

**United States Court of Appeals
for the Federal Circuit**

W.C.,
Petitioner-Appellant,

v.

**SECRETARY OF HEALTH AND HUMAN
SERVICES,**
Respondent-Appellee.

2012-5058

Appeal from the United States Court of Federal
Claims in case no. 07-VV-456, Judge Charles F. Lettow.

Decided: January 15, 2013

SYLVIA CHIN-CAPLAN, Conway, Homer & Chin-Caplan, P.C., of Boston, Massachusetts, argued for petitioner-appellant. Of counsel on the brief was RONALD C. HOMER.

DEBRA A. FILTEAU BEGLEY, Trial Attorney, Torts, Branch, Civil Division, United States Department of Justice, of Washington, DC, argued for respondent-appellee. With her on the brief were STUART F. DELERY, Acting Assistant Attorney General, RUPA

BHATTACHARYYA, Director, MARK W. ROGERS, Deputy Director, and VINCENT J. MATANOSKI, Assistant Director.

Before RADER, *Chief Judge*, PROST and Reyna, *Circuit Judges*.

RADER, *Chief Judge*.

The United States Court of Federal Claims affirmed the special master's decision denying W.C. (Petitioner) compensation under the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-1 to -34 (Vaccine Act). *W.C. v. Sec'y of Health & Human Servs. (Trial Court Decision)*, 100 Fed. Cl. 440 (2011). Because the special master's factual determinations were not arbitrary or capricious and the decision was in accordance with law, this court affirms.

I.

Petitioner alleges that an influenza vaccination he received at the age of thirty-four resulted in the onset of multiple sclerosis or significantly aggravated his preexisting, but asymptomatic, multiple sclerosis. *Trial Court Decision*, 100 Fed. Cl. at 443. Multiple sclerosis is a disorder of the central nervous system that causes clinical symptoms including weakness, loss of coordination, speech disturbances, and visual complaints. *Id.* at 443 n.2. The cause of multiple sclerosis is unknown. *W.C. v. Sec'y of Health & Human Servs. (Special Master Decision)*, No. 07-456V, 2011 WL 4537877, at *3 (Fed. Cl. Feb. 22, 2011). For many years, researchers have considered multiple sclerosis to be an autoimmune disease. *Id.* The disease may begin with a breach in the blood-brain barrier that allows cells from the immune system to cross into the brain. *Id.* These immune cells may mistakenly

attack the myelin sheath that coats nerve cells. *Id.* This attack would cause inflammation and subsequent scarring of the brain, called lesions. *Id.*

Petitioner suffers from the most common type of multiple sclerosis, known as relapsing remitting multiple sclerosis. *Id.* at *4. Patients with this type of multiple sclerosis usually have about one relapse of clinical symptoms per year. *Id.* “Much of the disease process is clinically silent,” meaning that a person can have active brain inflammation and develop new lesions without experiencing relapse (i.e., clinical symptoms). Bruce D. Trapp and Klaus-Armin Nave, *Multiple Sclerosis: An Immune or Neurodegenerative Disorder?*, 31 *Annu. Rev. Neurosci.* 247, 249 (2008). Brain imaging studies in patients with multiple sclerosis “indicate that inflammatory brain lesions can outnumber relapses by as much as 10 to 1.” *Id.* In this context, the term “clinical symptoms” refers to the outwardly-visible symptoms associated with a relapse (e.g., numbness and loss of motor function), as distinguished from clinically-silent brain lesions, which are also a symptom of multiple sclerosis.

