# In the United States Court of Federal Claims

No. 13-439V
(Filed Under Seal: December 14, 2017)[1]
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| **CAROLYNNE OLSON,** | * | |
| Petitioner, | * | Vaccine Act, 42 U.S.C. §§ 300aa-1 *et seq.*; Review of Special Master's Decision; Off-Table Injury; Rheumatoid Arthritis ("RA"); Human Papillomavirus ("HPV"); Gardasil Vaccine. |
| v. | * | |
| **SECRETARY OF HEALTH AND HUMAN SERVICES,** | * | |
| Respondent. | * | |

*Mitchel J. Olson*, Law Office of Mitchel J. Olson, JD, MD, Carlsbad, CA, for Petitioner.

*Jennifer L. Reynaud*, United States Department of Justice, Washington, DC, for Respondent.

## OPINION AND ORDER

**DAMICH**, Senior Judge:

On July 1, 2013, Petitioner filed a petition for compensation under the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-1 to -34 (2012) ("Vaccine Act"), claiming that the HPV Gardasil vaccine she received on July 1, 2010 caused her to develop rheumatoid arthritis ("RA"). On September 15, 2014, Respondent filed its Rule 4(c) Report asserting that Petitioner was not entitled to compensation because she could not carry the burden of proof under *Althen v. Sec'y of HHS,* 418 F.3d 1274, 1278 (Fed. Cir. 2005). After the Rule 4(c) Report was filed, the experts for each party submitted their reports. An entitlement hearing was held on March 27-28, 2017, and the parties agreed that no post-hearing briefing was needed. On July 14, 2017, Special Master Brian H. Corcoran denied compensation on the grounds that Petitioner did not establish by preponderant evidence that the vaccine caused her RA. *Olson v.*

[1] Vaccine Rule 18(b), contained in Appendix B of the Rules of the United States Court of Federal Claims, affords each party fourteen days in which to object to the disclosure of (1) trade secrets or commercial or financial information that is privileged or confidential of (2) medical information that would constitute "a clearly unwarranted invasion of privacy."

*Sec'y of HHS*, No. 13-439V, 2017 U.S. Claims LEXIS 1032, at 1 (Fed. Cl. Spec. Mstr. July 14, 2017) (hereinafter "*Olson*"). There was no motion for reconsideration, and this petition for review of the Special Master's decision followed on August 14, 2017.

In her motion for review, Petitioner requests this Court to enter judgment in her favor. In support, Petitioner argues that the Special Master's decision was arbitrary, capricious, contrary or otherwise not in accordance with law in that he: (1) misconstrued her theory, (2) raised her burden of proof, (3) erred in his conclusions, and (4) improperly weighed the evidence.

For the reasons set forth below, the Court holds that the Petitioner's arguments are without merit and that the Special Master's decision was not arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law. Petitioner's motion for review is, therefore, **DENIED**.

## I. BACKGROUND

### A. Medical History[2]

On July 1, 2010, Petitioner received an HPV Gardasil vaccine from her gynecologist, Angelica Zaid, M.D. At the time of the vaccination Petitioner was 52 years old, and was not within the medically targeted age group to receive the vaccine. Despite this, Petitioner asked to receive the vaccine in order to treat warts after learning from her daughter's dermatologist that it could be effective.

At the time of the vaccination, Petitioner's medical history was significant. She was being treated for hypothyroidism,[3] vitamin D deficiency, osteochondroma,[4] an Achilles tendon rupture, anemia, lifelong asthma, sinus pressure, facial pain, lung congestion, and chronic sinusitis.

Petitioner claims that within two weeks after the receipt of the vaccine she began to feel a burning sensation in both hands. However, the first medical record of these symptoms was made by Dr. Zaid on December 13, 2010, more than five months after the vaccination. During this visit, Petitioner reported to Dr. Zaid that she had developed "knuckle enlargement w[ith] pain" that was persistent after receiving the vaccine. *Olson*, at 4. For further treatment, Dr. Zaid referred Petitioner to rheumatologist Alexander Shikhman, M.D.

Petitioner saw Dr. Shikhman for the first time on February 22, 2011, and he noted that

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[2] The court derives Petitioner's medical history from the Special Master's decision.

[3] Hypothyroidism is defined as a "deficiency of thyroid activity." *Dorland's Medical Dictionary for Health Consumers*, The Free Dictionary, https://medical-dictionary.thefreedictionary.com/hypothyroidism, (last visited Dec. 7, 2017).

[4] Osteochondroma is defined as "a benign bone tumor consisting of projecting adult bone capped by cartilage projecting from the lateral contours of endochondral bones." *Dorland's Medical Dictionary for Health Consumers*, The Free Dictionary, https://medical-dictionary.thefreedictionary.com/osteochondroma, (last visited Dec. 7, 2017).

Petitioner's "clinical presentation [wa]s highly suspicious for *reactive* arthritis."[5] *Olson*, at 5 (emphasis added). Dr. Shikhman then ordered extensive laboratory testing. The results showed a mildly elevated sedimentation rate, as well as a positive Mycoplasma IgG antibody level – indicative of a prior resolved infection consistent with reactive arthritis. Petitioner's test results for rheumatoid factor and anti-citrullinated peptide antibodies ("ACPA") were negative. Rheumatoid factor and ACPA are two antibody markers that are strongly associated with RA. *Olson,* at 6.

