# In the United States Court of Federal Claims

**OFFICE OF SPECIAL MASTERS**
**No. 17-1257V**
**Filed: April 2, 2021**

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| GLENN REINHARDT,<br><br>Petitioner,<br><br>v.<br><br>SECRETARY OF HEALTH AND HUMAN SERVICES,<br><br>Respondent. | TO BE PUBLISHED<br><br>Influenza Vaccine; Bilateral Optic Neuritis ("ON") |

*Michael A. Baseluos*, Baseluos Law Firm PLLC, San Antonio, TX, for Petitioner
*Julia Martin Collison*, U.S. Department of Justice, Washington, DC, for Respondent

## RULING ON ENTITLEMENT[1]

**Oler**, Special Master:

On September 15, 2017, Glenn Reinhardt ("Petitioner") filed a petition for compensation under the National Vaccine Injury Compensation Program, 42 U.S.C. § 300aa-10, *et seq.*[2] (the "Vaccine Act" or "Program"). The petition alleges that Petitioner developed optic neuritis ("ON") as a result of the influenza ("flu") vaccine he received on October 11, 2016. Pet. at 1, ECF No. 1.

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

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

Upon review of the evidence submitted in this case, I find that Petitioner has met his burden in showing that the flu vaccination he received on October 11, 2016 caused him to develop ON. He is therefore entitled to compensation under the Vaccine Act.

## I. Procedural History

On September 15, 2017, Petitioner filed his petition ("Pet."), an expert report from Dr. Dean Cestari (Ex. 15) and Dr. Cestari's curriculum vitae (Ex. 16). The petition alleges that Petitioner developed bilateral optic neuritis after receiving the flu vaccine (specifically Afluria) resulting in irreversible legal blindness. Pet. at 1. On October 3, 2017, Petitioner filed the medical literature associated with Dr. Cestari's report and a Statement of Completion. Ex. 14; Ref. Nos. 1-54, ECF Nos.14-18; ECF No. 19.

On May 8, 2018, Respondent filed a Status Report acknowledging that the record was complete and indicating a willingness to participate in informal settlement discussions. ECF No. 28.

On September 9, 2018, while informal settlement negotiations were ongoing, Petitioner filed an expert report from Dr. Omid Akbari in support of his position. Ex. 2; ECF No. 32. On September 26, 2018, Petitioner filed the medical literature referenced in Dr. Akbari's expert report. Ex. 14; Ref. Nos. 1-53; ECF Nos. 37-41.

On October 11, 2019, after 15 months of informal settlement negotiations, Petitioner filed a status report stating, "Settlement negotiations have broken down and there is no value in continued extensions." ECF. No. 53. Petitioner requested that the matter be placed on the hearing docket. *Id*.

On December 13, 2019, Respondent filed an expert report from Dr. Timothy Vartanian (Ex. A) and Dr. Vartanian's CV. Ex. B; ECF No. 54. Respondent filed the medical literature referenced in Dr. Vartanian's first report on December 31, 2019. Exs. C-G; ECF No. 56.

On January 17, 2020, the parties filed a Joint Status Report in which Petitioner formally withdrew his theory of causation based on ASIA. ECF. No. 57. At the entitlement hearing, Petitioner confirmed that he was strictly relying on molecular mimicry as his medical theory of causation. Tr. at 66.

On March 26, 2020, I issued a Prehearing Order. ECF No. 60. An entitlement hearing was scheduled for May 21 and 22, 2020. ECF No. 60. I asked the parties to file all documents on which they intended to rely at the hearing no later than April 23, 2020. *Id*.

On March 31, 2020, Petitioner filed an expert report from Dr. Robert Turner, Dr. Turner's CV, and the medical literature cited in support of his findings. Exs. 27-28, ECF No. 61. On April 20, 2020, Petitioner filed a second expert report from Dr. Turner, the associated supplemental literature and MRI images. Supp. Ex. 28; Ref. Nos. 1-4; ECF. No. 64; Ex. 29; Supp. Ex. 29; ECF No. 64; Ex. 30; Supp. Exs. 1-17A; ECF No. 64-65.

On April 23, 2020, Petitioner filed an expert report from Dr. Martha Schatz, Dr. Schatz's CV, associated MRI reports and medical literature. Ex. 31-33; ECF No. 66. Petitioner also filed Power Point Presentations prepared by Dr. Akbari and Dr. Cestari. Exs. 34-35; ECF No. 66. On May 2, 2020, Petitioner filed the medical literature associated with Dr. Cestari's Power Point Presentation. Ex. 35; Ref. Nos. 1-4; ECF No. 80. On May 20, 2020, Petitioner filed an updated CV for Dr. Schatz. Ex. 1; ECF No. 102.

On April 24, 2020, Petitioner filed his prehearing memorandum, supplemental medical literature, and highlighted copies of Dr. Akbari's medical literature. Ex. 32; Supp. 1-2; ECF No. 69; Ex. 19; Ref. Nos. 1- 53; ECF Nos. 70-74. On April 30, 2020, Petitioner filed a second expert report from Dr. Akbari addressing the issues raised in Dr. Vartanian's first report along with additional medical literature. Ex. 37; ECF No. 75; Supp. Ex. 37; Ref. Nos. 1-15; ECF No. 75. On May 1, 2020, Petitioner filed a second expert report from Dr. Cestari and the related medical literature. Ex. 38; ECF No. 76; Supp. Ex. 38; Ref. Nos. 1-27; ECF Nos. 77-79. On May 7, 2020, Petitioner filed a Supplemental Brief and Prehearing Order. ECF No. 83.

On May 11, 2020, Respondent filed a Prehearing Brief, a Supplemental Report from Dr. Vartanian and the related medical literature. ECF Nos. 85; Exs. H-T; ECF No. 86. On May 13, 2020, Petitioner filed a Motion to Strike Dr. Vartanian's Report on the grounds that it was filed fewer than 10 days prior to the entitlement hearing and raised new issues and arguments not presented in his first report. ECF No. 88. On May 15, 2020, I issued an order denying Petitioner's Motion to Strike. ECF No. 98.

On May 19, 2020, Petitioner filed a Response to Respondent's Prehearing Brief. ECF No. 99. On May 20, 2020, Petitioner filed third expert reports from Dr. Cestari, Dr, Akbari and Dr. Turner including additional medical literature from Dr. Turner. Exs. 39-41; ECF No. 100; Supp. Ex. 41; Ref. Nos. 1-2; ECF No. 100.

I held an entitlement hearing on May 21 and 22, 2020. Due to the COVID-19 pandemic, the hearing was conducted via videoconference. On June 29, 2020, after the hearing, and with the permission of the Court, Petitioner filed a fourth expert report from Dr. Akbari and the associated medical literature. Ex. 43; ECF No. 107; Ex. 43; Ref. Nos. 1- 24; ECF Nos. 108-111. On July 10, 2020, Petitioner filed his Post-Hearing Brief specifically addressing *Althen* Prong One. ECF No. 115.

On August 26, 2020, Respondent filed a Post-Hearing Brief. ECF No. 119. On September 22, 2020, the parties filed a Joint Status Report stating that the record was complete. ECF No. 120. This matter is now ripe for adjudication.

## II. Medical Records

The parties agree that there are no medical facts in dispute with respect to Petitioner's medical records and Petitioner's timeline of symptoms. Joint Submission at 8; ECF No. 83; *see also* Ex. 11 (Petitioner Timeline of Symptoms).

### A. Relevant Pre-Vaccination History

Prior to October of 2016, with the exception of chronic sinusitis, Petitioner was a relatively healthy 44-year-old male with no significant medical history. Ex. 5 at 35. Prior to his influenza vaccination on October 11, 2016, Petitioner had no major issues with his eyes. Dr. Diana Gonzalez, an optometrist, conducted a routine eye exam on December 11, 2013, and noted no history of ocular surgery, trauma or injury, and an unremarkable ocular family history. Ex. 9 at 2. Petitioner had no complaints of physical ocular symptoms, routine headaches, double vision, visual floaters, light flashes, blurry vision, or uncomfortable vision. *Id*. Petitioner wore contact lenses for myopic astigmatism but was otherwise experiencing good/acceptable contact lens comfort, vision and eye health. *Id.* at 3.

Dr. Sebastian Mora, an ophthalmologist, conducted a routine eye exam on September 26, 2016. Ex. 3 at 3. The results of that exam were normal and demonstrated 20/15 visual acuity bilaterally (with contact lens correction). Ex. 14 at 2.

Petitioner's treating physician, Dr. Yoo, conducted routine physical examinations in October 2013 and June 2015. Bloodwork was unremarkable and exams were otherwise normal with the exception of symptoms of irritable bowel syndrome. Ex. 10 at 6.

