In the United States Court of Federal Claims

No. 15-1333V

(Filed Under Seal: December 28, 2018)
(Reissued: January 15, 2019)[1]

MARSHA DOUGHERTY,	*	
Petitioner,	*	National Childhood Vaccine Injury Act; Review of Special Master's Decision Denying Relief for Narcolepsy; Application of Althen Test; Assessment of Expert Testimony and Epidemiological Studies.
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

David P. Murphy, David P. Murphy & Associates, P.C., Greenfield, Indiana, for Petitioner.

Voris E. Johnson, Jr., with whom were *Chad A. Readler,* Acting Assistant Attorney General, *C. Salvatore D'Alessio,* Acting Director, Torts Branch, Civil Division, *Catharine E. Reeves*, Deputy Director, Torts Branch, Civil Division, *Gabrielle M. Fielding*, Assistant Director, Torts Branch, Civil Division, U.S. Department of Justice, Washington, D.C. for Respondent.

OPINION AND ORDER

WHEELER, Judge.

This vaccine case is before the Court on Petitioner's Motion for Review of the Special Master's July 5, 2018 decision denying compensation and dismissing the petition due to insufficient proof. Dougherty v. Sec'y of Health & Human Servs., No. 15-1333V,

[1] Pursuant to Rule 18(b) of the Court's Vaccine Rules, this opinion and order was initially filed under seal. As required under the Rules, each party was afforded 14 days from the date of issue, until January 11, 2019, to object to the public disclosure of any information furnished by that party. Neither party submitted any proposed redactions. The only changes to the original opinion and order are the addition of keywords and correction of minor typographical errors.

2018 WL 3989519 (Fed. Cl. Spec. Mstr. July 5, 2018). For the reasons explained below, the Court affirms the Special Master's dismissal decision.

On November 6, 2015, Marsha Dougherty ("Petitioner") filed a petition with this Court under the National Vaccine Injury Compensation Program, 42 U.S.C. §§ 300aa-1—34 ("Vaccine Act"). She seeks compensation for the narcolepsy with cataplexy[2] she claims to have developed as a result of a Fluzone influenza vaccine she received on November 7, 2012. In March 2016, Respondent filed the requisite Rule 4(c) Report, arguing that Petitioner had not met her burden of proof to show a causal connection between the flu vaccination and her narcolepsy. Dkt. No. 20. Petitioner and Respondent both filed expert reports and medical literature supporting their positions. An entitlement hearing before the Special Master was held on November 30 and December 1, 2017. On July 5, 2018, the Special Master issued her Decision denying compensation.

Background[3]

Petitioner's medical history prior to receiving the flu vaccine included complaints of abdominal pain, migraines, anxiety, hypertension, and neck pain. She had neck and spine surgery following an all-terrain vehicle accident in October 2008. On November 7, 2012, the day she received her flu vaccination, she was seeing her primary care physician, Dr. Neumann, for help with neck pain, anxiety, and hypertension. On December 4, 2012, Petitioner again visited Dr. Neumann's office complaining of increasing fatigue, having difficulty staying awake at times during the day. Her medications were adjusted. In a follow-up visit to Dr. Neumann on January 11, 2013, she reported continuing fatigue, and that she had pulled over while driving due to drowsiness. Dr. Neumann ordered a sleep study and again adjusted her medications. The sleep study performed on January 29, 2013, revealed "moderate mild to moderate obstructive sleep apnea (OSA)."

In April 2013, Petitioner made a follow-up visit to Dr. Neumann, who noted that Petitioner's migraines had not improved, and that she continued to have a lot of stress at home due to her living situation. Petitioner visited Dr. Neumann again on August 29, 2013, to discuss her experience while driving the day before when she passed out. She also reported that she had been having "staring episodes," noted by Dr. Neumann to be loss of consciousness and seizure. Dr. Neumann recommended she restrict driving.

Dr. Neumann referred Petitioner to a neurologist, Dr. Hemelt, whom Petitioner saw on September 10, 2013. The neurologist's notes show that Petitioner reported an episode

[2] Narcolepsy is described as "a chronic neurological disorder that affects the brain's ability to control sleep-wake cycles." Cataplexy is a "sudden loss of muscle tone" while awake, which results in a loss of voluntary muscle control. Narcolepsy Fact Sheet, National Institutes of Health, National Institute of Neurological Disorders and Stroke, https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Narcolepsy-Fact-Sheet.