Petitioner continued to see Dr. Shikhman until late in 2013. During this period, she continued to experience arthritis-like symptoms, although on occasion she felt better and had only minor joint pain. Experiencing worsening symptoms, Petitioner began treatment with Gregory Middleton, M.D., a rheumatologist, on September 10, 2013. Dr. Middleton diagnosed the Petitioner with "seronegative rheumatoid arthritis." *Olson*, at 11. "Seronegative" RA is a diagnosis of RA despite the absence in the blood of the two antibody markers (mentioned above) that are strongly associated with RA. Dr. Middleton also attributed the RA to her "immune system over-reaction from her 2010 HPV vaccine." *Id*. To date, Dr. Middleton continues to treat Petitioner for "mild but deforming seronegative inflammatory arthritis compatible with rheumatoid arthritis." *Olson*, at 12.

**B. Petitioner's Theory**

According to Petitioner's Motion for Review, her medical theory has the following components:

(1) While people with RA may have pre-existing risk factors or genetic predispositions to develop the condition, an additional environmental "trigger" or "second hit" is necessary to precipitate the autoimmune condition.

(2) Vaccines can be an environmental trigger for RA.

(3) Inflammatory lung conditions (as Petitioner had) create a significant risk of RA.

(4) Alum (an adjuvant in the HPV vaccine)[6] can act as an environmental trigger by activating inflammatory pathways in the lungs of people with inflammatory lung conditions. Petr.'s Mot. at 4.

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[5] "Reactive arthritis" is not rheumatoid arthritis. Reactive arthritis is "joint pain and swelling triggered by an infection in another part of the body. *MayoClinic.org*, "Reactive Arthritis," https://www.mayoclinic.org/diseases-conditions/reactive-arthritis/symptoms-causes/syc-20354838, (last visited Dec. 7, 2017).

[6] An "adjuvant" is "a substance that aids another, such as an auxiliary remedy." *Dorland's Medical Dictionary for Health Consumers*, The Free Dictionary, https://medical-dictionary.thefreedictionary.com/adjuvant, (last visited Dec. 7, 2017). In this case, the adjuvant boosts the immune system to make more antibodies with the result that the vaccine is more effective and long-lasting.

Petitioner called two expert witnesses, Dr. Gregory Middleton, a clinical rheumatologist, and Dr. Lawrence Mayer, a professor of epidemiology. Dr. Middleton prepared three expert reports and testified at the hearing; Dr. Mayer prepared one expert report and also testified at the hearing. Petitioner also submitted supportive medical literature.

According to the Special Master's summation of the expert reports and testimony, Dr. Middleton elaborated on Petitioner's medical theory attempting to link RA to the HPV vaccine. Essentially, Dr. Middleton's theory was that alum triggered certain protein complexes, called inflammasomes[7], which are

> "key to igniting the autoimmune process relevant to RA's pathogenesis. . . . Once such inflammasomes were activated by alum contained in a vaccine, an inflammatory process . . . central to RA began, because the inflammasomes themselves mediated the release of other proinflammatory cytokines[8] that fueled the process. Middleton Rep. at 12-13. [Dr. Middleton] thus posited that because alum has been demonstrated to stimulate these kinds of inflammasomes known to be factors in RA, there is a causal relationship between the vaccine and the pathogenesis of RA." *Id.* at 12.

Furthermore, Dr. Middleton linked the inflammasomes that contributed to RA as the same as those found in patents with inflammatory lung conditions. *Id.* at 13-14. According to the Special Master, "many articles Petitioner offered discuss or address the ACPAs[9] that are the result of citrullination,[10] a process widely understood to be an explanation for RA in numerous cases (and which allows a link to be drawn between chronic lung infections akin to what Mrs. Olson experienced and her RA)." *Olson,* at 63.

### C. The Special Master's Decision

According to *Althen v. Sec'y of HHS*, 418 F.3d 1274 (Fed. Cir. 2005), to establish a legal cause in a Non-Table Injury case, Petitioner must establish each of the three *Althen* prongs by

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[7] An inflammasome is "[a] multiprotein cytoplasmic complex which activates one or more caspases (proteins), leading to the processing and secretion of pro-inflammatory cytokines. *Sergen's Medical Dictionary*, The Free Dictionary, https://medical-dictionary.thefreedictionary.com/inflammasome, (last visited Dec. 7, 2017).

[8] A proinflammatory cytokine is "any of the circulating substances in the blood that deplete lean body mass in critical illness." *Medical Dictionary*, The Free Dictionary, https://medical-dictionary.thefreedictionary.com/proinflammatory+cytokines, (last visited Dec. 7, 2017).

[9] Anti-citrullinated protein antibodies ("ACPAs") are biomarkers strongly associated with RA. *Olson*, at 12.

[10] Citrullination is "the conversion of the amino acid arginine into citrulline (not one of 'the standard 20 amino acids encoded by DNA in the genetic code')". *Olson*, at 15 citing N. Sofat et al., *Interaction Between Extracellular Matrix Molecules and Microbial Pathogens: Evidence for the Missing Link in Autoimmunity with Rheumatoid Arthritis as a Disease Model*, 5 Frontiers in Microbiology 1-6 (2015) ("Sofat Article").

preponderant evidence: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a proximate temporal relationship between vaccination and injury. *Althen*, 418 F.3d at 1278. This is a non-table injury.[11]

The Special Master concluded: (1) that petitioner failed to present reliable, persuasive evidence of a medical theory causally connecting the HPV vaccination and RA under the facts and circumstances of this case (prong 1), (2) that petitioner failed to show a logical sequence of cause and effect between the HPV vaccine and petitioner's RA (prong 2), and (3) that petitioner failed to show that the timing between vaccination and the onset of petitioner's RA was medically appropriate for the HPV vaccine to be causative (prong 3).

