In the United States Court of Federal Claims

No. 10-565V
(Filed: May 25, 2016)*
***Opinion originally filed under seal on April 29, 2016**

MEGAN L. GODFREY, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	)	Vaccine Act; Motion for Review Following Remand, HPV Vaccine; Gardasil; Juvenile Ankylosing Spondylitis; Causation in Fact

M. Clay Ragsdale, Birmingham, AL, for petitioner. *Allison L. Riley*, Birmingham, AL, of counsel.

Jennifer L. Reynaud, Torts Branch, Civil Division, United States Department of Justice, Washington, DC, with whom were *Benjamin C. Mizer*, Principal Deputy Assistant Attorney General, *Rupa Bhattacharyya*, Director, *Vincent J. Matanoski*, Deputy Director, and *Catherine E. Reeves*, Assistant Director.

O P I N I O N

Firestone, *Senior Judge*.

Pending before the court is petitioner Megan L. Godfrey's ("petitioner") motion for review of the special master's October 27, 2015 decision on remand denying petitioner's claim for compensation under the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-1 to -34, as amended ("the Vaccine Act"). Petitioner's claim was initially denied in a decision published June 11, 2014. See Godfrey v. Sec'y of Health & Human Servs., No. 10-565V, 2014 WL 3058353 (Fed. Cl. June 11, 2014)

("Godfrey I"). The purpose of the remand was to determine whether the United States Court of Appeals for the Federal Circuit's intervening decision in Koehn v. Secretary of Health and Human Services, 773 F.3d 1239 (Fed. Cir. 2014), warranted a finding of liability in favor of petitioner. See Godfrey v. Sec'y of Health & Human Servs., No. 10-565V, 2015 WL 4972882 (Fed. Cl. Aug. 19, 2015) ("Godfrey II"). On October 27, 2015, the special master, after considering Koehn, issued a decision again denying entitlement to compensation under the Vaccine Act. See Godfrey v. Sec'y of Health & Human Servs., No. 10-565V, 2015 WL 10710961 (Fed. Cl. Oct. 27, 2015) ("Godfrey III").

On November 30, 2015, petitioner timely filed a motion for review of the special master's decision on remand. ECF No. 102. The Secretary of Health and Human Services ("respondent") filed a response on December 30, 2015. ECF No. 103. The court heard oral argument on April 25, 2016.

For the reasons below, petitioner's motion is **DENIED** and the special master's decision is **SUSTAINED**.

I. BACKGROUND

A. Petitioner's Medical History

Petitioner's undisputed medical history was described in the court's August 19, 2015 decision and is summarized as follows. She was born on August 1, 1989 and, aside from routine childhood illnesses, was healthy prior to the vaccination at issue. In high school, she participated in athletics, including cheerleading. Her family history includes Crohn's disease and rheumatoid arthritis. Petitioner also tested positive for HLA-B27, a

genetic marker that made her predisposed to developing juvenile ankylosing spondylitis ("JAS").[1]

On August 22, 2007, at age 18, petitioner received a single dose of the Gardasil HPV vaccine from her pediatrician. Four months later, on December 19, 2007, petitioner returned to her doctor complaining of sharp, intermittent pain in her left hip that had been ongoing for the previous three months. An x-ray of her hip indicated no problems and she did not report any recent injury. The next week, an MRI showed "[b]ilateral femoral benign fibrous dysplasia, greater on the left side than the right, and left-sided sacroiliitis, which the radiologist thought might have been inflammatory." A bone scan also indicated "increased activity at the left [sacroiliac] joint," similar to what could be seen "in osteomyelitis or in an inflammatory sacroiliitis." The parties stipulated that this pain established the onset of petitioner's JAS. Once diagnosed with JAS, petitioner began taking Infliximab injections, which she acknowledged were successful in terminating her JAS symptoms. None of petitioner's doctors expressly connected the Gardasil dose she received with her JAS.

