In the United States Court of Federal Claims

No. 15-51V
Filed: June 18, 2020[1]

DOUGLAS TULLIO,	*	
Petitioner,	*	**Vaccine Act; Motion for Review; Preponderance of the Evidence; Expert Opinions; Influenza Vaccine; Rheumatoid Arthritis; Epidemiology; Application of Althen Test.**
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Jennifer Ann Gore Maglio, Maglio Christopher and Toale, P.A., Sarasota, FL, for petitioner.

Dhairya D. Jani, Trial Attorney, Torts Branch, Civil Division, United States Department of Justice, Washington, D.C., for respondent. With him were **Heather L. Pearlman**, Assistant Director, Torts Branch, Civil Division, **Catherine E. Reeves**, Deputy Director, Torts Branch, Civil Division, **C. Salvatore D'Alessio**, Acting Director, Torts Branch, Civil Division, and **Ethan P. Davis**, Assistant Attorney General, Civil Division.

O P I N I O N

HORN, J.

On January 20, 2015, petitioner Douglas Tullio filed a petition for compensation with the National Vaccine Injury Compensation Program (Vaccine Program), under the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-1–300aa-34 (2012) (Vaccine Act), for an off-Table injury. See 42 U.S.C. § 300aa-11(c)(1)(C)(ii) (2012). Petitioner claimed that a September 29, 2012 fluzone high-dose influenza vaccination caused him to develop "rheumatoid arthritis." On December 19, 2019, Special Master Christian J. Moran of the United States Court of Federal Claims denied petitioner's claim for an award of compensation, finding that petitioner had not shown, by a preponderance of the evidence, that he is entitled to compensation under the Vaccine Act. See generally Tullio v. Sec'y of Health & Human Servs., No. 15-51V, 2019 WL 7580149 (Spec. Mstr. Fed. Cl. Dec. 19, 2019). On January 21, 2020, petitioner filed a motion for review in this

[1] Reissued for Publication: July 22, 2020. This Opinion was issued under seal on June 18, 2020. The parties did not propose redactions to the June 18, 2020 Opinion, thus, the court issues the decision without redactions for public distribution.

court of the Special Master's decision denying his claim pursuant to Rule 23 of the Vaccine Rules of the United States Court of Federal Claims (2019) (Vaccine Rules).

FINDINGS OF FACT

The following summary of the relevant facts regarding petitioner's medical history are established in the record before the court, many of which are not in dispute. On September 29, 2012, petitioner received a fluzone high-dose vaccination. According to the record before the court, at the time he received the vaccination, petitioner was working full-time with his wife, with whom he owned a business, and was sixty-nine years old. On October 12, 2012, petitioner saw an internist, Dr. John Samples, for the first time, at which time he complained that his legs "feel weaker." Thirteen days later, on October 25, 2012, petitioner once again visited Dr. Samples for an "[u]rgent overbooked visit," because petitioner complained of "diffuse body pain, worse since the last visit here 12 [sic] days ago." At that visit, petitioner had bloodwork done.

Throughout November and December of 2012, petitioner complained of pain and weakness in his legs to multiple medical providers. A diagnosis of possible Guillain-Barré syndrome (GBS) was considered, which led Dr. Mark Bouffard, a pain specialist, to refer petitioner to a neurologist, Dr. Catherine Brignoni, on November 28, 2012. On December 4, 2012, petitioner visited Dr. Brignoni with the chief complaint of "[p]ossible GBS, diffuse weakness and paresthesia after a flu vaccine." Dr. Brignoni conducted a neurological exam on petitioner, and based on the results, Dr. Brignoni began to treat petitioner for GBS. While Dr. Brignoni was treating petitioner for GBS, she stated "[h]e should not receive the flu vaccine any more [sic]." According to petitioner's medical records, the treatments to improve his pain from GBS "helped his bilateral shoulder pains and leg/thigh pains" initially, but "the weakness has not changed." This led petitioner to seek a second opinion from Dr. Perry Shieh at the University of California, Los Angeles, neurology department on January 18, 2013. Dr. Shieh recommended that petitioner see a rheumatologist.

Petitioner initially saw a rheumatologist, Dr. Sheri Hsu on January 30, 2013. At the first visit with Dr. Hsu, petitioner was not suffering from joint swelling, but was suffering from joint pain. At the January 30, 2013 visit, Dr. Hsu made a note in petitioner's medical records, "I am concerned about a pain syndrome associated with his flu vaccine." In February 2013, petitioner did complain of joint swelling. While treating petitioner, Dr. Hsu provided several different theories to explain petitioner's pain, including all of the following potential and distinct diagnoses: "seronegative RA [rheumatoid arthritis]," "Reactive arthritis," "Arthralgia," "DDD [degenerative disc disease] lumbar spine," and "Atrial fibrillation." (brackets added). By June 6, 2013, Dr. Hsu had diagnosed petitioner with "seronegative RA [rheumatoid arthritis]."[2] (capitalization in original) (brackets added).

[2] One of petitioner's experts Dr. Paul J. Utz testified at the hearing before Special Master Moran, regarding the distinction between two types of rheumatoid arthritis, seropositive and seronegative: "It is not a clean distinction. There is overlap between the two of them." Dr. Utz further testified that seronegative rheumatoid arthritis, "is more heterogenous in

According to the most recent medical records dated December 11, 2018 from Dr. Hsu, as well as petitioner's testimony at the March 6 through 8, 2019 hearing, petitioner was still suffering from rheumatoid arthritis.

On January 20, 2015, petitioner filed a petition within the statutory time period for filing a petition for compensation with the Vaccine Program pursuant to the Vaccine Act. In his petition, Mr. Tullio alleged, in relevant part:

> 6. To the current date, Petitioner continues to suffer from his vaccine-induced injury.
>
> 7. Petitioner's injuries are causally related to an adverse reaction to a vaccination or vaccinations listed in 42 U.S.C. § 300aa-14.
>
> 8. Petitioner's vaccine related injuries have lasted more than six months. See, e.g., P Ex. 10 at 2-3.

Petitioner also stated in his petition that "his condition continued and subsequent evaluation identified Petitioner's condition as a rheumatological injury, most likely reactive arthritis caused by his influenza vaccination. See, e.g., P Ex. 4 at 11-15; P Ex 17 at 18-19."[3]

On January 21, 2015, petitioner's case was assigned to Special Master Christian J. Moran. On January 22, 2015, petitioner filed eighteen exhibits, which included 1,257

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terms of presentation and joint involvement and things like that. They tend to have less severe disease." Dr. Utz testified that generally seronegative rheumatoid arthritis is determined by "the CCP test, which is just one test, is negative." Dr. Utz also testified, "CCP stands for cyclic citrullinated peptide." Dr. Mehrdad Matloubian, respondent's expert, testified, "[a]s we have understood more about pathogenesis of seropositive rheumatoid arthritis, this anti-citrullinated peptide antibody, ACPA, or anti-CCP is used to distinguish between people who are seropositive and seronegative RA [rheumatoid arthritis]." (brackets added). Respondent's expert Dr. Matloubian also testified, when asked "[d]oes seronegative RA [rheumatoid arthritis] in particular present heterogeneously?" responded: "It can." (brackets added).

[3] By the time of the March 6-8, 2019 hearing before Special Master Moran, both parties agreed that petitioner's diagnosis is seronegative rheumatoid arthritis, not reactive arthritis. At the hearing before Special Master Moran, petitioner's counsel asked petitioner's expert, Dr. Utz, the following question, "hindsight being 20/20, what do you believe that Mr. Tullio had after his September 2012 vaccination?" Dr. Utz responded, "I think this was all seronegative rheumatoid arthritis from the beginning." Respondent agreed in its February 19, 2019 pre-hearing submission, stating, "petitioner was ultimately diagnosed with seronegative RA [rheumatoid arthritis] by Dr. Hsu based on objective findings of synovitis on examination. Pet. Ex. 4 at 23. The parties' experts all agree with this diagnosis." (brackets added).

pages of contemporaneous records from physicians' offices and hospitals Mr. Tullio had visited prior to filing his petition. On January 22, 2015, Special Master Moran issued an Order which required petitioner to file a statement of completion once any "outstanding medical records and affidavits" were filed. On April 7, 2015, petitioner filed his statement of completion, after filing an affidavit by petitioner and additional medical records. Throughout the proceedings before Special Master Moran, however, petitioner continued to file updated medical records, with the last filing submitted to the court on March 7, 2019 during the hearing.

On June 17, 2015, respondent filed a Vaccine Rule 4c Report in which respondent stated "[n]either RA [rheumatoid arthritis] nor reactive arthritis are presumptive injuries following flu vaccine. Therefore, petitioner necessarily pursues a cause-in-fact claim." (brackets added). Respondent also contended in the Rule 4c Report, "[o]n the existing record, petitioner has failed to provide preponderant evidence in support of the petition for compensation." Respondent further stated:

> Without an expert opinion to support his claim, the sum total of petitioner's case is: that he received a flu vaccine on September 29, 2012; within three weeks developed a rheumatologic condition (either reactive arthritis or RA [rheumatoid arthritis]); and, no other cause for his condition has been identified. However, as the Federal Circuit has cautioned, "neither a mere showing of a proximate temporal relationship between vaccine and injury, nor a simplistic elimination of other potential causes of the injury suffices, without more, to meet the burden of showing actual causation." Moberly[ex rel. Moberly v. Sec'y of Health & Human Servs.], 592 F.3d [1315,] 1323-24 [(Fed. Cir. 2010)]; citing Althen[v. Sec'y of Health & Human Servs.], 418 F.3d [1274,] 1278 [(Fed. Cir. 2005)].

(brackets added).

During the proceedings before Special Master Moran, the parties in this case called four experts, two for the petitioner and two for the respondent, who filed, in total, ten expert reports. Petitioner's experts were Dr. Paul J. Utz and Dr. Lawrence Steinman. As of the most recent Curriculum Vitae filed on February 28, 2019, Dr. Utz is Board-certified in rheumatology and completed a residency in immunology and rheumatology. Dr. Utz also is the Director Emeritus of the Medical Scientist Training Program and Associate Director for Education of the Institute for Immunity, Transplantation, and Infection at Stanford University. In addition, Dr. Utz provides care at the Veterans Affairs Palo Alto Health Care Hospital and Clinics. Dr. Utz introduced and relied on the Bingham article and the Hennecke, Birnbaum, and Wooldridge papers. As of the most recent Curriculum Vitae filed on February 28, 2019, Dr. Steinman is a Board-certified neurologist and is a professor of neurology and neurological sciences at Stanford University. Dr. Steinman offered Blast search testimony. Respondent's experts were Dr. Mehrdad Matloubian and Dr. Neal Halsey. As of the most recent Curriculum Vitae filed on February 28, 2019, Dr. Matloubian is a Board-certified rheumatologist who practices rheumatology. Dr. Matloubian has a Ph.D. in virology. Dr. Matloubian is a Clinical Professor at University

of California San Francisco. Dr. Matloubian introduced and relied on the Westra, Malmström, Svendsen, James, and Snir studies. As of his most recent Curriculum Vitae filed on February 28, 2019, Dr. Halsey is Board-certified in pediatrics and pediatric infectious diseases. Dr. Halsey is the Director Emeritus of the Institute for Vaccine Safety at the Johns Hopkins Bloomberg School of Public Health. Dr. Halsey introduced and relied on the Bardage and Ray studies. The various articles, studies, and papers introduced by the experts are discussed more fully below.

