In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 17-1055V

(to be published)

ROSA MONZON,	*	
	*	
Petitioner,	*	Chief Special Master Corcoran
	*	
v.	*	
	*	Filed: June 2, 2021
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
	*	
Respondent.	*	
	*	

Joseph Vuckovich, Maglio Christopher & Toale, P.A., Washington, DC, for Petitioner

Dhairya Jani, U.S. Dep't of Justice, Washington, DC, for Respondent

ENTITLEMENT DECISION[1]

On August 4, 2017, Rosa Monzon filed a petition seeking compensation under the National Vaccine Injury Compensation Program (the "Vaccine Program")[2] alleging that the tetanus-diphtheria-acellular pertussis ("Tdap") vaccine that she received on April 12, 2016, caused her to develop polymyalgia rheumatica ("PMR"). *See* Petition ("Pet.") at 2. Petitioner's diagnosis was subsequently changed to rheumatoid arthritis ("RA"), and RA is the asserted injury in this case. Ex. 13 at 2; Petitioner's Prehearing Brief at 1.

[1] This Decision will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means the Decision will be available to anyone with access to the internet**. As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the published Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen (14) days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire Decision will be available to the public in its current form. *Id.*

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755 (codified as amended at 42 U.S.C. §§ 300aa-10–34 (2012)) (hereinafter "Vaccine Act" or "the Act"). All subsequent references to sections of the Vaccine Act shall be to the pertinent subparagraph of 42 U.S.C. § 300aa.

An entitlement hearing was held in this matter on February 5, 2021. After consideration of the record and testimony provided at hearing, I deny entitlement in this case. As discussed in more detail below, Petitioner has not preponderantly established that she likely experienced RA, rather than the preclinical version of it. At best, Petitioner experienced some post-vaccination symptoms likely attributable to the vaccine, but they did not reflect her claimed injury. And even if I had found that she likely did experience RA, she has not established that the Tdap vaccine could cause it, or that it did so in this case.

I. Medical History

A. *Medical History Prior to Vaccination*

Prior to her vaccination, Ms. Monzon was a healthy and active fifty-five-year-old woman with a medical history of hypertension, dyslipidemia, and irritable bowel syndrome, and no history of symptoms that could be deemed harbingers of RA. Pet. at 1; Ex. 2 at 2. On April 12, 2016, she visited Dr. Amir Goldenberg, her primary care physician, to establish care and receive treatment for hypertension. Ex. 2 at 15-17. At this same visit, she received the Tdap vaccine in her left deltoid. Ex. 1 at 1.

B. *Onset of Symptoms*

Ten days later, on April 22, 2016, Ms. Monzon presented to Memorial Healthcare System urgent care center in East Hollywood, Florida with complaints of generalized fatigue, neck pain, arm pain, a small hematoma at the Tdap injection site, and bilateral leg pain that she stated had "started after getting her tetanus vaccine." Ex. 2 at 35. She reported no fever, chills, paresthesia, or rash, however. *Id.* On exam, Petitioner had normal range of motion in her neck and extremities. *Id.* at 37. She was assessed with a "small Hematoma at site of injection of TDAP injection done one week ago" with reports of "associated fatigue and weakness," was prescribed steroidal medication, and instructed to return to the clinic in one week *Id.* at 38.

On May 4, 2016 (now approximately three weeks since the relevant vaccination), Petitioner was seen by Dr. Goldenberg for complaints of neck and lower back pain that she reported had returned two days following her completion of the steroidal medication. Ex. 2 at 52. Dr. Goldenberg's notes indicate that Petitioner's neck and back pain was reported to have "started 2 days after Tdap injection on 4/12/2016. She developed a small hematoma on the deltoid area but no surrounding erythema, fever or chills." *Id.* On exam, Petitioner had normal range of motion in her hips, but her cervical spine showed decreased range of motion with tenderness and spasm. *Id.* at 53-54. Dr. Goldenberg diagnosed a mild reaction to Tdap, cervicalgia, and lumbago that "[s]tarted after recent daily [sic] vaccination, likely adverse effect, flu like reaction." *Id.* at 55. He prescribed NSAIDs and local heat for the hematoma, a muscle relaxant, and administered an injection of Toradol, a pain killer. *Id.*

Ms. Monzon returned to urgent care on May 21, 2016, for evaluation of whole body weakness, aches, and pain that was mainly localized to her neck, buttocks, and posterior thighs. Ex. 2 at 74. She now reported that she could not bend over to pick anything up from the ground due to pain. *Id.* On exam, she had decreased range of motion in her neck, diffuse body muscle aches on palpation mainly in the posterior thigh, posterior neck, and gluteal muscles. *Id.* at 75. The diagnosis was cervicalgia and "adverse effect of pertussis vaccine." *Id.* at 76-77. She was prescribed an oral steroid and referred for a rheumatology consult. *Id.*

On May 31, 2016, Petitioner completed a Vaccine Adverse Event Reporting System ("VAERS") form reporting the date of vaccination and onset of alleged adverse event as April 14, 2016 (hence two days after vaccination) at 5:00 a.m. Ex. 9. On June 9, 2016, Petitioner returned to Dr. Goldenberg, who observed from lab testing an elevated erythrocyte sedimentation rate—a biomarker for the presentation of inflammation—and joint pain. Ex. 2 at 108. He urged her to consult with a rheumatologist. *Id.*

On June 16, 2016, Petitioner presented to rheumatologist Zabeth Cure Lopez, M.D., for evaluation. Ex. 10 at 171. Ms. Monzon now reported a two-month history of left arm pain following receipt of a Tdap vaccine, adding that she was fatigued because her neck pain disturbed her sleep, and also complained of myalgia, muscle cramps, numbness, and tingling. *Id.* On exam, she had full range of motion in all joints, negative fibromyalgia trigger points, bilateral trapezius spasm, and tenderness in her neck with related decreased range of motion. *Id.* Petitioner was diagnosed with low back pain, neck pain that "started after Tdap," and myalgia that was prominent in the neck and back. *Id.* Dr. Lopez ordered blood labs and recommended a neurological consult for possible Guillain-Barré syndrome ("GBS"). *Id.*