[3] Facts are drawn from the Special Master's Decision.

of losing consciousness while driving and waking up to find her car in a ditch. Her husband described times when Petitioner acted "differently," and sometimes confused. Dr. Hemelt noted that Petitioner's awareness problems were likely due to disordered sleep and maybe medication. She also wrote that the sleep problems could be caused by snoring and sleep apnea, perhaps combined with narcolepsy. She recommended further tests, medication adjustment, and continued driving restriction.

Two days after seeing Dr. Hemelt, Petitioner went to the emergency room at her local hospital because she had had two "trancelike seizures." She was discharged the same day, and the ER physician recommended that she expedite her further neurological tests. The next day Petitioner had another sleep study, again showing sleep apnea. A day later Petitioner underwent a multiple sleep latency test, which is used to diagnose narcolepsy. The test results were seen as consistent with narcolepsy, and Dr. Hemelt prescribed medication in light of that diagnosis. On September 30, 2013, Petitioner visited her primary care doctor, Dr. Neumann, who noted her recent diagnosis of narcolepsy and also observed that Petitioner told him she had done some research and found a link between the flu vaccine she had received and narcolepsy. At that time he noted that he had not heard of this connection before (although he later wrote two letters on Petitioner's behalf supporting her claim of a link between her flu vaccination and her narcolepsy). Two weeks later Petitioner visited Dr. Hemelt, whose notes also show that Petitioner spoke of a link with her flu vaccination. Dr. Hemelt noted that she was not aware of this association.

During the next years Petitioner continued treatment for narcolepsy and in March 2015, also began treatment for sleep apnea, starting use of a Continuous Positive Airway Pressure (CPAP) machine at night to help her breathing. In April 2015, she reported to her neurologist that the CPAP treatment for sleep apnea improved her symptoms of fatigue and sleepiness. However, she continued to suffer the effects of daytime sleepiness and was unable to work. Petitioner had a genetic test in December 2016, which showed she carries the gene associated with narcolepsy. In August 2017, she was granted Social Security disability benefits due to her diagnosis of narcolepsy with cataplexy.

Evidence Presented

Petitioner's Expert

Petitioner's expert, Dr. Marcel Kinsbourne, received his medical degree at Oxford University in the United Kingdom and is licensed in North Carolina, Massachusetts, and Virginia. He is board certified in pediatrics. The Special Master noted that Dr. Kinsbourne has had a long career in pediatrics and neurology starting in 1955, including serving on the staff at several hospitals as well as holding academic positions in pediatrics, neurology, and psychology in various universities. The Special Master observed that it has been "many years since Dr. Kinsbourne has regularly seen patients." Dougherty, 2018 WL 3989519 at *9. She stated further that while Dr. Kinsbourne is qualified as an expert in

neurology, he does not claim expertise specifically in narcolepsy outside his testimony in Vaccine Program cases.

Dr. Kinsbourne submitted an initial expert opinion, Dkt. No. 36, and followed it later with two supplemental reports. Kinsbourne Report, Dkt. Nos. 54 and 90. In his initial report, Dr. Kinsbourne described significant increases in the rate of narcolepsy in Western Europe and China after use of H1N1 vaccines, most frequently a formulation called Pandemrix, during a 2008-2010 pandemic. While H1N1 vaccines are also used in the United States under brands such as the Fluzone vaccine given to Petitioner, their formulation is different, notably in the absence of the adjuvant which is in the Pandemrix vaccines. Dr. Kinsbourne argued that flu vaccines themselves, with or without adjuvants, initiate an autoimmune attack in genetically susceptible individuals. In his first Report, he maintained that this autoimmune reaction is likely created by molecular mimicry which causes the body to attack and diminish its own hypocretin receptors regulating wakefulness, thereby causing narcolepsy. To support this theory, he cited a study known as the De La Herrán-Arita article[4]. He noted that the presence of adjuvants in a vaccine is irrelevant under this theory. He concluded that Petitioner's flu vaccination caused her narcolepsy with cataplexy "to a reasonable degree of medical probability."

