation of FluMist as that relevant to this case, he stated that the 2010-11 and 2011-12 seasonal influenza vaccine requirements were functionally the same. Second MacGinnitie Rep. at 3; *see* FDA News Release July 30, 2010, *FDA Approves Vaccines for the 2010-2011 Influenza Season* (Pet'r's Ex. 72) (ECF No. 31-8); FDA News Release July 18, 2011, *FDA Approves Vaccines for the 2011-2012 Influenza Season* (Pet'r's Ex. 73) (ECF No. 31-9). Thus, according

to Dr. MacGinnitie, the flu strain in the vaccine Mr. D'Tiole received was equivalent to the contents in the vaccine studied in Duffy, even though that study involved different years. *Id.* Overall, Dr. MacGinnitie maintained, the most logical interpretation of the data and literature presented in this case was that any increased risk of narcolepsy was associated only with the Pandemrix vaccine, and possibly a weaker correlation to the wild type flu infection. *Id.*

III. PROCEDURAL HISTORY

As noted above, Petitioner's parents originally filed this action in January 2015, alleging that his receipt of the flu vaccine in December 2011 caused him to develop narcolepsy with cataplexy. Petition at 1. About a month later Petitioner filed his first expert report from Dr. Steinman. ECF No. 9. Petitioner then filed medical records along with the literature offered by Dr. Steinman in support of his opinion, and then the Statement of Completion on March 31, 2015 (ECF No. 18).

Respondent filed her Rule 4(c) Report on July 13, 2015, asserting that Mr. D'Tiole was not entitled to compensation because he could not carry his burden of proof under *Althen*. Respondent's Rule 4(c) Report (ECF No. 21). Specifically, Respondent alleged that there was no evidence connecting Petitioner's proposed theory to the vaccine he received. ECF No. 21 at 5. Further, none of Petitioner's treating doctors had identified the vaccine as a potential cause of Petitioner's condition. *Id.* Respondent at that time also filed her own expert report from Dr. Kohrman. *See generally* First Kohrman Rep.

After the Rule 4(c) Report was filed, Petitioner filed a supplemental expert report from Dr. Steinman on September 28, 2015 (Second Steinman Rep.). This prompted Respondent to file in January 2016 additional expert reports of her own – a supplemental report from Dr. Kohrman, plus a new report from Dr. MacGinnitie. *See generally* Resp't's Exs. C and D, filed as ECF Nos. 28 and 29. The expert report filing continued, with Petitioner filing a third report from Dr. Steinman on January 19, 2016 (Third Steinman Rep.). Respondent for her part filed a supplemental report thereafter from Dr. MacGinnitie on February 3, 2016. Second MacGinnitie Rep.

I thereafter held a status conference with the parties to discuss the case's progress and possible resolution. I proposed that Respondent consider moving for a decision on the papers in lieu of hearing, since the case's history to date, plus my assessment of the nature of the disputed issues – issues that both side's experts had addressed in great detail – suggested to me that this would be the most expeditious approach to resolving the case. *See* Order, dated February 16, 2016. Respondent accepted my proposal, and after an extension of time so moved, on June 20, 2016 (ECF No. 36) ("Motion"). Petitioner opposed the motion on July 20, 2016 (ECF No. 37) ("Opp."), and then Respondent filed a reply on August 3, 2016 (ECF No. 38) ("Reply"). The matter is now ripe for resolution.

IV. PARTIES' RESPECTIVE ARGUMENTS

Respondent's motion argues in the main that Petitioner has not met the first *Althen* prong because he cannot offer a reliable scientific theory linking FluMist to narcolepsy. Motion at 7. In so arguing, Respondent particularly emphasized the findings from Duffy, while attempting to rebut Dr. Steinman's criticisms of the study's reliability. *Id.* at 7-9. Respondent also proposed that Dr. Steinman's own theory as to cross-reactivity between nucleoproteins from the flu vaccine and the hypocretin receptors was flawed and unreliable, for the reasons discussed above. *Id.* at 9-10. And she posited that Petitioner had only conclusorily alleged that the second two *Althen* prongs were met, without demonstrating real record support that reflected the theory working in real time. *Id.* at 10-12.

In reaction to the motion, Petitioner asserted that in fact he has met his burden for a non-Table claim under *Althen.* The theory proposed for causation is reliable (and was even deemed "superficially plausible" by Respondent's expert) and supported by evidence such as Han, which suggests an association between even the wild flu virus and narcolepsy. Opp. at 24-27. Duffy, he maintained, is too empirically flawed as a study, given Dr. Steinman's points about its methodologic weaknesses. *Id.* at 28-30. Otherwise, Petitioner argued that he had met the other *Althen* prongs; witness statements place onset in February 2012, which is a reasonable timeframe from the date of vaccination for the immunologic process proposed by Dr. Steinman to have occurred. *Id.* at 33-35. And Petitioner asserted that his parents' lack of knowledge about his receipt of FluMist, coupled with their laymen's unawareness of the possible causal relationship of the vaccine to his narcolepsy, explained why treaters had not linked his vaccination to his narcolepsy. *Id.* at 31-32.

Petitioner also strenuously objected to resolving this matter without a hearing, arguing that (i) disputed fact issues among the experts required they be allowed to testify live, (ii) testimony from Mr. D'Tiole and his family was also required in order to establish onset (as well as corroborate the fact that treaters were not informed of Petitioner's vaccination because his parents mistakenly deemed it unimportant), and (iii) resolving the matter without a hearing would violate his rights under Vaccine Rule 3(b). *Id.* at 13-18.