Regarding prong 1, the Special Master noted that it is reliably established that "adjuvants like alum help stimulate the innate immune system, thereby increasing the efficacy of vaccines." *Olson*, at 59. But the Special Master concluded that it is speculative whether this innate immune system stimulation "instigated by a single vaccine containing alum would be robust enough, and occur for long enough, to be pathogenic generally, let alone to cause RA." *Olson*, at 60. The Special Master noted that, although alum is used as an adjuvant in many vaccines, Petitioner offered no literature that concluded that alum was pathogenic: "If alum can cause RA, there should be more robust evidence that it is associated with other autoimmune conditions in different vaccines." *Olson*, at 62.

Regarding prong 2, the Special Master found that "her medical history does not provide the corroboration necessary to conclude that Petitioner's theory worked out as predicted." *Olson*, at 67.

Regarding prong 3, the Special Master concluded that, although Petitioner's RA-like symptoms occurred within one to two weeks of the vaccine, she failed to show that the timing of the onset of symptoms was "medically appropriate" under the proposed causation theory. Furthermore, the Special Master added that, since he had rejected Petitioner's theory in the context of the prong 1 analysis, "it does not matter that onset of the first obvious symptoms of Mrs. Olson's RA was temporally consistent with a theory that *itself* is not scientifically or medically reliable." *Olson*, at 70 (emphasis in original).

The Special Master came to these conclusions after reviewing the testimony of Petitioner and of the Petitioner's experts and their reports and after reviewing supportive medical literature, including some medical literature that was not filed by Petitioner. Of course, the Special Master also reviewed the testimony and reports of Respondent's expert, Dr. Robert Lightfoot, a rheumatologist.

[11] A Table Injury is "an injury falling within the Vaccine Injury Table - corresponding to one of the vaccinations in question within a statutorily prescribed period of time . . ." *Olson*, at 44.

## II. STANDARD OF REVIEW

Under the Vaccine Act, the Court may set aside a Special Master's findings of fact or conclusions of law only if they are found to be "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 42 U.S.C. § 300aa-12I(2)(B). With respect to findings of fact, the Special Master has broad discretion to weigh expert evidence and make factual determinations. *See Bradley v. Sec'y of HHS*, 991 F.2d 1570, 1575 (Fed. Cir. 1993). The Federal Circuit has clearly indicated its longstanding standard of review when the Court of Federal Claims hears petitions on review from the Special Masters:

> 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.

*Hodges v. Sec'y of HHS*, 9 F.3d 958, 961 (Fed. Cir. 1993) (internal citations omitted); *see also Snyder v. Sec'y of HHS*, 2014 U.S. App. LEXIS 1674, at 10-11 (Jan. 28, 2014) (quoting *Hodges*).

In *Hines v. Sec'y of HHS,* it was stated that "[i]f the special master has considered the relevant evidence of the record, drawn plausible inferences and articulated a rational basis for the decision, reversible error will be extremely difficult to demonstrate." 940 F.2d 1518, 1528 (Fed. Cir. 1991). This Court ought not to second-guess the Special Master's fact-intensive conclusions, particularly in cases "in which the medical evidence of causation is in dispute." *Hodges*, 9 F.3d at 961. In such cases, which often involve expert testimony, the Federal Circuit has "unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act." *Porter v. Sec'y of HHS*, 663 F.3d 1242, 1250 (Fed. Cir. 2011). "Such credibility determinations are 'virtually unreviewable'" on appeal. *Id.* at 1251. With respect to questions of law, legal rulings are reviewed *de novo* under the "not in accordance with law" standard. *See*, *e.g.*, *Moberly*, 592 F.3d at 1321; *Munn v. Sec'y of HHS*, 970 F.2d 863, 870 n.10 (Fed. Cir. 1992).

## III. DISCUSSION

When evaluating a motion for review, it is the Court's task to determine whether the Special Master properly considered the relevant evidence in the record, came to a factual conclusion based on plausible inferences, and provided a reasoned explanation in his or her decision. *Hines*, 940 F.2d at 1528. It is not the Court's task to second-guess the Special Master, especially in cases "in which the medical evidence of causation is in dispute." *Hodges*, 9 F.3d at 961. Thus, on review, the Court accords deference to the Special Master's factual findings and fact-based conclusions.

Petitioner raises 31 objections with respect to prongs one and two of the three prong *Althen* test. Petitioner did not raise any objections to the Special Master's decision with respect to prong three. In her motion for review, Petitioner argues that the Special Master (1) misconstrued her theory, (2) raised her burden of proof, (3) erred in his conclusions, and (4) improperly weighed the evidence. As discussed in depth below, these arguments are without merit.[12]

### A. *Althen* Prong 1 and Petitioner's Objections

Under the first prong of the *Althen* test, the Petitioner must establish by a preponderance of the evidence "a medical theory causally connecting the vaccination and the injury." *Althen*, 418 F.3d at 1278. This means that Petitioner must demonstrate that the vaccine can cause the injury that she has alleged by providing a "reputable medical theory." *Pafford v. Sec'y of HHS*, 451 F.3d 1352, 1355-56 (Fed. Cir. 2006) (citations omitted). Thus, it is not enough to establish a mere possibility that the vaccine caused the injury.