[1] JAS is a form of spondyloarthritis which involves inflammation at sites where ligaments and tendons attach to the bones. See Godfrey I, 2014 WL 3058353, at *11. In this regard it is different from other conditions such as systemic juvenile idiopathic arthritis ("SJIA") which was at issue in Koehn and affects the whole body. Godfrey III, 2015 WL 10710961, at *10.

B. The Chief Special Master's Decision (Godfrey I)

Petitioner filed her petition seeking compensation under the Vaccine Act on August 20, 2010. After a hearing, the chief special master issued a decision denying entitlement on June 11, 2014. See Godfrey I, 2014 WL 3058353, at *1.

The primary disputed issue in this case has been whether the single dose of Gardasil petitioner received on August 22, 2007 is causally connected to her development of JAS. At the hearing, petitioner's expert, Dr. Michael McCabe, Ph.D., testified that the Gardasil vaccine triggered the development of petitioner's JAS because studies show that Gardasil causes a release of pro-inflammatory proteins known as cytokines and that JAS has been shown to be triggered by environmental events that cause a sustained elevation of pro-inflammatory cytokines in genetically predisposed individuals such as petitioner. Thus, Dr. McCabe opined that the dose of Gardasil petitioner received acted like known JAS triggers by causing a release of pro-inflammatory cytokines. Dr. McCabe relied on Maxime Dougados & Dominique Baeten, Spondyloarthritis, 377 Lancet 2127 (2011) ("Dougados," Pet'r's Ex. 54) for his conclusion that environmental factors which result in a sustained elevation of pro-inflammatory cytokines play a role in the development or onset of JAS in genetically predisposed individuals. Specifically, the Dougados article noted that "[u]pon bacterial or mechanical stress, these pathways [stemming from HLA-B27] can lead to the abnormal production of proinflammatory cytokines . . . ." Dougados at 2130 (caption for figure 2).

In his testimony, Dr. McCabe conceded that "[a]bsolutely you need the sustained elevation of the cytokines . . . in order for the disease to manifest and to continue to

manifest." Tr. 57. He went on to state, however, that the sustained cytokine response "needn't be . . . coming from the vaccine throughout the course of th[e] disease." Id. Dr. McCabe suggested that "it's a useful analogy to say that it's a flip that was switched, a circuit was opened, a ball is pushed over to the apex of the hill and is going to roll down from there." Tr. 58. When asked what could cause petitioner's cytokine levels to remain elevated for four weeks, Dr. McCabe stated that "[h]er genetic background . . . causes a trigger to manifest in her as an abnormality." Tr. 84. Dr. McCabe also cited Morgan A. Marks, et al., Progesterone and 17β-Estradiol Enhance Regulatory Responses To Human Papillomavirus Type 16 Virus-Like Particles In Peripheral Blood Mononuclear Cells From Healthy Women, 17 Clinical & Vaccine Immunology 609 (2010) ("Marks," Pet'r's Ex. 87) as the best evidence that a dose of Gardasil can cause a sufficiently strong and sustained release of pro-inflammatory cytokines to trigger the development of JAS.

Dr. McCabe acknowledged that there was no direct evidence that petitioner had an inflammatory response to the Gardasil vaccine, but opined that he would expect a response during the four weeks after the vaccination based on several studies. For example, Dr. McCabe cited Ian H. Frazer, Measuring Serum Antibody to Human Papillomavirus following Infection or Vaccination, 118 (Supp. 1) Gynecologic Oncology S8 (2010) ("Frazer (2010)," Pet'r's Ex. 70) for its statement, regarding immunizations in general, that an individual's antibody response after a single immunization "reaches a plateau between 12 and 18 days after immunization, and then declines." Godfrey I, 2014 WL 3058353, at *15 (citing Tr. 81-82). Dr. McCabe then explained that cytokine levels would be increasing at the time antibody levels are declining because cytokines "are