Respondent's succinct reply repeated her earlier points for dismissal. Reply at 3-6. Respondent also again proposed that there was no need for a hearing, citing the fact that Vaccine Rule 8(d) allows special masters to determine when a hearing is necessary. *Id.* at 2.

V. APPLICABLE LEGAL STANDARDS

A. Claimant's 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).[18] 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 (which is the kind of claim asserted in this matter), a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen*: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *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

[18] 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).

this prong, the 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)). 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).

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).

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 Health & Human Servs.*, 100 Fed. Cl. 119, 136 (2011), *aff'd*, 463 F. App'x 932 (Fed. Cir. 2012); *Veryzer v. Sec'y 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." *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 Factual Determinations

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as "the results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & 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 a 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 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms. It is equally unlikely that pediatric neurologists, who are trained in taking medical histories concerning the onset of neurologically significant symptoms, would consistently but erroneously report the onset of seizures a week after they in fact occurred").

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, contemporaneously 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*, 968 F.2d 1226 (Fed. Cir.), *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 v. Sec'y of Health & Human Servs.*, 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992)). 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 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 over contrary testimony, 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 fora (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & 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 (1997)); *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).

D. Consideration of Medical Literature

Petitioner's expert filed some medical and scientific literature in this case, including articles offered in support of his causation theories. *See generally* Pet'r's Exs. 21 and 24-30. I have reviewed all of the medical literature submitted in this case, although my decision does not discuss each filed article in detail. *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). Petitioner in fact filed 55 articles, making a detailed written examination of every single one an arduous task. A write-up or summary of each within the body of this decision is not called for, however, in explaining my disposition of Petitioner's claim, although the items most significant to my determination, or to Petitioner's case, are discussed.

E. Determination to Resolve Case Without Hearing

Here, I have opted to decide entitlement based on written submissions and evidentiary filings, including the seven expert reports collectively filed by the parties. The Vaccine Act and Rules not only contemplate but encourage special masters to decide petitions on the papers rather than via evidentiary hearing, where (in the exercise of their discretion) they conclude that the former means of adjudication will properly and fairly resolve the case. Section 12(d)(2)(D); Vaccine Rule 8(d). The choice to do so has been affirmed on appeal. *See Hooker v. Sec'y of Health & Human Servs.,* No. 02-472V, 2016 WL 3456435, at *21 n.19 (Fed. Cl. Spec. Mstr. May 19, 2016) (citing numerous cases where special masters decided on the papers in lieu of hearing and that decision was upheld). I am simply not required to hold a hearing in every matter, no matter the preferences of the parties. *Hovey v. Sec'y of Health & Human Servs.,* 38

Fed. Cl. 397, 402-03 (1997) (special master acted within his discretion in denying evidentiary hearing); *Burns,* 3 F.3d at 417; *Murphy v. Sec'y of Health & Human Servs.,* No. 90-882V, 1991 WL 71500, at *2 (Ct. Cl. Spec. Mstr. Apr. 19, 1991).

ANALYSIS

After careful review of the expert reports, medical records, and the arguments of both sides, I conclude that Petitioner has not established preponderant evidence in favor of his claim.

A. Petitioner Has Not Established a Reliable Causation Theory.

The central weakness in Petitioner's case is his causation theory, offered in support of the first *Althen* prong. This determination does not turn on insufficiencies in expert credentials or credibility, but rather on fundamental holes in the theory itself, as evidenced by the reports and responsive statements made therein by each side's experts, as well as key literature offered to bulwark the theory. Petitioner has, in effect, attempted to leverage a theory that is reliable with respect to one form of the flu vaccine into a case involving a different form, but without showing that the theory is similarly reliable in the different setting.

Petitioner relies on Dr. Steinman's opinion that the H1N1 component in the FluMist form of the flu vaccine has the potential to interact (via the mechanism of molecular mimicry) with the hypocretin receptors in the brain. Important aspects of the theory are scientifically reliable. Thus, deficiencies in the hypocretin-mediated neurotransmission process have been persuasively linked to narcolepsy. *See, e.g.*, Nishino at 1; Peyron at 1; Ahmed II at 2. Similarly, there is plausible research (although, by Dr. Steinman's admission, it remains incomplete) suggesting that narcolepsy is likely an autoimmune-mediated condition. There is also reliable epidemiologic evidence linking Pandemrix in Europe to narcolepsy, and studies offered by Petitioner – in particular, the Ahmed articles co-authored by Dr. Steinman – refine the nature of the linkage further, concluding that the adjuvant contained in Pandemrix can probably be eliminated as a primary causal factor. This places the focus on the nucleoproteins in the H1N1 component, and the evidence that nucleoprotein antibodies are found in higher amounts in patients with narcolepsy who also received Pandemrix or a similar inactive flu vaccine.[19]

I do not dispute Dr. Steinman's qualifications or credibility on these matters. Dr. Steinman is often called upon in Program cases to testify about molecular mimicry as the agent for autoimmune and other conditions – and for good reason, given his ample expertise in studying the topic as it pertains to multiple sclerosis. *See* Pet'r's Ex. 62 at 2-3, 8-42 (listing all of

[19] I acknowledge Respondent's arguments about limits to the reliability of Ahmed II – given, for example, its limited sample size – but I need not evaluate whether it is sufficiently scientifically reliable in the first instance to find as I do, given the larger problem of extrapolating Ahmed II's results to a different form of the vaccine that has never been reliably associated with narcolepsy.

the literature Dr. Steinman has published on multiple sclerosis). Here, Dr. Steinman has co-authored two articles that directly pertain to the illness in dispute. He is a particularly apt expert for this case.