Petitioner alleges 18 total objections to the Special Master's decision with respect to prong 1. These objections can be grouped into three categories: whether the Special Master misapprehended Petitioner's theory (Objections 1, 3, 9, 16, and 17), increased Petitioner's burden of proof by requiring particular evidence (Objections 2, 6, 8, 10, 11, 12, 14, and 15), and erred in making his conclusions (Objections 4, 5, 7, 13, and 18).

Respondent argues that the Special Master properly weighed the evidence and declined to recognize Petitioner's theory as persuasive thus failing to meet her burden. Resp. at 8. Respondent maintains that Petitioner only suggested a theory of causation, whereas *Althen* and *Moberly* held that a petitioner must provide a persuasive medical explanation that is specific to the case and supported by reliable evidence. *Moberly*, 592 F.3d at 1322. According to Respondent, Petitioner did not meet this burden.

#### 1. The Special Master Did Not Misapprehend Petitioner's Theory.

Petitioner claims that the Special Master "misapprehended petitioner's medical theory" on five separate occasions with regard to *Althen* prong 1. Under Federal Circuit precedent, if a Special Master misapprehends a petitioner's theory, the Special Master's decision must be set aside. *Paluck v. Sec'y of HHS*, 786 F.3d 1373, 1380 (Fed. Cir. 2015). The Court holds that the Special Master did not misapprehend the Petitioner's theory.

*a. Objection 1*

According to the Motion for Review, "Petitioner introduced evidence that alum triggers 'inflammasomes,' which are immune cellular complexes that recognize 'danger signals,'

[12] The Court observes that after examining each of the 31 objections in detail, it is left with the general impression that Petitioner has cherry-picked sentences from the Special Master's opinion without close regard to their context.

including alum. Inflammasomes, in turn, activate particular cytokines that are centrally involved in asthma, bronchiectasis, and RA." Petr.'s Mot. at 5. Petitioner alleges that the Special Master "required evidence that cytokine upregulation [was] itself [a] trigger for RA." Obj. 1. In other words, the activation of particular cytokines was a trigger for RA. Petitioner notes that, in his opinion, the Special Master stated that:

> Petitioner has failed to demonstrate that cytokine upregulation allegedly resulting from vaccine administration is itself a trigger for RA. . .

*Olson*, at 60. Petitioner claims that it is not an element of her theory that cytokine upregulation is itself a trigger for RA but rather that something in the chemical environment can trigger inflammasomes. Petitioner's theory is a "chain reaction," that is, the alum in the HPV vaccine triggered inflammasomes which, in turn, activated particular cytokines centrally involved in RA.

The Court is puzzled that in her Motion for Review, the Petitioner, on the one hand, states that she did not argue that cytokine activation is a trigger for RA, when, on the other hand, (on the same page) she states that "[I]nflammasomes, in turn, activate particular cytokines that are centrally involved in asthma, bronchiectasis, and RA." Petr.'s Mot. at 5. It seems that the disagreement is between the Special Master's use of the word, "trigger," and her use of the word, "centrally involved."

In any event, there is a connection alleged by Petitioner's theory between RA and cytokine activation. In order for Petitioner's medical theory to be "reputable," it would seem that the connection between cytokine activation (mediated by inflammasomes) and RA must be plausibly one of cause and effect. The Special Master used the word "trigger" to represent this connection. It is not enough, it would seem, for the Petitioner to propose that cytokine activation is only "centrally involved." In other words, the Special Master understood the Petitioner's chain reaction theory but felt that the link between cytokine activation and RA was not sufficiently established to causally connect cytokine activation and RA.

Putting aside this cavil, on page 58 of the Special Master's opinion, the Special Master summarized Petitioner's theory clearly:

> Petitioner asserts that vaccines can function as the trigger that sets off the autoimmune process resulting in RA — particularly due to the inclusion of alum as an adjuvant.

*Olson*, at 58. He understood that she alleges that alum was the trigger that started the "chain reaction." The Special Master noted that Petitioner's theory

> established a general point — that many different environmental factors could initiate the process that would cause a susceptible individual to develop RA, and that it is not unreasonable to consider a vaccine . . . as one of those factors. But it remains a speculative issue as to whether cytokine production *instigated* by a single vaccine containing alum would be robust enough, and occur for long

enough, to be pathogenic generally, let alone to cause RA.

*Olson,* at 60 (emphasis added).

*b. Objection 3*

Petitioner also claims that the Special Master misconstrued her theory when he required evidence "that alum directly precipitates RA." Obj. 3. Similar to Objection 1, Petitioner asserts that she never claimed that alum precipitated RA. Instead, her theory was based on how the alum in the HPV vaccine was the environmental trigger.

In reviewing his decision, the Court notes that the Special Master found that Petitioner lacked "reliable scientific support," that alum "*could* precipitate RA." The Special Master did not require evidence that alum directly precipitates RA; he found that it *could* precipitate RA. The Special Master's use of the word "could" left open the possibility that alum could have caused the RA, but remained unconvinced, as he was unable to determine if her RA was caused by any other environmental factor. As such, he understood Petitioner's medical theory and did not require proof that alum directly precipitates RA, but concluded that Petitioner had not converted the possibility that alum precipitated RA into a reputable medical theory that explains how it could.

*c. Objection 9*

Petitioner also argues that the Special Master misunderstood her theory when he found that Petitioner "failed to prove that alum alone causes RA." Obj. 9. Petitioner argues that she never claimed "alum alone" causes RA but may only trigger RA in people with pre-existing lung conditions.