Medical professionals use magnetic resonance imaging (MRI) to observe lesions in the brain of a patient diagnosed with or suspected to have multiple sclerosis. *Id.* at *6. By administering a contrast agent called gadolinium before an MRI, medical professionals can locate active inflammation at the site of a brain lesion. *Id.* In active brain inflammation, a breakdown in the blood-brain barrier permits gadolinium to enter the brain. *Id.* When gadolinium enters the brain, active lesions appear on an MRI as “enhanced.” *Id.* After inflammation subsides, the body repairs the blood-brain barrier and lesions no longer appear enhanced. *Id.* Most new lesions (approximately 90%) first appear as enhanced on MRI for a period of time, while older lesions do not enhance. *Id.* The trial court dedicated considerable time to considering

the length of time that new lesions appear enhanced on MRI. *See* Part III. B. below.

Petitioner received the influenza vaccine on December 13, 2004. *Special Master Decision*, 2011 WL 4537877, at *1. Before then, Petitioner had no clinical symptoms of multiple sclerosis or other neurological problems. *Id.* On December 24, 2004, Petitioner experienced numbness in his left hand, arm, and the left side of his head and face. *Id.* An MRI performed on December 30, 2004 identified six scattered lesions in Petitioner's brain, none of which were enhanced on the gadolinium MRI. *Id.* at *7. The interpreting physician noted the "MRI in conjunction with the patient's clinical history suggest multiple sclerosis as a possible etiology." *Id.* at *1.

Petitioner experienced another episode of numbness and loss of motor function in his left hand and arm in January 2005. *Id.* at *2. Petitioner then saw a neurologist, Dr. John Hannam, who suggested that Petitioner might have multiple sclerosis. Dr. Hannam noted that "if [Petitioner] had [multiple sclerosis], I can't blame it on the flu shot." *Id.* Dr. Hannam recommended a second opinion from Dr. Rifaat Bashir, who specializes in multiple sclerosis. *Id.* Dr. Bashir noted that Petitioner's MRI "is certainly consistent with a demyelinating disease. He could have had a single isolated event possibly related to his vaccination which he did receive two weeks before the event." *Id.* After two additional MRIs, the latter of which showed a new, enhanced lesion, Dr. Bashir diagnosed Petitioner with multiple sclerosis. *Id.* at *3.

Petitioner filed a claim for compensation under the Vaccine Act in June 2007, alleging the influenza vaccine caused his multiple sclerosis or significantly aggravated his pre-existing, subclinical multiple sclerosis. In support of his claim, Petitioner presented an expert report and testimony by Dr. Carlo Tornatore, the director of the Multiple Sclerosis Center at Georgetown University

Hospital. *Id.* at *4. Dr. Tornatore opined that the influenza vaccine caused Petitioner’s multiple sclerosis through a process called “molecular mimicry.” *Id.* In this process, the immune system attacks normal proteins in the body because they are structurally similar to foreign substances, such as viral or bacterial peptides. *Id.* at *11. Specifically, Dr. Tornatore opined that portions of the influenza vaccine mimic myelin basic protein, a component of the central nervous system that is implicated in multiple sclerosis. *Id.* According to Dr. Tornatore’s theory, the influenza vaccine could trigger production of immune cells (called T-cells) that are “cross-reactive” with myelin and therefore attack the person’s own nerve cells. *Id.*

On February 22, 2011, the special master denied Petitioner compensation under the Vaccine Act. *Id.* at *1. The special master found Petitioner had multiple sclerosis before receiving the influenza vaccine and therefore the vaccine could not have caused Petitioner’s disease. *Id.* Further, the special master found Petitioner did not establish a plausible medical theory that the influenza vaccine causes significant aggravation of multiple sclerosis. *Id.* The Court of Federal Claims affirmed. *Trial Court Decision*, 100 Fed. Cl. at 456. Petitioner appeals, and this court has jurisdiction under 42 U.S.C. § 300aa-12(f).

II.

When reviewing decisions under the Vaccine Act, this court “performs the same task as the Court of Federal Claims and determines anew whether the special master’s findings were arbitrary or capricious.” *Lampe v. Sec’y of Health & Human Servs.*, 219 F.3d 1357, 1360 (Fed. Cir. 2000). This court reviews the special master’s legal determinations under a “not in accordance with law” standard. *Pafford v. Sec’y of Health & Human Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006).