Nevertheless, Petitioner's theory has a central reliability problem. Petitioner proposes that because Pandemrix has been credibly associated with narcolepsy, it is equally plausible that the FluMist formulation – an LAIV – of the vaccine would do the same, merely because it also contains the H1N1 wild virus strain. By Petitioner's admission, there is no direct evidence of this contention (although that fact does not mean the claim could not succeed, given the acceptance in the Program of the notion that vaccine injuries are rare and otherwise need not be proven with scientific certainty). *See, e.g.,* First Steinman Rep. at 21 ("I want to emphasize that there is no epidemiologic information linking FluMist to narcolepsy"). But the indirect evidence Petitioner relies upon does not adequately fill the gap. On the contrary – the Ahmed articles themselves undercut Petitioner's attempts to apply their findings to the present circumstances.

Both Ahmed articles explicitly acknowledge that the *form* of manufacture of the inactive flu vaccines (and specifically how manufacture caused a higher production of the nucleoprotein antigens believed to give rise to the antibodies that interfere with the hypocretin receptors) likely had something to do with the narcolepsy association. Thus, Pandemrix (strongly associated with narcolepsy) was not manufactured in the same manner as Focetria. Ahmed II at 1. At the same time, individuals whose antibody levels were tested in Ahmed II who had received Focetria had close to zero nucleoprotein antibodies – and Focetria was thus not associated with narcolepsy, likely because the cross-reactivity necessary to interfere with the hypocretin receptors could not occur. Ahmed II at 5 ("the trace amounts of [nucleoprotein] in Focetria would not elicit durable NP antibody responses necessary for subsequent cross-reactivity to HCRT receptor 2"), 7. Ahmed I and II thus stand for the proposition that something about the process of inactivating the viral strain in manufacturing that form of the flu vaccine is associated with increasing the number of nucleotide antibodies – not that the mere presence of H1N1 proteins in any form, and in any version of the flu vaccine, will inevitably result in sufficient levels of the antibodies to produce the same cross-reactive autoimmune process. The research explicitly does *not* state that, given its findings regarding concentrations of nucleoprotein antibodies in individuals who received Focetria.

This case, by contrast, involves a different form of the vaccine, subject to a wholly different manufacturing process in which the flu strain is live but attenuated. Other than also being an H1N1 strain, Petitioner has not shown why, or how, the LAIV version would be comparable to Pandemrix – or even Focetria, for that matter – in increasing the nucleoprotein antibodies.[20] Ahmed I for its part recognizes this as well – and, in particular, that an LAIV's viral

[20] Indeed, Respondent's experts, such as Dr. Kohrman, have persuasively demonstrated that the H1N1 strain used to manufacture FluMist may also be too different from the form studied in Ahmed II. Second Kohrman Rep. at 2-5.

elements are less likely to cross-react via the process of molecular mimicry (the mechanism proposed in this case for the autoimmune reaction) in comparison to how Pandemrix would, given its production of the nucleoprotein antibodies identified in Dr. Steinman's research at sufficient levels to interfere with the body's hypocretin receptors. Ahmed I at 5, Ahmed II at 4-5. Indeed, Dr. Steinman's research acknowledges that even forms of the flu vaccine (Focetria) more comparable to the version studied (Pandemrix) were not associated with narcolepsy. Ahmed II at 1 ("[c]urrently, no increased risk has been reported for the MF59-adjuvanted A(H1N1)pdm09 vaccine (Focetria), for which an estimated 6.5 million doses were distributed in EU/EEA, and 25 million doses were used in Europe and Latin America"). Accordingly, even if Dr. Steinman's research as reflected in Ahmed I and II is reliable, it has not been shown to be similarly reliable when applied to FluMist.

Another reliability deficiency with Petitioner's theory stems from the molecular mimicry mechanism that Petitioner proposes would cause the production of the nucleoprotein antibodies. It is well understood in the Vaccine Program that petitioners are not obligated to prove the mechanism posited as a component of their causation theory. *Knudsen v. Sec'y of Dep't of Health & Human Servs.,* 35 F.3d 543, 548-49 (Fed. Cir. 1994). Yet here, the proposed mechanism – that the fact that FluMist includes an H1NI viral strain from which the cross-reactivity necessary to produce the hypocretin receptor-interfering antibodies would emanate – is directly undercut by Dr. Steinman's own literature. FluMist, because it is an LAIV, may inherently be less likely to generate the cross-reactive molecular mimicry that Dr. Steinman posits would be the mechanism causing the autoimmune interference with the hypocretin receptors. *See* Ahmed I at 5.