The Special Master, again, understood Petitioner's theory and held that the studies submitted do "not explain why alum in a vaccine would likely initiate or increase," the development of RA and there was, "nothing specific enough regarding *any* of the possible triggers . . . to define how the triggering process would theoretically work." *Olson*, at 62 (emphasis in original). In other words, the Special Master did not conclude that Petitioner failed to show that "alum alone" caused RA, but rather found that Petitioner's theory did not establish how alum caused her to develop RA.

*d. Objection 16*

Petitioner also maintains that the Special Master misunderstood her theory as "dependent on citrullination." Obj. 16. Citrullination is important in explaining the link between RA and lung inflammation in general, and the link between Petitioner's lung inflammation and RA is part of her theory. (See p. 3 of this opinion.) It is discussed in the Sofat article, which was part of the medical literature submitted by Petitioner. (See footnote 10 above.)

The Special Master considered that the link between lung inflammation and RA was scientifically established, but he noted that the explanation in the submissions for this link

depended on citrullination. Citrullination is the process by which the amino acid arginine (found naturally in DNA) is converted into citrulline. *Olson*, at 15 citing Sofat article. As citrulline is not one of the amino acids found in DNA, the autoantibodies of the immune system may attack the citrulline, causing inflammation. Sofat Article at 1-2. This inflammation can occur in the lung and is also characteristic of RA. *Id.* These autoantibodies are called anti-citrullinated protein antibodies (ACPAs), and they are a scientifically accepted marker for RA. *Olson*, at 63. According to the Sofat article, relied upon by Dr. Middleton, Petitioner's expert, citrullination may first occur in the lungs before it occurs in the joints. But an indicator of citrullination is the existence of ACPAs, and Petitioner has never tested positive for ACPAs. *Olson*, at 63. (See p. 3 above.) Thus, the Special Master found that the evidence proposed by Petitioner was "ultimately inapposite to the present context." *Olson*, at 62.

Petitioner protests that "because the antibodies responsible for petitioner's RA . . . is not known, she is obviously unable to introduce evidence about how that autoantibody functions." Petr.'s Mot. at 15. But, unless Petitioner can propose a theory that does not rely upon citrullination to establish a link between lung inflammation and RA, we are left to imagine how lung inflammation is linked to RA. Furthermore, we are left to imagine how alum triggered the chain reaction that produced Petitioner's RA in the context of the link between lung inflammation and RA.

In sum, it appears that Petitioner did introduce a theory linking lung inflammation with RA that was dependent on citrullination. But this theory could not be linked to Petitioner's RA because she did not test positive for ACPAs, which are an effect of citrullination. Therefore, the Petitioner was thrown back to asserting that there are other explanations to explain the link—although Petitioner did not provide a plausible theory. It is not enough to satisfy *Althen* prong 1 to say that because the autoantibodies that may have caused Petitioner's RA were unknown, Petitioner is relieved from the obligation to provide a plausible scientific explanation for the element of her theory that involves a link between lung inflammation and RA.

The Special Master understood Petitioner's theory.

*e. Objection 17*

Petitioner also proffers that the Special Master misconstrued her theory by stating:

> Certainly Petitioner offered nothing reliable or persuasive . . . that suggests that alum plays any role in abetting the citrullination process.

*Olson*, at 64; Obj. 17.

In doing so, Petitioner claims that the citrullination process is not part of her theory, but rather that the alum activates particular pathways that are responsible for lung inflammation and these pathways have nothing to do with citrullination.

As noted above, citrullination was an explanation that an expert of Petitioner's used to explain the link between lung inflammation and RA, that link being an element of Petitioner's

theory. Insofar as citrullination provides this link, the Special Master noted that there was no reliable or persuasive evidence that alum would abet the citrullination process. Thus, the Special Master merely alludes to the fact that the Petitioner's evidence did not prove that alum abets the citrullination process. This statement is not equivalent to what Petitioner claims, that the Petitioner's theory rested upon the determination that alum abets the citrullination process. As such, he did not misapprehend Petitioner's theory.

**2. The Special Master Did Not Increase Petitioner's Burden of Proof.**

Petitioner's second group of objections is that the Special Master increased her burden of proof by requiring proof of specific biologic mechanisms, experimental evidence, other medical literature, required testimony of an immunologist, and cloaked the legal standard in a "credibility" determination. Specifically, Petitioner claims that the Special Master required evidence of a specific biologic mechanism for two components of her theory: linking alum to RA and demonstrating how environmental factors trigger RA.

Respondent argues that the Special Master recognized that a biological mechanism is not a required component of the Petitioner's medical theory, but because Petitioner offered a specific biological mechanism, the Special Master was then required to consider it. Resp. at 11. Respondent also argues that the Special Master did not require an immunologist; he simply took into consideration that Dr. Middleton was not an immunologist in finding Dr. Middleton's theory unpersuasive. Resp. at 11. Finally, Respondent reminds the Court that a Special Master is allowed to make credibility determinations and that such determinations should ordinarily be upheld on review, but its Response does not directly address Petitioner's "cloaking" argument. Resp. at 7.

*a. Objections 2, 10, 11, 12, 14, and 15*

As the Federal Circuit held in *Moberly,* the Special Master is endowed with the authority to weigh the evidence of a biological mechanism presented to him, and "[a]lthough a Vaccine Act claimant is not required to present proof of causation to the level of scientific certainty, 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 HHS*, 592 F.3d 1315, 1324 (Fed. Cir. 2010) (citing *Terran v. Sec'y of HHS,* 195 F.3d 1302, 1316 (Fed. Cir. 1999)). Thus, the Special Master is authorized to weigh the evidence of the Petitioner's biologic mechanism.