involved in bringing those antibody levels down." Tr. 83. However, Dr. McCabe agreed that there was no scientific evidence that a pro-inflammatory cytokine response would continue for four weeks after receiving a single dose of Gardasil and reiterated that his medical theory of causation did not require cytokine levels to be elevated "as elicited by the vaccine." Tr. 82. Dr. McCabe also cited Ian Frazer, Correlating Immunity with Protection for HPV Infection, 11 (Supp. 2) International Journal of Infectious Diseases (2007), S10 (2007) ("Frazer (2007)", Pet'r's Ex. 71);[2] Ligia A. Pinto, et al., HPV-16 L1 VLP Vaccine Elicits a Broad-Spectrum of Cytokine Responses in Whole Blood, 23 Vaccine 3555 (2005) ("Pinto (2005)," Pet'r's Ex. 73);[3] Alfonso García-Piñeres, et al.,

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[2] The chief special master described the study in the Frazer (2007) article as:

> An immunogenicity study of Gardasil show[ing] that the antibody [adaptive immune] response of the vaccinated group, who had received the complete three injection series, was approximately 10 to 100 times greater than the unvaccinated control group, who had prior natural infection. Among the vaccinated group, the [antibody or adaptive] immune response began approximately one month after the initial dose, peaked at approximately month seven, and thereafter declined to a plateau for two and a half years after the last dose.

Godfrey I, 2014 WL 3058353, at *10.

[3] The Pinto (2005) article was the subject of the Federal Circuit's discussion in Koehn. The Federal Circuit described the Pinto (2005) study as follows:

> [R]esearchers gave twenty female participants an HPV vaccine on the same three dose regimen as Gardasil, and drew blood before the first injection and one month after each of the second and third injections. The researchers either stimulated the blood samples with varying amounts of a virus-like particle in the vaccine or provided no stimulation at all. Cytokine levels were relatively consistent in the vaccinated blood that received no stimulation. Cytokine levels increased, however, for the vaccinated blood that received the virus-like particle . . . .

Koehn, 773 F.3d at 1242. However, neither Dr. McCabe nor the Federal Circuit found that the Pinto (2005) study provided evidence of a sustained release of pro-inflammatory cytokines after a single dose of Gardasil.

Cytokine and Chemokine Profiles following Vaccination with Human Papillomavirus Type 16 L1 Virus-Like Particles, 14 Clinical & Vaccine Immunology 984 (2007) ("García-Piñeres," Pet'r's Ex. 74);[4] Ligia A. Pinto, et al., Cellular Immune Responses to Human Papillomavirus (HPV)-16 L1 in Healthy Volunteers Immunized with Recombinant HPV-16 L1 Virus-Like Particles, 188 J. Infectious Diseases 327 (2003) ("Pinto (2003)," Pet'r's Ex. 75);[5] Thomas G. Evans, et al., A Phase 1 Study of a Recombinant Viruslike Particle Vaccine against Human Papillomavirus Type 11 in Healthy Adult Volunteers, 183 J. Infectious Diseases 1485 (2001) ("Evans," Pet'r's Ex. 76);[6] and C. Chao, et al., Surveillance of Autoimmune Conditions following Routine Use of Quadrivalent Human Papillomavirus Vaccine, 271 J. Internal Medicine 193 (2011) ("Chao," Pet'r's Ex. 80).[7]

[4] The study described in the García-Piñeres article measured cytokine levels before receiving an HPV vaccine and one month following the second dose of the vaccine.

[5] The study described in the Pinto (2003) article measured cytokine responses at one month after the second dose of an HPV vaccine and one month after the third dose.

[6] The study described in the Evans article was cited for "changes in lymphoproliferation [an immune response] . . . measured at six weeks." Tr. 80.

[7] The study described in the Chao article looked at the effects of Gardasil on nearly 190,000 women who received at least one dose of the vaccine. Godfrey I, 2014 WL 3058353, at *16 (citing Tr. 65). Dr. McCabe noted that the safety review committee identified the two months after receiving the first dose of Gardasil as a "risk period" for autoimmune conditions. Tr. 76. However, Dr. McCabe acknowledged that the Chao study "did not reveal an increased incidence of spondyloarthropathies like AS [ankylosing spondylitis] and JAS in the vaccinated population." Godfrey I, 2014 WL 3058353, at *16. Dr. McCabe "attributed the negative results to the rarity of the disease and the study lacking the power to detect a relationship of such a rare condition with the vaccine." Id.