On June 23, 2016, Petitioner was seen by a neurologist, Adnan Subei, D.O., who concluded that Petitioner was not likely suffering from GBS. Ex. 11 at 10. However, Dr. Subei did "think she developed some kind of an inflammatory reaction from the vaccine given her symptoms and lab markers." *Id.* He ordered an EMG/NCS of select muscles in the left arm to evaluate for mononeuropathy multiplex or demyelinating polyneuropathy (although no EMG/NCS results/records have been filed) and instructed Petitioner to continue follow-up with rheumatology. *Id.* On July 7, 2016, Petitioner returned to Dr. Lopez, who noted that Petitioner's exam results were consistent with her June 16, 2016 presentation. Ex. 3 at 2. The diagnosis was polymyalgia rheumatica ("PMR"), and Petitioner was prescribed Prednisone, to be taken twice a day for 30 days. *Id.*

Petitioner returned to Dr. Lopez for a follow-up visit on July 7, 2016. Ex. 3 at 2. Dr. Lopez noted that Petitioner's exam was unchanged since June 2016, and diagnosed Petitioner with PMR. *Id.* On August 11, 2016, however, Dr. Lopez amended the notes to Petitioner's medical record based on previously-ordered test results. *Id.* at 5-6. Her assessment was now (for the first time in the record) RA, based on "increased inflammatory markers and +CCP high titer." Ex. 6 at 7-10. As discussed below, the anti-cyclic citrullinated protein ("anti-CCP" or "+CCP") antibody is

highly associated with RA.

C. *Subsequent Treatment*

Petitioner continued to visit Dr. Lopez throughout the balance of 2016 and into mid-2017. Ex. 6 at 2, 5; Ex. 7 at 3; Ex. 10 at 175, 178, 181, 186, 278. On November 16, 2016, Dr. Lopez noted that Petitioner appeared to have no complaints. Ex. 7 at 1. In addition, exam revealed full range of motion in all joints with no synovitis. However, the typical tender points for fibromyalgia were positive. *Id.* at 3. Petitioner's diagnosis remained RA, but because there was "no clinical or laboratory evidence for disease activity," Dr. Lopez proposed to maintain existing treatment while tapering the Prednisone. *Id.* In keeping with this treatment plan, on February 9, 2017, Petitioner's dosage of Prednisone was reduced to 1 mg per day, and ceased entirely by April. Ex. 10 at 175, 178. Petitioner continued to take other prescription medications for treatment of fibromyalgia, however. *Id.*

On May 22, 2017—now a little more than a year since her symptoms began—Petitioner saw Dr. Goldenberg and reported that her RA was mostly controlled, and that she was no longer taking Prednisone. Ex. 10 at 300. Petitioner returned to Dr. Lopez on August 7, 2017, at which time she was without complaints of lower back pain, and she denied arthralgias or morning stiffness in her shoulders or hips. *Id.* at 183.

On May 5, 2018, Petitioner visited Dr. Gladys Nogueiras at MD Healthcare Hollywood in Hollywood, Florida for the first time. Ex. 44 at 178. Dr. Nogueiras took a medical history and noted that Petitioner had "no new complaints." *Id.* A physical exam revealed full range of motion in all extremities and no swelling. *Id.* at 182. Dr. Nogueiras noted that Petitioner's RA was stable, in treatment with Methotrexate (a common and effective RA-specific drug), and her fibromyalgia was stable in treatment with Duloxetine—both prescribed by her rheumatologist Dr. Lopez. *Id.* The plan was to follow-up in two weeks. *Id.*

On June 15, 2018 Petitioner was seen again at MD Healthcare Hollywood for a follow-up regarding Petitioner's lab results. Ex. 44 at 223-227. The assessment revealed that Petitioner's symptoms, including hypertension, lactose intolerance, and fibromyalgia were all stable on current treatments and a diet and exercise plan was discussed. *Id.* at 176. On September 14, 2018, Petitioner again visited Dr. Nogueiras where they discussed her dyslipidemia. *Id.* at 171. She was advised to continue with fish oil 2000 mg and begin Rosuvastatin 500mg with follow-up in three months. *Id.*

On January 11, 2019, Petitioner returned to MD Healthcare Hollywood following an acute illness including a cough and fever. Ex. 44 at 156. She was screened for pneumonia and prescribed an antibiotic. *Id.* at 158. A note by Dr. Nogueria indicated that Petitioner had continued taking Methotrexate to treat her RA symptoms until 2019, when the treatment was discontinued by Dr. Lopez "because of RA in remission for over 1 year." *Id.* at 8. Petitioner continued to follow-up for her on-going ailments and attend wellness checks with Dr. Nogueiras throughout 2019 and 2020.

See Id. 132-158.

II. Testimony at Hearing

A. *Ms. Monzon*

Petitioner provided an affidavit and testified at the hearing with the aid of an interpreter. *See* Affidavit, filed on July 9, 2020 as Ex. 41 (ECF No. 38-2) ("Affidavit"); Tr. 5-25. Petitioner resides in Hallandale, Florida, where she works as a housekeeper, and she received the Tdap vaccine there in April 2016. Id. at 6; Affidavit at 2. She was healthy prior to receipt of the vaccine, had not previously experienced arthritic-like pain, and had not been told by any treaters she might suffer from such a condition. Id. at 7-8. She also was not a smoker in her prior history. Id. at 24.