Petitioner attempted to close such gaps in his causation theory, but failed to do so persuasively, with his arguments consistently rebutted by evidence Respondent offered. First, Dr. Steinman argued in his reports that the wild H1N1 virus was in fact associated with narcolepsy (thus allowing for the conclusion that any vaccine containing the strain would also have the potential to cause narcolepsy). In support of this argument, he pointed to Han, which as noted above observed an association between the wild H1N1 virus in China and narcolepsy. As Respondent countered, however, there are facial difficulties with giving this particular study too much weight. First Kohrman Rep. at 10. Indeed, the Ahmed articles themselves noted the potential limitations of Han. *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 the flu generally). Thus, as recognized in Ahmed II, research regarding the Pandemrix-associated narcolepsy outbreak in Europe did not associate the wild virus with the condition either. Partinen II at 7. While it has not been shown herein that Han's findings are unreliable, its findings are too inconclusive generally to give them the weight urged by Petitioner.

Second, as Respondent pointed out, the Duffy epidemiologic study stood as very strong evidence rebutting an association between an LAIV containing the H1N1 strain and narcolepsy. As a general matter, it is true that Program petitioners need not offer epidemiologic evidence to establish their causation burden under *Althen*. Indeed, because vaccine injuries are rare events, the fact that a particular epidemiologic study suggests a vaccine is generally safe should not prevent a claimant from prevailing (assuming the other *Althen* factors are met). *See Harris v. Sec'y of Health & Human Servs.*, No. 10-322V, 2014 WL 3159377, at *11 (Fed. Cl. Spec. Mstr. June 10, 2014) (epidemiologic studies cannot absolutely refute causal connections, because it is possible that a larger study could always detect an increased risk).

But this does not mean that epidemiologic evidence relevant to a vaccine at issue in a case has no place in evaluating a claim – especially when the evidence is particularly on point and persuasive. *See, e.g., Godfrey v. Sec'y of Health & Human Servs.,* No. 10-565V, 2014 WL 3058353, at *19 (Fed. Cl. Spec. Mstr. June 11, 2014) ("this is not a case where epidemiologic evidence is lacking. The epidemiology exists, and is not supportive of the theory"), *mot. for review den'd*, No. 10-565V, slip op. (Apr. 29, 2016). To the contrary – in a case like the present, where a vaccine's formulation bears heavily on Petitioner's causation claim, and where Petitioner wants to leverage findings about a different vaccine formulation, epidemiologic evidence relevant to the version of the vaccine in dispute ought to be weighed against Petitioner's proof in evaluating whether he has carried his overall burden. *See W.C.*, 704 F.3d at 1361 (special master was not arbitrary in denying compensation, and noting that the special master properly relied on several epidemiological studies in reaching his decision); *Lampe*, 219 F.3d at 1365 (stating "[a]n epidemiological study may be probative medical evidence relevant to a causation determination"); *see also C.K. v. Sec'y of Health & Human Servs.*, 113 Fed. Cl. 757, 770 (2013) (a special master may evaluate contradictory evidence offered by Respondent).

Duffy involved a study of 650,995 vaccinated individuals in the 2009-10 flu season, but found **no** instances in which a child receiving the LAIV formulation of the flu vaccine developed narcolepsy in 180 days from vaccination – far fewer instances than the incidence rate would predict. Duffy at 2. In the 2010-11 season, only two cases were reported out of 870,530 individuals. *Id.* at 2-3. And of the 45,246 individuals between the ages of 10 and 19 who received an LAIV, none developed narcolepsy despite an incidence rate of 3.84 per 100,000 individuals (meaning .83 cases of narcolepsy would have been expected). Petitioner unconvincingly quibbles with aspects of Duffy. He argues that it has not been shown that the form of FluMist administered to him in 2011 was the same as that in the study, which involved the 2010-11 version – even though in fact it appears, based on the available unrebutted evidence, that the formulation was the same. Pet'r's Exs. 72 and 73; Third Steinman Rep. at 18 (stating that the 2010-11 and 2011-12 influenza vaccine requirements were the same).

Dr. Steinman also proposes that the incidence rate is unreliable and/or underpowered given how low it was. Yet (as Dr. MacGinnitie observed) the Duffy authors specifically took this fact into account, noting that even if it were increased ten-fold the result would be the same, with far fewer cases of actual narcolepsy occurring than what would be reasonably expected in the studied population.[21] An incidence rate is defined as the number of cases of a disease that develop during a specified period of time divided by the number of subjects in a study. Michael D. Green et al., Reference Guide on Epidemiology, in Reference Manual on Scientific Evidence 549, 567 (Federal Judicial Center, 3d ed. 2011) ("Green"). Epidemiologic studies can be limited in their ability to detect increased incidence rates of rare diseases, such as narcolepsy. *Harris,* 2014 WL 3159377, at *10. However, the predictive strength of an incidence rate is directly tied to the "power" of an epidemiologic study, which is in turn dependent on the sample size. *See* Green at 576, 582 (defining power as "the probability of finding a statistically significant association… (if it exists) in light of the sample sizes used") (citing *Proctor & Gamble Pharms., Inc. v. Hoffmann-LaRoche Inc.*, No. 06 Civ. 0034(PAC), 2006 WL 2588002, at *6 n.16 (S.D.N.Y. Sept. 6, 2006) ("the sample size of a well-designed randomized clinical is large enough to ensure a high . . . power of detecting a clinically important overall difference between two treatment groups")). A study with a greater sample size, and therefore sufficient statistical power, can more persuasively support a determination as to whether a causal link exists. *See* Green at 582.