Respondent's Experts

Dr. Thomas Scammell is a Professor of Neurology at Beth Israel Deaconess Medical Center, Boston Children's Hospital, and Harvard Medical School. He is board-certified in neurology, psychiatry, and sleep medicine, and for the last twenty years, has practiced as a neurologist, a clinical and basic researcher in sleep medicine, and a lecturer on narcolepsy and the neurobiology of sleep and wakefulness. He also has authored over one hundred publications, mostly focused on narcolepsy and sleep disorders, and is currently treating about sixty patients with narcolepsy. Scammell CV, Dkt. No. 47-2. After reviewing Petitioner's medical records, Dr. Scammell expressed doubts about Petitioner's diagnosis. He also stated that he reviewed the medical literature relating to the Fluzone vaccine and narcolepsy and found "little evidence that the Fluzone vaccine can cause narcolepsy." Scammell Report at 5, Dkt. No. 47-1. He pointed out that the association between H1N1 vaccines and narcolepsy has only been made for vaccines used outside the U.S., with different formulations. Id. at 9. He emphasized that the De La Herrán-Arita study cited by Dr. Kinsbourne to support a molecular mimicry theory had been retracted soon after publication.

Dr. Andrew MacGinnitie also provided an expert report on behalf of Respondent. MacGinnitie Report, Dkt. No. 47-3. He is an attending physician and Clinical Director for the Division of Immunology at Boston Children's Hospital, and a Professor of Pediatrics

[4] Alberto K. De la Herrán-Arita et al., CD4+ T cell autoimmunity to hypocretin/orexin and cross-Reactivity to a 2009 H1N1 influenza A epitope in narcolepsy, 5 Sci. Translational Med. 1 (2013), Dkt. No. 50-BB (hereinafter De La Herrán-Arita).

at Harvard Medical School. He is board-certified in both allergy/immunology and pediatrics. He sees "more than 1,500 patients" each year for a variety of immunologic diseases, including reactions to vaccines. MacGinnitie CV, Dkt. No. 47-4. Dr. MacGinnitie observed that there is "strong" epidemiological evidence linking narcolepsy with the Pandemrix vaccine used outside the U.S. in 2009, but that this is likely related to the adjuvant added to the Pandemrix. He noted that "[n]o increase in narcolepsy has been observed in individuals receiving influenza vaccines not containing adjuvants." He cited epidemiological studies of a possible link between seasonal flu vaccines (including Fluzone) and narcolepsy, including what is referred to as the Duffy study[5]. MacGinnitie Report at 8, Dkt No. 47-3. Those studies found no association with narcolepsy. He also pointed out that the De la Herrán-Arita article cited by Dr. Kinsbourne to support his molecular mimicry theory had been retracted.

Experts' Responses

Both Dr. Kinsbourne for Petitioner, and Dr. MacGinnitie for Respondent, filed supplemental reports in response to expert reports in opposition. Dr. Kinsbourne's second Expert Report, Dkt. No. 54, was addressed to Dr. Scammell's Report, and introduced a different theory by which a non-adjuvanted H1N1 vaccine such as Fluzone could have caused Petitioner's narcolepsy. Dr. Kinsbourne described an autoimmune reaction caused by the nucleoprotein in the influenza vaccine itself regardless of the presence of an adjuvant. He did not specifically address the De La Herrán-Arita study which had been retracted, but did offer literature to support this newly-presented theory, including the Ahmed study (2015)[6]. He concluded that even though this theory is "incomplete," it is a sufficient basis for "reasonable medical probability" that Petitioner's vaccination caused her narcolepsy.

Dr. MacGinnitie, Respondent's Expert, filed a response to Dr. Kinsbourne's second report, MacGinnitie Report, Dkt. No. 58-1. He described and then summarized the data in Ahmed supporting a link between the vaccine nucleoprotein and narcolepsy as "preliminary, resting on [a] single peer reviewed report that lacks appropriate controls and does not provide evidence" that antibodies are involved in causing the disease. Id., at 4. He repeated his opinion that Petitioner's narcolepsy was not the result of vaccination.

Dr. Kinsbourne filed a third Expert Report, Kinsbourne Supplementary Report, Dkt. No. 90-1, in which he discussed the Duffy epidemiological study finding no link between Fluzone and narcolepsy. This had been cited by both Dr. Scammell and Dr. MacGinnitie to support their opinions. Dr. Kinsbourne pointed out that Duffy and colleagues limited

[5] Duffy, J. et al. Narcolepsy and influenza A(H1N1) pandemic 2009 vaccination in the United States. 83 Neurology 1823-30 (2014), Dkt. No. 50-Z.