Ms. Monzon went on to describe her symptoms following the vaccination on April 12, 2016. Tr. at 8. She testified that the day after receiving the vaccination she felt pain in the injection arm and that two days after receiving the vaccination, she felt the need to rest more frequently and she began losing her physical strength. *Id.*; Affidavit at 2. Ms. Monzon explained that she went to the doctor on April 22, 2016 and she was very worried because she knew what was happening to her was not normal. Tr. at 10; Affidavit at 2. She explained that she had developed a hematoma on the injection site and that she also felt pain and weakness in her joints. *Id.*

Next, Ms. Monzon described a visit to a neurologist on June 23, 2016. Tr. at 10. She testified that she told the doctor she was experiencing rigidity in her neck, muscular pain, fatigue, and was having difficulty walking. *Id.* at 10-11. She also described a previous doctor visit, on June 6, 2016, with Dr. Lopez who prescribed her Prednisone for her symptoms. *Id.* at 11. Ms. Monzon indicated that the prescription alleviated her symptoms only slightly. *Id.* Ms. Monzon continued to follow up with her rheumatologist, Dr. Lopez, throughout the remainder of 2016, and the treatment she received was helpful, although her symptoms did not abate totally. *Id.* at 14. That fall, Petitioner was prescribed Methotrexate, which helped lessen her pain. *Id.* at 14-15.

By the summer of 2017, Petitioner learned from Dr. Lopez that if she did not maintain the medications she would likely see a recurrence of the more severe symptoms. Tr. at 15. She did so, finding that by the end of 2017 her pain was diminished and symptoms largely controlled, even though she still consistently felt fatigue. *Id.* As of 2018, Petitioner's pain persisted, albeit in a less intense manner, as she maintained her medicinal course, although she stopped taking Methotrexate when she left on a trip out of the United States (a pause that was not determined to have impacted her status, given the other medications she continued to take). *Id.* at 16-17. Ms. Monzon described her symptoms for 2019 as comparable to the past—persistent pain but controlled with her medications. *Id.* at 17-18.

B. *Daniel Wallace, M.D.*

Dr. Wallace provided three expert reports on Petitioner's behalf and provided testimony at

the hearing. Report, dated June 22, 2018, filed as Ex. 13 (ECF No. 19-2) ("First Wallace Rep."); Report, dated December, 21, 2018, filed as Ex. 30 (ECF No. 24-2) ("Second Wallace Rep."); Report, dated March 29, 2019, filed as Ex. 36 (ECF No. 25-2) ("Third Wallace Rep."); Tr. 26-113. Dr. Wallace maintained that Petitioner's Tdap vaccine was causally associated with her development of RA a short time later. First Wallace Rep. at 6.

Dr. Wallace is the Medical Director of the Wallace Rheumatic Study Center in Beverly Hills, California. *See* CV, dated December 21, 2018, filed as Ex. 31 (ECF No. 24-3) ("Wallace CV"). He obtained his medical degree from the University of Southern California and served his residency at Cedars-Sinai Medical Center in Los Angeles, California. *Id.* at 1. Dr. Wallace also completed a rheumatology fellowship at UCLA School of Medicine. *Id.* Currently, Dr. Wallace is an attending physician at Cedars Sinai Medical Center, a Clinical Professor of Medicine at David Geffen School of Medicine at UCLA, and the Associate director of the Rheumatology Fellowship Program and Professor of Medicine at Cedars-Sinai Medical Center. *Id.* Dr. Wallace has also published numerous books and articles and received various grants, including grants specifically for rheumatoid arthritis research. *Id.* at 4-6.

Dr. Wallace is board-certified in rheumatology and internal medicine. Tr. at 27. Most of his time is spent in clinical practice, and he has seen over a thousand patients with RA. *Id*. at 27-28. He otherwise teaches and conducts research—specifically in certain RA variants, like lupus, or Sjogren's syndrome. *Id.* at 27-28, 30. Dr. Wallace is not an immunologist or epidemiologist, however, and has no specific experience writing on or researching the alleged association between the Tdap vaccine and RA. *Id.* at 35, 89-90, 107-08.

Dr. Wallace's first report described RA as a chronic, progressive inflammatory disease which primarily affects the joints, attacking the synovium, or connective tissue "wrapping" found in the joints. First Wallace Rep. at 2; Tr. at 36, 45, 74, 84. RA is common in the United States, affecting upwards of two million people. Tr. at 36. Its clinical manifestations include arthralgia, swelling, redness, and limited range of motion. *Id.* Both steroids and non-steroidal inflammatory drugs are used to control symptoms, but do not stop the underlying progression of the disease. *Id.* RA is understood to have an autoimmune mechanism. *Id.* at 36. It also has a number of risk factors making it more likely, including family history/genetic susceptibility as well as gender. *Id.* at 85, 100. Although RA typically evolves over many months, it can present acutely and also go into remission, but can later be reactivated by infections like trauma, surgery, or comorbidity. *Id.* at 74, 84. Even though swelling is a common component of RA's presentation, Dr. Wallace noted that RA could initially present with simply pain, with swelling manifesting later. *Id.* at 44-45, 48.

Dr. Wallace differentiated RA from PMR, a separate condition that nevertheless can be difficult to distinguish from RA due to their overlapping clinical presentations. First Wallace Rep. at 2. Though both are chronic inflammatory conditions, PMR (which is also likely driven by an

autoimmune process) tends to be characterized by pain and stiffness in the shoulder and/or the pelvic girdle, rather than featuring RA's symmetric arthralgia in multiple sets of joints. *Id.;* Tr. at 36-37. Dr. Wallace also noted that RA and PMR differ in their biomarkers. An anti-CCP antibody test is highly relevant to diagnosing RA, since the presence of those antibodies are very specific to RA (but not to PMR). First Wallace Rep. at 2 (citing U. Sauerland et al., *Clinical Utility of the Anti-CCP Assay: Experiences with 700 Patients*, 1050(1) Ann. N.Y. Acad. Sci. 314-318 (2005), filed as Ex. 31 on December 21, 2018 (ECF No. 24-4) ("Sauerland")), 3; Tr. at 37, 39.[3] Dr. Wallace felt the initial speculation that Petitioner had PMR was not unreasonable, but that her later diagnosis was properly revised as more evidence for RA came in—in particular the proof provided by the positive anti-CCP test. Tr. at 37, 41, 43, 82.