The Special Master did not require proof of a specific biologic mechanism, epidemiological evidence, or other medical literature. In fact, the Special Master specifically noted that, "Program petitioners are not required to offer direct proof supporting their theory, or even any specific type of evidence, but instead may rely on circumstantial evidence." *Olson*, at 57. However, as Petitioner offered evidence of a specific biologic mechanism, the Special Master was then required to consider it and evaluate its persuasiveness.

After reviewing this evidence, the Special Master concluded that it was not persuasive, or in the case of the submitted medical literature, even applicable. For example, with regard to the specific biologic mechanism, because Petitioner identified only that component (the alum

adjuvant) of the HPV vaccine as potentially having caused RA, the Special Master concluded it was "critically important that Petitioner marshal reliable scientific or medical evidence suggesting that alum could precipitate RA." *Olson*, at 61. Thus, in addressing this issue, the Special Master was not requiring the Petitioner to show that alum was the sole trigger of the theory, but rather was pointing out that Petitioner had not shown it to be a trigger by preponderant evidence. The Special Master also discussed the kinds of evidence that, if present, would have assisted Petitioner in proving her theory, but did not require Petitioner to produce that evidence. *See Olson*, at 62 ("If alum can cause RA, there should be more robust evidence that it is associated with other autoimmune conditions in different vaccines.").

Moreover, after reviewing the medical literature, the Special Master noted that many of the articles offered relied on very different factual circumstances from those in this case and, therefore, gave them little weight. For instance, the Besnard article[13] was an animal study that explicitly excluded alum as part of the study. Ultimately, the Special Master found that these differences weakened the relevance and applicability of the articles. Thus, the Special Master properly considered the relevant evidence in the record, came to a factual conclusion based upon plausible inferences, and provided a reasoned explanation in his decision.

*b. Objections 6 and 8*[14]

Petitioner also alleges that the Special Master required her to provide the testimony of an immunologist, implying that only immunologists have the expertise to testify about complex immune processes. However, this argument is without merit. In his decision, the Special Master wrote:

> Dr. Middleton, though qualified to testify about RA generally and its possible etiology, lacked the specialized immunologic grounding necessary *to explain and defend in a persuasive manner the theory articulated in this case*, given that theory's dependency on complex immune system processes.

*Olson*, at 64 (emphasis added). Thus, it is clear to the Court that the Special Master did not require an immunologist, but rather articulated the reasons as to why Dr. Middleton was not persuasive—he could neither articulate nor could he defend in a persuasive manner his theory without more specialized knowledge of the immune system. Considering the complex factors involved, the Special Master properly weighed and considered the relevant evidence and provided a reasoned explanation in his decision.

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[13] A.-G. Besnard et al., *NLRP3 Inflammasome is Required in Murine Asthma in the Absence of Aluminum Adjuvant*, 66 Allergy 1047-57 (2011) ("Besnard"); *see Olson*, at 28.

[14] Objection 8 is entitled, "The decision cloaked an erroneous legal standard with a 'credibility determination.'" Petr's. Mot. at 10. But in the one-paragraph explanation of this objection, Petitioner merely asserts: "In this proceeding, the erroneous legal standard was that only immunologists have the expertise to testify about the complex immune processes involved in RA." Petr's Mot. at 11. She does not explain how this erroneous standard was "cloaked…with a credibility determination."

### 3. The Special Master Did Not Err In Making Factual Conclusions.

The remaining objections under *Althen* prong one is that the Special Master applied the wrong evidentiary standard which led to findings contrary to the factual record. However, the Special Master incorporated Petitioner's evidence and weighed the persuasiveness of her experts' theory and testimony. The Special Master repeatedly noted that, while Petitioner's theory has merit, it simply was not persuasive in this case.

The Special Master noted that the Petitioner offered persuasive evidence that, "persistent lung inflammation is often associated with RA," and that it is likely citrullination precedes ACPA production in the lungs. *Olson*, at 59.

However, the Special Master concluded that this was not enough to satisfy the burden under *Althen* prong 1 showing a medically plausible theory linking the vaccine to RA. The Special Master stated that even though some of the, "components of Petitioner's theory were facially sound or reliable (and that Respondent's expert on the injury at issue conceded certain points relevant to the science behind Petitioner's causation theory) [it] does not lead to the conclusion that the theory *as a whole* is reliable or persuasive." *Olson*, at 42 (emphasis in original).

As discussed above, the Special Master understood Petitioner's theory and was not persuaded by the medical theory of causation. He thus concluded that she failed to prove this by preponderant evidence. As the decision of the Special Master properly weighed and understood the evidence, his decision was not arbitrary, capricious, contrary or otherwise not in accordance with law and this Court will not second guess his fact intensive conclusions.

## B. *Althen* Prong 2 Objections

With respect to prong two of the *Althen* test, Petitioner alleges 13 total objections to the Special Master's decision. These objections can be grouped into four categories: whether the Special Master again misapprehended Petitioner's theory (Objection 28), increased Petitioner's burden of proof (Objections 19, 21, 22, 23, 25, 31), erred in making different evidentiary and legal conclusions (Objections 20, 27, 29, 30), and failed to give proper weight to Petitioner's expert testimony (Objections 24, 26).