[6] Ahmed SS, Volkmuth W, Duca J et al. Antibodies to influenza nucleoprotein cross-react with human hypocretin receptor-2. 2 Sci Translational Med. 294ra105 (2015), Dkt. No. 51-LL.

their study to an age range below 30, and since Petitioner was 44 years old at the time she received the flu vaccine, Duffy "casts no light" on vaccine causation in her case. Id. at 2. At the same time as the third Report was filed, Petitioner also submitted an expert report by a new contributor, Dr. S. Stanley Young. Statement of October 24, 2017, Dkt. No. 89-3. Dr. Young is an adjunct professor of statistics and biostatistics. He argued that flu vaccines cause the body to make antibodies which can damage the brain and cause narcolepsy in a person carrying the narcolepsy gene. He pointed out that this theory is supported by the work of Ahmed and colleagues. He discounted the significance of the Duffy study, claiming that study found it was neither the vaccine nor the adjuvant causing narcolepsy, but did not posit a cause. He argued that the Ahmed studies, which came out after Duffy, do show the cause: "antibodies to the nuclear protein, which is the current last man standing." Id. at 6.

Dr. MacGinnitie then addressed both Dr. Kinsbourne's third report and Dr. Young's report. MacGinnitie Third Expert Report, Dkt. No. 92-1. He observed that Ahmed's work does not show how the antibodies described cause brain damage leading to narcolepsy. He stated that while adjuvant may not be "*sufficient by itself* to cause narcolepsy, it does not change the fact that adjuvant is *required*." Id. at 1. And he defended the Duffy study: "Duffy remains strong evidence against a relation between non-adjuvanted vaccination and narcolepsy." Id. at 2.

The Special Master held an evidentiary hearing on November 30 and December 1, 2017, at which time she heard testimony from Petitioner and her family regarding her diagnosis, as well as from some of the parties' experts. She issued her opinion denying compensation on July 5, 2018.

Burden of Proof

Petitioner seeks recovery in this case for an "off-Table" injury, that is, an injury caused by a vaccine other than those injuries listed on the Vaccine Injury Table, 42 U.S.C. § 300aa-14(a). In off-Table injuries, claimants must show causation in fact by a preponderance of the evidence. 42 U.S.C. §§ 300aa-11(c)(1)(C)(ii), 300aa-13(a)(1)(A); see also Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1321 (Fed. Cir. 2010). The U.S. Court of Appeals for the Federal Circuit summarized the claimant's evidentiary burden associated with off-Table cases in Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005), holding that the claimant must establish by preponderant evidence:

> (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 proximate temporal relationship between vaccination and injury.

These factors are now commonly referred to as the three Althen prongs.

Special Master's Decision

The Special Master first found that Petitioner had established that she "more likely than not" suffered from narcolepsy with cataplexy. She then turned to Althen Prong One which requires proof of a medical theory showing the vaccination caused Petitioner's condition. She summarized the parties' expert arguments, and found Respondent's experts more persuasive in their position that there is no reliable evidence showing that nonadjuvanted flu vaccines such as Fluzone cause narcolepsy. She discussed two recent cases, both decided by the same Special Master, addressing this issue: McCollum v. Sec'y of Health & Human Servs., No. 14-790V, 2017 WL 5386613 (Fed. Cl. Spec. Mstr. Sept. 15, 2017), review denied, 135 Fed. Cl. 735 (2017), appeal docketed, No. 18-1623 (Fed. Cir. 2018), and D'Tiole v. Sec'y of Health & Human Servs., No. 15-85, 2016 WL 7664475 (Fed. Cl. Spec. Mstr. Nov. 28, 2016), review denied, 123 Fed. Cl. 421 (2017), aff'd, 726 Fed.App'x. 809 (Fed. Cir. 2018).

In D'Tiole, which involved FluMist, a vaccine similar to Fluzone, the Petitioner's expert made arguments akin to those presented in the instant case. The expert maintained that the vaccine caused an autoimmune reaction through molecular mimicry, citing studies of Pandemrix for support. Respondent's experts, including Dr. MacGinnitie, focused on the differences between Pandemrix and the vaccine at issue, as has been done in this case. They also cited the Duffy study to show there is no connection between narcolepsy and the flu vaccines used in the U.S. The Special Master in that case dismissed Petitioner's claim, finding that Petitioner had not shown a reliable theory applicable to FluMist.

In McCollum, Dr. Kinsbourne also served as an expert for Petitioner and offered the same causation theory he presented here. The Special Master in McCollum again dismissed the claim, citing the Duffy study as "the sole relevant epidemiologic evidence regarding . . . the flu vaccine administered in the U.S." 2017 WL 5386613 at *17.