On January 4, 2019, petitioner submitted his pre-hearing brief to Special Master Moran. The Special Master, however, indicated in an order on January 22, 2019 that "Mr. Tullio's brief did not persuasively advocate his case, and he was instructed to file an amended brief." Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *4. On January 28, 2019, according to Special Master Moran, the petitioner "filed an amended and improved brief." Id. Petitioner's January 28, 2019 pre-hearing brief alleged that "[t]he primary issue in controversy in this case is Althen[v. Secretary of Health & Human Services] prong I, whether or not the influenza vaccination can cause RA [rheumatoid arthritis]." (brackets and emphasis added). Petitioner also stated he is "not required to introduce evidence of epidemiologic studies" because "[s]uch an approach would be inconsistent with allowing 'the use of circumstantial evidence envisioned by the preponderance standard and negates the system created by Congress.'" (quoting Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1280). Regarding expert's opinions that are not directly supported by literature, petitioner stated the expert's opinion "can also surpass the threshold requirement for reliability, provided that the expert explains his process at arriving at that opinion by scientific methodology." (citing Daubert v. Merrell Dow Pharmaceuticals, Inc., 43 F.3d 1311, 1319 (9th Cir.), cert. denied, 516 U.S. 869 (1995)). Petitioner alleged "[t]hrough expert testimony consistent with his medical course, Petitioner provides preponderant evidence that he suffered RA [rheumatoid arthritis] as the result of an aberrant, individual immune response to what should have been a beneficial influenza vaccination in 2012." (brackets added). Petitioner also noted thirteen cases in which a Special Master of the United States Court of Federal Claims has granted compensation for a petitioner who developed rheumatoid arthritis after an influenza vaccination.[4]

[4] Petitioner's statement in its January 28, 2019 pre-hearing brief is misleading. Although the cases that petitioner cited granted compensation for petitioners who received influenza vaccinations that the petitioners alleged led to rheumatoid arthritis, the respective Special Masters did not find causation. The petitioners and respondents in each of those cases stipulated that petitioners were entitled to compensation, but the respondent denied the influenza vaccinations led to petitioners' injuries. See Egan v. Sec'y of Health & Human Servs., No. 15-976V; Zimmerman v. Sec'y of Health & Human Servs., No. 14-323V; Walker v. Sec'y of Health & Human Servs., No. 14-921V; Ward v. Sec'y of Health & Human Servs., No. 16-72V; Stolowski v. Sec'y of Health & Human Servs., No. 12-635V; Miller v. Sec'y of Health & Human Servs., No. 13-837V; Hambleton v. Sec'y of Health & Human Servs., No. 13-819V; Scales v. Sec'y of Health & Human Servs., No. 13-501V; Habchy v. Sec'y of Health & Human Servs., No. 11-680V; Wallace v. Sec'y of Health & Human Servs., No. 11-627V; DeMartini v. Sec'y of Health & Human

Respondent filed its final pre-hearing submission on February 19, 2019, in which respondent contended, "[i]n evaluating the reliability of petitioner's expert's opinion, a special master 'may conclude that there is simply too great an analytical gap between the data and the opinion proffered.'" (quoting Cedillo v. Sec'y of Health & Human Servs., 617 F.3d 1328, 1339 (Fed. Cir. 2010)). Respondent stated, "[g]eneric theories of causation are patently insufficient to meet petitioner's burden of proof." (citing Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339, 1350-51 (Fed. Cir. 2010)). Respondent argued that the absence of an association between the flu vaccine and rheumatoid arthritis "is striking, given the high incidence of influenza infection globally and the numerous articles that have been published on both influenza and RA [rheumatoid arthritis]." (brackets added). Regarding the comment by Dr. Hsu, petitioner's treating rheumatologist, at Mr. Tullio's first visit that stated "I am concerned about a pain syndrome associated with his [petitioner's] flu vaccine," the respondent noted "it does not appear from her [Dr. Hsu's] later medical records that once she diagnosed petitioner with seronegative RA [rheumatoid arthritis], that she ever mentioned the flu vaccine as a cause of his condition." (brackets added). Finally, respondent stated "[t]here is no 'appropriate' timeframe within which medical science would expect RA [rheumatoid arthritis] to occur following the administration of the flu vaccine, because the flu vaccine does not cause RA [rheumatoid arthritis]." (brackets added).

From March 6, 2019 until March 8, 2019, Special Master Moran held an entitlement hearing in San Francisco, California to determine whether petitioner should receive compensation under the Vaccine Act, at which petitioner and all four experts testified. On December 19, 2019, after describing the relevant medical events in petitioner's history and reviewing the evidence in the record before him, including the expert opinions offered by both petitioner and respondent, Special Master Moran issued his decision denying petitioner's claim of entitlement to compensation. The Special Master found petitioner had failed to carry his burden of proving how the flu vaccine had caused his rheumatoid arthritis.

With regard to the first prong of the Althen test, described more fully below, "a medical theory causally connecting the vaccination and the injury," Althen v. Secretary of Health & Human Services, 418 F.3d at 1278,[5] Special Master Moran concluded that the evidence presented by petitioner regarding molecular mimicry "fell short" of being persuasive to establish petitioner's case. See Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *22. The Special Master indicated that the epidemiological evidence presented by respondent "weakens the reliability of opinions that the flu vaccine

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Servs., No. 12-734V; Gifford v. Sec'y of Health & Human Servs., No. 10-325V; Merrill v. Sec'y of Health & Human Servs., No. 7-278V.

[5] The three prongs described in Althen v. Secretary of Health & Human Services, are: "(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 v. Sec'y of Health & Human Servs., 418 F.3d at 1278.

can cause rheumatoid arthritis." Id. at *11. Special Master Moran also wrote "there is ample legal justification for considering epidemiological studies in determining whether the flu vaccine can cause rheumatoid arthritis." Id. at *8. Special Master Moran disputed the proposition urged by petitioner – that petitioner's T cell repertoire was so rare that it would not have been detected by epidemiology. Special Master Moran stated: "As Dr. Halsey pointed out, epidemiological studies have identified that the risk of developing Guillain-Barré syndrome after flu vaccination is increased by one case or two cases per million doses of vaccination. This example refutes a commonly offered argument that epidemiological studies cannot detect rare events." Id.

Despite finding that "Mr. Tullio did not meet his burden of proof for Althen prong one," Special Master Moran reviewed "the remaining two Althen prongs . . . for completeness." Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *27. Special Master Moran reviewed petitioner's claim under the second prong of the Althen test, whether there exists a "logical sequence of cause and effect." Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1278. Special Master Moran stated "[t]he lack of support from treating doctors is consistent with the lack of information about the cause of rheumatoid arthritis. As explained much earlier in section I.B of this decision, the cause of rheumatoid arthritis is not known." Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *28. Special Master Moran stated, "given this information, it would be surprising for a doctor to tell Mr. Tullio that the flu vaccination caused his rheumatoid arthritis." Id. The Special Master found "Mr. Tullio also has not established, by preponderant evidence, a logical sequence of cause and effect." Id. at *5.

In addition, Special Master Moran examined the case in the context of the third prong of the Althen test, "a showing of a proximate temporal relationship between vaccination and injury." Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1278. Based only on Dr. Utz's testimony that molecular mimicry would take at least one week, and Dr. Matloubian's testimony that molecular mimicry would take between one and six weeks, Special Master Moran made his finding that "the appropriate time period would be one to six weeks." Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *27. As a result, because the petitioner had reported experiencing calf pain approximately one week after receiving the flu vaccination and had complained to Dr. Samples of "diffuse body pain" on October 25, 2012, about one month after the vaccination, Special Master Moran concluded that "[b]oth dates fit within the accepted temporal interval of one to six weeks. Therefore, if Mr. Tullio had established prong one, he would have also established prong three." Id. As a result of his review of the record before him Special Master Moran denied petitioner's claim for compensation. Thereafter, petitioner filed the motion for review currently under consideration on January 21, 2020.[6] The government responded on February 19, 2020, and petitioner filed his reply on April 14, 2020. On April 28, 2020, this court held a telephonic oral argument.

[6] Mr. Tullio's motion for review was filed within the statutory time period on Tuesday, January 21, 2020 because Monday, January 20, 2020 was a federal holiday and this court was closed.

D I S C U S S I O N

When reviewing a Special Master's decision, the assigned Judge of the United States Court of Federal Claims shall:

> (A) uphold the findings of fact and conclusions of law of the special master and sustain the special master's decision,
> (B) set aside any findings of fact or conclusions of law of the special master found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law and issue its own findings of fact and conclusions of law, or
> (C) remand the petition to the special master for further action in accordance with the court's direction.

42 U.S.C. § 300aa-12(e)(2) (2018). The legislative history of the Vaccine Act states: "The conferees have provided for a limited standard for appeal from the [special] master's decision and do not intend that this procedure be used frequently, but rather in those cases in which a truly arbitrary decision has been made." H.R. Rep. No. 101-386, at 517 (1989) (Conf. Rep.), reprinted in 1989 U.S.C.C.A.N. 3018, 3120.

In Markovich v. Secretary of Health & Human Services, the United States Court of Appeals for the Federal Circuit wrote, "[u]nder the Vaccine Act, the Court of Federal Claims reviews the Chief Special Master's decision to determine if it is 'arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with the law.' 42 U.S.C. § 300aa-12(e)(2)(B)." Markovich v. Sec'y of Health & Human Servs., 477 F.3d 1353, 1355-56 (Fed. Cir.), cert. denied, 552 U.S. 816 (2007); see also K.G. v. Sec'y of Health & Human Servs., 951 F.3d 1374, 1379 (Fed. Cir. 2020); Oliver v. Sec'y of Health & Human Servs., 900 F.3d 1357, 1360 (Fed. Cir. 2018) (citing Milik v. Sec'y of Health & Human Servs., 822 F.3d 1367, 1375-76 (Fed. Cir. 2016)); Deribeaux ex rel. Deribeaux v. Sec'y of Health & Human Servs., 717 F.3d 1363, 1366 (Fed. Cir.), reh'g and reh'g en banc denied (Fed. Cir. 2013) (The United States Court of Appeals for the Federal Circuit stated that "we 'perform[ ] the same task as the Court of Federal Claims and determine[ ] anew whether the special master's findings were arbitrary or capricious.'" (brackets in original) (quoting Lampe v. Sec'y of Health & Human Servs., 219 F.3d 1357, 1360 (Fed. Cir. 2000))); W.C. v. Sec'y of Health & Human Servs., 704 F.3d 1352, 1355 (Fed. Cir. 2013); Hibbard v. Sec'y of Health & Human Servs., 698 F.3d 1355, 1363 (Fed. Cir. 2012); de Bazan v. Sec'y of Health & Human Servs., 539 F.3d 1347, 1350 (Fed. Cir. 2008); Avera v. Sec'y of Health & Human Servs., 515 F.3d 1343, 1347 (Fed. Cir.) ("Under the Vaccine Act, we review a decision of the special master under the same standard as the Court of Federal Claims and determine if it is 'arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law.'" (quoting 42 U.S.C. § 300aa-12(e)(2)(B))), reh'g and reh'g en banc denied (Fed. Cir. 2008); Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1277; Faup v. Sec'y of Health & Human Servs., 147 Fed. Cl. 445, 458 (2019); Dodd v. Sec'y of Health & Human Servs., 114 Fed. Cl. 43, 47 (2013); Taylor v. Sec'y of

Health & Human Servs., 108 Fed. Cl. 807, 817 (2013). The arbitrary and capricious standard is "well understood to be the most deferential possible." Munn v. Sec'y of Health & Human Servs., 970 F.2d 863, 870 (Fed. Cir. 1992). The United States Court of Appeals for the Federal Circuit has indicated that:

> These standards vary in application as well as degree of deference. Each standard applies to a different aspect of the judgment. Fact findings are reviewed by us, as by the Claims Court judge, under the arbitrary and capricious standard; legal questions under the "not in accordance with law" standard . . . ; and discretionary rulings under the abuse of discretion standard. The latter will rarely come into play except where the special master excludes evidence.

Munn v. Sec'y of Health & Human Servs., 970 F.2d at 871 n.10; see also Carson ex rel. Carson v. Sec'y of Health & Human Servs., 727 F.3d 1365, 1369 (Fed. Cir. 2013); Deribeaux ex rel. Deribeaux v. Sec'y of Health & Human Servs., 717 F.3d at 1366; W.C. v. Sec'y of Health & Human Servs., 704 F.3d at 1355; Griglock v. Sec'y of Health & Human Servs., 687 F.3d 1371, 1374 (Fed. Cir. 2012); Porter v. Sec'y of Health & Human Servs., 663 F.3d 1242, 1249 (Fed. Cir. 2011) (citing Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d at 1345) (explaining that the reviewing court "do[es] not reweigh the factual evidence, assess whether the special master correctly evaluated the evidence, or examine the probative value of the evidence or the credibility of the witnesses—these are all matters within the purview of the fact finder") reh'g and reh'g en banc denied (Fed. Cir. 2012); Dodd v. Sec'y of Health & Human Servs., 114 Fed. Cl. at 56. "[T]he special masters have broad discretion to weigh evidence and make factual determinations." Dougherty v. Sec'y of Health & Human Servs., 141 Fed. Cl. 223, 229 (2018).

> With regard to both fact-findings and fact-based conclusions, the key decision maker in the first instance is the special master. The Claims Court owes these findings and conclusions by the special master great deference – no change may be made absent first a determination that the special master was "arbitrary and capricious."

Munn v. Sec'y of Health & Human Servs., 970 F.2d at 870; see also 42 U.S.C. § 300aa-12(e)(2)(B).

Generally, "if the special master 'has considered the relevant evidence of record, drawn plausible inferences and articulated a rational basis for the decision, reversible error will be extremely difficult to demonstrate.'" Hibbard v. Sec'y of Health & Human Servs., 698 F.3d at 1363 (quoting Hines v. Sec'y of Health & Human Servs., 940 F.2d 1518, 1528 (Fed. Cir. 1991)); see also Porter v. Sec'y of Health & Human Servs., 663 F.3d at 1253-54; Lampe v. Sec'y of Health & Human Servs., 219 F.3d at 1360; Avila ex rel. Avila v. Sec'y of Health & Human Servs., 90 Fed. Cl. 590, 594 (2009); Dixon v. Sec'y of Health & Human Servs., 61 Fed. Cl. 1, 8 (2004) ("The court's inquiry in this regard must therefore focus on whether the Special Master examined the 'relevant data' and articulated a 'satisfactory explanation for its action including a rational connection

between the facts found and the choice made.'" (quoting Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co., 463 U.S. 29, 43 (1983) (quoting Burlington Truck Lines, Inc. v. United States, 371 U.S. 156, 168 (1962)))).