### B. Relevant Post-Vaccination History

On October 11, 2016, Petitioner had follow-up appointment with his ENT, Dr. Christine Gilliam, in connection with a sinus infection. Ex. 1 at 4. Dr. Gilliam noted that Petitioner was feeling well, with no fever, headache or runny nose. *Id*. At that visit, Petitioner received his first ever influenza vaccination. *Id*.

On October 24, 2016, Petitioner saw Dr. Mora, complaining of obstructed vision in his right eye starting on October 23, 2016, 12 days after his vaccination. Ex. 3 at 5. Dr. Mora diagnosed Petitioner with serious maculopathy and referred Petitioner to a retina specialist, Dr. Thomas Oei, for further examination. *Id*. Dr. Oei observed an abnormality in the optic nerve and diagnosed Petitioner with ischemic optic neuropathy but noted that further testing was necessary. Ex. 4 at 4. Dr. Oei referred Petitioner to Dr. Schatz, a neuro-ophthalmologist. *Id*. On October 26, 2016, prior to seeing Dr. Schatz, Petitioner telephoned Dr. Oei to inform him that Petitioner's vision had further deteriorated. *Id*. Dr. Oei recommended that Petitioner go to the nearest emergency room. *Id*. Petitioner was admitted to University Hospital that day and remained for a period of three weeks. *Id*.

Upon his admission to University Health System, the differential diagnosis for Petitioner's vision loss and bilateral optic disc swelling was broad, including vascular, infectious, inflammatory, post infectious, post-vaccine, metabolic, hereditary, comprehensive, and neoplastic causes. Ex. 5 at 28. Over the next few days, Petitioner underwent an extensive diagnostic work up looking for an infectious or autoimmune etiology in order to formulate a treatment plan. *Id.* at 20-28.

Petitioner's treating team performed a myriad of tests including, but not limited to, vision screening, bilateral vision exams, field of view testing, carotid ultrasound, CT scan, multiple MRIs of the brain and orbits, blood sample testing, cerebral spinal fluid (CSF) testing, chest x-ray, stool sample testing, lumbar puncture, neurological exams, and infectious disease evaluations. Ex. 5 at 76-118. All testing and lab work were either negative or non-diagnostic, ruling out multiple potential causes including viral infection, bacterial infection, fungal infection, structural issues, parasites, medication responses, environmental factors, brain issues, and abnormal CSF pressure. *Id.; see also* Joint Submission at 7.

Despite having no clinical symptoms or positive lab results, Petitioner was treated empirically for several conditions in an effort to increase his chances of recovery. Ex 5. at 72. Petitioner was started on IV steroids followed by oral steroids. *Id*. Petitioner was treated for Bartonella Hensley IgG[3] (cat scratch fever) with a course of antibiotics. *Id*. He was also treated for neuromyelitis optica spectrum disease ("NMO") with five days of plasma exchange. *Id*. Ultimately, there was no noticeable improvement and Petitioner's vision worsened. *Id*.

Petitioner was discharged from the hospital on November 14, 2016, with a diagnosis of bilateral optic neuritis. Ex. 8 at 10. He completed his oral steroid treatment on January 4, 2017, and although his disk swelling slowly receded, his visual field never fully returned. *See* Ex. 9 at 10. On February 15, 2017, Dr. Chan, a low vision specialist, determined that Petitioner was legally blind and issued a certificate a legal blindness. *Id*.; Ex. 12. On February 16, 2017, Dr. Schatz assessed Petitioner with post vaccine autoimmune optic neuritis based on the exclusion of other possible etiologies and the temporal association with the flu vaccine administered two weeks prior. Ex. 9 at 22. At the time of the entitlement hearing, he had not had a recurrence of symptoms. Tr. at 124.

## III. Expert Reports and Testimony

Petitioner filed a total of 11 expert reports authored by four experts: Dr. Dean Cestari, Dr. Omid Akbari, Dr. Martha Schatz and Dr. Robert Turner. *See* Ex. 14 ("First Cestari Rep."); Ex. 38 ("Second Cestari Rep."); Ex. 39 ("Third Cestari Rep."); Ex. 19 ("First Akbari Rep."); Ex. 37 ("Second Akbari Rep."); Ex. 40 ("Third Akbari Rep."); Ex. 37 ("Fourth Akbari Rep."); Ex. 32 ("Schatz Rep."); Ex. 28 ("First Turner Rep."); Ex. 29 ("Second Turner Report"); Ex. 41 ("Third Turner Rep.").

Respondent filed two expert reports, both authored by Dr. Timothy Vartanian. *See* Ex. A ("First Vartanian Rep."); Ex. H ("Second Vartanian Rep.).

For the sake of clarity, my summary of the expert reports and testimony will be divided as follows: (1) those portions of the reports and testimony that address Petitioner's medical theory of causation, and (2) those portions of the reports and testimony that address *Althen* prongs two and three.

[3] Petitioner's initial lab work came back borderline positive for Bartonella Hensley IgG. His subsequent PCR amplification test, a more precise test for Bartonella came back negative, and Bartonella was ruled out as the cause of Petitioner's vision loss. Tr. at 119-22.

## A. Expert Reports re: Medical Theory of Causation

### 1. Dr. Akbari's First Report

Dr. Akbari has a B.S. and a M.S. in general and medical microbiology, and a Ph.D. in molecular and cellular immunology. Ex. 18 at 1. (hereinafter "Akbari CV"). He is a Professor of Medicine and a Professor of Immunology at University of Southern California, USC, Keck School of Medicine. Tr at. 12. Dr. Akbari is actively involved in researching the role immune tolerance plays in triggering an autoimmune disease. Tr. at 14. Dr. Akbari has specifically studied immune regulation/dysregulation after influenza infection and vaccination. *Id.* Several years ago, his lab designed a new universal vaccine against the influenza virus for which they won several awards. *Id.* at 15-16. Dr. Akbari's lab has also conducted studies of viral-induced autoimmunity and immune-mediated diseases that cause blindness. *Id.* at 15. Dr. Akbari has been the recipient of the Henning Loewenstein Award for best practice and research in immunology and the Pharmacia Award for the best immunology research. *Id.* The results of his research have been published in several high impact journals such as New England Journal of Medicine, Journal of Clinical Investigation, Journal of Experimental Medicine, Nature Immunology, Nature Medicine, and Journal of Immunology. *Id.* at 16.

In Dr. Akbari's first report, having reviewed Petitioner's medical records, he concluded "to a high degree of certainty, and by a preponderance of the scientific evidence, had it not been for the flu vaccination, particularly the first exposure to flu vaccine, [Petitioner] would not have developed symptoms such as optical neuritis, blurred vision and vision loss." First Akbari Rep. at 17. Dr. Akbari's report referenced 53 pieces of medical literature in support of his opinion.

Dr. Akbari's research revealed that "the theory of molecular mimicry and vaccine homology support that influenza immunization can plausibly[4] cause an adverse immune cross reaction and result in the onset of local optic neuro-degeneration observed in this case." First Akbari Rep. at 4. First, Dr. Akbari found that the Afluria vaccine is partially composed of the H1N1 vaccine, a vaccine which has been widely studied and has been shown to contain two separate six amino acid sequences that mimic those found in components of the myelin sheath. *Id.* at 10-11; *see also* Markovic–Plese, et al., *High level of cross-reactivity in influenza virus hemagglutinin-specific CD4+ T-cell response: Implications for the initiation of autoimmune response in multiple sclerosis*, 169 J NEUROIMMUNOL 31-38 (2005) (filed as Ex. 19, Ref. No. 27), KW Wucherpfennig & JL Strominger, *Molecular mimicry in T cell-mediated autoimmunity: viral peptides activate human T cell clones specific for myelin basic protein*. 80 CELL 5, 695- 705 (1995) (filed as Ex. 28) (hereinafter "Wucherpfennig1"). Dr. Akbari has also located research showing that the H1N1 vaccine is capable of triggering an autoimmune response resulting in a demyelinating disease. First Akbari Rep. at 12; *see also* Nachamkin, et al., *Anti-ganglioside antibody induction by swine (A/NJ/1976 /1-Il Nl) and other influenza vaccines: insights into*

[4] During the entitlement hearing, Dr. Akbari clarified his use of the terms "plausible" and "reasonable" as being "our language in science. . . . but that doesn't mean that we are not sure." Tr. at 21-22. "Whenever the possibility of something is anything greater than 51 percent or 60 percent, we say it is plausible or it is believed." Tr. at 22.

*vaccine-associated Guillain-Barre syndrome*, 198 J INFECT DIS. 2, 226-33 (2008) (filed as Supp. Ex. 19, Ref. No. 34) (hereinafter "Nachamkin").