The anti-CCP antibody plays a significant role in RA's pathogenesis, and Dr. Wallace briefly described how the antibody is scientifically understood to come into being. Certain individuals possess a genetic mutation that causes a particular protein, arginine, to be incorrectly converted (via a process called "citrullination") into citrulline—triggering production of antibodies against the citrulline that also cross-react against joint tissues, furthering the pathogenesis of RA. First Wallace Rep. at 3; Tr. at 38. This citrullination process is thought to occur in the oral cavities or lungs, and can be exacerbated by smoking, poor oral hygiene, or other lung-impacting factors, like pollutants. Tr. at 85. It is rare for an individual to be diagnosed with RA and not test positive for the anti-CCP antibodies—although a person can be "seropositive" for the antibodies long before they develop clinical symptoms of RA. *Id.* at 39-41.

As noted above, Dr. Wallace opined that Ms. Monzon likely had RA, and was thus correctly diagnosed with it. Tr. at 37, 38. She tested positive for the anti-CCP antibodies, and in fact possessed them well before receiving the Tdap vaccine deemed causal in this case. Tr. at 37, 42-43, 66, 86, 103; *see also* Ex. 6 at 8. Indeed, her clinical presentation would have led Dr. Wallace to conduct testing for the antibody, since it appeared she might have RA based on her symptoms. *Id.* at 41, 82. In addition, Ms. Monzon at one point early in her course tested positive for the existence of inflammatory biomarkers, further suggesting an RA process was occurring. *Id.* at 43-44, 46-47, 49; First Wallace Rep. at 3 (citing N. Shadick et al., *C-Reactive Protein in the Prediction of Rheumatoid Arthritis in Women*, 166 Arch. Intern. Med. 2490-2494 (2006), filed as Ex. 22 on June 22, 2018 (ECF No. 20-2)).[4] Dr. Wallace went so far as to propose that the mere evidence of the anti-CCP antibodies was *itself* suggestive of ongoing inflammation. Tr. at 46-47, 50-51.

[3] A review of 700 patients revealed a sensitivity to RA in 74 percent of subjects with the anti-CCP antibody, and a specificity for RA in over 90 percent. Anti-CCP reactivity can be seen in other conditions, but at lower rates: systemic lupus (12.7%), Sjogren's syndrome (3.3%), polymyalgia rheumatica (<5%). First Wallace Rep. at 2 (citing Sauerland).

[4] Dr. Wallace deemed this evidence more significant than observations by Dr. Lopez at the time that there was "no evidence of [RA] disease activity" otherwise. Tr. at 49

By contrast, Dr. Wallace did not accept Respondent's proposed counter-diagnosis of preclinical RA. Tr. at 72. He allowed that the preclinical classification (which he defined as the possession of anti-CCP antibodies without other clinical symptoms characteristic of RA) had medical acceptability. *Id.*; K. Mankia et al., *Preclinical Rheumatoid Arthritis: Progress Toward Prevention*, 68(4) Arthritis & Rheumatology 779-788 (2016), filed as Ex. 37 on March 29, 2019 (ECF No. 25-3). However, he concluded that Petitioner's course was not consistent with it. First Wallace Rep. at 4. Even though Petitioner never went on to exhibit certain classic RA features, such as swollen joints, RA is a progressive disease—and therefore patients do not always display these symptoms right away. Tr. at 45. Moreover, prompt treatment with steroids and Methotrexate can limit or suppress swelling symptoms, so that they do not become clinically apparent until years after onset, if ever. *Id.* at 45-46. And Dr. Wallace emphasized his conclusion that the temporal association of Petitioner's post-vaccination onset was diagnostically-meaningful. *Id.* at 72.[5]

Dr. Wallace similarly rejected the suggestion that Petitioner might be better understood as suffering from fibromyalgia (which was in effect mistaken, early on, by Petitioner's treaters to be RA). Fibromyalgia, he explained, is a "central desensitization syndrome" characterized by muscle aches and pain when touched, and not itself a disease, making it possible for Ms. Monzon to have had it and RA concurrently. Tr. at 50. In the absence of an alternative explanation for the anti-CCP results (which would have no bearing on fibromyalgia), Dr. Wallace concluded that the most medically sound explanation was that she did in fact have RA (with fibromyalgia only a secondary condition). Second Wallace Rep. at 3.

Next, Dr. Wallace addressed his primary causal contention: that the Tdap vaccine was the "inciting event" for the initiation of Petitioner's RA. Tr. at 37. He began with what is known generally about potential associations between vaccines and RA, which he characterized as "obvious." *Id.* at 58; First Wallace Rep. at 3. Though rare, stimulation of the immune system with vaccinations has been associated with flares of preexisting autoimmune disease, like RA, and causing new autoimmune reactions. First Wallace Rep. at 3, citing L. Calabrese et al., *Checkpoint Immunotherapy: Good for Cancer Therapy, Bad for Rheumatic Diseases*, 76(1) Ann. Rheum. Dis. 1-3 (2017), filed as Ex. 26 on June 22, 2018 (ECF No. 20-6); Y. Segal et al., *Vaccine-Induced Autoimmunity: the Role of Molecular Mimicry and Immune Crossreaction*, 14 Cellular & Molec. Immun. 1-9 (2018), filed as Ex 27 on June 22, 2018 (ECF No. 20-7)). A vaccine could thus theoretically "light up somebody who is predisposed to RA." Tr. at 52, 62-63.

Dr. Wallace placed particular emphasis on a recent meta-analysis of the risk of RA after

[5] Dr. Wallace also took issue with a contention in one of Dr. Oddis's reports that the positive anti-CCP antibody findings could have been incorrect, arguing that the testing was sensitive enough to render this extremely unlikely. Second Wallace Report at 2. However, Dr. Oddis acknowledged at hearing that it was only a possibility that Petitioner's anti-CCP antibody test was a false positive, and he seemed to some extent to abandon this argument at trial. Tr. at 187. I find it more likely than not that the positive anti-CCP antibody testing results received for Petitioner in the summer of 2014 were accurate.

vaccinations. First Wallace Rep. at 4 (citing B. Wang et al., *Vaccinations and Risk of Systemic Lupus Erythematosus and Rheumatoid Arthritis: A Systemic Review and Meta-Analysis*, 16 Autoimmunity Rev. 756-765 (2017), filed as Ex. 25 on June 22, 2018 (ECF No. 20-5) ("Wang")). Based on an aggregated overview of sixteen observational studies, Wang noted an "obvious association between vaccination and increased risk of RA." First Wallace Rep. at 5; Wang at 762. Dr. Wallace deemed Wang's findings to have statistical significance, although he admitted that they did not amount to a scientific certainty. Tr. at 57, 86.