As noted by the United States Court of Appeals for the Federal Circuit:

> Congress assigned to a group of specialists, the Special Masters within the Court of Federal Claims, the unenviable job of sorting through these painful cases and, based upon their accumulated expertise in the field, judging the merits of the individual claims. The statute makes clear that, on review, the Court of Federal Claims is not to second guess the Special Masters [sic] fact-intensive conclusions; the standard of review is uniquely deferential for what is essentially a judicial process. Our cases make clear that, on our review . . . we remain equally deferential. That level of deference is especially apt in a case in which the medical evidence of causation is in dispute.

Deribeaux ex rel. Deribeaux v. Sec'y of Health & Human Servs., 717 F.3d at 1366-67 (modification in original) (quoting Hodges v. Sec'y of Health & Human Servs., 9 F.3d 958, 961 (Fed. Cir. 1993)); Hibbard v. Sec'y of Health & Human Servs., 698 F.3d at 1363; Locane v. Sec'y of Health & Human Servs., 685 F.3d 1375, 1380 (Fed. Cir. 2012). The United States Court of Appeals for the Federal Circuit has explained that the reviewing courts "'do not sit to reweigh the evidence. [If] the special master's conclusion [is] based on evidence in the record that [is] not wholly implausible, we are compelled to uphold that finding as not being arbitrary and capricious.'" Deribeaux ex rel. Deribeaux v. Sec'y of Health & Human Servs., 717 F.3d at 1367 (modification in original) (quoting Lampe v. Sec'y of Health & Human Servs., 219 F.3d at 1363); see also K.G. v. Sec'y of Health & Human Servs., 951 F.3d at 1379 ("With respect to factual findings, however, we will uphold the special master's findings of fact unless they are clearly erroneous." (citing Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1278)); Hibbard v. Sec'y of Health & Human Servs., 698 F.3d at 1363 (citing Cedillo v. Sec'y of Health & Human Servs., 617 F.3d at 1338).

The United States Court of Appeals for the Federal Circuit has explained that:

> A petitioner can establish causation in one of two ways. Id. [Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d at 1341] If the petitioner shows that he or she received a vaccination listed on the Vaccine Injury Table, 42 U.S.C. § 300aa–14, and suffered an injury listed on that table within a statutorily prescribed time period, then the Act presumes the vaccination caused the injury. Andreu[ex rel. Andreu] v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1374 (Fed. Cir. 2009). Where, as here, the injury is not on the Vaccine Injury Table, the petitioner may seek compensation by proving causation-in-fact.

Milik v. Sec'y of Health & Human Servs., 822 F.3d at 1379 (citing Andreu ex rel. Andreu v. Sec'y of Health & Human Servs., 569 F.3d at 1374); see also W.C. v. Sec'y of Health & Human Servs., 704 F.3d at 1356; Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d at 1346; Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1356 (Fed. Cir.), reh'g and reh'g en banc denied (Fed. Cir. 2006), cert. denied, 551 U.S. 1102 (2007); Grant v. Sec'y of Health & Human Servs., 956 F.2d 1144, 1147-48 (Fed. Cir. 1992); Faup v. Sec'y of Health & Human Servs., 147 Fed. Cl. at 458; Dodd v. Sec'y of Health & Human Servs., 114 Fed. Cl. at 50; Paluck v. Sec'y of Health & Human Servs., 104 Fed. Cl. 457, 467-68 (2012); Fesanco v. Sec'y of Health & Human Servs., 99 Fed. Cl. 28, 31 (2011).

For petitioner to establish a *prima facie* case in a vaccine case, decisions of the Federal Circuit permit the use of circumstantial evidence, which the court described as "envisioned by the preponderance standard" and by the vaccine system created by Congress, in which "close calls regarding causation are resolved in favor of injured claimants" without the need for medical certainty. See Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1280; see also Cloer v. Sec'y of Health & Human Servs., 654 F.3d 1322, 1332 n.4 (Fed. Cir. 2011), cert. denied, 566 U.S. 956 (2012); Andreu ex rel. Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1379 (Fed. Cir. 2009) ("In Althen, however, we expressly rejected the Stevens test, concluding that requiring 'objective confirmation' in the medical literature prevents 'the use of circumstantial evidence . . . and negates the system created by Congress' through the Vaccine Act." (modification in original)); La Londe v. Sec'y of Health & Human Servs., 110 Fed. Cl. 184, 198 (2013) ("Causation-in-fact can be established with circumstantial evidence, i.e., medical records or medical opinion."), aff'd, 746 F.3d 1344 (Fed. Cir. 2014). The Althen court further noted that "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 v. Sec'y of Health & Human Servs., 418 F.3d at 1280 (citing Knudsen ex rel. Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 549 (Fed. Cir. 1994)); see also W.C. v. Sec'y of Health & Human Servs., 704 F.3d at 1356.

When proving eligibility for compensation for a petitioner of an off-Table injury under the Vaccine Act, such as the one filed by Mr. Tullio, petitioner may not rely on his or her testimony alone. According to the Vaccine Act, "[t]he special master or court may not make such a finding based on the claims of a petitioner alone, unsubstantiated by medical records or by medical opinion." 42 U.S.C. § 300aa-13(a)(1). A petitioner who meets his or her burden is entitled to recovery under the Vaccine Act, unless the respondent proves by preponderant evidence that the injury was caused by factors unrelated to the vaccine. See Stone v. Sec'y of Health & Human Servs., 676 F.3d 1373, 1379-80 (Fed. Cir. 2012); Walther v. Sec'y of Health & Human Servs., 485 F.3d 1146, 1151 (Fed. Cir. 2007); see also Rus v. Sec'y of Health & Human Servs., 129 Fed. Cl. 672, 680 (2016) (citing 42 U.S.C. § 300aa-13(a)(1)(B); Shalala v. Whitecotton, 514 U.S. 268, 270-71 (1995)). "But, regardless of whether the burden of proof ever shifts to the respondent, the special master may consider the evidence presented by the respondent in determining whether the petitioner has established a *prima facie* case." Rus v. Sec'y of Health & Human Servs., 129 Fed. Cl. at 680 (citing Stone v. Sec'y of Health & Human Servs., 676 F.3d at 1379; de Bazan v. Sec'y of Health & Human Servs., 539 F.3d at 1353).

Petitioner also must prove causation-in-fact in an off-Table injury. See Grant v. Sec'y of Health & Human Servs., 956 F.2d at 1147-48. The United States Court of Appeals for the Federal Circuit has held that causation-in-fact in the Vaccine Act context is the same as the "legal cause" in the general torts context. See Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352 (Fed. Cir. 1999). Therefore, drawing from the Restatement (Second) of Torts, the vaccine is a cause-in-fact when it is "'a substantial factor in bringing about the harm.'" de Bazan v. Sec'y of Health & Human Servs., 539 F.3d at 1351 (quoting the Restatement (Second) of Torts § 431(a) (1965)); see also Oliver v. Sec'y of Health & Human Servs., 900 F.3d at 1361 (citing Moberly ex rel. Moberly v. Sec'y of Health & Human Servs., 592 F.3d at 1321); Deribeaux ex rel. Deribeaux v. Sec'y of Health & Human Servs., 717 F.3d at 1367 ("To prove causation, a petitioner must show that the vaccine was 'not only a but-for cause of the injury but also a substantial factor in bringing about the injury.'" (quoting Shyface v. Sec'y of Health & Human Servs., 165 F.3d at 1352–53)). A "'substantial factor' standard requires a greater showing than 'but for' causation." de Bazan v. Sec'y of Health & Human Servs., 539 F.3d at 1351 (citing Shyface v. Sec'y of Health & Human Servs., 165 F.3d at 1352). "However, the petitioner need not show that the vaccine was the sole or predominant cause of her injury, just that it was a substantial factor." Id. (citing Walther v. Sec'y of Health & Human Servs., 485 F.3d 1146, 1150 (Fed. Cir. 2007)). A Judge of the United States Court of Federal Claims has explained the relationship between "but-for" causation and "substantial factor" in Deribeaux ex rel. Deribeaux v. Secretary of Health & Human Services:

> The de Bazan [v. Sec'y of Health & Human Servs., 539 F.3d at 1351] court defined but-for causation as requiring that "the harm be attributable to the vaccine to some nonnegligible degree," and noted that, although substantial is somewhere beyond the low threshold of but-for causation, it does not mean that a certain factor must be found to have definitively caused the injury. Id. [de Bazan v. Sec'y of Health & Human Servs., 539 F.3d at 1351] Accordingly, a factor deemed to be *substantial* is one that falls somewhere between causing the injury to a non-negligible degree and being the "sole or predominant cause." Id.
>
> This definition of substantial—somewhere between non-negligible and predominant—is applicable to respondent's burden to prove a sole substantial factor unrelated to the vaccine. Accordingly, a respondent's burden is to prove that a certain factor is the only *substantial* factor—one somewhere between non-negligible and predominant—that caused the injury.

Deribeaux ex rel. Deribeaux v. Sec'y of Health & Human Servs., 105 Fed. Cl. 583, 595 (2012), aff'd, 717 F.3d 1363 (Fed. Cir.), reh'g and reh'g en banc denied (Fed. Cir. 2013) (emphasis in original).

In order to recover under the Vaccine Act, a petitioner "must show, by a preponderance of the evidence, 'that the injury or death at issue was caused by a

vaccine.'" Milik v. Sec'y of Health & Human Servs., 822 F.3d at 1379; (quoting Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d at 1341 (citing 42 U.S.C. §§ 300aa–11(c)(1), –13(a)(1))); see also Oliver v. Sec'y of Health & Human Servs., 900 F.3d at 1361; W.C. v. Sec'y of Health & Human Servs., 704 F.3d at 1355-56 ("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.'" (quoting 42 U.S.C. § 300aa–11(c)(1)(C))); see also Boatmon v. Sec'y of Health & Human Servs., 941 F.3d 1351, 1355, 1359 (Fed. Cir. 2019); Oliver v. Sec'y of Health & Human Servs., 900 F.3d at 1360; La Londe v. Sec'y of Health & Human Servs., 746 F.3d 1334, 1339 (Fed. Cir. 2014); Lombardi v. Sec'y of Health & Human Servs., 656 F.3d 1343, 1350 (Fed. Cir. 2011) ("A petitioner seeking compensation under the Vaccine Act must prove by a preponderance of the evidence that the injury or death at issue was caused by a vaccine."); Faup v. Sec'y of Health & Human Servs., 147 Fed. Cl. at 458; see also Shapiro v. Sec'y of Health & Human Servs., 105 Fed. Cl. 353, 358 (2012), aff'd, 503 F. App'x 952 (Fed. Cir. 2013); Jarvis v. Sec'y of Health & Human Servs., 99 Fed. Cl. 47, 54 (2011). "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." W.C. v. Sec'y of Health & Human Servs., 704 F.3d at 1356 (quoting Moberly ex rel. Moberly v. Sec'y of Health & Human Servs., 592 F.3d at 1322); Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1278; Hines v. Sec'y of Health & Human Servs., 940 F.2d at 1525.

While scientific certainty is not required, the Special Master "is entitled to require some indicia of reliability to support the assertion of the expert witness." Moberly ex rel. Moberly v. Sec'y of Health & Human Servs., 592 F.3d at 1324; see also Hazlehurst v. Sec'y of Health & Human Servs., 88 Fed. Cl. 473, 439 (2009), aff'd, 604 F.3d 1343 (Fed. Cir. 2010) (quoting Andreu ex rel. Andreu v. Sec'y of Health & Human Servs., 569 F.3d at 1379). The United States Supreme Court has explained that:

> Claimants who show that a listed injury first manifested itself at the appropriate time are prima facie entitled to compensation. No showing of causation is necessary; the Secretary bears the burden of disproving causation. A claimant may also recover for unlisted side effects, and for listed side effects that occur at times other than those specified in the Table, but for those the claimant must prove causation.

Bruesewitz v. Wyeth LLC, 562 U.S. 223, 228-29 (2011) (footnotes omitted); see also Kennedy v. Sec'y of Health & Human Servs., 99 Fed. Cl. 535, 539 (2011), aff'd, 485 F. App'x 435 (Fed. Cir. 2012).

The Federal Circuit in Althen v. Secretary of Health & Human Services defined a three-prong test by which a petitioner can meet his or her burden to establish causation in an off-Table injury case:

> To meet the preponderance standard, [petitioner] must "show a medical theory causally connecting the vaccination and the injury." Grant v. Sec'y of Health & Humans Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992) (citations omitted). A persuasive medical theory is demonstrated by "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury[,]" the logical sequence being supported by "reputable medical or scientific explanation[,]" i.e., "evidence in the form of scientific studies or expert medical testimony[.]" Grant [v. Sec'y of Health & Human Servs.], 956 F.2d at 1148. [Petitioner] may recover if she shows "that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Shyface[v. Sec'y of Health & Human Servs.], 165 F.3d at 1352-53. Although probative, neither a mere showing of a proximate temporal relationship between vaccination and injury, nor a simplistic elimination of other potential causes of the injury suffices, without more, to meet the burden of showing actual causation. See Grant[v. Sec'y of Health & Human Servs.], 956 F.2d at 1149. Concisely stated, [petitioner's] burden is to show by preponderant evidence that the vaccination brought about [the] 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.

Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1278 (first three sets of brackets in original); see also Boatmon v. Sec'y of Health & Human Servs., 941 F.3d at 1354-55; Oliver v. Sec'y of Health & Human Servs., 900 F.3d at 1361; Deribeaux ex rel. Deribeaux v. Sec'y of Health & Human Servs., 717 F.3d at 1367; Porter v. Sec'y of Health & Human Servs., 663 F.3d at 1249; Moberly ex rel. Moberly v. Sec'y of Health & Human Servs., 592 F.3d at 1322; Pafford v. Sec'y of Health & Human Servs., 451 F.3d at 1355; Capizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1324 (Fed. Cir. 2006); Faup v. Sec'y of Health & Human Servs., 147 Fed. Cl. at 458; C.K. v. Sec'y of Health & Human Servs., 113 Fed. Cl. 757, 766 (2013).

With regard to the first Althen prong, "a medical theory causally connecting the vaccination and the injury," Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1278, the Federal Circuit in Althen analyzed the preponderance of evidence requirement as allowing medical opinion as proof, even without scientific studies in medical literature that provide "objective confirmation" of medical plausibility. See id. at 1278, 1279-80; see also Shapiro v. Sec'y of Health & Human Servs., 105 Fed. Cl. at 358. In rejecting a requirement that a claimant under the Vaccine Act prove confirmation of medical plausibility from the medical community and medical literature, the Althen court turned to the analysis undertaken in Knudsen ex rel. Knudsen v. Secretary of Health & Human Services, 35 F.3d at 549. See Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1279-80. In Knudsen ex rel. Knudsen v. Secretary of Health & Human Services, the United States Court of Appeals for the Federal Circuit wrote, "to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the

vaccine compensation program. The Vaccine Act does not contemplate full blown tort litigation in the Court of Federal Claims." Knudsen ex rel. Knudsen v. Sec'y of Health & Human Servs., 35 F.3d at 549. The Federal Circuit in Knudsen stated further:

> The Court of Federal Claims is therefore not to be seen as a vehicle for ascertaining precisely how and why DTP [diphtheria-tetanus-pertussis vaccine] and other vaccines sometimes destroy the health and lives of certain children while safely immunizing most others. This research is for scientists, engineers, and doctors working in hospitals, laboratories, medical institutes, pharmaceutical companies, and government agencies. The special masters are not "diagnosing" vaccine-related injuries. The sole issues for the special master are, based on the record evidence as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the [petitioner's] injury or that the [petitioner's] injury is a table injury, and whether it has not been shown by a preponderance of the evidence that a factor unrelated to the vaccine caused the child's injury. See 42 U.S.C. § 300aa-13(a)(1), (b)(1).

Id. (brackets added).

> The Federal Circuit also has indicated that:
>
> Although a finding of causation "must be supported by a sound and reliable medical or scientific explanation," causation "can be found in vaccine cases . . . without detailed medical and scientific exposition on the biological mechanisms." Knudsen v. Sec'y of the Dep't of Health & Human Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994). It is not necessary for a petitioner to point to conclusive evidence in the medical literature linking a vaccine to the petitioner's injury, as long as the petitioner can show by a preponderance of the evidence that there is a causal relationship between the vaccine and the injury, whatever the details of the mechanism may be.

Simanski v. Sec'y of Health & Human Servs., 671 F.3d 1368, 1384 (Fed. Cir. 2012) (omission in original).

Regarding the use of epidemiological evidence in a case in which causation is at issue, the United States Court of Appeals for the Federal Circuit has found that a Special Master may consider epidemiological evidence in determining causation. See Andreu ex rel. Andreu v. Sec'y of Health & Human Servs., 569 F.3d at 1379 ("Although Althen[v. Secretary of Health & Human Services,] and Capizzano[v. Secretary of Health & Human Services] make clear that a claimant need not produce medical literature or epidemiological evidence to establish causation under the Vaccine Act, where such evidence is submitted, the special master can consider it in reaching an informed judgment as to whether a particular vaccination likely caused a particular injury." (brackets added)); see also Grant v. Sec'y of Health & Human Servs., 956 F.2d at 1149 ("These

epidemiological studies are probative medical evidence relevant to causation."); Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1280.

The second prong of the Althen test requires the petitioner to demonstrate "a logical sequence of cause and effect, showing that the vaccination was the reason for the injury" by a preponderance of the evidence. See Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1278; see also Pafford v. Sec'y of Health & Human Servs., 451 F.3d at 1355. In order to prevail, the petitioner must show "that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1278 (quoting Shyface v. Sec'y of Health & Human Servs., 165 F.3d at 1352). In Capizzano v. Secretary of Health & Human Services, the Federal Circuit stated, "'[a] logical sequence of cause and effect' means what it sounds like – the claimant's theory of cause and effect must be logical. Congress required that, to recover under the Vaccine Act, a claimant must prove by a preponderance of the evidence that the vaccine caused his or her injury." Capizzano v. Sec'y of Health & Human Servs., 440 F.3d at 1326 (quoting 42 U.S.C. §§ 300aa-11(c)(1)-13(a)(1) (2006)); see also Cozart v. Sec'y of Health & Human Servs., 126 Fed. Cl. 488, 498 (2016). The Federal Circuit has found that treating physicians' opinions can help satisfy the second prong of the Althen test:

> Such testimony is "quite probative" since "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." Id. [Capizzano v. Sec'y of Health & Human Servs., 440 F.3d at 1326] (citations and internal quotation marks omitted); see also Althen[v. Sec'y of Health & Human Servs.], 418 F.3d at 1279–80 (noting that the Vaccine Act provides for the use of "medical opinion as proof" of causation); Zatuchni v. Sec'y of Health & Human Servs., 69 Fed. Cl. 612, 623 (Fed. Cl. 2006) (relying heavily on the testimony of treating physicians in concluding that Vaccine Act causation had been established).

Andreu ex rel. Andreu v. Sec'y of Health & Human Servs., 569 F.3d at 1375 (first set of brackets in original); see also Paluck v. Sec'y of Health & Human Servs., 786 F.3d at 1385 (finding "the special master erred in disregarding contemporaneous statements from K.P.'s [petitioners' minor child] treating physicians regarding the cause of his neurodegeneration" and "[a]s we explained in Andreu, '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.' [Andreu ex rel. Andreu v. Sec'y of Health & Human Servs.,] 569 F.3d at 1375" (brackets added)).

The third prong of the Althen test requires the petitioner to demonstrate, by a preponderance of evidence, "a proximate temporal relationship between vaccination and injury." Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1278. The United States Court of Appeals for the Federal Circuit emphasized the importance of a temporal relationship in Pafford v. Secretary of Health & Human Services, when the court noted that "without some evidence of temporal linkage, the vaccination might receive blame for

events that occur weeks, months, or years outside of the time in which scientific or epidemiological evidence would expect an onset of harm." Pafford v. Sec'y of Health & Human Servs., 451 F.3d at 1358. Requiring evidence of strong temporal linkage is consistent with the third requirement articulated in Althen because "[e]vidence demonstrating petitioner's injury occurred within a medically acceptable time frame bolsters a link between the injury alleged and the vaccination at issue under the 'but-for' prong of the causation analysis." Pafford v. Sec'y of Health & Human Servs., 451 F.3d at 1358 (citing Capizzano v. Sec'y of Health & Human Servs., 440 F.3d at 1326). The Pafford court further explained,

> [i]f, for example, symptoms normally first occur ten days after inoculation but petitioner's symptoms first occur several weeks after inoculation, then it is doubtful the vaccination is to blame. In contrast, if symptoms normally first occur ten days after inoculation and petitioner's symptoms do, in fact, occur within this period, then the likelihood increases that the vaccination is at least a factor. Strong temporal evidence is even more important in cases involving contemporaneous events other than the vaccination, because the presence of multiple potential causative agents makes it difficult to attribute "but-for" causation to the vaccination. After all, credible medical expertise may postulate that any of the other contemporaneous events may have been the sole cause of the injury.

Id. A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." de Bazan v. Sec'y of Health & Human Servs., 539 F.3d at 1352. Determining what constitutes a medically appropriate timeframe, thus, is linked to the petitioner's theory of how the vaccine can cause petitioner's injury. See id.; see also K.T. v. Sec'y of Health & Human Servs., 132 Fed. Cl. 175, 186 (2017); Shapiro v. Sec'y of Health & Human Servs., 101 Fed. Cl. 532, 542 (2011).

According to the court in Capizzano v. Secretary of Health & Human Services, evidence used to satisfy one of the Althen prongs may overlap with and be used to satisfy another prong. See Capizzano v. Sec'y of Health & Human Servs., 440 F.3d at 1326 ("We see no reason why evidence used to satisfy one of the Althen [v. Secretary of Health & Human Services, 418 F.3d at 1278] prongs cannot overlap to satisfy another prong." (brackets added)). If a petitioner satisfies the Althen test, the petitioner prevails, "unless the [government] shows, also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine." Knudsen ex rel. Knudsen v. Sec'y of Health & Human Servs., 35 F.3d at 547 (brackets in original; quotation omitted).

The Special Master has discretion to determine the relative weight of evidence presented, including contemporaneous medical records and oral testimony. See Burns v. Sec'y of Health & Human Servs., 3 F.3d 415, 417 (Fed. Cir. 1993) (finding that the Special Master had thoroughly considered evidence in record, had discretion not to hold an additional evidentiary hearing); Hibbard v. Sec'y of Health & Human Servs., 698 F.3d at 1368 (finding it was not arbitrary or capricious for the Special Master to weigh diagnoses

of different treating physicians against one another, including when their opinions conflict).

> "Clearly it is not then the role of this court to reweigh the factual evidence, or to assess whether the special master correctly evaluated the evidence. And of course we do not examine the probative value of the evidence or the credibility of the witnesses. These are all matters within the purview of the fact finder."

Dodd v. Sec'y of Health & Human Servs., 114 Fed. Cl. at 56 (quoting Munn v. Sec'y of Health & Human Servs., 970 F.2d at 870 n.10); see also Rich v. Sec'y of Health & Human Servs., 129 Fed. Cl. 642, 655 (2016); Paluck v. Sec'y of Health & Human Servs., 104 Fed. Cl. at 467 ("So long as those findings are 'based on evidence in the record that [is] not wholly implausible,' they will be accepted by the court." (quoting Lampe v. Sec'y of Health & Human Servs., 219 F.3d at 1363 (alteration in original))). "Determinations subject to review for abuse of discretion must be sustained unless 'manifestly erroneous.'" Heddens v. Sec'y of Health & Human Servs., 143 Fed. Cl. 193 (2019) (quoting Piscopo v. Sec'y of Health & Human Servs., 66 Fed. Cl. 49, 53 (2005) (citations omitted)).

Additionally, a Special Master is "not required to discuss every piece of evidence or testimony in [his or] her decision." Snyder ex rel. Snyder v. Sec'y of Health & Human Servs., 88 Fed. Cl. 706, 728 (2009) (brackets added); see also Paluck v. Sec'y of Health & Human Servs., 104 Fed. Cl. at 467 ("[W]hile the special master need not address every snippet of evidence adduced in the case, see id. [Doe v. Sec'y of Health & Human Servs., 601 F.3d 1349, 1355 (Fed. Cir. 2010)], he [or she] cannot dismiss so much contrary evidence that it appears that he 'simply failed to consider genuinely the evidentiary record before him.'" (brackets added) (quoting Campbell v. Sec'y of Health & Human Servs., 97 Fed. Cl. 650, 668 (2011))).

With regard to the Special Master's weighing of evidence when testimony conflicts with contemporaneous medical records, a Special Master generally should afford contemporaneous medical records greater weight than conflicting testimony offered after the fact. See Murphy v. Sec'y of Health & Human Servs., 23 Cl. Ct. 726, 733 (1991) (citing United States v. United States Gypsum Co., 333 U.S. 364, 396 (1947) ("It has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")), aff'd, 968 F.2d 1226 (Fed. Cir.) reh'g denied, (Fed. Cir. 1992). This is because medical records, created contemporaneously with the events they describe are presumed to be accurate and complete. See Cucuras v. Sec'y of Health & Human Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993).

As discussed above, petitioner must prove by a preponderance of the evidence that his rheumatoid arthritis was caused by the influenza vaccination he received. See 42 U.S.C. § 300aa-11(c)(1)(C)(ii)(I). If the Special Master's decision was not arbitrary, capricious, or not in accordance with the law, the reviewing court shall uphold that decision. See 42 U.S.C. § 300aa-12(e)(2). Special Master Moran spent significant amounts of time in his decision devoted to the details of the scientific and medical

evidence, although often without offering definitions of the scientific and medical terms he used in his decision. Also, given that the petitioner has the burden of proof, the Special Master's decision oddly starts his discussion of the experts' opinions by first reviewing the respondent's experts, and then goes on to review the petitioner's experts. Nonetheless he did carefully try to review the record before him, including petitioner's medical history, the expert reports, and information provided to him at the hearing over which he presided.