Dr. Akbari cited two studies showing that cross-reactive T cells created in response to the H1N1 vaccine have been shown to cause ON in both rat models and rhesus monkeys. First Akbari Rep. at 11; *see also* Weilbach, et al., *T-cell receptor V beta- element expression in peripheral nerves of Lewis rats suffering from experimental autoimmune neuritis*, 79 J NEUROIMMUNOL 1, 69-75 (1997) (filed as Ex. 19, Ref No. 29) (hereinafter "Weilbach"); Bajramovic, et al., *Oligodendrocyte-specific protein is encephalitogenic in rhesus macaques and induces specific demyelination of the optic nerve*, 38 EUR J IMMUNOL. 5, 1452-64 (2008) (filed as Ex. 19, Ref. No. 30) (hereinafter "Bajramovic"). Similarly, Dr. Akbari presented research suggesting that T cells targeted to attack myelin basic protein ("MBP") share a peptide sequence with the flu virus. First Akbari Rep. at 11; *see also* Wucherpfennig1; Wucherpfennig, et al., *Recognition of the Immunodominant Myelin Basic Protein Peptide by Autoantibodies and HLA-DR2- restricted T Cell Clones from Multiple Sclerosis Patients*, 100 J CLIN INVEST 5, 1114-22 (1997) (filed as Ex. 19, Ref. No. 31) (hereinafter "Wucherpfennig2").

To show that it is medically likely for the flu vaccine to cause ON in humans, Dr. Akbari cited to the Karussis study which identified 21 patients who reported having an adverse reaction to the flu vaccine within approximately 14 days of vaccination. First Akbari Rep. at 10; *see also* D. Karussis & P. Petrou, *The spectrum of post-vaccination inflammatory CNS demyelinating syndromes*, 13 AUTOIMMUNITY REVIEWS 215-24 (2014) (filed as Ex. 19, Ref. No. 26) (hereinafter "Karussis"). Of those 21 cases, "optic neuritis was the prominent clinical presentation."[5] *Id*. Based on all of the medical literature, Dr. Akbari concluded that "the scientific research supports the assertion that stimulation of the immune system following vaccination, followed by the production of antibodies in response to the vaccine is a plausible[6] medical theory causally linking the flu vaccination with the development of Petitioner's symptoms including optical neuritis and vision loss." *Id*. at 18.

Dr. Akbari opined that the potential for molecular mimicry is high given that T cells need only recognize a few amino acids of an antigenic peptide to induce an autoimmune response. First Akbari Rep. at 6. Yet, the incidence of autoimmune disease "is only estimated to develop in approximately 3-8% of the population." *Id.* at 9. Dr. Akbari explained that the immune system has many checkpoints which likely prevent a high incidence of autoreactive T cells from multiplying and establishing pathology in the majority of individuals. *Id.*; Tr. at 54-55. With respect to the remaining 3-8%, Dr. Akbari stated that certain individuals may be more susceptible or genetically predisposed to developing an autoimmune disease. First Akbari Rep. at 16.

Dr. Akbari explained that the scientific community now believes that the immune system's inability to control an autoimmune response, rather than molecular mimicry alone, is the main reason certain individuals develop an autoimmune disease. First Akbari Rep. at 10. The immune system's effector T cells are known to help eliminate different types of pathogens. *Id.* at

[5] Two other demyelinating diseases were also reported in relation to the influenza vaccine: myelitis and encephalitis. Tr. at 82.

[6] *See supra* note 4.

7. Regulatory T lymphocytes (Tregs) express cytokines which actively suppress the T effectors and prevent them from getting out of control, i.e. otherwise attacking healthy cells due to molecular mimicry. *Id.* at 7, 10. When Tregs are either insufficient or overwhelmed by T effectors, this results in an "adverse autoimmune reaction upon stimulation of the immune system from infection or vaccination." *Id.* at 8. Notably, research has shown that the number of Tregs in patients with ON is significantly decreased. *Id.* at 7; *see also* Kebir, et al., *Human TH17 lymphocytes promote blood-brain barrier disruption and central nervous system inflammation*, 2007 NAT MED 13, 1173-75 (2007) (filed as Ex. 19, Ref. No. 11); Cong, et al., *Change of Th17 Lymphocytes and Treg/Th17 in Typical and Atypical Optic Neuritis*, 11 PLOS ONE 1, e0146270 (2016) (filed as Ex. 19, Ref. No. 15); G Chen, et al., *mTOR regulates neuroprotective effect of immunized CD4+Foxp3+ T cells in optic nerve ischemia*, 2016 SCI REP. 6, 37805 (2016) (filed as Ex. 19, Ref. No 16); Y Liu, et al., *Roles of Treg/Th17 Cell Imbalance and Neuronal Damage in the Visual Dysfunction Observed in Experimental Autoimmune Optic Neuritis Chronologically*, 17 NEUROMOLECULAR MED. 4, 391-403 (2015) (filed as Ex. 19, Ref. No. 22).

2. Dr. Vartanian's First Report

Dr. Vartanian is a board-certified neurologist who subspecializes in the research and care of patients with inflammatory demyelinating diseases. Ex. B at 1 (hereinafter "Vartanian CV"). Dr. Vartanian taught at Harvard Medical School from 1992-2009 and is currently a Professor of Neurology and Neuroscience at Weill Cornell Medical College of Cornell University. *Id*. at 2. He is the attending neurologist at New York Presbyterian Hospital; Chief Scientist at Neurogen Research Foundation; and Director of the Judith Jaffe Multiple Sclerosis Center at Beth Israel Deaconess Medical Center. *Id*. at 2-3,7. Dr. Vartanian has published over 60 peer-reviewed papers and is a peer editor for many publications, some of which include Journal of Cell Biology, Journal of Neuroscience, Brain, Developmental Neuroscience, and Annals of Neurology. *Id*. at 11-19.

Dr. Vartanian's first report challenged Dr. Akbari's medical theory of causation on the grounds that there is no convincing evidence of an association between the flu vaccine and ON (bilateral or unilateral). First Vartanian Rep. at 12. Particularly, Dr. Vartanian stated that Dr. Akbari failed to provide evidence showing that the flu vaccine can stimulate autoantibody production resulting in optic neuritis; failed to show how a peptide without much homology can bind and activate the immune system (with or without vaccination); failed to explain why the majority of people receiving the flu vaccine fail to develop an autoimmune disease; and finally, failed to provide evidence of a molecular or cellular mechanism that reduces Tregs following vaccination. *Id*. at 11. With respect to Karussis, Dr. Vartanian noted that inflammatory disease following vaccination does not prove that the vaccination caused the disease. *Id.* at 12.

3. Dr. Akbari's Second Report

Dr. Akbari wrote his second report in response to Dr. Vartanian's first expert report. In it, he stated that Dr. Vartanian requires specific evidence of an occurrence "that has evaded researchers for over 30 years. This narrow view of requiring scientific certainty ignores the plethora of evidence that supports causation, [and] overlooks current emerging concepts involving the complex induction of immune-mediated diseases." Second Akbari Rep. at 1. A great deal of

Dr. Akbari's second report restated the findings in his first report that specifically address the issues raised by Dr. Vartanian. *See generally*, Second Akbari Rep.

4. Dr. Vartanian's Second Report

Dr. Vartanian reiterated that Petitioner has not established an epidemiological association between the flu vaccine and optic neuritis. Second Vartanian Rep. at 5. He argued that Dr. Akbari failed to identify the T cells or antibodies directed against Petitioner's target antigens and the molecular mimics of those antigens. *Id*. Dr. Vartanian also pointed to the absence of any study replicating Dr. Akbari's theory in animal models. *Id*.

Dr. Vartanian argued that if the flu vaccine shares a meaningful sequence homology with MBP, one would predict a much higher incidence of post-vaccination auto-immune demyelination given the prevalence of seasonal flu vaccinations. *Id*. at 7. He cited to the Silvanovich study for the proposition that "searches for short amino acid sequence matches of eight amino acids or fewer to identify proteins as potential cross-reactive allergens is a product of chance and adds little value to the allergy assessments for newly expressed proteins." *Id*. at 7; *see also* Silvanovich, et al., *The value of short amino acid sequence matches for prediction of protein allergenicity*, 90 TOXICOL SCI. 1, 252-58 (2006) (filed as Ex. Q) (hereinafter "Silvanovich"); Trost, et al., *Bacterial peptides are intensively present throughout the human proteome*, 1 SELF/NONSELF 1, 71-74 (2010) (filed as Ex. R) (hereinafter "Trost") (suggesting that about 50,000 perfect sequences, each 9 amino acids long, are shared between 40 bacterial proteomes and about one third of the human proteome). Based on his research, Dr. Vartanian concluded that there is no statistical association between the flu vaccine and demyelinating diseases, "let alone a high incidence of CNS demyelinating disease post-vaccination." *Id*. at 6.