Importantly, Wang was not restricted to evaluation of the impact of Tdap or other vaccines with a tetanus component. Wang at 759. Indeed, Dr. Wallace specifically acknowledged that only three of the sixteen studies cited in Wang clearly, or even arguably, included the Tdap vaccine in their analysis (one of which was one of the primary items of literature relied upon by Respondent, as discussed below). Tr. at 105-06; Wang at 759. Petitioner filed those studies after the hearing, and subsequent close review confirmed they said little about a Tdap-RA association. *See generally* P. Ray et al., *Risk of Rheumatoid Arthritis Following Vaccination with Tetanus, Influenza and Hepatitis B Vaccines Among Persons 15-59 Years of Age*, 29 Vaccine 6592-6597, at 6592 (2011), filed as Ex. 47 on Feb. 8, 2021 (ECF No. 48-3) ("Ray"); T. Verstraeten, et al., *Analysis of Adverse Events of Potential Autoimmune Etiology in a Large Integrated Safety Database of AS04 Adjuvanted Vaccines*, 26 Vaccine 6630-6638 at 6637 (2008), filed as Ex. 48 on Feb. 8, 2021 (ECF No. 48-4) ("Verstraeten").

Ray, for example, was a large retrospective study involving a cohort analysis of nearly 400 cases of new-onset RA in vaccinated and unvaccinated people, as well as a case-control study of 37 cases of new-onset RA. Ray at 6592. Ray's authors found no statistically significant association between exposure to tetanus vaccine and development of RA. *Id.* at 6592, 6595. Verstraeten was an integrated analysis aimed at assessing the safety of AS04-adjuvanted vaccines, like the human papillomavirus vaccine ("HPV"), with regard to adverse events of potential autoimmune etiology. Verstraeten at 6630. Tdap does not contain this adjuvant. In randomized controlled trials including over 68,000 subjects, HPV, hepatitis B, and genital herpes simplex virus vaccines (AS04 adjuvanted) were analyzed in an integrated analysis of individual data. *Id.* Verstraeten's authors actually found no evidence of an increase in relative risk associated with AS04-adjuvanted vaccines. *Id.* Thus, Verstraeten not only did not evaluate the alleged RA-Tdap association, but found no association for the vaccines it *did* consider.

Dr. Wallace's discussion of specific items of literature referenced in Wang also included an article relied upon by Respondent to rebut any Tdap-RA association. *See* C. Bengtsson et al., *Common Vaccinations Among Adults do not Increase the Risk of Developing RA: Results from the Swedish EIRA Study*, 69 Ann. Rheum. Dis. 1831-1833 (2010), filed as Ex. D on October 1, 2018 (ECF No. 22-2) ("Bengtsson"). Bengtsson looked at a possible association between vaccination in adults and the risk of developing RA, analyzing data from a Swedish population-based RA case-

control study encompassing 1,998 incident cases of RA. Bengtsson at 1831. Bengtsson found no increased risk of RA following vaccination in general or for any specific vaccination studied. *Id.*

Dr. Wallace criticized Bengtsson, however, as under-powered in an epidemiologic sense, given its relatively-small sample size, especially when compared to some of the studies referenced in Wang, and also observed that the study relied on a subject sample that was arbitrary in defining a relevant timeframe for purposes of assessing post-vaccination risk. Tr. at 53-55, 62. Indeed, Dr. Wallace pointed out that Wang was not only the more recent item of literature, but had expressly *included* Bengtsson's findings, while still concluding overall that vaccines could be associated with RA. *Id.* at 56; Wang at 759, 763. And overall, although Dr. Wallace could not identify an epidemiological association between immunization and RA, he did not consider this to undermine his theory, since the absence of a statistically significant risk did not mean zero risk. Second Wallace Rep. at 3.

Besides Wang, Dr. Wallace discussed some case reports. The first involved a recurrence of reactive arthritis after a booster dose of tetanus toxoid. A. Kaul et al., *Recurrence of Reactive Arthritis after a Booster Dose of Tetanus Toxoid*, 61 Ann. Rheum. Dis. 185 (2002), filed as Ex. 19 on June 22, 2018 (ECF No. 19-8) ("Kaul"). The patient, a 24-year old male, presented with acute swelling of the right ankle two weeks after receiving the immunization. Kaul at 1. The second case report involved a 34-year old woman in 1986 who developed a severe local reaction three weeks after receiving the second dose of the tetanus toxoid. A. Jawad, et al., *Immunization Triggering Rheumatoid Arthritis?*, 48 Annals of the Rheumatic Disease 185 (1989), filed as Ex. 18 on June 22, 2018 (ECF No. 19-7) ("Jawad"). The patient's RA was almost completely resolved in one year. *Id.* at 185. The third case report involved two patients who developed RA following immunization against diphtheria, poliomyelitis and tetanus toxoid. J. Maillefert et al., *Arthritis Following Combined Vaccine against Diphtheria, Poliomyelitis, and Tetanus Toxoid*, 18 Clinical & Experimental Rheumatology 255-56 (2000), filed as Ex. 21 on June 22, 2018 (ECF No. 19-10) ("Maillefert"). One patient developed post-immunization mono-arthritis of the knee that regressed following synovectomy. Maillefert at 255. Five years later, the arthritis recurred after a booster vaccine injection. *Id.* The other patient developed arthritis of the ankle one day following immunization that persisted for three days. *Id.*

Dr. Wallace proffered the mechanism of molecular mimicry in a genetically-predisposed individual as a plausible mechanism by which one or more vaccine components could cause an autoimmune response. Tr. at 95. He described molecular mimicry as a process in which antibodies formed in response to stimulation of the immune system by a pathogen or vaccine attack the body's own tissues. First Wallace Rep. at 3 (citing M. Van Gemeren et al., *Vaccine-Related Autoimmune Hepatitis: The Same Disease as Idiopathic Autoimmune Hepatitis? Two Clinical Reports and Review*, 52:1 Scandinavian J. of Gastroenterology 18-22 (2017), filed as Ex. 24 on June 22, 2018 (ECF No. 20-4)). This cross-reaction is mediated by similarities in amino acid structure between

the body's own proteins and those of the vaccine. *Id.* Dr. Wallace maintained that such an autoimmune process mediated by molecular mimicry could occur in response to any antigen component of a vaccine—and thus in the case of the Tdap vaccine, the tetanus, diphtheria, or pertussis antigen components might have prompted this cross- reaction. First Wallace Rep. at 4. He did, however, note that certain case reports placed particular emphasis on the tetanus toxoid component. *Id.* at 5 (citing Maillefert).