As indicated above, petitioner submitted his medical records and offered two experts, Dr. Paul J. Utz and Dr. Lawrence Steinman to support petitioner's theory of molecular mimicry and his theory of causation. At the oral argument before this court, petitioner's counsel indicated: "Dr. Steinman looked at the BLAST searches, Dr. Utz looked at the articles on both, the HA collagen and how the T cells bond, but also on how the tetramers, which are a portion that have the specific peptide complexes, how those create these bonds." (capitalization in original). Dr. Utz's original expert report, submitted on February 29, 2016, discussed petitioner's theory of molecular mimicry, including "[w]hen an immune response to a nonself antigen such as components of an influenza vaccine cross reacts with self molecules, the process is termed 'molecular mimicry.'" Dr. Utz stated in his February 29, 2016 original expert report that the medical theory of causation proffered by petitioner is that "the vaccine triggered activation of B and/or T lymphocytes through molecular mimicry, formation of immune complexes, cross-priming, or a combination of these." Dr. Utz also stated in his February 29, 2016 original expert report that "[m]any arthritides including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), Lyme arthritis, serum sickness, and parvovirus infection are postulated to be (SLE [systemic lupus erythematosus], RA [rheumatoid arthritis]) or known to be (the remaining illnesses), caused by exposure to an infectious antigen or foreign antigen." (capitalization in original) (brackets added). Dr. Utz cited the Clifton O. Bingham III and Malini Moni article (the Bingham article) in his November 7, 2016 first supplemental expert report and stated "the Bingham article does not link influenza vaccination and RA [rheumatoid arthritis]; however, it clearly shows that another expert considers molecular mimicry to be a possible trigger in RA [rheumatoid arthritis], in contrast to the position taken by Dr[.] Matloubian." (brackets added). The Bingham article, titled, "Periodontal disease and rheumatoid arthritis: the evidence accumulates for complex pathobiologic interactions," published in May 2013, examined "the associations between periodontal disease and rheumatoid arthritis." In the article, molecular mimicry is not mentioned by name. The authors state that when other researchers "immunized" animals "using Pg-enolase and human a-enolase" that "the study demonstrated that a Pg protein could induce arthritis and propagate an immune response against citrullinated peptides." (emphasis in original). Regarding this statement in the Bingham article, Dr. Utz stated "the authors clearly describe the ability of a bacterial protein to break tolerance and to cause arthritis in an animal model, acting as a molecular mimic."

In his November 7, 2016 first supplemental expert report, Dr. Utz also cited to the Jens Hennecke and Don C. Wiley paper (the Hennecke paper), titled, "Structure of a Complex of the Human α/β T Cell Receptor (TCR) HA1.7, Influenza Hemagglutinin Peptide, and Major Histocompatibility Complex Class II Molecule, HLA-DR4 (DRA*0101 and DRB1*0401): Insight into TCR Cross-Restriction and Alloreactivity," published

February 25, 2002. (capitalization in original). Dr. Utz stated "the authors demonstrate that a cross-reactive peptide (ie, [sic] a molecular mimic) derived from the hemagglutinin molecule from influenza was able to bind the DR4 MHC molecule." (capitalization in original). The authors of the Hennecke paper described the findings of the study as: "This structural study of TCR cross-reactivity emphasizes how MHC sequence differences can affect TCR binding indirectly by moving peptide atoms." (capitalization in original). Dr. Utz stated, regarding the findings of this study, "this paper only demonstrates that DR4 can bind an influenza or collagen peptide; it does not demonstrate that T cell receptors (TCRs) on human T cells can recognize collagen or influenza peptides." (capitalization in original). Dr. Utz, in his September 4, 2018 third supplemental expert report also introduced the Michael E. Birnbaum, Juan L. Mendoza, Dhruv K. Sethi, Shen Dong, Jacob Glanville, Jessica Dobbins, Engin Özkan, Mark M. Davis, Kai W. Wucherpfennig, and K. Christopher Garcia paper (the Birnbaum paper) as support for molecular mimicry and stated "autoimmune T cells have the ability to be activated by immunogens encountered in the environment, which may serve as the triggers for the initiation of autoimmunity." The Birnbaum paper, titled, "Deconstructing the peptide-MHC specificity of T cell recognition," published on May 22, 2014, examined "[d]econstructing the peptide-MHC specificity of T cell recognition." (capitalization in original). The Birnbaum paper stated:

> While the naturally occurring peptides in this study were found as a proof of principle for our methodology, they further support the hypothesis that autoimmune T cells have the ability to be activated by immunogens encountered in the environment, which may serve as the triggers for the initiation of autoimmunity.

Dr. Utz in his September 4, 2018 third supplemental expert report also introduced the Linda Wooldridge, Julia Ekeruche-Makinde, Hugo A. van den Berg, Anna Skowera, John J. Miles, Mai Ping Tan, Garry Dolton, Mathew Clement, Sian Llewellyn-Lacey, David A. Price, Mark Peakman, and Andrew K. Sewell paper (the Wooldridge paper), titled, "A Single Autoimmune T Cell Receptor Recognizes More Than a Million Different Peptides," published November 18, 2011. (capitalization in original). The Wooldridge paper researchers stated, "[a] single autoimmune T cell receptor recognizes more than a million different peptides."

In his June 8, 2017 second supplemental expert report, Dr. Utz also stated that the evidence he provided should be sufficient to support molecular mimicry, but that he cannot prove that molecular mimicry can occur without "culturing these autoreactive, stimulated, expanded T cells and transferring them into an asymptomatic healthy human subject to attempt to induce RA [rheumatoid arthritis] in fulfillment of Koch's postulates,[7] an experiment that would be completely unethical." (emphasis in original) (brackets and footnote added). Dr. Utz also admitted in his September 4, 2018 third supplemental expert report, "I have not proven that the molecular mimic influenza peptides directly influence the same T cells that are activated by collagen peptides." (emphasis in original). Dr. Utz,

[7] Dr. Utz does not define "Koch's postulates" in his expert report.

nonetheless, stated in his September 4, 2018 third supplemental expert report, "[i]n many cases, I have successfully argued for molecular mimicry just by" "show[ing] sequence homology between a vaccine component and a self molecule," without citing to those other cases.

In his November 7, 2016 first supplemental expert report, Dr. Utz indicated that because rheumatoid arthritis is so heterogenous in its pathology it is difficult to determine a cause. Dr. Utz then listed environmental factors that "the vast majority of rheumatologists and immunologists would agree" contribute to rheumatoid arthritis. Dr. Utz acknowledged environmental factors that contribute to rheumatoid arthritis in his November 7, 2016 first supplemental expert report, such as use of "tobacco," "age, sex, family history, and gingivitis, among others." Dr. Utz also stated in his February 29, 2016 original expert report, "my search identified no epidemiological link between RA [rheumatoid arthritis] and influenza vaccination." (brackets added). Dr. Utz, however, stated in his February 29, 2016 original expert report that "many studies and textbooks postulate that RA [rheumatoid arthritis] can be caused by viruses themselves, or by other inflammatory triggers" without citing to the studies or textbooks to which he was referring. (brackets added). Dr. Utz also stated in his February 29, 2016 original expert report that petitioner's T cell repertoire, which is the type of cell that would mistake a foreign antigen for a self antigen to cause molecular mimicry, is so rare that "epidemiologic studies will not have the power to capture rare, patient-specific events such as occurred in Mr[.] Tullio's case."[8]

[8] The court notes that Dr. Utz had been the retained expert in Parker v. Secretary of Health & Human Services, No. 14-979V, 2019 WL 3425297 (Fed. Cl. Spec. Mstr. June 24, 2019). Because Dr. Utz was a retained expert in Parker v. Secretary of Health & Human Services, petitioner had requested access to the hearing transcripts in the Parker case, which was denied by the Special Master during the course of the proceedings before him. In the motion for review to this court, petitioner also requested access to the hearing transcripts in Forrest v. Secretary of Health & Human Services, No. 14-1046V, 2019 WL 925495 (Fed. Cl. Spec. Mstr. Jan. 28, 2019), in which Dr. Steinman was an expert witness. To explain the issues petitioner raises, petitioner states in his motion for review, "[i]t is erroneous and harmful to Petitioner to permit a credibility determination of his expert based on extra-judicial information inaccessible to Petitioner." Petitioner also states: "This situation underscores the problems inherent in the Special Master's pre-hearing order denying Petitioner's request for the transcript of a related proceeding." It is not apparent that the position taken by Dr. Steinman in Forrest v. Secretary of Health & Human Services or by Dr. Utz in Parker v. Secretary of Health & Human Services would have undermined the opinions as expressed in the instant case. The court believes that the unavailability of the two hearing transcripts to petitioner would not have altered the consideration given to the opinions offered by those two petitioner's experts, impacted concerns about Dr. Steinman's credibility expressed by the Special Master in his decision, or go to the credibility of Dr. Utz. This court, therefore, considers review by the petitioner of the transcripts in Parker and Forrest not necessary nor of assistance to this court in its review of the Special Master's decision, and the Special Master did not err when he denied petitioner's request for the Parker transcript. Moreover, as discussed below, Mr.

With respect to the "evidence regarding experiments on the hemagglutinin in flu virus and collagen," Special Master Moran found that the papers Dr. Utz relied upon to assert the molecular mimicry theory to be "relatively unimportant" because the studies "basically report on how an antigen-presenting cell interacts with hemagglutinin and with collagen," and not "whether T cells bind to the hemagglutinin and/or collagen as presented through the antigen-presenting cell." See Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *14, *16. Special Master Moran found that, without the theory that hemagglutinin and collagen are molecular mimics having been tested, a "gap of knowledge and evidence exist[s]." See id. at *24. During the course of the case before the Special Master, respondent offered expert testimony to refute petitioner's offers of proof and to refute petitioner's evidence. The respondent's expert Dr. Matloubian agreed with petitioner's expert Dr. Utz in that the presentation of rheumatoid arthritis can be heterogenous, however, Dr. Matloubian asserted in his June 10, 2016 original expert report, "[f]or molecular mimicry to be relevant to an autoimmune disease and the vaccine in question, the natural infection itself, i.e. with influenza virus in this case, should also lead to development of that disease in some people." (emphasis in original).

In his decision, Special Master Moran also relied on and discussed a number of previously decided vaccine cases to bolster his conclusion to deny compensation to petitioner, including W.C. v. Secretary of Health & Human Services and Caves v. Secretary of Health & Human Services, as part of his analysis of petitioner's theory of molecular mimicry. See W.C. v. Sec'y of Health & Human Servs., 704 F.3d 1352 (Fed. Cir. 2013); Caves v. Sec'y of Health & Human Servs., 100 Fed. Cl. 119, 135 (2011), aff'd, 463 F. App'x 932 (Fed. Cir. 2012). In W.C. v. Secretary of Health & Human Services, petitioner alleged that his influenza vaccination caused aggravation to his multiple sclerosis (MS) through the process of molecular mimicry. The United States Court of Appeals for the Federal Circuit in W.C. v. Secretary of Health & Human Services described the evidence presented by a petitioner:

> The special master found that "[m]olecular mimicry is a well-regarded theory in some contexts," Special Masters 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 [v. Secretary of Health & Human Services], 618 F.3d at 1345 (holding "a petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case").
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> 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

Tullio failed to offer sufficient evidence to meet his burden of proving that his rheumatoid arthritis was caused by the influenza vaccination petitioner received. See Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *28.

> 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.

W.C. v. Sec'y of Health & Human Servs., 704 F.3d at 1360. In W.C. v. Secretary of Health & Human Services, the Federal Circuit outlined the reasons, which were also identified by the Special Master, as to why the petitioner's theory of molecular mimicry was insufficient to prove petitioner's case, finding, "Petitioner provided no evidence that the portions of the influenza virus shown by Wucherpfennig [referred to in the quote immediately above] to mimic myelin basic protein were present in the influenza vaccine Petitioner received," and "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. at 1360-61 (brackets added). The Federal Circuit in W.C. v. Secretary of Health & Human Services also found that two studies which examined patients with MS relied upon by the Special Master showed that MS was not exacerbated by the influenza vaccination to be more persuasive than petitioner's expert's theory and affirmed the denial of compensation by the Special Master. See id. at 1361.

The second case regarding molecular mimicry that Special Master Moran discussed was Caves v. Secretary of Health & Human Services, a case also decided by Special Master Moran, and which was then affirmed by Judge Bush of the United States Court of Federal Claims. Subsequently, the United States Court of Appeals for the Federal Circuit affirmed the Court of Federal Claims' decision. See generally Caves v. Sec'y of Health & Human Servs., 463 F. App'x 932 (Fed. Cir. 2012). In the Court of Federal Claims decision, the Judge found:

> The theory of molecular mimicry does not apply specifically to petitioner's case; on the contrary, that general theory could be used to demonstrate an association between virtually any combination of antigens and autoimmune injuries. Without any empirical evidence that the theory actually applies to the influenza vaccine and TM [transverse myelitis], the first prong of Althen would be rendered meaningless.

Caves v. Sec'y of Health & Human Servs., 100 Fed. Cl. at 135.