Here, Duffy's sample size was generally large enough to render its incidence rate projections reliable, despite Dr. Steinman's claims to the contrary.[22] Thus, from a scientific standpoint – and from applying the *Daubert* criteria that govern reliability determinations in Program cases – I find that Duffy contradicts Petitioner's argument about the likelihood that the FluMist form of the vaccine could cause narcolepsy, given the failure of observed, real-world instances to rise anywhere close to the expected incidence rate. *Daubert*, 43 F.3d at 1321 (citing *DeLuca v. Merrell Dow Pharm., Inc*., 911 F.2d 941, 958 (3rd Cir. 1990)) ("[f]or an epidemiological study to show causation under a preponderance standard, 'the relative risk of ... [the defect or injury] arising from the epidemiological data . . . will, at a minimum, have to exceed '2'").

[21] Dr. Steinman further argues that the low incidence rate could be attributable to the fact that those with the genetic defect giving them a propensity to develop narcolepsy, like Mr. D'Tiole, are less common in the United States than abroad, where the Pandemrix/inactivated form of vaccine has been shown to be linked to the condition. Third Steinman Rep. at 9-10. But Dr. MacGinnitie persuasively established that incidence would also be affected by population size, rather than just the prevalence of the genetic allele. Second MacGinnitie Rep. at 2. Because the United States' population is much larger than both Finland and Sweden, the study would have likely shown more cases of narcolepsy if a link did in fact exist.

[22] There is also some irony in Dr. Steinman's objection that Duffy was underpowered, and hence unreliable – since his own research from Ahmed II, so heavily relied upon by Petitioner to establish a relationship between the flu vaccine and narcolepsy based upon the presence of nucleoprotein autoantibodies, ***involved only 20 individuals***.

The basis for my determination herein to give Duffy more weight than Petitioner urges can also be understood by reiteration of a prior point. In this case, to the extent *any* flu vaccine has been associated with narcolepsy, that association is the result of epidemiologic evidence involving Pandemrix only. Dr. Steinman's own literature, especially Ahmed I and II, only underscored the extent to which questions about formulation likely matter. And Petitioner has heavily relied on other epidemiologic evidence involving the wild virus, like Han. Given the backdrop, epidemiologic evidence involving the specific vaccine formulation at issue in this case becomes especially relevant – and the conclusions of such evidence therefore become more probative.[23]

I again acknowledge that components of Petitioner's theory in this case have reliable foundations, even if some of the research relied upon remains preliminary, as Dr. Steinman has admitted. Petitioner's theory could well become more reliable once there is stronger proof linking the LAIV form of the H1N1 flu vaccine, or better and more consistent evidence linking the H1N1 wild virus alone, to narcolepsy. Studies measuring the nucleoprotein antibody levels in individuals vaccinated with FluMist would also be useful in supporting the theory. *See* Ahmed II at 8 (noting that these kind of findings would constitute a step toward understanding vaccine-associated narcolepsy, and therefore future studies would be beneficial to further understand the mechanism linking narcolepsy and the flu vaccine). At present, however, Dr. Steinman's own research suggests that the theory he proposes applies only to a form of the flu vaccine not at issue in this case. It therefore lacks sufficient reliability in this context to carry Petitioner's *Althen* prong one burden.

Petitioner and his expert protest that the Vaccine Act's evidentiary requirements do not demand scientific exactitude, and thus for me to find the first prong has not been satisfied is to unfairly increase his burden of proof. *See, e.g.,* Opp. at 24-25, Second Steinman Rep. at 8. But I have not done so in my analysis. For, even if a petitioner need only demonstrate a "plausible" theory, the scientific evidence offered to meet that standard must *itself* be reliable, based on the same standards that would apply to it outside the courtroom. *Kumho Tire Co., Ltd. v. Carmichael,* 526 U.S. 137, 152 (1999) (*Daubert* factors exist "to make certain that an expert, whether basing testimony upon professional studies or personal experience, employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field").

Thus, although the Vaccine Act does not require a petitioner to prove with scientific certainty that his theory is plausible (and special masters make legal determinations about

[23] Indeed, in this case Petitioner has arguably put epidemiologic evidence directly into contention. Where a petitioner relies on such evidence to suggest a vaccine likely could cause a particular disease or condition, then he must also persuasively explain or rebut contrary evidence – he cannot simply take refuge behind the general proposition that Vaccine Act claimants need not usually offer such evidence.

evidentiary weight – not scientific determinations), it *does* require a chain of reliable propositions supporting petitioner's theory – and here important links in the chain are missing. It is simply too great of a leap for me to conclude that, because one form of the flu vaccine may plausibly cause narcolepsy due to manufacturing differences that promote an excess of certain antigens that could theoretically provoke an autoimmune reaction, a significantly different form of the vaccine would necessarily have the same effect in the United States – especially given reliable epidemiologic evidence to the contrary, as well as admissions found in Petitioner's own scientific evidence.

B. The Other *Althen* Elements Have Not Been Met

Although my decision turns on Petitioner's inability to offer a persuasive and reliable theory of causation, I also find that the other *Althen* prongs have not been met, for reasons somewhat independent of the above analysis.