Adjuvants contained in vaccines could also, in Dr. Wallace's view, play a role in adverse autoimmune reactions. First Wallace Rep. at 4. Adjuvants are purposely used as immunogenicity-enhancing agents which can help prompt an adaptive immune response (in which the body "learns" how to manufacture antibodies specific to the vaccine's antigens, so that it will know how to fight a wild infection in the future). *Id.* However, adjuvants might also trigger undesired autoimmune reactions in individuals with a genetic susceptibility (specifically those carrying certain HLA-DRB1 alleles highly associated with RA), leading to an abnormal immune response and development of full-blown autoimmune disorders. *Id.* (citing Y. Shoenfeld et al., *"ASIA" – Autoimmune/Inflammatory Syndrome Induced by Adjuvants*, 36(1) J. of Autoimmunity 4-8 (2011), filed as Ex 23 on June 22, 2018 (ECF No. 20-3).[6] Some of the HLA-DRB1 alleles implicated in autoimmune reactions to adjuvants are also important markers for RA, with more than 80 percent of RA patients carrying at least one of these alleles. *Id.* (citing S. Kerlan-Kandon et al., *HLA-DRB1 Transcripts in Rheumatoid Arthritis*, 124 Clinical & Experimental Immun. 142-9 (2001), filed as Ex. 20 on June 22, 2018 (ECF No. 19-9)).

A third, less well-developed mechanistic explanation considered by Dr. Wallace was an anamnestic immune response. Tr. at 69. This can occur when an individual has had some prior exposure to an antigen (whether in vaccination, an infectious incident, or some other environmental factor), resulting in a greater autoimmune response to a subsequent exposure. *Id.* at 70-71. But Dr. Wallace offered little corroborative support for this contention, and acknowledged he lacked the expertise to assign this proposed mechanism much evidentiary significance. *Id.* at 77.

Dr. Wallace found support for his causation theory in Ms. Monzon's medical record. Petitioner had experienced no pre-existing conditions that could have caused RA-like symptoms, and around the time of her vaccination she was not subject to any infections or trauma that could have possibly induced RA. First Wallace Rep. at 6. In addition, two of Petitioner's treating

[6] The ASIA theory for adjuvant-induced autoimmunity has never been deemed medically reliable in any prior Program cases. *See generally Morris v. Sec'y of Health & Human Servs.,* No. 12-415V, 2016 WL 3022141, at *12 (Fed. Cl. Spec. Mstr. Apr. 1, 2016) (discussing lack of reliability of ASIA theory); *Rowan v. Sec'y of Health & Human Servs.,* No. 10-272V, 2014 WL 7465661, at *16 (Fed. Cl. Spec. Mstr. Dec. 8, 2014), *mot. for review den'd,* 2015 WL 3562409 (Fed. Cl. May 18, 2015); *D'Angiolini v. Sec'y of Health & Human Servs.,* No. 99-578V, 2014 WL 1678145, at *60 (Fed. Cl. Spect. Mstr. Mar. 27, 2014), *mot. for review den'd,* 122 Fed. Cl. 86 (2015), *aff'd,* 645 F. App'x 1002 (Fed. Cir. 2016).

physicians stated in their notes that her Tdap immunization had some connection to her RA-like symptom. *Id.* And testing results (which revealed the presence of the anti-CCP antibodies plus some inflammation biomarkers) were all consistent with an ongoing course of RA, as well as her symptoms and response to treatment. *Id.* Overall, in Dr. Wallace's view a patient in whom a systemic inflammatory process is already underway would, all other things being equal, be more likely to experience an adverse autoimmune-mediated reaction to vaccination. Second Wallace Rep. at 2. Here, he maintained, Petitioner's possession of anti-CCP antibodies reflected the presence of systemic inflammation. Tr. at 38.

Finally, Dr. Wallace addressed the temporal association between Petitioner's vaccination and clinical onset of her RA. First Wallace Rep. at 5; Second Wallace Rep. at 5. An autoimmune process mediated by molecular mimicry could commence rapidly following vaccination, although the exact time when such a process becomes symptomatic would vary considerably from one patient to the next. First Wallace Rep. at 5. Thus, Petitioner's asserted two-day post-vaccination onset was medically acceptable. Tr. at 96. In support, Dr. Wallace cited one case report in which he claimed the patient developed arthritis approximately 24 hours after tetanus/diphtheria/polio immunization. *Id.* (citing Jawad). However, the Jawad subject in fact developed RA three weeks after a second dose of tetanus toxoid. *Id.* at 1.

Responding to Dr. Oddis's opinion that there is no evidence in the literature that a specific RA autoantibody like anti-CCP can develop so quickly (i.e. just over two months) after a vaccine, Dr. Wallace restated his opinion that an autoimmune process mediated by molecular mimicry could commence rapidly following vaccination, with specific timeframes varying depending on the patient. Second Wallace Rep. at 5. Therefore, in his view the close temporal association of vaccination and symptom onset in Petitioner's case further strengthened the hypothesis that the former caused the latter. *Id.;* Tr. at 72-73.