The Vaccine Act created the National Vaccine Injury Compensation Program, which allows certain petitioners to be compensated upon showing, among other things, that a person “sustained, or had significantly aggravated” a vaccine-related “illness, disability, injury, or condition.” 42 U.S.C. § 300aa-11(c)(1)(C). The Vaccine Act provides two avenues to compensation: “table” claims and “off-table” claims. *Althen v. Sec’y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005). In a table claim, the petitioner benefits from a statutory presumption of causation upon showing that the injury is listed in the Vaccine Injury Table for the vaccine received and occurred within the time period in the table. 42 U.S.C. § 300aa-14(a); see *Althen*, 418 F.3d at 1278. If the injury is not listed in the table, the petitioner must prove actual causation by a preponderance of the evidence. 42 U.S.C. §§ 300aa-11(c)(1)(C)(ii), 300aa-13(a)(1); *Moberly v. Sec’y of Health & Human Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010). Multiple sclerosis is not on the Vaccine Injury Table. See 42 C.F.R. § 100.3 (2012).

In this off-table case, the petitioner must show that it is “more probable than not” that the vaccine caused the injury. *Althen*, 418 F.3d at 1279–80. This level of proof does not require scientific certainty, nor epidemiologic studies such as might be needed for a theory to achieve “general acceptance in the scientific or medical communities.” *Andreau v. Sec’y of Health & Human Servs.*, 569 F.3d 1367, 1378 (Fed. Cir. 2009) (internal quotations omitted). Indeed, “the purpose of the Vaccine Act’s preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof of how vaccines affect the human body.” *Althen*, 418 F.3d at 1280.

Nonetheless, the petitioner must do more than demonstrate a “plausible” or “possible” causal link between the vaccination and the injury; he must prove his case by a preponderance of the evidence. *Moberly*, 592

F.3d at 1322. Specifically, a petitioner seeking to prove causation in an off-table case must provide: “(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. “[N]either a mere showing of a proximate temporal relationship between vaccination and injury, nor a simplistic elimination of other potential causes of the injury suffices, without more, to meet the burden of showing actual causation.” *Id.* (citing *Grant v. Sec’y of Health & Human Servs.*, 956 F.2d 1144, 1149 (Fed. Cir. 1992)).

In this case, Petitioner argues in the alternative that if the influenza vaccine did not cause his multiple sclerosis, then it significantly aggravated his preexisting condition. This court has not previously addressed the proof required to establish a *prima facie* case of significant aggravation for an off-table claim.

In *Whitecotton v. Sec’y of Health & Human Servs.*, 81 F.3d 1009, 1107 (Fed. Cir. 1996), this court articulated a four-prong test to evaluate an on-table significant aggravation claim. *Whitecotton* requires the special master to compare the injured person’s condition prior to vaccination with his or her current condition to determine whether a significant aggravation occurred, and then determine whether the first symptom of aggravation occurred within the time period in the Table. *Id.* If so, the petitioner receives the statutory presumption that the vaccine caused the aggravation.

Here, Petitioner asserts that the Vaccine Act “does not make a distinction between on-Table and off-Table claims of significant aggravation.” Pet’r’s Br. 10–11. He therefore suggests that under *Whitecotton*, he need only show that his condition worsened after administration of

the vaccine, and that the aggravation occurred within a medically appropriate time frame. *Id.*

This argument runs counter to the language of the statute. The statute distinguishes table claims from off-table claims for both initial onset and significant aggravation cases. See 42 U.S.C. § 300aa-11(c)(1)(C)(i) (table claims) and § 300aa-11(c)(1)(C)(ii) (off-table claims). For off-table claims that an injury was *either* “sustained, or [] significantly aggravated,” a petitioner must show the vaccine “caused” the injury or aggravation. § 300aa-11(c)(1)(C)(ii). As this court previously observed in the context of on-table claims, “[t]he statutory requirements to make out a *prima facie* significant aggravation claim are analogous to those required to make out a *prima facie* initial onset claim.” *Whitecotton*, 81 F.3d at 1103. Thus, a petitioner in an off-table case must show the vaccine actually caused the significant aggravation—not just that, accepting petitioner’s medical theory as sound, the person’s condition worsened within a medically-acceptable time frame.