A case not relied upon or cited by the Special Master, but relevant to the instant case, is a decision discussing molecular mimicry issued by United States Court of Appeals for the Federal Circuit. See generally Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339. The evidence the petitioner in Broekelschen v. Secretary of Health

& Human Services offered to "connect[ ] the molecular mimicry theory to the flu vaccine" was "a literature review based on two papers from the early 1950s, which in turn considered vaccine cases between 1929 and 1952." Id. at 1350. The Federal Circuit in Broekelschen v. Secretary of Health & Human Services affirmed the Special Master's decision that petitioner "had not provided a 'reliable medical or scientific explanation' sufficient to prove by a preponderance of the evidence a medical theory linking the flu vaccine to anterior spinal artery syndrome." Id. at 1351 (quoting Knudsen ex rel. Knudsen v. Sec'y of Health & Human Servs., 35 F.3d at 548). Although Mr. Tullio provided more evidence than a literature review of two 1950s studies, Mr. Tullio failed to "provide evidence that any peptide from the influenza vaccine he received was cross-reactive with" the specific T cells. See W.C. v. Sec'y of Health & Human Servs., 704 F.3d at 1360–61; see also Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d at 1351. When arriving at his decision, Special Master Moran was justified in focusing on petitioner's expert Dr. Utz and respondent's expert Dr. Matloubian, who shared concerns that the cause of rheumatoid arthritis is unknown. The Special Master rationally could conclude that that the influenza vaccination petitioner received was not the cause of Mr. Tullio's rheumatoid arthritis. As Dr. Utz testified at the hearing before Special Master Moran: "It is currently not known what causes rheumatoid arthritis." In response to the question from respondent's counsel at the hearing before Special Master Moran: "Does the medical community know what causes rheumatoid arthritis?" Dr. Matloubian testified: "No." As discussed further below, based on a review of the record before the court, the Special Master was justified to require more evidence than what was in the record to support petitioner's allegations that petitioner's influenza vaccination caused the petitioner's rheumatoid arthritis. The Special Master's conclusion was not arbitrary or capricious based on his in-depth examination of the record before him. The Special Master also stated:

> The mechanistic evidence tends to align with the epidemiologic evidence, which did not detect an increased incidence of rheumatoid arthritis following flu vaccination. Thus, exclusively for the reasons set forth . . . Mr. Tullio has failed to carry his burden of presenting a reliable and persuasive theory that the flu vaccine can cause rheumatoid arthritis.

Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *22 (internal references omitted). Special Master Moran, therefore, concluded that petitioner had not satisfied his burden to prove by a preponderance of evidence that petitioner had presented a "logical sequence of cause and effect," and his conclusions were not arbitrary or capricious. See Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1278; see also Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *5.

At the oral argument before this court, petitioner's counsel, however, stated that, in addition to relying on the studies regarding hemagglutinin and collagen introduced by Dr. Utz, petitioner also tried to rely on "how the tetramers, which are a portion that have the specific peptide complexes, how those create these bonds." Respondent's expert Dr. Matloubian had introduced the information regarding tetramers in his November 16, 2018 second supplemental expert report, in part in response to petitioner's expert Dr. Utz

indicating that testing his theory of molecular mimicry only would be possible through unethical means.[9] Dr. Matloubian also stated in his November 16, 2018 second supplemental expert report, "[u]sing current immunological tools and techniques, such as widely available tetramers, the question of whether the same T cell receptor can recognize both collagen and HA peptides bound to the same HLA can be readily addressed." Dr. Matloubian described tetramers by stating, "these tools allow identification of T cells that recognize a specific MHC-peptide complex (i.e., T cells that are specific for HLA-DR4 containing the HA peptide or HLA-DR4 containing the collagen II peptide)." (capitalization in original). Petitioner did not address the theory of tetramers until petitioner's expert Dr. Utz testified at the March 6-8, 2019 hearing before Special Master Moran, in response to a question from petitioner's counsel, "[h]ow would you go about observing molecular mimicry in one of your patients in a clinical setting?" Petitioner's expert Dr. Utz replied:

> In a clinical setting, to observe molecular mimicry or study it would be an enormous challenge. So one of the things would be to identify collagen antibodies. That would be one thing that would be supportive. Those assays are not available in clinical labs to my knowledge. I have never ordered one. They are only available in a research lab.
>
> The second would be to create tetramers which Dr. Matloubian has provided three [sic] exhibits on tetramers. Tetramers are MHC molecules that are loaded in this case with DR4, loaded with collagen, or with HA.

The four studies on tetramers introduced by Dr. Matloubian in his first and second supplemental reports were the Svendsen, Snir, James, and Malmström studies. Special Master Moran evaluated the four studies regarding tetramer experiments introduced by respondent. Special Master Moran found that the petitioner's contention that tetramer experiments can "explain how the flu vaccine can cause rheumatoid arthritis" "lacks persuasive value because Dr. Utz extends the studies beyond what the authors of those studies reported." Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *18. The Special Master evaluated the Pia Svendsen, Claus B. Andersen, Nick Willcox, Anthony J. Coyle, Rikard Holmdahl, Thomas Kamradt, and Lars Fugger study (the Svendsen study), titled, "Tracking of Proinflammatory Collagen-Specific T Cells in Early and Late Collagen-Induced Arthritis in Humanized Mice" accepted for publication on

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[9] According to the Benaroya Institute, a source cited by Dr. Matloubian in his November 16, 2018 second supplemental expert report, tetramers are "are a multivalent synthetic mimic of the peptide binding proteins found on the surface of antigen presenting cells." Scientists & Laboratories: Tetramer Core Laboratory, Benaroya Research Institute, https://www.benaroyaresearch.org/what-is-bri/scientists-and-laboratories/core-labs/tetramer -core-laboratory (last visited on June 18, 2020). Dr. Utz testified at the hearing as to his definition of tetramers: "Tetramers are MHC molecules that are loaded in this case with DR4, loaded with collagen, or with HA. Four of them tether together and they have fluorophores on them so they glow. You can use those to look at antigen-specific T cells." (capitalization in original).

August 10, 2004, which was introduced by Dr. Matloubian in his November 16, 2018 second supplemental expert report. The Special Master described three experiments which took place to try to determine whether B or T cells "initiated the disease," when "struggling to understand the pathology of rheumatoid arthritis." See id. In order to test the theory, the researchers had used petri dishes and mice. One experiment referenced in the Svendsen study involved mice being immunized with collagen, hemagglutinin with an adjuvant, as well as an adjuvant, and saline. Blood was drawn from mice lymph nodes thirteen days after immunization of collagen, hemagglutinin with an adjuvant, as well as an adjuvant, and saline, and "researchers determined the frequency of the targeted T cells, expressed as a percentage of T cells" that responded. See id. The frequency of the T cells from the hemagglutinin-immunized mice that were stained with hemagglutinin tetramer was 0.86 percent and with a collagen tetramer was 0.08 percent. Dr. Utz testified that 0.08 demonstrates cross-reactivity between hemagglutinin and collagen. The Omri Snir, Mary Rieck, John A. Gebe, Betty B. Yue, Crystal A. Rawlings, Gerald Nepom, Vivianne Malmström, and Jane H. Buckner study (the Snir study), titled, "Identification and Functional Characterization of T Cells Reactive to Citrullinated Vimentin in HLA–DRB1*0401–Positive Humanized Mice and Rheumatoid Arthritis Patients," which was published in October 2011, was introduced by Dr. Matloubian in his November 16, 2018 second supplemental expert report. (capitalization in original). In the Snir study the "hemagglutinin antigen tetramer was used as a negative control." In addition in the Eddie A. James, Mary Rieck, Jennifer Pieper, John A. Gebe, Betty B. Yue, Megan Tatum, Melissa Peda, Charlotta Sandin, Lars Klareskog, Vivianne Malmström, and Jane H. Buckner study (the James study), titled, "Citrulline-Specific Th1 Cells Are Increased in Rheumatoid Arthritis and Their Frequency Is Influenced by Disease Duration and Therapy," published in July 2014, also introduced by Dr. Matloubian in his November 16, 2018 second supplemental expert report, the peptide control was again hemagglutinin. (capitalization in original). In the Vivianne Malmström, Anca I. Catrina and Lars Klareskog study (the Malmström study), titled, "The immunopathogenesis of seropositive rheumatoid arthritis: from triggering to targeting," published December 5, 2016, likewise was introduced by Dr. Matloubian in his February 23, 2017 first supplemental expert report. In the Malmström study, hemagglutinin from the influenza vaccination is described as "an unrelated antigen" to the research regarding seropositive rheumatoid arthritis, similar to how hemagglutinin was a control in the James study. When Special Master Moran asked petitioner's expert Dr. Utz at the hearing before him about the statement that hemagglutinin is an unrelated antigen to seropositive rheumatoid arthritis, Dr. Utz responded that "they are using these tetramers as a control. They are not studying mimicry. They are not studying people like Mr. Tullio. So they are using this as a control for a totally different purpose."

At the oral argument before this court, petitioner's counsel argued that, in addition to the expert reports provided by Dr. Utz and the tetramer experiments introduced by respondent, petitioner also relies on petitioner's expert Dr. Lawrence Steinman's "BLAST searches."[10] (capitalization in original). Petitioner's expert Dr. Steinman, in his November

[10] At the hearing before Special Master Moran, Dr. Steinman described the Blast searches as a computer program "aligning vast domains of these proteins and assigning weights

7, 2016 original expert report, discussed the similarities between hemagglutinin, the protein in the influenza vaccination, and that the "major proteins considered to be the major targets of the response in RA [rheumatoid arthritis] are collagen, fibrinogen, enolase and vimentin (8)." (brackets added). Dr. Steinman conducted what he called Blast searches to determine "any relevant molecular mimics between" the proteins and the components of the influenza vaccination the petitioner received by searching a National Institute of Health database of amino acids. The enolase and hemagglutinin peptide sequence homology[11] was deemed "relevant" by Dr. Steinman because the "peptides of enolase and the hemagglutinin from the 2012 vaccine have 5 of 12 or 4 of 11 identities with 2 close matches within 12 amino acids, making it 7 of 12 positives." The protein vimentin also was deemed by Dr. Steinman to have relevant molecular mimics because there were "4 of 12 identical, 5 of 12 positive, and 5 of 13 identical and 6 of 13 positive" in the sequence homology Blast search. Regarding fibrinogen, Dr. Steinman stated there was "a 4 of 7 identity and a 5 of 7 positivity" with hemagglutinin, which meant "this was sufficient to induce clinical autoimmune disease." Finally, in his November 7, 2016 original expert report regarding collagen, Dr. Steinman stated, "[t]here were many molecular mimics but these two above are stunning, including a 6 of 11 with four consecutive IDENTICAL amino acids between collagen and the Hemagglutinin from Influenza Virus A/Victoria/361/2011." (capitalization in original). Dr. Steinman stated that "[s]trikingly, there are extensive molecular mimics between the contents of the 2012 influenza vaccine received by Petitioner and the critical antigens that are associated with rheumatoid arthritis." (emphasis in original omitted).

Regarding Dr. Steinman's Blast searches, offered in support of petitioner's case, respondent's expert Dr. Matloubian, in his June 10, 2016 original expert report, stated the

> presence of linear sequence homology does not necessarily translate to immunogenicity. Proteins consist of linear sequence of amino acids but fold into complex three-dimensional structures. Therefore, the same sequence of amino acids may be on the surface of one protein, and thus easily accessible to antibodies, while in another protein the same sequence could be buried inside the molecule and hidden from those antibodies.

Disputing petitioner's theory of sequence homology, Dr. Matloubian also stated in his February 23, 2017 first supplemental expert report:

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and actually lining them up." Regarding the Blast searches, which petitioner's counsel called the "Steinman study" at the oral argument, this court asked the petitioner's counsel: "You cannot tell me that Dr. Steinman's experimentation had anything to do with either high dose Fluzone influenza vaccine or rheumatoid arthritis. Is that correct?" Petitioner's counsel responded: "Yes, ma'am."

[11] Dr. Steinman, who performed the Blast searches, stated that sequence homology, in his view, has an "operational definition that a sequence of 12 or fewer amino acids that are identical at 4 positions."

> Even though the same peptide sequence of 7-12 amino acids can occur in two different proteins, its proper processing could be affected by the surrounding amino acid sequences resulting in differences in the ability of MHC molecules to present them to T cells. Because of these caveats, in science, the standards of proof for molecular mimicry are quite high and sequence homology itself is not sufficient evidence.

Moreover, Dr. Matloubian stated in his February 23, 2017 first supplemental expert report that researchers generally focused much more heavily on studying the structure of proteins, rather than on the sequence of proteins, because most algorithms regarding sequence "have low accuracy for predicting MHC class II restricted epitopes, underscoring the principle that just finding sequence homology in several proteins does not imply antigenicity, let alone molecular mimicry." (emphasis in original). In his November 16, 2018 second supplemental expert report, Dr. Matloubian stated: "Just because two peptides (small pieces of protein) may share similar sequences and even bind to the same major histocompatibility complex (MHC/HLA) does not necessarily mean that the same T cell can see them as similar (i.e. does not mean that they have the same 'immunologic epitope')." (capitalization in original) (emphasis omitted). In addition, Dr. Matloubian stated in his November 16, 2018 second supplemental expert report that in order for molecular mimicry to occur "at the T cell level, the same T cell must recognize both the influenza peptide and the RA [rheumatoid arthritis] peptide associated with MHC/HLA." (capitalization in original) (emphasis omitted) (brackets added).