Respondent highlights that in order to satisfy prong two of *Althen*, Petitioner must establish by a preponderance of the evidence that "a logical sequence of cause and effect showing that the vaccination was the reason for the injury," and that this is usually supported by Petitioner's medical records. *Althen,* 418 F.3d at 1278. Then applying this standard to the facts of the case the Respondent concludes that, "[m]ost devastating to petitioner's case is that repeated testing confirmed that she did not have the requisite antibodies that would be present if the citrullination process described by Dr. Middleton had actually occurred in her body." Resp. at 13. In other words, because the Petitioner lacked the antibodies associated with this process she failed to establish the "logical sequence of cause and effect." *Althen*, 418 F.3d at 1278.

### 1. The Special Master Did Not Misapprehend Petitioner's Theory Under *Althen* Prong 2.

Petitioner claims that the Special Master "misapprehended the theory of alum as a trigger of RA." Petr.'s Mot. at 22. Petitioner argues that "*no* part of petitioner's medical theory posits 'persistent pathogenic cytokine upregulation' after alum administration. Rather . . . petitioner's medical theory is that alum can be an environmental "trigger" for RA in a person with a chronic inflammatory lung condition." Petr.'s Mot. at 23 (emphasis in original). In other words, "Petitioner's medical theory is that alum can be an environmental trigger for RA by heightening the inflammation in a person with a pre-existing inflammatory lung condition[;] th[is] does not require that there be a "persistent" elevation in inflammation "primarily in the first six months to a year after vaccination." Petr.'s Mot. at 23.

In support of this argument, the Petitioner relies on the following excerpt from the Special Master's decision:

> Most significantly, the record does not reflect the existence of an ongoing inflammatory process that would establish the persistent, pathogenic cytokine upregulation that Petitioner's theory envisions after administration of an alum-adjuvanted vaccine.

*Olson*, at 67. However, after reviewing the evidence provided, the Special Master found that:

> [Petitioner's] medical history does not provide the corroboration necessary to conclude that Petitioner's theory worked out as predicted — and leaves open the possibility that other factors were more likely to have precipitated her RA than the vaccine.

*Olson*, at 67. Therefore, the Special Master was discussing *how* and *why* he was unable to determine which "factor" caused Petitioner's RA, namely, because Petitioner's medical history did not corroborate with her own theory of causation. The Special Master explained:

> [Petitioner was] missing are other pieces of proof that, under Petitioner's causation theory, should have been reflected in the medical records. In particular, Petitioner has consistently tested negative for ACPAs — even though citrullination, and its connection to persistent inflammatory conditions in the lung, was repeatedly referenced in both Petitioner's literature and Dr. Middleton's testimony as significant in establishing an individual's susceptibility to RA given longstanding respiratory problems.

*Olson*, at 68. Thus, after reviewing the evidence, he did not misconstrue Petitioner's theory, but held it to be inconsistent with her causation theory. Therefore, as the Special Master understood Petitioner's theory and properly reviewed the relevant evidence, his conclusion was not arbitrary, capricious, contrary or otherwise not in accordance with law.

**2. The Special Master Did Not Increase Petitioner's Burden of Proof.**

Petitioner's second category of arguments under prong 2 of *Althen* maintains that the Special Master impermissibly raised the burden of proof by requiring: (1) "her to negate possibilities and alternatives that might have occurred," (2) "evidence of causation relating to other vaccines," (3) "evidence of other autoimmune conditions," (4) epidemiological evidence, (5) "evidence of pathological markers," and (6) "test results consistent with the medical theory." *See* Petr.'s Mot at Objs. 19, 21, 22, 23, 25, and 31.

Petitioner argues that the Special Master required her to negate any alternatives and this raised her burden of proof. However, he wrote that Petitioner's theory, "*leaves open the possibility* that other factors were more likely to have precipitated," the RA. *Olson*, at 67 (emphasis added). This statement does not require Petitioner to negate anything, but rather highlighted weaknesses in the medical theory proffered by her. Thus, the Special Master did not raise Petitioner's burden.

With regard to Petitioner's argument that the Special Master raised her burden of proof by requiring her to provide "evidence of causation relating to other vaccines," and "evidence of other autoimmune conditions," these arguments lack merit. In his decision, the Special Master was not persuaded by her theory that alum in the vaccine caused her RA. As the Special Master explained,

> The fact that many vaccines also contain alum but have not been implicated in RA or other autoimmune conditions as alleged herein also merits some weight. *See, e.g., Johnson v. Sec'y of HHS*, No. 10-578V, 2016 U.S. Claims LEXIS 1284, *8-9 (Fed. Cl. Spec. Mstr. Aug. 18, 2016) (noting the unreliability of the theory that if an adjuvant can cause an autoimmune disease, it could cause any autoimmune disease). If alum can cause RA, there should be more robust evidence that it is associated with other autoimmune conditions in different vaccines.

*Olson*, at 62 (emphasis added). This statement only indicates that if Petitioner's theory that alum in Gardasil caused RA could be proven, other evidence would exist indicating that alum in other vaccines caused for instance RA, or other autoimmune conditions. As such, the Special Master was not persuaded and this Court will not second guess his decision.

Further, Petitioner's attempt to equate the lack of "more robust evidence," to requiring epidemiological evidence, along with the allegation that the Special Master required evidence of pathological markers and "test results consistent with the medical theory," is misleading. As explained above, the "more robust evidence" was made regarding the persuasiveness of the theory, and not the type of evidence provided. Therefore, the Special Master did not require epidemiological evidence.