In *Loving v. Sec’y of Health & Human Servs.*, 86 Fed. Cl. 135, 144 (2009), the Court of Federal Claims articulated a six-factor test for proof of off-table significant aggravation claims. The *Loving* test combines the first three *Whitecotton* factors, which establish significant aggravation, with the *Althen* factors, which establish causation. We hold that the *Loving* case provides the correct framework for evaluating off-table significant aggravation claims. A petitioner must prove by preponderant evidence that the vaccination caused significant aggravation by showing:

- (1) the person’s condition prior to administration of the vaccine, (2) the person’s current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person’s current condition con-

stitutes a “significant aggravation” of the person's condition prior to vaccination, (4) a medical theory causally connecting such a significantly worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) . . . a proximate temporal relationship between the vaccination and the significant aggravation.

Id. at 144.

III.

A.

In analyzing Petitioner’s claim that the influenza vaccine caused his multiple sclerosis, the special master identified a “preliminary question” of whether Petitioner had subclinical multiple sclerosis before the vaccination. *Special Master Decision*, 2011 WL 4537877, at *5. Because the special master found it was more likely than not that Petitioner had multiple sclerosis before receiving the vaccine, he recognized the vaccine could not have caused the disease. *Id.* at *5–8. The special master therefore denied compensation without applying the three-factor causation test set forth in *Althen*. *Id.* at *8; *cf. Althen*, 418 F.3d at 1278.

The special master cited *Broekelschen v. Secretary of Health & Human Services*, 618 F.3d 1339 (Fed. Cir. 2010) as support for resolving a preliminary issue before conducting an *Althen* analysis. In *Broekelschen*, this court held the special master did not err by preliminarily determining which of two possible diagnoses was correct before determining whether the vaccine caused the condition. *Id.* at 1350. Unlike in *Broekelschen*, the parties in this case agree on Petitioner’s diagnosis. Because the issue is whether the vaccine caused Petitioner’s multiple

sclerosis, the special master should have expressly applied the analysis set forth in *Althen*.

While this court disagrees with the special master's suggestion that *Althen* could be bypassed in this case, the Court of Federal Claims correctly determined the error was harmless. See *Trial Court Decision*, 100 Fed. Cl. at 451. The special master's finding that Petitioner had multiple sclerosis before receiving the vaccine means that Petitioner did not establish a "logical sequence of cause and effect showing that the vaccination was the reason for [his] injury" as required by prong two of *Althen*. 418 F.3d at 1278. If a petitioner has a disorder before being vaccinated, the vaccine logically cannot have caused the disorder.

Additionally, prong three of *Althen* requires a "medically-acceptable temporal relationship" between vaccination and onset of symptoms. *Id.* at 1281; *De Bazaan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1353 (Fed. Cir. 2008) (holding a petitioner's causation claim may fail because disease onset occurs "too early to be attributable to the vaccine"). In this case, Petitioner's first episode of numbness occurred eleven days after the vaccination—a time period which the government's expert agreed would be consistent with Petitioner's medical theory that the influenza vaccine triggered an immune-mediated disorder. However, the special master found Petitioner's first symptom of multiple sclerosis—telltale lesions in the brain—appeared before the vaccination. *Special Master Decision*, 2011 WL 4537877, at *8. This finding implies that the disease onset did not occur "within a time frame for which . . . it is medically acceptable to infer causation-in-fact," such that Petitioner's claim did not meet *Althen* prong three. *De Bazaan*, 539 F.3d at 1352.