Finally, Dr. Vartanian opined that even assuming the flu vaccine were capable of triggering a demyelinating autoimmune response, Dr. Akbari failed to show that the flu vaccine contains an adjuvant capable of penetrating the blood brain barrier ("BBB") of the CNS. *Id*. at 7.

5. Dr. Akbari's Third Report

In response Dr. Vartanian's references to Silvanovich and Trost, Dr. Akbari noted that Silvanovich relates to pollens, and that allergens have no relevance to this case.[7] Third Akbari Rep. at 2. Similarly, Trost addresses bacterial sequences, none of which have any relevance to this case. *Id*. at 1.

6. Dr. Akbari's Fourth Report

Dr. Akbari's fourth report, filed after the entitlement hearing, addressed two articles concerning the BBB cited by Dr. Vartanian in his second report and discussed at length by Dr. Vartanian at the entitlement hearing. Dr. Akbari agreed that penetrating the CNS is a requirement

[7] Dr. Akbari also noted that both the Trost and Silvanovitch articles were published in low impact journals. Third Akbari Rep. at 1-2. Trost has only been cited five times in the past ten years, Silvanovitch 13 times in the past 14 years. *Id*.

for inducing a demyelinating condition; however, he did not find the articles cited by Dr. Vartanian to be relevant to Petitioner's case.[8] Fourth Akbari Rep. at 2. Dr. Akbari opined that it is important to distinguish the BBB from the Blood Retina Barrier ("BRB") and the Blood Ocular Barrier ("BOB"). *Id.* at 3. The BRB and BOB surrounding the optic nerves are very delicate and many studies have shown that they do not block complete access to the optic nerve. *Id.* at 3, *citing* Hofman, et al., *Lack of blood-brain barrier properties in microvessels of the prelaminar optic nerve head*, 2001 INVEST OPHTHALMOL VIS SCI 42, 895-901 (2001) (filed as Supp. Ex. 43, Ref. No. 3); Diaz-Coranguez, et al., *The inner blood-retinal barrier: Cellular basis and development*, 2017 VISION RES 139, 123-37 (2017) (filed as Supp. Ex. 43, Ref. No. 4). Dr. Akbari reported that the "[i]nfluenza vaccine is known to induce specific T cells that can disrupt BRB and cause optic neuritis." Fourth Akbari Rep. at 3, *citing* Kebir, et al., *Human TH17 lymphocytes promote blood-brain barrier disruption and central nervous system inflammation*, 2007 NAT MED 13, 1173-75 (2007) (filed as Supp. Ex. 43, Ref. No. 5).

### B. Expert Testimony re: Medical Theory of Causation

#### 1. Dr. Akbari's Expert Testimony

Dr. Akbari testified that molecular mimicry via the influenza vaccine was a substantial factor in Petitioner's development of optic neuritis. Tr. at 21, 23-24. Dr. Akbari presented the court with a power point presentation thoroughly laying out his theory connecting the flu vaccine to Petitioner's ON via molecular mimicry. *See* Ex. 34.

First, Dr. Akbari discussed the Nachamkin article, which found that H1N1 vaccines contain structures that can induce anti-ganglioside antibodies in mice. Tr. at 48-49. Nachamkin provides evidence that the H1N1 vaccine is capable of triggering an autoimmune response resulting in a demyelinating disease. *Id*.

Next, Dr. Akbari discussed the Weilbach article, which found that rats injected with T cells targeted to attack MBP (a component of the myelin sheath) started to experience blindness due to demyelination of the nervous system. Tr. at 49-51. Similarly, Bajramovic found that rhesus monkeys injected with T cells targeted to attack oligodendrocyte-specific protein resulted in inflammatory responses throughout the central nervous system, specifically causing demyelination of the optic nerve resulting in blindness. *Id*. According to Dr. Akbari, both Weilbach and Bajramovic provide evidence that autoreactive T cells are capable of damaging the central nervous system ("CNS") and causing blindness. *Id*.

Finally, Dr. Akbari discussed the two Wucherpfennig studies which found that T cells isolated from the blood of patients with multiple sclerosis, based upon their reactivity to MBP, share a peptide sequence with the flu virus. Tr. at 51-52. The Wucherpfennig studies provide an example of molecular mimicry with influenza strains contained in the same vaccine that Petitioner received. Tr. at 52.

[8] Dr. Akbari's Fourth Report was filed after the entitlement hearing, with permission of the court, given that Dr. Vartanian's Second Report and supporting literature was filed fewer than 10 days before the hearing and raised new issues not presented in his first report.

To tie all of this research together, Dr. Akbari discussed Karussis, which he explained is not a single case study but a meta-analysis. Tr. at 53. Karussis collected all of the reported adverse events related to vaccines in the United States from 1979-2003. *Id*. The search located a total of 71 reported cases, 21 of those specifically related to the flu vaccine. *Id*. Of those 21 cases, nine reported optic neuritis as the adverse effect.[9] Tr. at 54. According to Dr. Akbari, Karussis is evidence of a real-world association between the flu vaccine and the development of ON in human beings. Tr. at 55.

Dr. Akbari testified that the low rate of autoimmune responses following vaccination is a testament to the safety of vaccines and the efficiency of the immune system. Tr. at 62-63. Yet, "safety and rarity do not rule out the scientific plausibility[10] of adverse immune responses." *Id.* at 63. Dr. Akbari opined that in addition to a molecular mimic triggering an autoimmune response, Petitioner did not have a sufficient level of regulatory T cells to contain that response, and that is why he developed optic neuritis following his influenza vaccination. *Id.* at 79.

In the absence of a clinical lab test that can prove that the flu vaccine caused Petitioner's optic neuritis via molecular mimicry, Dr. Akbari testified that one must make a determination based on many factors including the medical history of that particular patient, the timing of clinical presentation of symptoms, the composition of the vaccine, and the existence of clinical factors to support a diagnosis. *Id.* at 74. Having considered the totality of the circumstances in this case, Dr. Akbari is of the opinion that it is more than 51% likely that the flu vaccine was a substantial factor causing Petitioner's condition. *Id.*

Highly relevant to this case, in Dr. Akbari's opinion, is the fact that Petitioner developed ON after receiving his first ever influenza vaccination. Tr. at 98. Many people get the flu vaccine every year. *Id.* If something goes wrong after the 10th, 11th, or 12th vaccination, one needs "to look at what were the difference between that particular influenza vaccine or situation of that day or situation of patient at the time, and others." *Id*. When a person develops a reaction to a vaccine after the first one, that has to be one of the factors considered as playing an important role. *Id.* at 98-99.

According to Dr. Akbari, another highly relevant factor is that the Afluria package insert warns that "Neurological disorders temporally associated with influenza vaccination, such as optic neuritis, have been reported." Tr. at 83; Ex. 2. Petitioner began to experience vision loss approximately 12 days after receiving the Alfuria vaccine, consistent with the onset of symptoms reported in Karussis. Tr. at 84-85.

2. Dr. Vartanian's Expert Testimony

Dr. Vartanian testified that molecular mimicry, as it has been presented, is a nonviable hypothesis, based on a lack of evidence. Tr. at 315, 333. Dr. Vartanian believes the theory is flawed on the grounds that a six amino acid sequence is too short to be of any relevance. *Id.* at 331-33.

[9] Two other demyelinating diseases were also reported in relation to the influenza virus: myelitis and encephalitis. Tr. at 82.

[10] *See supra* note 5.

Dr. Vartanian quoted Trost which revealed that human proteins share thousands of matches with bacterial and viral peptides suggesting "that autoimmune diseases should have a much higher incidence than actually observed, both in the total number of individuals affected and the number of autoimmune pathologies per individual." *Id.* at 333, *quoting* Trost.

Dr. Vartanian testified at length regarding Dr. Akbari's failure to show that the influenza vaccine contains an adjuvant capable of penetrating the blood brain barrier of the CNS. Citing the Brabb study, Dr. Vartanian listed two requirements for inducing a demyelinating autoimmune disease: (1) exposure to an organism/bacteria/virus/vaccine that activates the immune response in the periphery, and (2) penetration, via damage, to the CNS barriers. Tr. at 335, Brabb, et al., *Triggers of autoimmune disease in a murine TCR-transgenic model for multiple sclerosis*, 159 J IMMUNOL 1, 497-507 (1997) (filed as Ex. J); *see also* Owens, et al., *Perivascular spaces and the two steps to neuroinflammation*, 67 J NEUROPATHOL EXP NEUROL 12, 1113-21 (2008) (filed as Ex. P). In animal models, for example, simply injecting an animal with MBP will not trigger a demyelinating disease unless you add the pertussis toxin which targets and opens the BBB. Tr. at 335-37. Dr. Vartanian found nothing in the influenza vaccine that would allow it to breach the BBB. *Id.* at 346.