First, the "did cause," second *Althen* prong has not been met with preponderant evidence. Mr. D'Tiole cannot establish that he in fact experienced an autoimmune process, in the manner outlined by Dr. Steinman's theory, culminating in his narcolepsy. The record lacks direct[24] or indirect evidence of the existence of an autoimmune post-vaccination reaction, reflected by some other test result or symptom. What is left is the fact that (crediting Ms. DePlush's statements) Petitioner began to experience some narcolepsy symptoms after his February 2012 surgical procedure, and then additional symptoms several months later, with nothing in the intervening period to suggest any progression or continuation of symptoms. This does not constitute a coherent, logical sequence of cause and effect that could persuasively be related to his December 2011 vaccination. Dr. Steinman largely appears to assume that the fact that narcolepsy followed vaccination is proof enough of a relationship – an assumption the Program soundly rejects. *See, e.g.*, *Moberly*, 592 F.3d at 1323 ("neither a mere showing of a proximate temporal relationship between vaccination and injury, nor a simplistic elimination of other potential causes of the injury suffices, without more, to meet the burden of showing actual causation"); *Grant*, 956 F.2d at 1148.

Second (and with respect to the third *Althen* prong), Petitioner has not adequately demonstrated that the proposed timeframe in which he would be expected to experience the autoimmune process interfering with his hypocretin production, and resulting in narcolepsy, was medically reasonable. It is true that Dr. Steinman's theory proposes a timeframe that is fairly long, and which has some reliable basis. Working from the Pandemrix literature, plus Han, Dr.

[24] Thus, there is no evidence that Petitioner had any of the H1N1-derived nucleoprotein antibodies that would theoretically interact with his hypocretin production – although I acknowledge that this evidentiary omission does not deserve significant weight, since it is not likely any of Mr. D'Tiole's treaters would have even thought to look for the presence of these antibodies in the first place.

Steinman posits that the autoimmune reaction could take several months to develop, since narcolepsy is itself usually diagnosed in such a time lag after vaccination or likely infection date. First Steinman Rep. at 17, 19. Given that Petitioner experienced his symptoms no sooner than about seven to eight weeks from his receipt of FluMist, and no later than April 2012 (which the medical records suggest, based on the first time he mentioned his symptoms to a treater), Petitioner's reported onset is well within that timeframe.[25]

However, the medical records are inconsistent on the scope or progression of these symptoms in the ten months after Mr. D'Tiole received the vaccine. Thus, although there is evidence of onset in the late winter of 2012, the records from Petitioner's neurologic and epilepsy consult in October 2012 make little mention of sleep problems as Petitioner's primary concern, and do not themselves corroborate the earlier records. And, as noted above, there is zero record evidence that evinces the existence of an autoimmune process occurring in the seven months after vaccine administration. It is therefore impossible to conclude that the proposed timeframe actually played out as would be expected. Dr. Steinman has also not offered an explanation for why an individual's narcolepsy would take such a stuttering, up and down course under his theory, with the molecular mimicry mechanism he posits beginning at the time of vaccination but thereafter taking over nine months to develop, with many subsequent lulls.[26]

C. A Hearing Was Not Necessary to Resolve this Case

In deciding as I do, I am declining Petitioner's request that I conduct a hearing. The choice of how best to resolve this case is a matter that lies generally with my discretion, but given Petitioner's protestations I shall explain my reasoning.

A hearing usually provides a petitioner with the opportunity to put on live testimony, which aids the special master most in cases where witness credibility is at issue, or where there is a need to pose questions to a witness in order to obtain information not contained in, or not self-evident from, the existing filings. *See, e.g.*, *Hooker*, 2016 WL 3456435, at *21 (discussing a

[25] It should be noted that the literature discusses this timeframe in relation to *diagnosis* of narcolepsy, not onset – and thus suggests that onset would be sooner. *See* S. Nevsimalova, *Narcolepsy in Childhood*, 2009 Sleep Medicine Reviews 13, at 2 (Pet'r's Ex. 35) (ECF No. 11-8).

[26] For added background in evaluating whether the timing of onset in this case was medically acceptable, it is instructive to compare this case with the only other reasoned decision of which I am aware addressing the propensity of some forms of the flu vaccine to cause narcolepsy, *Garrison v. Sec'y of Health & Human Servs*., No. 14-762V, 2015 WL 7424016 (Fed. Cl. Spec. Mstr. Oct. 29, 2015). The petitioner in *Garrison* received the flu vaccine in November 2011, and (as medical records plainly established) began experiencing sleepiness and related symptoms within a week or two. By May 2012, she was diagnosed with narcolepsy. *Garrison*, 2015 WL 7424016, at *1-2. Temporally this onset is far closer to the vaccine's administration than in the present case, where (even if I accept Petitioner's assertions about onset occurring in February 2012) there is a two-month lag, followed by a fluctuating course of symptoms over the next six months. Moreover, the medical records in this case are inconsistent on onset, with some suggesting Mr. D'Tiole's narcolepsy did not begin until March or April 2012.

special master's discretion in holding a hearing and the factors that weighed against holding a hearing in this matter); *Murphy*, 1991 WL 71500, at *2 (no justification for a hearing where the claim is fully developed in the written records and the special master does not need to observe the fact witnesses for the purpose of assessing credibility). It may also, in certain circumstances, permit a claimant to expand upon or illuminate points already set forth in paper filings, or respond to unanticipated questions raised in the matter – but again, only where necessary to reach a decision.