C. *Chester V. Oddis, M.D.*

Dr. Oddis, a rheumatologist, prepared one report on behalf of Respondent and provided testimony at the hearing. Report, dated September 28, 2018, filed as Ex. A (ECF No. 21-1) ("Oddis Rep."); Tr. at 114-210. Dr. Oddis opined that Petitioner's presentation, clinical descriptions, and immediate onset of symptoms were most consistent with "preclinical" RA, and that the Tdap vaccine could not otherwise cause this to occur. Wallace Rep. at 5.

Dr. Oddis received his bachelor's degree in biochemistry from the University of Pittsburg. Dr. Oddis Curriculum Vitae, filed as Ex. B-1 on Sept. 28, 2018 (ECF No. 21-2) ("Oddis CV") at 1. He then obtained his medical degree from Pennsylvania State University College of Medicine where he also completed his residency in internal medicine. Oddis CV at 1. He then completed a fellowship in rheumatology at the University of Pittsburg School of Medicine. *Id.* He is board certified in internal medicine and rheumatology. *Id.* at 3. Dr. Oddis is currently Professor of

Medicine in the Division of Rheumatology and Clinical Immunology and Director of the Myositis Center in the School of Medicine at the University of Pittsburg. *Id.* at 2. His primary area of research and clinical care is in the clinical, epidemiologic, serologic and treatment aspects of the idiopathic inflammatory myopathies (myositis) and autoimmune interstitial lung disease. *Id.* Dr. Oddis has also published numerous journal articles on these subjects. *Id.* at 2, 4-15. Although his focus is different, Dr. Oddis also regularly sees patients with RA, and he would deem a handful to be properly diagnosed with preclinical RA. Tr. at 116, 117. He does not have epidemiologic expertise. *Id.* at 166.

Dr. Oddis began his testimony with a review of the same RA concepts discussed by Dr. Wallace. He acknowledged RA to be autoimmune in pathogenesis, featuring small joint inflammatory arthropathy and usually "synovitis," or inflammation of the joint lining. Tr. at 120-21. The classic clinical signs and symptoms of RA include objective inflammation of the joints, stiffness and pain in the small joints of the hands and feet predominantly, and evidence of abnormal autoantibodies in laboratory tests. *Id.* at 121-22. Dr. Oddis acknowledged that the presence of anti-CCP antibodies is an important criterion for RA's diagnosis, adding that these particular antibodies can long predate clinical symptoms. *Id.* at 122, 174. However, despite the specificity of the anti-CCP antibody for RA, Dr. Oddis would not exclusively rely on their presence to diagnose RA in an individual. *Id.* at 153, 185-86. RA's true cause remains unknown, and although it has many risk factors, Dr. Oddis disputed vaccines are among them, stressing that rheumatologists readily encourage their patients to be vaccinated. *Id.* at 154-55, 56, 190.

Dr. Oddis also outlined the concept of preclinical RA, which he defined as a period in time for a patient where there is detectable autoimmunity, plus or minus inflammation, that otherwise predates the onset of clinically apparent or classic rheumatic disease. Tr. at 123; Oddis Rep. at 4 (quoting K. Deane et al., *Pathogenesis and Prevention of Rheumatic Disease: Focus on Preclinical RA and SLE*, 10 Nat. Rev. Rheumatol. 212-214 (2014) at 212, filed as Ex. C on October 1, 2018 (ECF No. 22-1) ("Deane")). Preclinical RA is a relatively new diagnostic classification, and can be applied both where a person presents with nonspecific RA-like symptoms, or tests positive for anti-CCP antibodies in the absence of confirming clinical symptoms. Tr. at 123, 126; Deane at 213 ("the measure of tissue injury that should be used to define the onset of clinically apparent disease…is an important consideration in characterizing the preclinical period").

Because preclinical RA overlaps to some extent with full RA, it would be easy in treatment to confuse the two. Thus, a patient might receive common RA treatment based on a few clinical indicia plus a positive anti-CCP antibody test, even though all criteria for the disease itself had not been met. Oddis Rep. at 4. Dr. Oddis admitted, however, that in his experience the antibodies would not be looked for absent some strong clinical hint that RA might exist. Tr. at 124. The best treatment course for persons thought to have preclinical RA would be to follow them over time, watching to see whether their presentation evolved into the more classic form of RA. *Id.* Dr. Oddis could only speculate how often preclinical RA does so evolve (and he has personally only observed 20 to 25 patients to whom he would apply the new diagnostic classification). *Id.* at 125, 127-28.

Petitioner, Dr. Oddis maintained, was best diagnosed with preclinical RA that had (to date) never actually evolved into classic RA. Tr. at 161, 180-81, 183-84. To support this contention, Dr. Oddis conducted a painstakingly-specific review of Petitioner's medical history. Oddis Rep. at 2; Tr. at 132-48. Her initial post-vaccination treater visits (in late-April and early-May 2016) featured non-specific complaints that allowed no definitive diagnosis, as she presented only with joint pain not also accompanied by RA's characteristic swelling. Tr. at 132-33.

By Petitioner's first rheumatology visit with Dr. Lopez on June 16, 2016 (Ex. 3 at 4), the clinical impression was that Petitioner had low back pain, cervicalgia (neck pain), and myalgia. Oddis Rep. at 2; Tr. at 137. No likelihood of RA is mentioned. Oddis Rep. at 2. She also had full range of motion of all her joints, and no synovitis and or tender points of fibromyalgia, but focal tenderness of the trapezius muscles was noted. *Id.* (citing Ex. 3 at 4). Dr. Oddis discounted the possibility that Ms. Monzon had initially experienced some form of vaccine-induced reactive arthritis, arguing that the sole evidence to support anything inflammatory was occurring was her high ESR rate from the May 21, 2016 doctor's visit (Tr. at 134, 207), followed by a high CRP in June (Tr. at 137), but ultimately he could not opine what the etiology of her initial symptoms represented. Tr. at 209.