### C. Expert Reports re: *Althen* Prongs Two and Three

All of Petitioner's experts agree with Petitioner's diagnosis of vaccine-induced ON. Dr. Cestari, Dr. Turner and Dr. Vartanian spent a great deal of time debating whether ON was the proper diagnosis in their reports. At the entitlement hearing Dr. Vartanian agreed that bilateral optic neuritis was the most likely diagnosis; however, he does not believe that it was vaccine-induced. Tr. at 354. Instead, Dr. Vartanian suggested that Petitioner's condition was anti-MOG[11] induced. My discussion of the expert reports and testimony will be limited to that issue.

#### 1. Dr. Schatz's Report

On April 23, 2020, Petitioner filed an expert report authored by Dr. Martha Schatz. Ex. 32 (hereinafter "Schatz Rep."). Dr. Schatz is a board-certified ophthalmologist specializing in neuro-ophthalmology. Ex. 42 at 2 (hereinafter "Schatz CV"). She is a Professor of Clinical Ophthalmology at University of Texas Health Science Center of San Antonio. *Id*. at 1. Dr. Schatz has maintained a clinical practice since 1998 and is currently the Chief Ophthalmologist at Pediatric Ophthalmologist Service. *Id*. at 14. She is published in a variety of peer reviewed journals and is regularly invited to speak on topics related to neuro-ophthalmology. *Id*. at 9-11. Dr. Schatz served as Petitioner's treating physician during his stay at University Hospital.

Dr. Schatz's report explains her reasons for ultimately diagnosing Petitioner with post-vaccine ON: (1) the temporal association between the vaccination and his vision loss, and (2) his

[11] MOG stands for myelin oligodendrocyte glycoprotein. Tr. at 193. MOG proteins provide structural integrity to the myelin sheath. Tr. at 193. When anti-MOG antibodies attack the MOG proteins, they cause demyelination. Tr. at 194.

symptoms were more characteristic of other reported cases of post-vaccine ON, despite the fact that those cases are rare. *Id*. at 5. Petitioner was not responsive to any treatments for other known causes of bilateral optic neuritis, such as NMO-Spectrum and anti-MOG, and all other possible etiologies had been ruled out. *Id*. at 4-5. "Some would suggest that [Petitioner] had simply idiopathic optic neuritis, a diagnosis used when there is no other cause definitely found when a patient presents with his first episode. However, [Petitioner] did have another probable etiology - his first influenza vaccination two weeks prior to vision loss." *Id*. at 5.

2. Dr. Cestari's First Report

Petitioner filed Dr. Cestari's first report as an exhibit accompanying his petition. Ex. 1 (hereinafter "First Cestari Rep."). Dr. Cestari received his B.A. from Colgate University and his M.D. from Tel Aviv University. Ex. 15 at 2 (hereinafter "Cestari CV"). He is board certified as a neurologist and ophthalmologist. *Id*. He is one of roughly ten neuro-ophthalmology specialists in the United States. Tr. at 166. Dr. Cestari subspecializes in optic nerve disease and in treating double vision. *Id*. He is a professor of Ophthalmology at Harvard Medical School and an assistant clinical professor of Optometry at the New England College of Optometry. Cestari CV at 3. Dr. Cestari has had an active medical and surgical practice at Massachusetts Eye and Ear Infirmary since 2006, where he also serves as the fellowship director of neuropathology. *Id.* at 35; Tr. at 168. He performs clinical and translational research, is well published in many peer-reviewed publications, and regularly gives local, regional, national and international talks. Cestari CV at 29-32; Tr. at 169-72.

Dr. Cestari reviewed Petitioner's medical records and agreed with the diagnosis of vaccine-induced bilateral optic neuritis. "Influenza vaccination-associated optic neuritis is a rare occurrence and its diagnosis is one of exclusion and can only be made when all other possible causes are ruled out." First Cestari Rep. at 16. Dr. Cestari emphasized that he has rarely seen "a more complete, thorough and exhaustive evaluation and work up looking for an etiology of a bilateral optic neuropathy that included four MRIs of the brain and orbits as well as every conceivable blood test and a spinal tap." *Id.* at 17. It is Dr. Cestari's opinion that, given the extensive negative medical findings, the theory of how a vaccine can induce optic neuritis presented by Dr. Akbari, and the temporal relationship between the onset of visual symptoms 12 to 14 days following flu vaccine, "the only possible explanation for Petitioner's signs and symptoms is a post vaccination optic neuritis." *Id*.

Dr. Cestari explained that proving causation of an extremely rare side effect can be difficult, and that clinicians often rely on published case reports to lend support to a causal relationship between a mediation and a side effect. First Cestari Rep. at 14. "The most convincing support for a causal relationship between the influenza vaccine and optic neuritis comes from a report of a challenge-rechallenge case in which a 59-year-old woman developed bilateral optic neuritis on 2 separate occasions, 1 year apart, after consecutive annual influenza vaccinations." First Cestari Rep. at 16; *see also*, *Id.* at 14. T.P. Hull & J.H. Bates, *Optic neuritis after influenza vaccination,* 124 AM J OPHTHALMOL 5, 703-04. (1997) (filed as Ex. 14, Ref. No. 39) (hereinafter "Hull").

For proof of a temporal relationship, Dr. Cestari cited to the Stübgen article, showing that as of 2013, there have been 38 reports of presumed post-vaccination optic neuritis, either bilateral or unilateral, all occurring an average of two to three weeks after vaccination. First Cestari Rep. at 15; *see also* Stübgen, J.P., *A literature review on optic neuritis following vaccination against virus infections*, 12 AUTOIMMUN REV 10, 990-97 (2013) (filed as Ex. 14, Ref. No. 14) (hereinafter "Stübgen").

3. Dr. Vartanian's First Report

Dr. Vartanian's first report mainly disputed Petitioner's diagnosis on the grounds that optic neuritis is almost always contrast-enhancing on MRI, and Petitioner's MRIs were normal. First Vartanian Rep. at 9.[12]

Dr. Vartanian does not agree that Petitioner's work-up excluded all other known causes of bilateral optic neuritis on the grounds that the empirical treatment for suspected NMO and anti-MOG-related ON was neither sufficient nor diagnostically informative. First Vartanian Report at 10. He argued that case reports do not prove causation and concluded: "To a reasonable degree of medical certainty, the visual loss experienced by petitioner is not due to vaccine-induced inflammatory/autoimmune optic neuritis." *Id*. at 13.

4. Dr. Turner's First Report

Dr. Turner's first report was limited to his review of Petitioner's MRIs and his opinion that the MRIs represent an inflammatory optic neuritis. *See generally*, First Tuner Rep.

5. Dr. Turner's Second Report

In his second report, Dr. Turner opined that the "optimum timing for MRI enhancement of the optic nerve is within 4 weeks of symptomatology." Second Tuner Rep. at 1; *see also* Zhang, et al., *MRI texture heterogeneity in the optic nerve predicts visual recovery after optic neuritis*, 2014 NEUROIMAGE CLIN. 4, 302-07 (2014) (filed as Supp Ex. 29, Ref. No. 1) (hereinafter "Zhang"). Thus, in Dr. Turner's opinion, the MRI studies conducted at University Hospital on October 27, 2016 are consistent with a vaccine injury. *Id*. at 2. He stated: "Although the MRI does not indicate causality between the vaccine and Petitioner's clinical state, it does support a temporal relationship." *Id*.

6. Dr. Cestari's Second Report

In his second report, Dr. Cestari stated that Petitioner has atypical bilateral ON, and that atypical bilateral ON can usually be attributed to one of three identifiable causes: NMO, anti-MOG, or vaccination. Second Cestari Rep. at 9. Petitioner's symptoms were inconsistent with a diagnosis of either NMO or anti-MOG induced ON, leaving vaccine-induced ON as the only viable etiology. *Id*. at 11.

[12] This opinion was later retracted at the evidentiary hearing after Dr. Vartanian had an opportunity to review Dr. Turner's reports. Tr. at 354.

Dr. Cestari reported that Petitioner did not and still does not fit the anti-MOG clinical profile. *See* discussion of anti-MOG clinical characteristics *infra* at 16.