Respondent's experts, Dr. Carlos Rose, M.D., and Dr. Burton Zweiman, M.D., challenged Dr. McCabe's causation theory. They agreed that certain environmental factors that cause a sustained elevation of pro-inflammatory cytokines, such as gastrointestinal and genitourinary bacteria and mechanical stress (specifically chronic physical micro-trauma), can trigger JAS in genetically predisposed individuals. However, they disagreed with Dr. McCabe's theory that a single dose of the Gardasil vaccine would be sufficient to trigger JAS. First, they explained that there was no medical evidence to support a link between petitioner's single dose of Gardasil and the development of JAS. Second, they opined that even assuming Dr. McCabe's theory was possible, any release of pro-inflammatory cytokines following one dose of Gardasil would have been too transient to have the alleged effect. Dr. Zweiman testified that because an individual's innate immune response does not have "immunologic memory such as one finds in adaptive responses, . . . to get a repeat or continued elaboration of the products of inflammatory cytokine, you have to have continued stimulation by the initial stimulus." Godfrey I, 2014 WL 3058353, at *20 (citing Tr. 179-80). To result in the sustained elevated levels of pro-inflammatory cytokines required under Dr. McCabe's theory, "for the most part one needs to have a continued stimulation of more production by cells," of which there was no evidence presented. Id. (citing Tr. 202-03).

Respondent's experts also noted that there was no evidence to suggest that petitioner experienced a release of pro-inflammatory cytokines following her HPV vaccination. Given petitioner's genetics and medical history, respondent's experts suggested that petitioner's development of JAS following her Gardasil vaccination was

"simply coincidental" or that some other activity, such as petitioner's cheerleading, might have provided sustained trauma or stress and triggered her JAS.

The chief special master determined based on the evidence she received that petitioner had failed to meet her burden of proof under the Vaccine Act. The chief special master explained that the evidence showed that petitioner's JAS was attributable to her "genetic background, coupled with a family history and the presence of a known 'trigger' for development of JAS," which the chief special master identified as petitioner's cheerleading. The chief special master noted that there was no evidence that petitioner had experienced elevated levels of pro-inflammatory cytokines following her vaccination, that a transient increase in cytokines cannot cause JAS, or that the elevated levels from a single dose of Gardasil would have remained sustained for a long enough period to trigger JAS. The chief special master also found that the link between the onset of petitioner's JAS and her HPV vaccination was too speculative in that petitioner's imaging studies showed that JAS was present in both hips, even though petitioner complained of pain in only one hip, and thus it was uncertain how long petitioner had JAS. The chief special master stated that the imaging suggested that petitioner's JAS may have existed before she received the vaccination but did not yet cause any pain. For these principal reasons, the chief special master denied the petition.

C. This Court's Remand Decision (Godfrey II)

On review before this court, petitioner argued that the Federal Circuit's decision in Koehn, 773 F.3d at 1239, which had been issued after the chief special master's decision, demonstrated that petitioner's expert, Dr. McCabe, had presented a viable medical theory

of causation and that the chief special master had erred in rejecting petitioner's expert's theory in favor of respondent's experts' opinions. As discussed in the remand decision, Koehn involved a claim by a 13-year-old female who developed an auto-inflammatory disease known as systematic juvenile idiopathic arthritis ("SJIA") following receipt of two of three HPV vaccine doses. 773 F.3d at 1240-41. In this case, as in Koehn, petitioner relied on the testimony of Dr. McCabe to support her claim that the vaccine had triggered her disease by releasing pro-inflammatory cytokines. Id. at 1242. Also in this case, as in Koehn, respondent relied on the testimony of Dr. Rose to rebut Dr. McCabe's theory. Id. The special master in Koehn determined that the petitioner had not met her burden of presenting a legally probable medical theory of causation and for that reason as well as others denied the petition. On appeal, the Federal Circuit affirmed the special master's rejection of Ms. Koehn's claim but stated in dicta that the special master had "committed several errors" in rejecting the medical theory proffered by Dr. McCabe. Id. at 1243. Specifically, the Federal Circuit stated:

> Had the Special Master properly evaluated the evidence, we believe the Special Master would have likely found that Koehn met her burden [of establishing a medical theory causally connecting the vaccination and the injury]. The Pinto [(2005)] article demonstrated that the participants who received the HPV vaccine had increased levels of the same cytokines dysregulated in SJIA. Dr. Rose asserted that the article showed increased levels only when the vaccinated blood received a stimulus. Koehn['s expert, Dr. McCabe,] explains, however, that measurement of cytokine levels can only occur in blood samples outside the body, and the only way to "replicate what is going on in the body" is to introduce an antigen to the blood sample assay. A stimulus was therefore necessary to measure cytokine levels. Especially given the low incidence rate of SJIA, requiring a measurement without a stimulus would have compelled Koehn to present more than what is scientifically possible or legally necessary. Thus, Koehn likely presented a viable, "legally probable" medical theory that "there

> would only be an upregulation in cytokines [that are associated with SJIA] if those cells are told to do so [by the HPV vaccine.]"

Id. at 1244 n.1 (citations omitted). Based on the Federal Circuit's statement and petitioner's reliance in part on the same Pinto (2005) study in this case, this court elected to remand the matter for the special master to determine in the first instance whether Dr. McCabe's medical causation theory should be reconsidered in light of Koehn.

D. The Special Master's Decision on Remand (Godfrey III)

On remand, a new special master to whom this case had been reassigned after the chief special master retired determined that the Federal Circuit's footnote in Koehn regarding Dr. McCabe's medical theory did not require any change in the chief special master's causation finding in this case. In deciding that petitioner's expert had failed to establish causation, the special master explained that even if Dr. McCabe had, based on the Pinto (2005) study, established a viable theory of causation in Koehn, the facts in the present case were sufficiently different as to warrant a different outcome. First, the special master noted that petitioner's disease, JAS, is distinct from SJIA, the illness at issue in Koehn. SJIA is not linked to a specific genetic marker, whereas JAS is directly linked to the HLA-B27 gene. In addition, SJIA affects the entire body and petitioner's JAS was specific to her hips. Second, the special master noted that while Dr. McCabe relied on the Pinto (2005) study to support his medical theory that pro-inflammatory cytokines are linked to both diseases, support for the medical causation theories were not identical. In Koehn, Dr. McCabe cited studies linking vaccines to SJIA, but, in this case, he did not cite any studies linking vaccines to JAS. Third, the special master noted that

Dr. McCabe testified that JAS's manifestation was dependent on a "sustained elevation" of cytokines but did not offer any reliable evidence indicating that a single dose of Gardasil would cause such an elevation. At the entitlement hearing, Dr. McCabe conceded that there was no scientific evidence to suggest that a single dose of Gardasil could trigger elevated release of pro-inflammatory cytokines for a 1-month period, such that it could be linked to petitioner's development of JAS. To the contrary, evidence was presented to show that Gardasil produces only a transient increase in cytokine levels. Based on these distinctions, the special master determined that Dr. McCabe had not demonstrated a legally probable medical theory connecting petitioner's JAS with her receiving a single dose of Gardasil. Accordingly, the special master concluded that the Federal Circuit's statements in Koehn did not alter the chief special master's conclusion that Dr. McCabe had failed to present a legally sufficient medical theory of causation in this case.