In this case, live witness testimony was not required in order for me to reach a reasoned decision, which did not turn on a credibility determination. The largest weakness in Petitioner's case is his causation theory as proposed by Dr. Steinman. Dr. Steinman's credibility on the topic at hand was established by his reports, burnished by his reputation and credentials (given that he frequently appears in Program cases as an expert).[27] Indeed, it is evident that both sides have offered expert opinions from individuals with the necessary backgrounds and experience to give them. Thus, I need not hear Dr. Steinman (or any expert for that matter in this case) "live" to weigh his theory, since personally evaluating his candor was not required for me to decide the case.

I further note that Petitioner had sufficient opportunity to present his arguments, along with supportive expert testimony. Petitioner offered ***three*** reports from Dr. Steinman, providing ample elaboration of his views as well as reacting to the critiques lobbed by Respondent's experts in their own reports. The timing of the filing of these reports illuminates the numerous opportunities Petitioner had to bulwark his theories in light of Respondent's challenges, and thus the extent to which he has had a "full and fair" opportunity to make his case. Thus, Dr. Steinman's first report was filed less than one month after the case's initiation in early 2015, with the second (responding to the points raised by Dr. Kohrman) filed in September of that same year. The third supplemental report (which, at 23 pages, was nearly as long as the first report) followed Dr. Kohrman's supplemental report and Dr. MacGinnitie's first report, both of which were filed in early 2016.

In addition, I note that the parties' experts thoroughly addressed the issues relevant to causation in their reports, allowing me to discern the problems with Petitioner's theory that I have identified above without needing to question any expert directly about a topic that had only occurred to me. Respondent's experts squarely challenged in their reports the extent to which the Ahmed I and II findings about Pandemrix applied to FluMist. *See, e.g.,* First MacGinnitie Rep. at 9 ("Flumist and Pandemrix are very different vaccines administered by different routes and causing distinct immune responses," and "narcolepsy has only been associated with a specific

[27] I also note that I have personally heard Dr. Steinman testify several times in different Program cases, and thus had repeated opportunities to observe him and weigh his personal credibility. While I have not always found his opinion persuasive with respect to a given claim, I have never doubted his competency or expertise.

type of subunit vaccine"). In turn, Petitioner and his expert were clearly made aware of Respondent's arguments, and Dr. Steinman endeavored in his two supplemental reports to answer and rebut all of them. I had no additional questions to pose to Dr. Steinman that he had not already answered, or had been given the opportunity to answer.[28]

I similarly did not need to hear directly from Petitioner or his family members. There are many cases where witness testimony about the nature of a symptom or its onset is critical to determining a fact issue. *See, e.g.*, *Rich v. Sec'y of Health & Human Servs.*, No. 12-742V, 2015 WL 5882324 (Fed. Cl. Spec. Mstr. Sept. 16, 2016) (fact hearing required witness testimony to determine onset of petitioner's ADEM symptoms); *Reddy v. Sec'y of Health & Human Servs*., No. 13-208V, 2015 WL 5578610 (Fed. Cl. Spec. Mstr. Aug. 26, 2015) (determining onset of symptoms through witness testimony at fact hearing to resolve whether claim was timely filed); *Bray v. Sec'y of Health & Human Servs.*, No. 10-207V, 2014 WL 5025173 (Fed. Cl. Spec. Mstr. Sept. 16, 2014) (case required witness testimony to determine if petitioner received the flu vaccine). In such instances, it is necessary to evaluate the witness's demeanor live in order to determine how much weight to give a factual allegation. But here, I can dispense with live testimony – and even credit all of the witness testimony as set forth in written declarations as true – but still reach the same conclusion.

For example, Petitioner argues that fact witnesses in this case would attempt to establish that onset of petitioner's narcolepsy occurred around the time of his operation in February 2012. Opp. at 18. Some of this testimony would be in opposition to medical records – for example, those records where Petitioner or his family proposed a somewhat later onset. But even if I simply accept as true Petitioner's assertion that onset began around the time of his February 2012 surgical procedure, my finding that Petitioner has not demonstrated that FluMist *could cause* narcolepsy remains. Finding in favor of Petitioner on the onset issues after hearing such testimony would not cause him to prevail.

Petitioner also proposes that some of his narcolepsy treaters might have identified the FluMist vaccine as a trigger for his narcolepsy had they been aware that he received it, thus strengthening his call for live testimony about onset. Opp. at 17-18. While treater views are important in Program cases, however, the assumption that a treater would have offered support for FluMist's causal role is speculative. Moreover, the particular treater identified, Dr. Mignot,[29] was known to Petitioner and could easily have been contacted (whether in the course of this

[28] Importantly, six months passed from the date of Dr. Steinman's third expert report and Petitioner's brief filed in opposition to Respondent's motion – giving him even more time, had he so chosen, to file additional statements from Dr. Steinman (or other experts) on the issues in contention.

[29] Notably, this is the same Dr. Mignot whose research findings on a component of Dr. Steinman's overall theory about autoantibodies blocking hypocretin receptors could not be replicated – a failure that Dr. Steinman opted to characterize as fraudulent in nature. Third Steinman Rep. at 1-5.

matter or in briefing the motion to dismiss) and asked to make a supporting declaration based on the known fact that Mr. D'Tiole received the FluMist vaccine, but was not.[30] Dr. Mignot has offered opinions about the propensity of the flu vaccine to cause narcolepsy before in other cases, and his unavailability herein has not been established. *See, e.g., Garrison*, 2015 WL 7424016, at *7.[31] In any event, I need not accept a treater opinion, or give it the weight urged by a claimant, that itself is not reliable or founded on reliable evidence – and because Dr. Steinman's opinion has not been found to be reliable when applied to FluMist, the fact that a treater might espouse the same theory would not alter my conclusion. *Synder,* 88 Fed. Cl. at 746 n.67.