7. Dr. Vartanian's Second Report

Dr. Vartanian argued that anti-MOG should not be ruled out, especially now that anti-MOG testing is available. Second Vartanian Rep. at 8. Dr. Vartanian stressed that Petitioner should be tested, and if the tests come back positive, Petitioner can be treated to avoid a relapse. *Id*. at 8.

Dr. Vartanian also stated that: "The distinguishing features of anti-MOG NMO are dramatic swelling of the intro-ocular segment of the optic nerve, longitudinal twisting of the optic nerve, and peri-neural enhancement, none of which I see in the [MRIs] taken from petitioner." Second Vartanian Rep. at 5.

8. Dr. Cestari's Third Report

Dr. Cestari's third report criticized Dr. Vartanian's suggestion that Petitioner should undergo anti-MOG testing on the grounds that "he DOCUMENTS IN HIS REPORT THAT MR. REINHARDT'S MRI FINDINGS ARE INCONSISTENT WITH ANTI-MOG OPTIC NEURITIS and I agree!!!" Third Cestari Rep. at 13 (emphasis in original). Consequently, "there is no reason to obtain anti-MOG testing now. Mr. Reinhardt does not fit the clinical or radiologic profile of a patient with anti-MOG optic neuritis. He has had no recurrences of optic neuritis." *Id*.

9. Dr. Tuner's Third Report

In his third report, Dr. Turner stated that his review of Petitioner's MRIs did not reveal any anti-MOG characteristics. Third Turner Rep. at 1. Dr. Turner also noted that Dr. Vartanian refuted his own theory by admitting that Petitioner's MRIs do not support an anti-MOG diagnosis. *Id*. at 2.

**D. Expert Testimony re: *Althen* Prongs Two and Three**

1. Dr. Schatz's Testimony

Dr. Schatz's testified that by empirically treating Petitioner with corticosteroids, the treating team was able to rule out anti-MOG induced ON. After receiving IV steroids followed by three months of oral steroids "[h]is disk swelling slowly receded, went down, and his vision -- and his visual field never returned." Tr. at 124; *see also* Ex. 5 at 72; Ex. 9 at 17. Furthermore, even had anti-MOG testing been available in 2016, Petitioner did not fit the clinical profile, and testing Petitioner now would not reveal anything about his immune status back in 2016. Tr. at 137, 158.

In addition to excluding other possible etiologies, Dr. Schatz testified that there "were features of [Petitioner's] case that stood out as specific for vaccine-related optic neuritis." Tr. at 153. One was the temporal course of his presentation, 12 days after his first ever influenza vaccine. Additionally, although there is no established medical literature discussing the clinical conditions

of vaccine-induced ON, Dr. Schatz testified that anecdotal case reports do exist; and when compared to case reports concerning anti-MOG related ON, Petitioner's symptoms were more consistent with the vaccine-related cases. Tr. at 154, 161.

2. Dr. Cestari's Testimony

Dr. Cestari testified that although anti-MOG induced ON is a relatively new clinical entity, it was once considered to be an extension of multiple sclerosis. Tr. at 134. Thus, researchers have known about it and written about it for a long time. *Id.* Dr. Cestari testified that so much anti-MOG research and literature exists that we can get a good sense of what does and does not fit the clinical profile. *Id.*at 402. After considering the anti-MOG literature, Dr. Cestari opined that "the preponderance of evidence does not support that diagnosis." *Id.* at 395.

Anti-MOG associated optic neuritis has distinct clinical manifestations. Tr. at 195. It typically occurs in young women. *Id.* at 395. It is usually unilateral, and it is usually associated with a good prognosis. *Id.* In general, about half of patients will have complete recovery or significant recovery if treated with corticosteroids. *Id.* at 195. But the "hallmark of patients with anti-MOG antibodies and optic neuritis is recurrence." *Id.* at 194. Autoimmune diseases naturally have a tendency to recur because there is a chronic ongoing level of inflammation, and in anti-MOG patients the rate of recurrence is 80-84% within one year. *Id.* at 197-98, 403, 404.

When compared to vaccine-induced ON, "there should not be recurrence if there was a one-time trigger." Tr. at 197. Petitioner has gone almost four years without any recurring symptoms, and the proper diagnosis becomes clearer the longer you wait. *Id.* at 404. "I would expect that within three and a half years, if this was anti-MOG optic neuritis, and he's not on maintenance, therapy [for] immunosuppression, he should have another event, and he hasn't." *Id.*

Dr. Cestari also testified that Petitioner received a flu vaccination 12 days prior to the onset of his symptoms, so that has to be a consideration. Tr. at 395. We know that the Afluria insert warns that cases of optic neuritis have been reported post-vaccination. *Id.* As a neuro-ophthalmologist, when a patient presents with some kind of vision loss, part of Dr. Cestari's review is to ask, "have you had any kind of immunization in the last 30 days, because we know that the literature, medical literature, supports the possibility that this could happen." *Id.* at 398. In Dr. Cestari's opinion "the preponderance of evidence makes it much more likely that the influenza vaccination that Petitioner received substantially contributed to the development of his optic neuritis." *Id.* at 399.

3. Dr. Turner's Testimony

Dr. Turner testified that his review of Petitioner's MRIs revealed that they were 100 percent abnormal. Tr. at 275. On October 27, 2016, both of Petitioner's optic nerves were showing enhancement. *Id.* at 275-76. "So, without question, the MRI study, you can take this to the bank on this one image alone, shows enhancement." *Id.*; *see also* Supp. Ex. 5 (Image 9 Series 13001).

Dr. Turner does not believe that Petitioner's MRIs exhibited any of the radiological features of anti-MOG ON. Tr. at 299-300. The Chen article found that the MRIs of anti-MOG

patients show long segment (more than 50%) enhancement of the anterior segment of both optic nerves, perioptic soft tissue involvement, and enhancement of the optic nerve sheath." *Id.* at 297; *see also* Chen, et al., *Myelin Oligodendrocyte Glycoprotein Antibody (MOG-lgG)-Positive Optic Neuritis: Clinical Characteristics, Radiologic Clues and Outcome*, 2018 AM. J. OPTHALMOL. 195, 8-15 (2018) (filed as Ex. 38, Ref. No. 6). According to Dr. Turner, Petitioner's MRIs did not show involvement of the perioptic soft tissue or enhancement of the optic nerve sheath. *Id.* at 297. Petitioner's optic nerve enhancement was roughly 7 millimeters in a 5-centimeter structure – certainly not more than 50%. *Id*. As referenced in Dr. Vartanian's second report, Dr. Turner also did not observe any longitudinal twisting of the optic nerve or paraneural enhancement." Tr. at 299.

4. Dr. Vartanian's Testimony

Dr. Vartanian does not believe that the evidence is sufficient to prove that Petitioner's ON was vaccine induced. Tr. at 324. According to Dr. Vartanian, everyone agrees that this is a complex and unusual case, but "[n]o one can say, with authority, that this is vaccine related when there is no vaccine related clinical syndrome that is well described." Tr. at 326, 328. Dr. Vartanian testified that case reports are completely unreliable in connection with vaccine-induced autoimmune diseases "when you think of how frequent vaccines -- influenza vaccines are given to how many people, the -- you know, pure chance of someone getting a vaccine and two weeks, three weeks, a month later having some clinical event is actually quite high." *Id.* at 345-46.

Dr. Vartanian is of the opinion that the most appropriate diagnosis for Petitioner is anti-MOG induced ON. Tr. at 325. Dr. Vartanian testified that as an autoimmune condition, anti-MOG fits nicely with Petitioner's molecular mimicry theory. *Id.* at 328. Yet, Dr. Vartanian admitted that Petitioner does not fit the classical clinical presentation of anti-MOG ON. In discussing this apparent contradiction, Dr. Vartanian testified that not every patient presents with the same clinical features, and that Petitioner has an atypical form of anti-MOG ON. *Id.* at 326, 377. "Unusual presentations, uncommon presentations, partial, you know, phenotypes happen all the time." *Id.* at 367.

## IV. Applicable Law

### A. Petitioner's Burden in Vaccine Program Cases

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

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

Under the first prong of *Althen*, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs*., 35 F.3d 543, 548 (Fed. Cir. 1994). Proof that the proffered medical theory is reasonable, plausible, or possible does not satisfy a petitioner's burden. *Boatmon v. Sec'y of Health & Hum. Servs*., 941 F.3d 1351, 1359-60 (Fed. Cir. Nov. 7, 2019).