The special master went on to examine whether, even assuming Dr. McCabe had presented a viable medical theory of causation, petitioner could satisfy the other requirements necessary to establish her vaccine injury claim. The special master considered whether petitioner could show a logical sequence of cause and effect between her vaccine and JAS. He also addressed whether she could establish a temporal relationship between her vaccination and injury. With regard to these requirements, the special master noted that none of petitioner's treaters linked her vaccination with her subsequent illness and that there was no "evidence (such as test results) that would lend credence to Dr. McCabe's theory by showing it 'working' in real time." Godfrey III,

2015 WL 10710961, at *14. The special master also found that Dr. McCabe did not sufficiently explain why a one-month interval between petitioner's Gardasil vaccination and her first symptoms was medically acceptable. For these reasons as well, the special master concluded that petitioner had not established causation and thus was not entitled to compensation.

II. JURISDICTION AND LEGAL STANDARDS

To receive compensation under the Vaccine Act, a petitioner must show that she has sustained an injury listed in the Vaccine Injury Table ("Table"), 42 U.S.C. § 300aa-14, within the time frame prescribed or that she suffered an "off-Table" injury as a result of receipt of a covered vaccine. See 42 U.S.C. § 300aa-11(c)(1). If a petitioner presents a Table claim, the petitioner is granted a presumption of causation if she shows that she suffered an injury listed in the Table and that the injury occurred within the prescribed time period. See Andreu ex rel. Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1374 (Fed. Cir. 2009). In an off-Table case, like the present case, a petitioner does not receive a presumption of causation and instead must prove by a preponderance of the evidence that the injury was "caused in fact" by the vaccine. See Paluck v. Sec'y of Health & Human Servs., 786 F.3d 1373, 1379 (Fed. Cir. 2015) (citing Andreu, 569 F.3d at 1374).

In the seminal case Althen v. Secretary of Health & Human Services, 418 F.3d 1274, 1278 (Fed. Cir. 2005), the Federal Circuit established a three-pronged test to determine whether a petitioner in an off-Table case has met her burden. The Althen test requires petitioners to show by preponderant evidence:

> (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury.

Id. Specifically, a petitioner must offer a medical theory that answers affirmatively the question that the vaccine at issue can cause the type of injury alleged. This showing of causation requires "a reputable medical or scientific explanation that pertains specifically to the petitioner's case, although the explanation need only be 'legally probable, not medically or scientifically certain.'" Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339, 1345 (Fed. Cir. 2010) (quoting Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994)).

In addition to showing that the vaccine at issue can cause a particular injury, a petitioner must prove by a preponderance of the evidence that the vaccine could have actually caused the injury in the specific case. Althen, 418 F.3d at 1278. With respect to the temporal association, a petitioner must show that the onset of symptoms also occurred within a medically acceptable timeframe. Koehn, 773 F.3d at 1244 (citing de Bazan v. Sec'y of Health & Human Servs., 539 F.3d 1347, 1352 (Fed. Cir. 2008)).

Once the petitioner satisfies this burden under Althen, she "is entitled to compensation unless the government demonstrates by a preponderance of the evidence that the injury was in fact caused by factors unrelated to the vaccine." Paluck, 786 F.3d at 1379 (citing 42 U.S.C. § 300aa-13(a)(1)(B)).

This court has jurisdiction to review the decisions of a special master under 42 U.S.C. § 300aa-12(e)(2). The court uses three distinct standards of review in Vaccine

Act cases: findings of fact are reviewed under the arbitrary and capricious standard, questions of law under the not in accordance with law standard, and discretionary rulings under the abuse of discretion standard. See Masias v. Sec'y of Health & Human Servs., 634 F.3d 1283, 1287-88 (Fed. Cir. 2011); Munn v. Sec'y of Health & Human Servs., 970 F.2d 863, 870 n.10 (Fed. Cir. 1992); see also 42 U.S.C § 300aa-12(e)(2)(B). In this connection, the court does 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." Lampe v. Sec'y of Health & Human Servs., 219 F.3d 1357, 1360 (Fed. Cir. 2000) (internal quotation marks omitted) (quoting Munn, 970 F.2d at 871). If the special master "has considered the relevant evidence of record, drawn plausible inferences and articulated a rational basis for the decision," then "reversible error is extremely difficult to demonstrate." Id. at 1360 (internal quotation marks omitted) (quoting Hines ex rel. Sevier v. Sec'y of Health & Human Servs., 940 F.2d 1518, 1528 (Fed. Cir. 1991)).