This point underscores another reason for forgoing a hearing. As noted above, the deficiency in Petitioner's causation theory was discernible from review of the expert reports alone. Dr. Steinman proposed that the presence of the H1N1 wild virus component in FluMist would likely have the same impact as that component contained in different form of vaccine. But the very studies he helped author, and that he cites in support of his theory, *themselves* point to a contrary conclusion: that it was the manner in which the H1N1 components were affected by inactivation, rather than the mere inclusion of the flu virus in any vaccine, that played the primary role in causing narcolepsy. My conclusions about the deficiencies in Petitioner's theory were derived from close consideration of the parties' competing reports and their supporting literature, and did not require me to question them (any more than I would be obligated to question them at hearing).

Petitioner insists that the mere fact that his expert embraces an opinion in opposition to the Respondent's experts means that there exist "genuine issues of fact that must be fleshed out further with witness testimony." Opp. at 15. But this misconstrues the factors I am to weigh in deciding when a hearing is required. Prior decisions have recognized that a special master's discretion in deciding whether to conduct an evidentiary hearing "is tempered by Vaccine Rule 3(b)," or the duty to "afford[] each party a full and fair opportunity to present its case." *Hovey*, 38 Fed. Cl. at 400-01, *citing* Rule 3(b). But the rule also includes the obligation of creation of a record "sufficient to allow review of the special master's decision." *Id.* Thus, the fact that a claim is legitimately disputed, such that the special master must exercise his intellectual faculties in

[30] Dr. Mignot began treating Petitioner in 2014. This matter was filed in 2015, but Petitioner only offered expert support for his claim from Dr. Steinman. I did not indicate my intent to permit Respondent to make a motion for a ruling on the record until March 2016. Petitioner subsequently filed his opposition to Respondent's motion on July 20, 2016 (ECF No. 37). No reason has been provided why Dr. Mignot could not have been, or was not, asked to provide support for Petitioner's argument herein at any time in 2015 or this year.

[31] *Garrison* was decided in favor of the petitioner, but in circumstances in which Respondent did not offer her own expert, and opted instead simply to request a ruling on the record based upon the petitioner's submissions. *Garrison*, 2015 WL 7424016, at *1 (Respondent filed only a Rule 4(c) Report requesting a ruling on the record). Accordingly, the special master's determination was based mainly on whether the petitioner had offered sufficient proof to meet the *Althen* prongs, without confronting the issues herein.

order to decide a matter, is not itself grounds for a trial (for if it were, trials would be required in every disputed case).

Rather, the standard is whether Petitioner has had a fair chance to present his case – and here he has. This is not a case where the diagnosis is in dispute, such that I would benefit from hearing an expert explain his interpretation of the record. The issue disputed by the experts – whether research involving Pandemrix applies to FluMist – is self-evident from their reports. As previously noted, moreover, I have deemed Petitioner's allegations about onset as true, removing another disputed fact that under other circumstances might have required an evidentiary hearing to resolve. The experts all had ample opportunity to review each other's opinions and respond accordingly, in keeping with the "full and fair opportunity" duty that informs whether to hold a hearing. And those reports, plus the ample medical and scientific literature offered in connection therewith, were all filed – thus providing the record necessary to resolve a motion for review, should Petitioner choose to exercise that opportunity. Resolution of the primary disputed issue – the first *Althen* prong – did not require live testimony simply because it was a contested matter.

The third reason for not holding a hearing is less substantively important, but still significant. The Vaccine Program is currently inundated with cases, with filings growing at a rate faster than the existing special masters (whose numbers are limited by the Vaccine Act itself) can handle. *See Hooker,* 2016 WL 3456435, at *22 ("[t]he special masters of this court, designated to decide these cases, now face nearly overwhelming numbers of cases on each of their dockets, being required to resolve many more cases than in past years, but with the same number of special masters"). This means that legitimately contested matters cannot possibly be heard promptly after they are ready, even discounting the need to schedule hearings at times mutually-convenient to counsel, witnesses, and experts.[32] Under such circumstances, special masters must necessarily reserve trials for matters where live witness testimony is vital to resolution. Other cases, no matter how hotly contested, can be fairly, and efficiently, resolved on the papers, even if they call for close review of the file and painstaking evaluation of expert positions. This case presents such an instance.

[32] This case, for example, could not have been heard until the second half of 2017 at the earliest, given my present calendar schedule for entitlement hearings – which at the moment anticipates conducting ten individual hearings before Memorial Day 2017. Thus (and taking into account usual post-trial briefing), had I scheduled this case for hearing, it is unlikely I would have completed a decision in the matter before mid-2018. By contrast, this written decision is being released in 2016, and less than six months from the date the case was ripe for decision.

CONCLUSION

The record does not support Mr. D'Tiole's contention that the FluMist form of the flu vaccine could cause his narcolepsy or cataplexy, or did so. There is no more than a temporal relationship between vaccination and his subsequent symptoms – and, moreover, one that is not particularly close, and which the proposed theory is somewhat vague in addressing. Petitioner has not established entitlement to a damages award.[33]

IT IS SO ORDERED.

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

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