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). However, special masters are "entitled to require some indicia of reliability to support the assertion of the expert witness." *Boatmon*, 941 F.3d at 1360, *quoting Moberly*, 592 F.3d at 1324. Special Masters, despite their expertise, are not empowered by statute to conclusively resolve what are complex scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Hum. Servs*., 121 Fed. Cl. 230, 245 (2015), *vacated on other grounds*, 844 F.3d 1363 (Fed. Cir. 2017); *see also Hock v. Sec'y of Health & Hum. Servs*., No. 17-168V, 2020 U.S. Claims LEXIS 2202 at *52 (Fed. Cl. Spec. Mstr. Sept. 30, 2020).

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

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence also present in the record. *Hibbard v. Sec'y of Health & Hum. Servs*., 100 Fed. Cl. 742, 749 (2011), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Caves v. Sec'y of Health & Hum. Servs*., No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 Fed. App'x 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Hum. Servs*., 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Hum. Servs*., 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem*., 503 F. App'x 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs*., No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

### B. Law Governing Analysis of Fact Evidence

The parties agree that there are no medical facts in dispute with respect to Petitioner's medical records and Petitioner's timeline of symptoms. Joint Submission at 8, ECF No. 83; *see also* Ex. 11 (Petitioner Timeline of Symptoms). Accordingly, Petitioner's medical records are presumed to accurate and complete and are afforded substantial weight. *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Hum. Servs*., 95 Fed. Cl. 598, 608 (2010); *Lowrie v. Sec'y of Health & Hum. Servs.*, No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005).

### C. Analysis of Expert Testimony

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

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora. *Daubert* factors are employed by judges to exclude evidence that is unreliable and potentially confusing to a jury. In Vaccine Program cases, these factors are used in the weighing of the reliability of scientific evidence. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted").

Respondent frequently offers one or more experts of his own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)). A "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly*, 592 F.3d at 1324. Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Id.* at 1325-26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations").

### D. Consideration of Medical Literature

Although this decision discusses some but not all of the medical literature in detail, I reviewed and considered all of the medical records and literature submitted in this matter. *See Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though [s]he does not explicitly reference such evidence in h[er] decision."); *Simanski v. Sec'y of Health & Hum. Servs.*, 115 Fed. Cl. 407, 436 (2014) ("[A] Special Master is 'not required to discuss every piece of evidence or testimony in her decision.'" (citation omitted)), *aff'd*, 601 F. App'x 982 (Fed. Cir. 2015).

## V. Analysis

### A. Preponderant Evidence Establishes that Petitioner Suffers from ON

Dr. Vartanian suggests that anti-MOG induced ON is the more appropriate diagnosis in this case. Tr. at 325. Yet, Dr. Vartanian admits that Petitioner does not fit the clinical profile. Second Vartanian Rep. at 5.; Tr. at 368-71. He claims that Petitioner has a rare or atypical form of anti-MOG but did not provide any medical literature in support of his theory. Tr. at 372-73. The lack of medical literature, he argues, is due to the fact that anti-MOG ON is a relatively new entity and the medical research is evolving. *Id.* at 374.

Ultimately, Dr. Vartanian's criticisms of the vaccine-induced diagnosis come down to a disagreement concerning Petitioner's clinical course of treatment: "regardless of the case and its outcome," if he were my patient he would be checked repeatedly for aquaporin-4 and anti-MOG every few months, at least for a year or two. Tr. at 324, 375. The fact that Petitioner has not only surpassed the two years of testing proposed by Dr. Vartanian without a relapse but has also gone more than five years now without a relapse is sufficient to persuade me that Petitioner's condition was not anti-MOG induced. My finding is based on Dr. Cestari's testimony that recurrence is the hallmark of anti-MOG optic neuritis, and on the medical literature submitted by both Dr. Cestari and Dr. Vartanian. *See* Cobo-Calvo, et al., *MOG antibody-related disorders: common features and uncommon presentations*, 264 J NEUROL 9, 1945-55 (2017) (finding a relapsing course in 44–83%

of patients more commonly involving the optic nerve) (filed as Ex. D); Jarius, et al., *MOG-IgG in NMO and related disorders: a multicenter study of 50 patients, Part 2: Epidemiology, clinical presentation, radiological and laboratory features, treatment responses, and long-term outcome*, 2016 13 J NEUROINFLAMMATION 279 (2016) (filed as Ex. 38, Supp. Ref. No. 12) (finding that of the 50 MOG-IgG-positive patients studied, 80% first relapsed within a median of 5 months and concluding MOG-IgG-related CNS autoimmunity requires consistent treatment and care); Ramanathan, et al., *Antibodies to myelin oligodendrocyte glycoprotein in bilateral and recurrent optic neuritis*, 1 NEUROIMMUNOL NEUROINFLAMM 4, (2014) (MOG antibody–associated BON is a relapsing disorder that is frequently steroid responsive and often steroid dependent) (filed as Ex. N).

I have also considered the relative strength of the expert opinions in this case. While Dr. Vartanian is clearly qualified to opine on the matters before the court, Dr. Cestari is one of approximately ten neuro-ophthalmology specialists in the United States. He subspecializes in optic nerve disease and treats patients for these conditions. Because of this expertise, I have given greater weight to his opinion than to that of Dr. Vartanian.

I will next address each of the *Althen* prongs in the order of their significance to this case.

**B. *Althen* Prong One**

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

Petitioner has alleged an "off-Table" injury, and thus must prove by preponderant evidence a medical theory causally connecting the flu vaccine to his bilateral optic neuritis. Petitioner theorizes that the flu vaccine caused his ON by means of molecular mimicry. The theory of molecular mimicry explains how an infection or vaccine can lead to an autoimmune disease. First Akbari Rep. at 4. When a foreign antigen and an antigen produced by the body share certain attributes, such as similar protein peptides or a similar structural architecture, the immune system can mistakenly attack the self-produced antigen due to its similarities with the foreign "mimic." First Akbari Rep. at 5; Tr. at 25, 31. A demyelinating disease is an autoimmune disease that occurs when the immune system attacks part of the body's central nervous system. Tr. at 27.

The optic nerve is part of the CNS and is surrounded by a myelin sheath, similar to the rubber coating around a copper wire. Tr. at 193. The myelin sheath insulates the optic nerve and ensures that the electric impulses to and from the nerve are transmitted efficiently. *Id.* When the myelin sheath is damaged due to an autoimmune disease, it results in a demyelinating disease, i.e., optic neuritis. *Id.* at 21.

At the outset, I note that the Vaccine Program generally recognizes that the flu vaccine is capable of causing a demyelinating condition. Notably, Guillain-Barré syndrome is recognized as an "on-Table" injury caused by seasonal influenza vaccines. 42 C.F.R. § 100.3(a)(XIV)(D). With

respect to "off-Table" injuries, the following cases have held that the flu vaccine caused or significantly aggravated a CNS demyelinating condition: *Hitt v. Sec'y of Health & Hum. Servs.*, No. 15-1283V, 2020 WL 831822 (Fed. Cl. Spec. Mstr. Jan. 24, 2020) (finding the flu vaccine caused the Petitioner's MS); *Calise v. Sec'y of Health & Hum. Servs.*, No. 08-865V, 2011 WL 1230155, at *27 (Fed. Cl. Spec. Mstr. March 14, 2011) (finding that the flu vaccine is capable of breaching the blood-brain barrier and triggering NMO); *Brown v. Sec'y of Health & Hum. Servs.*, No. 09-426V, 2011 WL 5029865, at *41 (Fed. Cl. Spec. Mstr. Sept. 30, 2011) (finding the flu vaccine caused Petitioner's ADEM); *Hayes v. Sec'y of Health & Hum. Servs.*, No. 06-738V, 2010 WL 2985632, at *3 (Fed. Cl. Spec. Mstr. July 12, 2010) (finding that, by the process of molecular mimicry, the flu vaccine was a substantial cause of Petitioner's transverse myelitis, ADEM, bilateral optic neuritis, and developmental delay).

Molecular mimicry is also a well-established theory in the Vaccine Program and has been persuasively linked to different immune-mediated conditions. *See e.g. W.C. v. Sec'y of Health & Hum. Servs.*, No. 07-456V, 2011 WL 4537877, at *11 (Fed. Cl. Spec. Mstr. Feb. 22, 2011), (finding that molecular mimicry is a well-regarded theory in some contexts), *mot. for rev. denied*, 100 Fed. Cl. 440 (2011), *aff'd*, 704 F.3d 1352 (Fed. Cir. 2013); *H.J. v. Sec'y of Health & Hum. Servs.*, No. 011-0301V, 2015 WL 6848357 (Fed. Cl. Spec. Mstr. Nov. 6, 2015) (finding that Petitioner's Rheumatoid Arthritis was more likely than not caused by molecular mimicry following the Tdap vaccine); *Day v. Sec'y of Health & Hum. Servs*, No. 12-630V, 2016 WL 6237236 (Fed. Cl. Spec. Mstr. Nov. 15, 2015) (finding that Gardasil and flu vaccine led Petitioner to develop neuromyelitis optica via molecular mimicry); *Salmins v. Sec'y of Health & Hum. Servs*., No. 11–140V, 2014 WL 1569478 (Fed. Cl. Spec. Mstr. Mar. 31, 2014) (finding that HPV vaccine caused Petitioner to develop GBS via molecular mimicry); *Roberts v. Sec'y of Health & Hum. Servs.*, No. 09-427V, 2013 WL 5314698 (Fed. Cl. Spec. Mstr. Aug. 29, 2013) (finding that Tdap vaccine led Petitioner to develop transverse myelitis via molecular mimicry ); *Hayes*, 2010 WL 2985632, at *3 (finding that, by the process of molecular mimicry, the flu vaccine was a substantial cause of Petitioner's transverse myelitis, ADEM, bilateral optic neuritis, and developmental delay).