Because a petitioner must establish "all three prongs of the *Althen* test," *id.*, it was not necessary for the special

master to evaluate whether Petitioner established a medical theory as required by *Althen* prong one. The lack of a logical sequence of cause and effect, and the lack of a “medically-acceptable temporal relationship” between the vaccination and disease onset, prevented Petitioner from establishing his claim. In sum, the special master’s finding that Petitioner had multiple sclerosis before he was vaccinated necessarily implies that Petitioner could not demonstrate causation under *Althen*.

B.

The special master’s underlying factual findings that Petitioner had multiple sclerosis before receiving the influenza vaccine were not arbitrary or capricious. The special master carefully evaluated the clinical record, expert testimony, and medical literature in finding it is “more probable than not that at least some, if not all, of the six lesions detected on [Petitioner’s] December 30, 2004 MRI existed before the December 13, 2004 flu vaccination.” *Special Master Decision*, 2011 WL 4537877, at *8.

The parties dispute the implications of the December 30, 2004 MRI that the trial court used to gauge when Petitioner developed multiple sclerosis. *See id.* at *6. The December 30, 2004 MRI showed six lesions in Petitioner’s brain, none of which were enhanced by gadolinium. *Id.* at *7. The government’s expert, Dr. Arun Venkatesan, an assistant professor in the Department of Neurology at John Hopkins University, testified that “if the vaccination caused the lesions, at least one of them should have been enhanced when the MRI was done 17 days after vaccination.” *Id.* Petitioner’s expert, Dr. Tornatore, responded that the December 30, 2004 MRI was “not useful in determining whether the lesions were present before the vaccination.” *Id.* at *6.

Dr. Venkatesan supported his opinion with a published article studying the duration of gadolinium enhancement of lesions identified in weekly MRIs performed on multiple sclerosis patients. Francois Cotton et al., *MRI Contrast Uptake in New Lesions in Relapsing-Remitting MS followed at Weekly Intervals*, 60 *Neurology* 640–646 (2003) (Cotton Study). The Cotton Study determined the average duration of enhancement was “3.07 weeks,” while the median duration was “2 weeks.” *Id.* at 642. Importantly, because MRIs were performed only once per week, a lesion that appeared enhancing for “1 week” may have been enhancing for anywhere from one to thirteen days. *Id.* at 641. For example, a lesion that appeared enhanced on only the second weekly scan could have appeared the day after the first weekly scan and enhanced until the day before the third weekly scan (13 days), or it could have enhanced only on the day of the MRI in which it appeared (1 day). Similarly, a “2 week” enhancement means the lesion was enhancing for 8–20 days, and “3 weeks” means the lesion appeared enhanced for 15–27 days. *See Special Master Decision*, 2011 WL 4537877, at *7. The Cotton Study’s finding that the median enhancement was “two weeks” indicates that one-half of the observed lesions lasted “two weeks” (i.e., 8–20 days) or less, while one-half lasted “two weeks” or more. *Id.*

Dr. Venkatesan explained that, under the medical theory proposed by Dr. Tornatore, lesions “would take at least a few days and potentially even a week or two” after the vaccination to develop. *Id.* (quoting Hearing Tr. 302). Thus, if Petitioner’s vaccination on December 13, 2004 had caused him to develop multiple sclerosis, lesions could have developed as early as December 16, 2004 or as late as December 27, 2004. *Id.* Adding the median duration of enhancement from the Cotton Study of 8–20 days, a lesion that developed on the earliest possible date

(December 16, 2004) would have appeared enhanced on MRI until between December 24, 2004 and January 5, 2005. Alternatively, adding the average enhancement duration of 15–27 days, the earliest possible lesion would have enhanced until at least December 31, 2004.