Regarding Dr. Steinman's Blast searches, Special Master Moran wrote that because all proteins "are built from the same 20 amino acids, it is inevitable that some sequences of amino acids will repeat." Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *15. In this respect, Special Master Moran indicated that "the finding of sequence homology does not necessarily mean the similarity has significance to the immune system." Id. Special Master Moran also noted that "scientists have identified the portions of the flu virus that are peptides and created a database of them. Dr. Matloubian queried the database to see whether the epitopes that Dr. Steinman had identified appeared in the database. Dr. Matloubian disclosed that he did not find any positive hits." Id. After his review of the record before him, Special Master Moran found the Blast research to be unpersuasive because of Dr. Steinman's "lack of meaningful response" when compared to respondent's expert, Dr. Matloubian's, conclusion, who searched the influenza virus peptide database, as opposed to a more general database. See id.

After reviewing the record before him, Special Master Moran stated petitioner's expert Dr. Steinman "misses its mark" when Dr. Steinman "added a critique that those studies[12] were not relevant to Mr. Tullio's situation because none of those studies

[12] Although not clear in the Special Master's decision, based on the hearing transcript, Dr. Steinman seemed to be referring to the Ray and Bardage studies discussed below. The Bengtsson study, also discussed below, could also have been included because petitioner argues that petitioner also would not have qualified for that vaccination. The

involved the exact vaccine that he received." Id. at *11 (footnote added). Dr. Steinman testified at the hearing before Special Master Moran: "And again, I state in my report, referring to Dr. Matloubian's Exhibit CC [the Ray study] where he talks about vaccines from the 1997 to 1999 season, that that epidemiology is totally irrelevant because those vaccines didn't have the 2009 A/California, the 2011 A/Victoria, the 2010 B/Wisconsin because it was only 1999." (brackets added). Dr. Steinman also testified: "Generally speaking, there's a whole problem with lumping all influenza vaccines into one boat because, as I said this morning, they're seasonal. The CDC [Center for Disease Control] nominates well ahead of time the virus strains. The virus strains differ from year to year. And we know, for instance, that one year a virus strain that was used with an adjuvant, not here, but it led to an outbreak of narcolepsy." (brackets added). Regarding this argument offered by petitioner, Special Master Moran stated:

> Dr. Matloubian tested the degree of difference among various iterations of flu vaccines. Using the same methodology Dr. Steinman used to determine the degree of homology between a component of the flu vaccine and a component of joint tissue . . . Dr. Matloubian found that the flu vaccines retain at least 90 percent homology across the years.[13] When asked about this approach, Dr. Steinman did not contest Dr. Matloubian's findings.

Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *11 (internal citations omitted) (footnote added). The Special Master also concluded that "Dr. Steinman's challenge to the usefulness of epidemiologic studies not involving the 2015 [sic] flu vaccine that Mr. Tullio received is not persuasive. Instead, the epidemiologic studies are persuasive. As such, the epidemiological evidence weakens the reliability of opinions that the flu vaccine can cause rheumatoid arthritis." Id.

In Moberly ex rel. Moberly v. Secretary of Health & Human Services, the United States Court of Appeals for the Federal Circuit found, "[a]s a general matter, epidemiological studies are designed to reveal statistical trends only for a carefully constructed test group. Such studies provide no evidence pertinent to persons not within the parameters of the test group." Moberly ex rel. Moberly v. Sec'y of Health & Human Servs., 592 F.3d at 1324 (finding that because petitioner could not have belonged to a test group that the study could not apply to petitioner). In Lampe v. Secretary of Health &

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hearing transcript, however, cited by the Special Master cited only petitioner's references to the Ray and Bardage studies.

[13] In this statement, Special Master Moran appears to be referring to a database introduced and examined by respondent's expert Dr. Matloubian. According to the Special Master's decision, "scientists have identified the portions of the flu virus that are peptides and created a database of them. Dr. Matloubian queried the database to see whether the epitopes that Dr. Steinman had identified appeared in the database. Dr. Matloubian disclosed that he did not find any positive hits." Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *15.

Human Services, the United States Court of Appeals for the Federal Circuit also found that because petitioner did not fit into the study's "paradigm" that the study could not "shed light on the issue of causation in her case." Lampe v. Sec'y of Health & Human Servs., 219 F.3d at 1366.[14]

In his decision, Special Master Moran criticized petitioner's expert Dr. Steinman for "suggesting that his methods in forming an opinion in a legal proceeding are less stringent than if he were submitting his theory for peer review." Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *24. Regarding Dr. Steinman, Special Master Moran noted, "if he were trying to publish a paper in a peer-reviewed journal, he would do more, such as model his theory in mice." Id. Special Master Moran further wrote:

> Dr. Steinman stated that his work is sufficient for a court but not for the broader community. Tr. 354 ("And that's about the best I could do and that's the foundation of a theory for this Court. I'm not applying for a prize. I'm just saying that this is where an experiment led me [to that says could a vaccine that has the components of Mr. Tullio's that are shared with those antigens that are imputed to be involved in the pathogenesis of rheumatoid arthritis, could they have done it?]").

Id. (brackets added). Special Master expressed concern that "Dr. Steinman seemed to indicate that he expressed opinions, as an expert, more readily than he would outside a legal proceeding" and that "[o]ther special masters have expressed similar concerns." Id. at *26 (citing D.G. v. Sec'y of Health & Human Servs., No. 11-577V, 2019 WL 2511769, at *182 (Fed. Cl. Spec. Mstr. May 24, 2019); Chinea v. Sec'y of Health & Human Servs., No. 15-095V, 2019 WL 1873322, at *19 (Fed. Cl. Spec. Mstr. Mar. 15, 2019), aff'd, 144 Fed. Cl. 378, 386-87 (2019)). Special Master Moran wrote in his decision that Dr. Steinman's approach on behalf of the petitioner was inconsistent with the United States

[14] The court notes that in an unpublished decision, McCollum v. Secretary of Health & Human Services, the United States Court of Appeals for the Federal Circuit upheld a Special Master's determination that the studies regarding the adjuvanted H1N1 Pandemrix vaccination and narcolepsy were not persuasive to petitioner's case because petitioner in that case received the unadjuvanted influenza vaccination. See McCollum v. Sec'y of Health & Human Servs., 760 F. App'x 1003, 1008-09 (Fed. Cir. 2019). In another unpublished decision cited by petitioner, D'Toile v. Secretary of Health & Human Services, the United States Court of Appeals for the Federal Circuit found appropriate the lack of deference given to a study involving Pandemrix when the petitioner received a different influenza vaccination than Pandemrix. See D'Tiole v. Sec'y of Health & Human Servs., 726 F. App'x 809, 811 (Fed. Cir. 2018). Thereafter, in a decision issued by another Judge of the United States Court of Federal Claims, Dougherty v. Secretary of Health & Human Services, the Judge cited D'Tiole and found that the Special Master had reasonably found insufficient evidence existed to support that the petitioner's narcolepsy was caused by the influenza vaccination because the vaccination was sufficiently different from Pandemrix. See Dougherty v. Sec'y of Health & Human Servs., 141 Fed. Cl. at 229-30.

Supreme Court's decision in Kumho Tires Co., Ltd. v. Carmichael, 526 U.S. 137 (1999), because testimony in the courtroom should employ "'the same level of intellectual rigor that characterizes the practice of an expert in the relevant field.'" Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *26 (quoting Kumho Tires Co., Ltd. v. Carmichael, 526 U.S. at 152). In a somewhat contradictory statement, Special Master Moran also wrote in his decision, "[h]owever, Dr. Steinman's approach might be consistent with a view that distinguishes scientists from participants in the civil litigation." Id. (citing Andreu ex rel. Andreu v. Sec'y of Health & Human Servs., 569 F.3d at 1380).

Another of the petitioner's arguments before this court is that the Special Master erred because "[t]he weight placed on the epidemiological evidence herein influenced the Decision's entire causation analysis." Petitioner argues that "the Special Master should have rejected the epidemiology herein as not dispositive and of little persuasive value, as opposed to finding it 'powerful.'" (quoting Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *11, *27). Although at the oral argument before this court, petitioner's counsel indicated that, in part, "Petitioners [sic] weren't [sic] relying on epidemiological studies in support of their [sic] position. Only Respondent was relying on them to counter the Petitioner's position," petitioner also referred to some of the respondent's evidence to support his case, as described above regarding tetramers. Petitioner points to four studies that the Special Master allegedly relied on too heavily: the Ray, Bengtsson, Bardage, and Westra studies, each of which was introduced by the respondent. The Paula Ray, Steven Black, Henry Shinefield, Aileen Dillon, Diane Carpenter, Edwin Lewis, Pat Ross, Robert T. Chen, Nicola P. Klein, Roger Baxter study (the Ray study), titled, "Risk of rheumatoid arthritis following vaccination with tetanus, influenza and hepatitis B vaccines among persons 15-59 years of age," published on July 16, 2011, introduced by Dr. Halsey in his February 23, 2017 original expert report, examined influenza, hepatitis B, and tetanus vaccinations from 1997 until 1999 in individuals from the ages of 15-59. To rebut Dr. Steinman's contention that the studies on influenza vaccinations from other years are inapplicable, specifically the years covered in the Ray study, Dr. Matloubian stated in his February 23, 2017 first supplemental expert report:

> Two out of the four sequences are identical between the 1998-1999 strain and the 2012-2013 one (Figure 3). The other two, only differ by one amino acid between the two strains, resulting in 12 out of 13 in one case and 10 out of 11 in the other case of identical amino acids. This type of similarity is what Dr. Steinman would term 'stunning' and is more remarkable than any he has described in his report. (Ex. 40 at 20).

Petitioner claims in his motion for review that the Ray study raised by respondent should not be dispositive, because "the high-dose influenza vaccine received by Petitioner was not available during those years." Petitioner also argues that petitioner would not have qualified for the Ray study because "Petitioner was too old."

The Camilla Bengtsson, Meliha C. Kepetanovic, and Henrik Källberg, et al. study (the Bengtsson study), titled, "Common vaccinations among adults do not increase the risk of developing rheumatoid arthritis: results from the Swedish EIRA study," published

on July 5, 2010, also introduced by respondent, although not through an expert, was conducted from 1996-2006, and the class of people studied were from the ages of 18-70 living in Sweden. Additionally, the Bengtsson study noted that "[s]pecific vaccinations studied were flu, tetanus, diphtheria, tickborne encephalitis, hepatitis (A, B, C), polio and pneumococcus." The Bengtsson study stated, "it is unlikely that vaccinations in general should be considered as a major risk factor for RA [rheumatoid arthritis]." (brackets added). Petitioner claims in his motion for review he would not have qualified for the respondent-introduced Bengtsson study because "Respondent offered no evidence that the influenza vaccination given in Sweden in 1998 was similar to the high-dose vaccine given to Petitioner in 2012."

The Carola Bardage, Ingemar Persson, Åke Örtqvist, Ulf Bergman, Jonas F Ludvigsson, and Fredrik Granath study (the Bardage study), titled, "Neurological and autoimmune disorders after vaccination against pandemic influenza A (H1N1) with a monovalent adjuvanted vaccine: population based cohort study in Stockholm, Sweden," published in 2011, introduced by Dr. Halsey in his February 23, 2017 expert report, was conducted with individuals who lived in Stockholm county, Sweden from January 1, 1998, through at least October 1, 2009. These individuals received the H1N1 influenza vaccination Pandemrix, and the researchers found that the risk for rheumatoid arthritis for those who received the vaccination remained "unchanged." Petitioner also argues that the respondent-introduced Bardage study should not be heavily relied upon because, "epidemiological and other evidence involving the Pandemrix vaccine have been consistently rejected by special masters in decisions approved by this Court and the Federal Circuit."

The Johanna Westra, Christien Rondaan, Sander van Assen and Marc Bijl study (the Westra study), titled, "Vaccination of patients with autoimmune inflammatory rheumatic diseases," published in March 2015, introduced by Dr. Matloubian in his June 10, 2016 original expert report stated:

> In most of the latest studies of the efficacy of influenza vaccination in patients with RA [rheumatoid arthritis], safety is considered and yet no significant influence of vaccination on disease activity has been reported. Also, in pre-post studies after influenza vaccination, patients with RA [rheumatoid arthritis] did not experience increased disease activity.