Also, as discussed above, the Special Master took into consideration all the evidence provided and ultimately concluded that he could not find what the "most likely cause was, given the total absence of any of the biomarkers/antibodies most associated with the disorder." To the Special Master, this was the most persuasive evidence. *Olson,* at 69. And because, "Petitioner

has never tested positive for those autoantibodies . . . she cannot credibly propose a theory involving a process that she cannot also establish occurred to her." *Olson*, at 63.

The Special Master did not require any of the evidence described above to establish a logical sequence of cause and effect, but properly considered the relevant evidence in the record, came to a factual conclusion based on plausible inferences, and provided a reasoned explanation in the decision.

**3. The Special Master Did Not Err In Making Factual Conclusions.**

The Petitioner alleges that the Special Master erred in making findings contrary to the factual record. Particularly, Petitioner alleges that the Special Master erred when he: "based findings on evidence not in the record," found that she "did not have an active immune-mediated disease course," lacked "tests that supported her theory," and failed to recognize that Petitioner established a plausible medical theory. *See* Petr.'s Objs. 20, 27, 29, and 30. Upon review, these allegations are without merit.

*a. Objection 20*

Petitioner claims that the Special Master based findings of fact on evidence not in the record by taking into account the lack of evidence that alum causes RA. In support, Petitioner points to this statement by the Special Master, "The fact that many vaccines also contain alum but have not been implicated in RA or other autoimmune conditions as alleged herein also merits some weight." *Olson*, at 62.

However, this statement recognizes the weakness of Petitioner's overall theory, that alum has not been shown to trigger RA in any vaccine, and does not support the conclusion that he considered evidence not in the record.

*b. Objection 27*

Petitioner also argues that, in general, the Special Master erred when he failed to find that Petitioner established a logical sequence of cause and effect between the receipt of the vaccine and injury. Petitioner maintains that her biologically plausible theory, "combined with a close temporal proximity of vaccine administration and the onset of RA, is a valid basis for a medical opinion that there is a logical sequence of cause and effect between vaccine and injury." Petr's Mot. at 22.

However, as discussed *supra*, the Special Master did not find her medical theory to be plausible, thus failing the first element. Moreover, Petitioner's evidence on this prong rests solely upon the temporal relationship; this is not enough to establish a link. *See Grant v. Sec'y of HHS*, 956 F.2d 1144, 1147-48 (Fed. Cir. 1992) ("the petition must affirmatively demonstrate that the injury or aggravation was caused by the vaccine. Simple similarity to conditions or time periods listed in the Table is not sufficient evidence of causation.").

According to the Special Master, Petitioner failed to show by preponderant evidence that

affirmatively demonstrated that the injury was caused by the vaccine, the Special Master concluded that she failed to meet her burden under *Althen*. This conclusion is not arbitrary, capricious, contrary or otherwise not in accordance with law.

*c. Objections 29 and 30*

Petitioner maintains that the Special Master's finding that Petitioner "didn't have tests that supported her theory was a factual inference wholly unsupported by the record," and was arbitrary.[15] Petr.'s Mot. at 24. Petitioner derives this argument from the following statement by the Special Master:

> Petitioner has also **pointed to no testing results or other laboratory proof** (primarily in the first six months to a year after vaccination) that would establish that her causation theory was occurring as expected, such as results evidencing the presence of ongoing inflammation.

*Olson*, at 67 (bold in original). However, this is not an arbitrary finding by the Special Master. The Special Master found that:

> *The record* does not reflect the existence of an ongoing inflammatory process that would establish the persistent, pathogenic cytokine upregulation that Petitioner's theory envisions after administration of an alum-adjuvanted vaccine. Overall, as Dr. Lightfoot observed in his report, Mrs. Olson's case of RA was on the mild end of the spectrum — reflected in its lengthy course, her ability to tolerate the associated pain while conducting her life, and the lack of evidence demonstrating a more progressively severe trajectory.

*Olson*, at 67 (emphasis added).

Thus, as the Special Master makes clear, Petitioner failed to meet her burden based upon the record as it was in front of him. As such, the Special Master was not arbitrary, capricious, contrary or otherwise not in accordance with law.

**4. The Special Master Properly Weighed the Evidence**

The remaining objections relate to the Special Master's weight to particular testimony. The first objection relates to the Special Master's alleged failure to accord weight to Petitioner's epidemiologist expert, Dr. Mayer. The second relates to the Special Master's alleged failure to not consider the opinion of the treating physician, Dr. Middleton.

As discussed, the Special Master took into consideration the testimony of Petitioner's

[15] Petitioner also argues that the Special Master's finding that she both had RA and "failed to demonstrate the existence of an active immune-mediated disease course," are inconsistent and an abuse of discretion. *Olson*, at 68. However, the Special Master did not accord this "absence of testing" any "excess weight." *Olson*, at 68 n.25.

epidemiologist expert, Dr. Mayer; he was just not persuaded by him.

As to the testimony of the physician, Dr. Middleton, "a treating physician's opinion on vaccine causation is only as strong as the underlying basis for the opinion." *See Perreira v. Sec'y of HHS*, 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994). As discussed at length above, the Special Master was not persuaded by Dr. Middleton's "underlying basis" for his theory of causation. As such, the Special Master properly weighed Dr. Middleton's testimony.

## IV. CONCLUSION

For the reasons stated above, the Court **DENIES** Petitioner's motion for review and **SUSTAINS** the decision of the Special Master. The clerk is directed to enter the judgment accordingly.

**IT IS SO ORDERED.**

s/ Edward J Damich
EDWARD J. DAMICH
Senior Judge