The special master acknowledged that the “timeline can be compressed” so that a lesion could have developed and become non-enhancing within the seventeen day window between Petitioner’s vaccination and his MRI. *Id.* at *8. Nonetheless, he found it improbable that *all six lesions* identified in Petitioner’s December 30, 2004 MRI would have developed and become non-enhancing in less than the average amount of time reported by the Cotton Study. *Id.* The Cotton Study supports the trial court’s finding because “[d]ifferent lesions in a same patient appeared to develop largely independent of each other and demonstrated large variation in the duration of enhancement . . .” Cotton Study, *supra*, at 640. In other words, the Cotton Study indicates it is unlikely that Petitioner regularly exhibits lesions with a short duration of enhancement.

Ultimately, it is Petitioner’s burden to prove causation by preponderant evidence. 42 U.S.C. § 300aa-13(a)(1)(A); *Althen*, 418 F.3d at 1278. The special master carefully considered the evidence in the record, drew plausible inferences, and articulated a rational basis for his determination that, more likely than not, Petitioner’s lesions existed before he received the influenza vaccination on December 13, 2004. *Special Master Decision*, 2011 WL 4537877, at *8; *see Lampe*, 219 F.3d at 1360 (discussing arbitrary and capricious standard of review). This court does not find the special master’s determination arbitrary or capricious. Consequently, because Petitioner did not show a logical sequence of cause and effect or a medically-acceptable time period between the vaccination and disease onset, this court affirms the denial of benefits

on Petitioner's claim that the influenza vaccine caused his multiple sclerosis.

IV.

Petitioner claims that, if he had preexisting multiple sclerosis when he received the influenza vaccine, the vaccination significantly aggravated his condition. The special master applied the correct law in evaluating this claim under *Loving*. 86 Fed. Cl. at 144. The special master found dispositive the fourth item of the *Loving* test, which requires petitioner to present a medical theory connecting his significantly worsened condition to the vaccination. *Special Master Decision*, 2011 WL 4537877, at *9.

As noted above, Petitioner's medical theory is that, through the process of molecular mimicry, the influenza vaccine triggered an immune response which released T-cells that were cross-reactive with myelin. *Trial Court Decision*, 100 Fed. Cl. at 454. Some of those T-cells crossed into Petitioner's brain, where they attacked the myelin coating on his nerve cells. This induced an immune cascade resulting in inflammation, demyelination, and nerve damage characteristic of multiple sclerosis.

The government's expert, Dr. Venkatesan, agreed that molecular mimicry is accepted as playing a role in the autoimmune disease Sydenham's chorea. *Id.* Medical science generally accepts that Sydenham's chorea develops as a result of immune response cross-reactivity following infection with streptococcus bacteria. *Id.* The special master found that "[m]olecular mimicry is a well-regarded theory in some contexts," *Special Master Decision*, 2011 WL 4537877, at *11, but correctly required additional evidence showing that molecular mimicry can cause the influenza vaccine to significantly aggravate multiple sclerosis, see *Broekelschen*, 617 F.3d at 1345 (holding "a petitioner must provide a reputable medical or scientific

explanation that pertains specifically to the petitioner's case").

In support of his theory that molecular mimicry between the influenza virus and myelin caused Petitioner's multiple sclerosis, Dr. Tornatore relied primarily on an article by Wucherpfennig and Strominger at Harvard University's Department of Molecular and Cellular Biology. Kai Wucherpfennig & Jack L. Strominger, *Molecular Mimicry in T Cell-Mediated Autoimmunity: Viral Peptides Activate Human T Cell Clones Specific for Myelin Basic Protein*, 80 Cell 695 (1995). The Wucherpfennig article showed that human myelin basic protein-specific T-cell clones derived from the blood of multiple sclerosis patients were "cross-reactive" with one peptide from a wild influenza Type A strain. *Id.* at 697. Dr. Tornatore testified that this evidence, demonstrating that influenza proteins can stimulate T-cells specific to myelin basic protein, makes it "beyond plausible" that the influenza vaccine could stimulate the immune response that led Petitioner to develop multiple sclerosis. J.A. 170.