III. DISCUSSION

At issue in this case is whether petitioner has met her burden to prove causation under the Althen standards for her "off-Table" vaccine injury claim. As discussed above, in Koehn, the Federal Circuit suggested that the special master in that case had erred in rejecting Dr. McCabe's medical theory of causation based on concerns about the same Pinto (2005) study that Dr. McCabe relied upon in this case. The Federal Circuit explained that it believed the Pinto (2005) study was credible and that the study supported the conclusion that the Gardasil vaccine can cause an increased level of pro-

inflammatory cytokines, which can be a trigger for the development of SJIA. Because Dr. McCabe had opined in this case that pro-inflammatory cytokines were associated with triggering JAS, the matter was remanded. On remand, the special master determined that Koehn did not require a change from the chief special master's initial decision rejecting Dr. McCabe's causation theory.

Petitioner argues that the special master's decision on remand was arbitrary, capricious, and not in accordance with law. In particular, petitioner argues that the special master failed to properly apply the Federal Circuit's rationale from Koehn. Pet'r's Mot. 14. Petitioner argues that the Koehn panel found, based on the results of the Pinto (2005) study, that Gardasil likely "does, in fact, cause an increase in cytokines sufficient to trigger an autoinflammatory condition." Id. In effect, petitioner argues that this conclusion alone is sufficient to establish a legally probable medical theory in her case.

Respondent argues that there are material differences between Koehn and this case, including the dosage of the Gardasil vaccine received by the petitioners and the diseases at issue, and that the special master in this case was justified in rejecting Dr. McCabe's theory of causation. Specifically, respondent argues that under Dr. McCabe's theory of causation in this case, it was not enough for Dr. McCabe to opine that petitioner's vaccination led to a release of pro-inflammatory cytokines; he needed to also offer evidence that a single dose of Gardasil could cause an increase in cytokines that lasted long enough to trigger the development of JAS. In this connection, the special master expressly found that "Dr. McCabe did not offer sufficient persuasive proof that

such an increase [in pro-inflammatory cytokines] would be sustained enough (and over the time that lapsed between Ms. Godfrey's vaccination and development of hip pain symptoms) after a single Gardasil dose to result in JAS." Godfrey III, 2015 WL 10710961, at *11 (citation omitted).

The court reviews the special master's decision to determine whether it is supported and concludes for the reasons that follow that it is. At the entitlement hearing, Dr. McCabe endeavored to link petitioner's vaccination to her development of JAS by relying on studies that show Gardasil can cause a release of pro-inflammatory cytokines. Dr. McCabe acknowledged, however, that the Pinto (2005) study did not provide evidence of what cytokine levels might have looked like during the month after a single Gardasil dose because the individuals in the Pinto (2005) study were sampled only before the initial dose of an HPV vaccine and 1 month after the second and third doses of the vaccine. Tr. 63-64. Thus, the Pinto (2005) study did not address whether a single dose of Gardasil can produce sustained pro-inflammatory cytokine levels that could trigger JAS. Given the undisputed evidence that JAS may be triggered by environmental factors giving rise to a sustained pro-inflammatory cytokine response, it was rational for the special master to conclude that an adequate medical theory would require a showing that a single dose of the Gardasil vaccine can result in a sustained pro-inflammatory cytokine response.

In this connection, the court finds that petitioner's reliance on the Marks study to suggest that Dr. McCabe demonstrated that the vaccine elevates pro-inflammatory cytokine levels for a period of time is misplaced. The Marks study measured cytokine

levels at 72 hours after immunization with an HPV vaccine. Indeed, Dr. McCabe, referring to the results of the Marks study at the entitlement hearing, stated that "[i]t's not a sustained elevation. . . . It's being measured at 72 hours . . . ." Tr. 55.