In the instant case the Special Master determined that Petitioner's experts were not able to refute the arguments presented by Dr. Scammell and Dr. McGinnitie, and for that reason found that Petitioner failed to satisfy her burden under Althen Prong One. As to Prong Two, the Special Master noted that without a reasonable medical theory shown under Prong One, an analysis of Prong Two is not very meaningful, but the Special Master pointed out that Petitioner did not present any evidence supporting an autoimmune reaction in her case. In sum, the claims of her expert were insufficient to "meet the preponderant standard in the face of relevant and credible epidemiological studies, well-versed opposing experts, and Petitioner's reliance on a retracted article." Dougherty, 2017 WL 3989519 at *47.

Motion for Review

Petitioner argued in her Motion for Review that the Special Master improperly increased Petitioner's burden of proof to show a causation theory. Dr. Kilbourne's opinion, that "a nucleoprotein in Fluzone caused Marsha, a genetically predisposed person, to develop narcolepsy" should have been enough, since "[n]either the Act nor Althen requires Marsha to identify the specific protein . . . ." Mot. for Review at 5, Dkt. No. 101. Rather, all Petitioner need show is a "scientifically reasonable theory." Id. In Petitioner's second objection to the Decision, she argued that the Special Master ignored an abstract from the journal SLEEP, submitted by Petitioner in Dkt. No. 89-10. Petitioner maintained that this article rebuts the conclusions of the Duffy article and provides "stronger proof" that nonadjuvanted flu vaccines can cause narcolepsy. Id. at 8.

Respondent answered Petitioner's Motion by emphasizing Petitioner's failure to present adequate proof of her expert's theory, a theory that had been deemed unpersuasive in two recent Vaccine Program cases, D'Tiole and McCollum, as noted by the Special Master in this case. Resp't Resp. to Mot. for Review, Dkt. No. 105. With regard to Petitioner's claim that the Special Master ignored the SLEEP abstract, Respondent pointed out that the abstract was filed as an attachment to Dr. Young's Expert Report and only briefly mentioned in his Report. In addition, Petitioner did not call Dr. Young to testify at the evidentiary hearing and Dr. Kinsbourne did not mention this study at all. Further, it is not clear whether this abstract was ever published, which can add to the significance of studies.

Standard of Review

This Court has jurisdiction to review decisions of the special masters in accordance with provisions of the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-12(e)(1) - (2). Under those provisions, this Court will only set aside findings of fact or conclusions of law found to be "arbitrary, capricious, an abuse of discretion or otherwise not in accordance with law." 42 U.S.C. § 300aa-12(e)(2)(B). With respect to findings of fact, the special masters have broad discretion to weigh evidence and make factual determinations. As to questions of law, the legal rulings made by a special master in connection with a vaccine claim are reviewed de novo, under a "not in accordance with the law" standard. The Special Master's findings of fact receive deferential review under an "arbitrary and capricious" standard, while the Court reviews legal conclusions under the "not in accordance with law" standard and discretionary rulings for an "abuse of discretion." Munn v. Sec'y of Health & Human Servs., 970 F.2d 863, 870 n.10 (Fed. Cir. 1992). "Weighing the persuasiveness of particular evidence often requires a finder of fact

to assess the reliability of testimony, including expert testimony, and we have made clear that the special masters have that responsibility in Vaccine Act cases." Moberly ex rel. Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1325 (Fed. Cir. 2010).

Conclusion

The Court has carefully considered the parties' arguments, the evidence of record, and the Special Master's decision on entitlement, and is satisfied that the Special Master set forth a reasonable basis for her decision. The Special Master reasonably found here that there was insufficient evidence to support Petitioner's claim that the Fluzone vaccination was the cause of her narcolepsy. She addressed two recent cases addressing this issue, and reasonably explained why Petitioner's arguments in this case failed to establish any persuasive differences from those cases. She reiterated the strength of the Duffy study at this stage of narcolepsy research. As the Federal Circuit noted in D'Tiole, nothing in prior Vaccine Program case law "requires the Special Master to ignore probative epidemiological evidence that undermines petitioner's theory." 726 Fed.App'x. 809, 811.

For these reasons the Special Master's Decision is AFFIRMED and accordingly, Petitioner's Motion for Review is DENIED.

IT IS SO ORDERED.

s/Thomas C. Wheeler
THOMAS C. WHEELER
Judge