Dr. Akbari testified that Petitioner's first flu vaccination contained components that share a similar structure or sequence with components of the myelin sheath, and more likely than not, the flu vaccine triggered an autoimmune response that was capable of penetrating the CNS and damaging Petitioner's optic nerve. A central component of Dr. Akbari's theory is that certain people may be predisposed to autoimmunity, thus accounting for the low rate of autoimmune responses following vaccination.

Several studies support Dr. Akbari's theory in this case. The Wucherpfennig studies demonstrate that T cells isolated from the blood of patients with multiple sclerosis share a peptide sequence with the flu virus. Tr. at 51-52. These studies provide an example of molecular mimicry with influenza strains contained in the same vaccine that Petitioner received. *Id.* at 52.

The Nachamkin article found that H1N1 vaccines contain structures that can induce anti-ganglioside antibodies in mice. Tr. at 48-49. Nachamkin provides evidence that the H1N1 vaccine (a component of which was included in Petitioner's 2016 flu vaccine) is capable of triggering an autoimmune response resulting in a demyelinating disease. *Id.*

Additionally, the Karussis meta-analysis described nine reported cases of optic neuritis following flu vaccine. *See* Ex. 19, Ref. No. 26. While case reports are not robust evidence, they do constitute some evidence with which petitioners can meet their burden in the Vaccine Program. *See Contreras v. Sec'y of Health & Hum. Servs.*, 107 Fed. C. 280 (Fed. Cl. 2012); *see also Capizzano* 440 F.3d at 1325-26.

Dr. Vartanian's discussion of epidemiologic studies, animal models and identification of specific peptide structure/sequences and molecular mimics before attributing causality to the flu vaccine is contrary to Vaccine Program case law. Petitioners are not required to identify "specific biological mechanisms" to establish causation, nor are they required to present "epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities." *Capizzano*, 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280). It is not Petitioner's burden to prove his theory with this level of specificity. *Knudsen*, 35 F.3d at 549.

In evaluating the evidence that has been presented, I find that Dr. Akbari has provided a sound and reliable medical theory demonstrating that the flu vaccine can cause bilateral optic neuritis. Accordingly, I find that Petitioner has carried his burden of proof with respect to the first *Althen* prong.

**B. *Althen* Prong Three**

Under *Althen* prong three, a petitioner must establish the "timeframe forwhich it is medically acceptable to infer causation," and he must demonstrate that the onset of his disease occurred within that timeframe. *Shapiro v. Sec'y of Health & Hum. Servs.,* 101 Fed. Cl. 532, 542-43 (2011), *recons. denied after remand on other grounds*, 105 Fed. Cl. 353 (2012), *aff'd without op.,* 503 F. App'x 952 (Fed. Cir. 2013). Petitioner received the flu vaccine on October 11, 2016. On October 23, 2016, Petitioner first reported symptoms of ON, 12 days following his vaccination. Both sides agree that Petitioner experienced his first clinical sign of ON on this date. Joint Submission at 8, ECF No. 83; *see also* Ex. 11 (Petitioner Timeline of Symptoms).

Dr. Schatz testified that the onset of Petitioner's disease 12 days after his flu vaccination is a medically acceptable temporal interval and consistent with the theory of molecular mimicry. Tr. at 143-44. Dr. Akbari explained that after immunization, it takes three to five days for the antigen to get picked up by an antigen-presenting cell. Tr. at 97. Any adverse immune reaction would generally begin around day five, peaking around days seven to ten. *Id.* Both Dr. Akbari and Dr. Cestari provided evidence demonstrating that two to three weeks was the average timeframe for the onset of ON following a flu vaccination. Dr. Akbari cited Karussis in which the meta-data reflected the onset of ON following the flu vaccination occurred at an average of two to three weeks. *Id.* at 54. Dr. Cestari discussed the Stübgen and Hull articles evidencing a two to three-week temporal relationship. First Cestari Rep. at 14-15.

Petitioner also cited to Shindler in support of the third *Althen* prong. *See* Shindler, et al., *Retinal ganglion cell loss induced by acute optic neuritis in a relapsing model of multiple sclerosis*, 12 MULTIPLE SCLEROSIS 526-32 (2006) (filed as Ex. 43, Ref. No. 23) (hereinafter "Shindler"). In

this study, the authors examined the relationship between inflammation and retinal ganglion cell loss during acute optic neuritis. Shindler at 526. During the course of the study, the authors found that "No optic neuritis was detected prior to day 9 following immunization. Incidence of optic neuritis was 30% at day 9 and increased to over 70% by day 11, remaining high through day 18." *Id.* Although the mice in this study were immunized with proteolipid protein peptide 139_151 and not the flu vaccine, this study does provide some support for Petitioner's contention that the onset of ON 12 days after vaccination was medically appropriate.

I also note that Dr. Vartanian testified he did not dispute any of the expert reports with respect to the concept that 12-14 days "fits within our temporal understanding of when T cell and antibody responses are generated." Tr. at 356.

Based on the existing medical literature and expert testimony, I find that onset of ON 12 days after flu vaccination is an acceptable timeframe in which to infer causation. I further find that Petitioner has established the onset of his symptoms occurred within that timeframe. Petitioner has satisfied the third *Althen* prong.

### C. *Althen* Prong Two

Under *Althen's* second prong, a petitioner must "prove a logical sequence of cause and effect showing that the vaccination was the reason for the injury." *Althen*, 418 F.3d at 1278.

The fact that Petitioner has already established *Althen* prongs one and three bolsters his ability to establish that the flu vaccination was in fact the cause of his condition. "Medical opinions that explain how a vaccine can cause the injury alleged coupled with evidence demonstrating a close temporal relationship "are quite probative" in proving actual causation. *Capizzano*, 440 F.3d at 1358; *see also Contreras*, 107 Fed. Cl. at 295 (finding that there is a "logical overlap between the three *Althen* prongs, and evidence that goes towards proving one prong may also be probative for another").

#### 1. Petitioner's Treating Physician

Dr. Schatz's explained the exhaustive testing and treatment that Petitioner had undergone prior to receiving the diagnosis of vaccine-induced ON. Schatz Rep. at 2. In addition to ruling out all other possible etiologies for bilateral optic neuritis, she highlighted the importance of this being Petitioner's first flu vaccination. *Id*. at 5. "Some would suggest that [Petitioner] had simply idiopathic optic neuritis, a diagnosis used when there is no other cause definitely found when a patient presents with his first episode. However, [Petitioner] did have another probable etiology - his first influenza vaccination two weeks prior to vision loss." *Id*. Because she is Petitioner's treating physician, I find Dr. Schatz's opinion to be especially probative. In weighing the evidence in Vaccine Program cases, the opinions of treating physicians are favored "as they 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." *Althen*, 418 F.3d at 1280.

Dr. Schatz's diagnosis is supported by both Dr. Cestari and Dr. Turner. It is Dr. Cestari's opinion that, "Given the extensive negative work-up, the biologically plausible theory of how a

vaccine can induce optic neuritis and the temporal relationship of the onset of visual symptoms 12 to 14 days following receiving the influenza vaccination, the only possible explanation for Petitioner's signs and symptoms is a post vaccination optic neuritis." *Id*.

I find Dr. Schatz's assessment of Petitioner's condition to be reasonable and persuasive. I find that the flu vaccine, more likely than not, *did cause* Petitioner's ON. Thus, Petitioner has satisfied the second *Althen* prong.

## VI. Conclusion

Upon careful evaluation of all the evidence submitted in this matter, including the medical records, the testimony, as well as the experts' opinions and medical literature, I conclude that Petitioner has met his burden of proof under *Althen*. Accordingly, Petitioner is entitled to compensation. An order regarding damages will issue shortly.

**IT IS SO ORDERED.**

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