The special master noted, however, that the Wucherpfennig article showed three other peptides derived from the wild influenza virus were not cross reactive with the myelin basic protein-specific T-cells. Wucherpfennig & Strominger, *supra*, at 698 (Table 1); *Special Master Decision*, 2011 WL 4537877, at *12. In other words, only certain portions of the influenza virus generated a cross-reactive immune response.

Petitioner provided no evidence that the portions of the influenza virus shown by Wucherpfennig to mimic myelin basic protein were present in the influenza vaccine Petitioner received. *Special Master Decision*, 2011 WL 4537877, at *12. Petitioner also did not provide evidence that any peptide from the influenza vaccine he received was cross-reactive with myelin basic protein-specific T-cells. *Id.* The special master reasonably considered the

lack of evidence connecting the cross-reactivity observed by Wucherpennig to the facts of Petitioner's case to weigh "against finding that Dr. Tornatore's opinion is persuasive." *Id.*; see *Moberly*, 592 F.3d at 1324 (holding special master did not err in rejecting a theory of causation where "there was no evidence in the record suggesting that the proposed mechanism was at work in [the petitioner's] case").

Moreover, the special master credited several published studies of multiple sclerosis patients who received the influenza vaccine showed no aggravation of symptoms following vaccination. *Special Master Decision*, 2011 WL 4537877, at *14–15. The Confavreaux study, involving 643 patients with multiple sclerosis, found that "commonly administered vaccinations (specifically, against tetanus, hepatitis B and influenza) do not increase the risk of relapse in patients with multiple sclerosis." Christian Confavreaux et al., *Vaccinations and the Risk of Relapse in Multiple Sclerosis*, 344 *New England J. of Med.* 319 (2001). Confavreaux found the "odds ratio" of a relapse in the two months following the flu shot was 1.08, meaning there was a slightly higher rate of relapse in patients who had the vaccine, but the difference was not statistically significant. *Id.* at 324.

Similarly, the Miller article reported a randomized, double-blind trial of influenza immunization in 104 multiple sclerosis patients. A.E. Miller et al., *A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial of Influenza Immunization in Multiple Sclerosis*, 48 *Neurology* 312 (1997). The patients were divided into two groups, one of which received the influenza vaccine while the other received placebo. The patients were monitored for relapses in the six months following vaccination. The authors found "[i]nfluenza immunization in [multiple sclerosis] patients is neither associated with an increased exacerbation rate in the post-vaccination period nor a

change in disease course over the subsequent 6 months.” *Id.* at 312. Petitioner emphasizes that the vaccinated group had nearly twice as many patients experience relapse during the six months following vaccine administration than the placebo group (eleven vs. six). This difference was not statistically significant. *Id.* at 313. Moreover, the authors noted that the average time between vaccination and relapse was higher in the vaccine group than the placebo group, indicating the difference in relapse rate between the two groups was due to random variation rather than a causal connection to the vaccine. *Id.*

The special master evaluated all of the evidence of record, and found that the large studies of multiple sclerosis patients “reinforce Dr. Venkatesan’s opinion that the theory offered by Dr. Tornatore is ‘extremely unlikely.’” *Special Master Decision*, 2011 WL 4537877, at *15 (quoting Tr. 149–50). The special master correctly applied the law in requiring Petitioner to demonstrate by preponderant evidence that the influenza vaccine caused significant aggravation of Petitioner’s multiple sclerosis. This court cannot say that the special master’s evaluation of the expert testimony or weighing of the scientific evidence was arbitrary or capricious.

V.

Therefore, for the reasons discussed above, this court affirms the judgment of the Court of Federal Claims upholding the special master’s decision denying Petitioner compensation under the Vaccine Act.

AFFIRMED