(internal references omitted) (brackets added). According to the Westra study researchers, corticosteroids, methotrexate, TNF inhibitor, and anti-IL-6-receptor antibody have "no significant influence on influenza vaccination," while the methotrexate plus TNF inhibitor, anti-CD20 antibody, and abatacept "can cause a reduced immune response to vaccination." (capitalization in original). Using the Westra study as support in his February 23, 2017 first supplemental expert report, Dr. Matloubian stated that "even though it [the influenza vaccination] elicits an immune response, the influenza vaccine does not exacerbate the disease." (brackets added). Dr. Matloubian, in his February 23, 2017 first supplemental expert report described the results of the Westra study: "although these RA [rheumatoid arthritis] patients were on immunosuppressive therapy, they still made an

immune response to the influenza vaccine, but did not have an exacerbation of their RA [rheumatoid arthritis]." (brackets added). Petitioner notes, however, that he "would not have been included in" the respondent-introduced Westra study because "he was not already suffering RA [rheumatoid arthritis] and receiving serious immune-modifying medications at the time of vaccination."[15] (brackets added).

As noted above, the Special Master examined in detail the epidemiological studies presented and wrote that the respondent's epidemiological studies were "persuasive" and "powerful." See Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *11, *27. Special Master Moran concluded his discussion of the first prong of the Althen test by stating "the powerful epidemiologic evidence does not support this [petitioner's] hypothesis." Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *27 (brackets added); see also Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1278. The Special Master also stated, "[n]evertheless, it remains the case that, as Vaccine Program precedent indicates, epidemiology is not dispositive." Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *11. Special Master Moran also provided a cautionary note to his findings by stating, "[r]egardless, this case does not turn on why experts presented the opinions they presented. Instead, the case resolves on the (lack of) persuasiveness of the theory that the flu vaccine can cause rheumatoid arthritis via molecular mimicry." See id. at *27. Although the Special Master in his decision appears to give more credence to the respondent's experts than to petitioner's experts, he did carefully review all the evidence before him in reaching his ultimate conclusion denying compensation and was not arbitrary or capricious in doing so.

As also discussed above, the United States Court of Appeals for the Federal Circuit has addressed the weight that epidemiological evidence should play in a Special Master's decision, for example, in Grant v. Secretary of Health & Human Services. See Grant v. Sec'y of Health & Human Servs., 956 F.2d at 1145-49. In Grant v. Secretary of Health & Human Services, the petitioner received the Quadrigen vaccination as an infant, to protect petitioner from diphtheria, pertussis, tetanus, and polio, which petitioner alleged caused his encephalopathies. See id. at 1145-46. The respondent in Grant introduced epidemiological evidence which demonstrated that children who had received the diphtheria, pertussis, and tetanus (DPT) vaccination, which is different than the Quadrigen vaccination, experienced the same amount of infantile spasms as those who did not receive the DPT vaccination. See id. at 1148-49. The Federal Circuit in Grant v. Secretary of Health & Human Services approved the Special Master's reliance on the scientific evidence presented by the petitioner regarding the Quadrigen over the respondent's presentation of DPT epidemiology because "the epidemiological studies cited by the Secretary in this appeal related to a general DPT vaccine, not the Quadrigen vaccine," and the epidemiology was "not dispositive of the actual causation question in this case." See id. at 1149. In Heddens v. Secretary of Health & Human Services, a decision issued by a Judge of the United States Court of Federal Claims, a petitioner

[15] In his decision, Special Master Moran did not indicate that the patients in the Westra study were all taking immune-modifying medications.

alleged that a human papillomavirus (HPV) vaccination caused her MS. See Heddens v. Sec'y of Health & Human Servs., 143 Fed. Cl. at 195. In her motion for review, the petitioner in Heddens v. Secretary of Health & Human Services argued that the Special Master's reliance on epidemiology which did not examine HPV and MS was appropriate. See id. at 197-98. The Judge in Heddens v. Secretary of Health & Human Services found that, because the Special Master "considered the epidemiological evidence presented by respondent, but did not treat that evidence as weighing heavily against petitioner," that the Special Master did not abuse his discretion. See id. at 198. The Judge also stated that because there was no indication that the Special Master "regarded the epidemiological evidence with what petitioner calls 'fervor,'" that the weight given to epidemiological evidence did not heighten petitioner's burden. See id. at 199.

Petitioner also appeals the Special Master's finding that petitioner did not satisfy the second prong of the Althen test, that there was a "logical sequence of cause and effect" from the vaccine to petitioner's injury. See Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1278. Petitioner argues in his motion for review, "[a]lthough it briefly discussed Althen prong two, the decision failed to set forth whether this prong was satisfied, likely as a result of its conclusion on prong one," and petitioner, therefore, requests "that any remand include an instruction to evaluate Petitioner's evidence on Althen prong two in accordance with Capizzano[v. Secretary of Health & Human Services, 440 F.3d at 1326]." (brackets added). Respondent argues, however, that the Special Master made a proper finding that petitioner had not established a logical sequence of cause and effect because the Special Master found that Dr. Hsu did not associate petitioner's rheumatoid arthritis with the flu vaccine in the petitioner's medical records once petitioner had received the rheumatoid arthritis diagnosis. Respondent also argues that "the Special Master provided a sound reason, based on a contextual analysis of the record as a whole, to conclude that no treating physician persuasively opined that the flu vaccination caused petitioner's RA [rheumatoid arthritis]." (brackets added). Petitioner's reply to respondent in this court concedes that Special Master Moran had come to the conclusion that petitioner had not satisfied the second prong of Althen. Petitioner, therefore changed his argument in this court to argue that "requiring multiple treator attributions in order to reach an acceptable level of persuasiveness is not in keeping with case law." (citing Paluck v. Sec'y of Health & Human Servs., 786 F.3d at 1385-86). As stated above, the United States Court of Appeals for the Federal Circuit has found that treating physician statements are considered "quite probative" because "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." Capizzano v. Sec'y of Health & Human Servs., 440 F.3d at 1326 (internal quotation marks omitted); see also Andreu ex rel. Andreu v. Sec'y of Health & Human Servs., 569 F.3d at 1375.

In Capizzano v. Secretary of Health & Human Services, the United States Court of Appeals for the Federal Circuit found "[a]s far as the second prong is concerned, in our view, the chief special master erred in not considering the opinions of the treating physicians who concluded that the vaccine was the cause of Ms. Capizzano's injury." Capizzano v. Sec'y of Health & Human Servs., 440 F.3d at 1326. Regarding petitioner's

physicians, Special Master Moran noted petitioner's visits to Dr. Samples, Dr. Bouffard, Dr. Brignoni, and Dr. Shieh, before addressing the consultations with petitioner's rheumatologist, Dr. Hsu, including Dr. Hsu's statement, that "I am concerned about a pain syndrome associated with his flu vaccine." Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *28. The Special Master stated that "after Dr. Hsu diagnosed Mr. Tullio with rheumatoid arthritis, she did not associate his disease with his flu vaccination." Id. As discussed above, the petitioner's treating doctors were unable to diagnose petitioner's disease for months. Petitioner came to Dr. Hsu initially with an incorrect diagnosis of Guillain-Barré syndrome, which has been recognized by the Secretary of Health and Human Services to be associated with the influenza vaccination. See Vaccine Injury Table, 42 C.F.R. § 100.3(a) (2019) (associating "Seasonal Influenza vaccines" with "Guillain-Barré Syndrome" "3-42 days" after vaccine administration). After diagnosing petitioner with rheumatoid arthritis, however, Dr. Hsu did not mention the influenza vaccination in the medical records of when she saw petitioner. Therefore, Special Master Moran did not discount the treating physician's statement, but Special Master Moran took the entire record into consideration when he found that the second prong of the Althen test, "logical sequence of cause and effect," was not satisfied because "no treating doctor has persuasively opined that the flu vaccination caused Mr. Tullio's rheumatoid arthritis." Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *28; see also Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1278.

Special Master Moran also stated that "[t]he lack of support from treating doctors is consistent with the lack of information about the cause of rheumatoid arthritis" because "the cause of rheumatoid arthritis is not known." Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *28. According to Special Master Moran, "when epidemiologic studies have explored a potential association, they have not found an increased incidence of rheumatoid arthritis in people who received the flu vaccine." Id. Also according to Special Master Moran, "given this information, it would be surprising for a doctor to tell Mr. Tullio that the flu vaccination caused his rheumatoid arthritis. See Tr. 219 (Dr. Utz stating that he has never told any of his rheumatoid arthritis patients that flu vaccination caused their rheumatoid arthritis)." Id.

The final, and most unusual, section in Special Master Moran's decision is the "Testability" section. See id. at *22-*26. Special Master Moran stated, "Dr. Utz and Dr. Steinman have presented a hypothesis—hemagglutinin and collagen are molecular mimics—that is testable, but has not been tested directly." Id. at *24. Special Master Moran also stated, "[i]f Dr. Steinman or Dr. Utz had conducted experiments about molecular mimicry, the results could have assisted Mr. Tullio in meeting his burden of proof." Id. at *25. Special Master Moran goes so far as to state:

> The Vaccine Program would seem to allow for time to seek approval from an overseeing institution, to carry out the experiment, and to submit an article for peer review because the pace of litigation has dramatically slowed. Mr. Tullio's case came to hearing approximately four years after it was filed and this time was relatively quick. Moreover, the presence of

> approximately $4 billion in the Vaccine Injury Compensation Trust Fund suggests that money is available to pay for experiments.

Id. at *25 n.23. Then, at the end of the section regarding testability, Special Master Moran presented a caveat that applied to the entire section:

> As discussed in sections A and B, the epidemiology and the mechanistic evidence do not support a finding that the hypothesis of molecular mimicry between flu vaccine and hemagglutinin is sound and reliable. Therefore, the lack of testing does not affect the outcome of the case—if this section on testability were excised from the decision, the undersigned still would have found that Mr. Tullio did not establish prong 1 [of the Althen test].

Tullio v. Sec'y of Health & Human Servs., 2019 WL 7580149, at *26 (brackets added).

This court notes that at the oral argument before this court, the petitioner explicitly rejected the Special Master's suggestion that petitioners in the Vaccine Program should perform experiments to assist in providing proof for his or her case. In particular, the petitioner's attorney stated at the oral argument that the idea of testing "is not really a practical approach," because "it raises a lot of concerns for Petitioner, because as in this case, first of all, I mean, who is going to do this research?" Further, petitioner argued at the oral argument, that requiring testing "would not resolve their cases quickly" and "it could be prohibitive, and if they [petitioners] were at a risk of losing the funds they put into research, then it would, you know, be a reasonable basis type of analysis where they would not be reimbursed their costs, then you have the -- it would be highly troubling." (brackets added). In addition, petitioner states in his motion for review that testing is "impractical," asking:

> Would petitioners be expected to delay already crucially needed compensation while their experts engage in testing? Would petitioners be required to bear the cost of such testing unless and until it is reimbursed through the granting of a motion for fees and costs? Would petitioners run the risk of not being compensated for the costs of testing if their claims prove unsuccessful and are challenged as not having a reasonable basis? What is the practicality of finding expert researchers willing to sideline present research and academic focus to run the experiments proposed in the Decision?

Respondent stated in its response to petitioner's motion for review in this court, regarding the Special Master's testability comments that "his discussion as to testability of petitioner's causation theory was clearly dicta." Moreover, as noted above, the United States Court of Appeals for the Federal Circuit in Knudsen ex rel. Knudsen v. Secretary of Health & Human Services outlined the role of the United States Court of Federal Claims in deciding cases in the Vaccine Injury Compensation Program:

> The Court of Federal Claims is therefore not to be seen as a vehicle for ascertaining precisely how and why DTP and other vaccines sometimes destroy the health and lives of certain children while safely immunizing most others. This research is for scientists, engineers, and doctors working in hospitals, laboratories, medical institutes, pharmaceutical companies, and government agencies. The special masters are not "diagnosing" vaccine-related injuries. The sole issues for the special master are, based on the record evidence as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the [petitioner's] injury or that the [petitioner's] injury is a table injury, and whether it has not been shown by a preponderance of the evidence that a factor unrelated to the vaccine caused the child's injury. See 42 U.S.C. § 300aa-13(a)(1), (b)(1).

Knudsen ex rel. Knudsen v. Sec'y of Health & Human Servs., 35 F.3d at 549 (brackets added); see also Broekelschen v. Health & Human Servs., 618 F.3d at 1345; Andreu ex rel. Andreu v. Sec'y of Health & Human Servs., 569 F.3d at 1382.

In sum, after reviewing the evidence in the record before him, Special Master Moran found that the petitioner had failed to meet his burden of proving "a medical theory causally connecting the vaccination and the injury" with "some indicia of reliability to support the assertion of the expert witness." Althen v. Sec'y of Health & Human Servs., 418 F.3d at 1278; Moberly ex rel. Moberly v. Sec'y of Health & Human Servs., 592 F.3d at 1324.

C O N C L U S I O N

Upon review of the record before this court, including the medical records, the expert reports, the testimony taken at the hearing before Special Master Moran, and Special Master Moran's decision, this court finds that Special Master Moran's decision, which concluded that the petitioner had failed to prove, by a preponderance of the evidence, a medical theory of causation connecting the influenza vaccination to the petitioner's allegation that the vaccination caused his rheumatoid arthritis, was not arbitrary or capricious. The Special Master's ruling on entitlement denying compensation to petitioner is **AFFIRMED**. The Clerk of the Court is instructed to enter **JUDGMENT** consistent with this Opinion.

IT IS SO ORDERED.

s/Marian Blank Horn
MARIAN BLANK HORN
Judge