Finally, the court finds that Dr. McCabe's suggestion that a single dose of Gardasil could trigger sustained, elevated levels of pro-inflammatory cytokines for an individual in petitioner's circumstances, because it could be viewed as the last straw or tipping point, was not supported. When asked what could cause petitioner's cytokine levels to remain elevated for four weeks, Dr. McCabe stated that "[h]er genetic background . . . causes a trigger to manifest in her as an abnormality." Tr. 84. However, Dr. McCabe did not provide any scientific evidence in support of this theory.

The special master also had before him the testimony of respondent's experts, Dr. Rose and Dr. Zweiman, who explained that even if pro-inflammatory cytokines play a role in the development of JAS, the evidence showed that the Gardasil vaccine causes nothing more than a transient increase in pro-inflammatory cytokines such that the vaccine is not capable of triggering JAS. Tr. 178-80. Dr. Zweiman "rejected Dr. McCabe's assertions regarding the role of the vaccine in the JAS disease process, noting that under Dr. McCabe's theory, in order to cause JAS, cytokine production would have to occur in a 'prolonged, consistent fashion.'" Godfrey I, 2014 WL 3058353, at *18 (citing Tr. 200). Dr. Zweiman explained that because an individual's innate immune response does not have "immunologic memory such as one finds in adaptive responses, . . . to get a repeat or continued elaboration of the products of inflammatory cytokine, you have to have continued stimulation by the initial stimulus." Id. at *20 (citing Tr. 179-80).

To result in the sustained elevated levels of pro-inflammatory cytokines required under Dr. McCabe's theory, "for the most part one needs to have a continued stimulation of more production by cells," of which there was no evidence presented. Id. (citing Tr. 202-03).

Based on the evidence presented, the court finds that the special master's conclusion that petitioner failed to establish a legally probable medical theory of causation under Althen prong one must be sustained.[8] The special master had sufficient evidence before him to conclude that petitioner failed to show that a single dose of the Gardasil vaccine could cause a sustained pro-inflammatory cytokine response of the kind associated with environmental factors that have been shown to trigger the development of JAS. Petitioner's failure to establish the first Althen prong is fatal to her claim. See, e.g., Koehn, 773 F.3d at 1244 (finding that a petitioner's failure to establish any of the three Althen prongs is dispositive).[9]

[8] Having found that the special master's rejection of petitioner's medical theory was not arbitrary, capricious, or not in accordance with law, the court does not reach petitioner's argument that the special master erred by making a distinction between the onset of her symptoms and the onset of her disease.

[9] Even assuming that a single dose of Gardasil could cause a sustained release of pro-inflammatory cytokines, and that reaction could lead to the development of JAS, the court finds that the special master's conclusions regarding petitioner's failure to meet the other two Althen prongs are also supported. Dr. McCabe did not provide any evidence in support of his claim that petitioner actually experienced a sustained release of pro-inflammatory cytokines after receiving her Gardasil vaccination. When asked for evidence that petitioner had an abnormally high level of pro-inflammatory cytokines at any time during the month after she received her vaccine, Dr. McCabe acknowledged that no tests had been conducted and that "there is nothing that's really all that convincing that she had any inflammatory response or anything going on as a consequence of elevated, pro-inflammatory cytokines after her immunization." Tr. 74. In addition, Dr. McCabe could not explain why a one-month interval between petitioner's HPV vaccination and her first symptoms of JAS was medically acceptable. Dr. McCabe stated that

IV. CONCLUSION

For the reasons set forth above, the court finds that special master's decision on remand denying entitlement was not arbitrary, capricious, or not in accordance with law. Accordingly, petitioner's motion for review is **DENIED** and the special master's decision on remand is **SUSTAINED**. The clerk is directed to enter judgment accordingly.

IT IS SO ORDERED.

s/Nancy B. Firestone
NANCY B. FIRESTONE
Senior Judge

"[i]t's really a matter of just proximity to the trigger" and agreed that the only evidence was the "literal temporal relationship . . . and nothing more." Tr. 84.