Dr. Oddis also highlighted a lack of treater support for an RA diagnosis overall (although he could not dispute the existence of *some* evidence supporting it). Petitioner's managing rheumatologist, Dr. Lopez, initially did not believe that Ms. Monzon had RA. Oddis Rep. at 2. Dr. Lopez had only embraced RA after the positive anti-CCP antibody test results. Tr at 138-39, 184. But thereafter, in all subsequent medical record notes, Dr. Lopez never observed any of the characteristic features of RA, or other laboratory or clinical evidence of RA disease activity in many of her clinical notes. *Id.* Other treaters also made no note of clinical findings consistent with RA. *Id.* at 123-38. Indeed, after the June and July 2016 visits, PMR appeared to be the preferred diagnosis, and it remained so until the positive anti-CCP test results were obtained. *Id.* at 138; Ex. 6 at 2-3. And by October 2016, when Petitioner was being treated for RA (mainly on account of the anti-CCP antibody findings), fibromyalgia had entered the differential (a significant development in Dr. Oddis's view). Tr. at 140; Ex. 6 at 2-3.

By the fall of 2016, Ms. Monzon was receiving RA-specific medications like Methotrexate (again, without her symptoms having begun to include classic indicia such as swelling). Tr. at 140-41. But she also began to receive treatments specific for fibromyalgia and chronic pain, like Cyclobenzaprine and Duloxetine. *Id.* at 141-42; Ex. 10 at 173-175. Several months into 2017, however, there was no change in her clinical presentation, with no manifestation of previously-absent RA symptoms, and she ceased taking an anti-inflammatory drug. Tr. at 142; Ex. 10 at 176-178. Then, by June of 2017, Petitioner's treater notes record "no disease activity" and "[t]he fibromyalgia was better on the combination of Cyclobenzaprine and Duloxetine." Tr. at 143 (quoting Ex. 10 at 179-182). Dr. Oddis deemed these records to establish "a classic scenario of preclinical [RA]," since Petitioner's presentation was still mostly characterized by the existence of the anti-CCP antibodies but without fully-corroborating clinical indicia of RA. Tr. at 144-45.

At hearing, Dr. Oddis also discussed the updated medical records for 2018 that had been filed after he had prepared his written report, and in his view they strongly supported the conclusion that Petitioner suffered from preclinical RA. Tr. at 146. Thus, by the spring and summer of 2018, it was evident that Petitioner had full range of motion of all of the joints, no evidence of any RA disease activity, and also showed marked improvements in her fibromyalgia symptoms given the disease-specific treatments she had been receiving. Tr. at 146; Ex. 39 at 2; Ex. 42 at 22. Then, by October 2018 Petitioner was taken off Methotrexate, while continuing to receive the fibromyalgia medications. Tr. at 147; Ex. 38 at 8. But even six months later she displayed "no clinical or lab evidence of [RA] disease activity." *Id*. Her presentation was similarly consistent even by October 2020. Tr. at 148; Ex. 43 at 2. Thus, additional evidence from Petitioner's medical treatment history did not reveal disease progression or symptoms recurrence.

Dr. Oddis made a point of discussing Petitioner's suggestion that the absence of certain commonly-associated RA symptoms in her history, such as swelling, could be attributed to the success of RA-specific treatments in suppression expression of such symptoms. Tr. at 149, 154. Although he allowed for the possibility that RA-specific medication, like Methotrexate, might ameliorate some RA symptoms, he pointed out (based on the totality of Petitioner's record) that even after Petitioner later ceased these medications, she experienced no "documented joint inflammation . . . or an abnormal physical examination consistent with rheumatoid arthritis." *Id.* at 149, citing Ex 8 at 4. As a result, Dr. Oddis remained convinced Petitioner had never progressed out of preclinical RA. Tr. at 153-54.

Turning to Dr. Wallace's causation theory, Dr. Oddis denied that reliable evidence existed to suggest RA could be caused or triggered by the Tdap vaccine. Tr. at 161-62; Oddis Rep. at 5. Patients with established autoimmune rheumatic disorders were encouraged to receive appropriate vaccination, suggesting as an overall matter that the risk of adverse reaction was low. Oddis Rep. at 5; Bengtsson at 1833. Dr. Oddis acknowledged that molecular mimicry was a medically-acceptable mechanistic explanation for many autoimmune disease processes, as well as the fact that the Tdap vaccine amounts to an antigenic stimulus that, in the setting of a genetic tendency to develop an autoimmune disorder, could theoretically play a triggering role. *Id.*; Tr. at 194. But Bengtsson, a case-controlled[7] study, had observed no increased RA risk post-vaccination (for *any* vaccine), including in a subset of patients with anti-CCP positivity. *Id.* (citing Bengtsson at 1831); Tr. at 156. While Dr. Oddis agreed that (as argued more extensively by Dr. Wallace) Bengtsson had some methodologic flaws, he felt those same kinds of critiques could also be applied to the single-patient case studies relied upon by Petitioner, and overall that Bengtsson still had persuasive force. *Id*. at 156-59, 199.

Dr. Oddis also spent some time discussing the Wang meta-analysis cited by Dr. Wallace in support of the proposition that vaccines can cause RA. Tr. at 163. Although he deemed Wang

[7] A case-control study compares a group with a disease or condition to a control group without the condition. *Snyder v. Sec'y of Health & Hum. Servs.*, No. 01-162V, 2009 WL 332044 at *199 (Fed. Cl. Spec. Mstr. Feb. 12, 2009).

helpful in generating hypotheses regarding association between vaccines and RA, he felt the article was not sufficient to establish causality. *Id.* at 164. Wang in his view made broad generalizations, relying on findings involving different kinds of vaccines (with a minority of its referenced articles even involving the Tdap vaccine), and therefore its conclusions were more of an intriguing hypothesis than reliable causal evidence. *Id.* at 163-65.

Dr. Oddis similarly discounted some of the case reports cited by Dr. Wallace in his expert report. Kaul, for example, involved a diagnosis (reactive arthritis) not at issue, while Jawad was over 30 years old, and thus relied on somewhat outdated criteria for defining RA, and also involved a longer onset timeframe. Tr. at 168-71, 177. Overall, Dr. Oddis characterized case reports as "interesting" but of limited value with respect to causation. *Id.* at 167-68, 205.

Regarding the timeframe for onset, Dr. Oddis indicated his openness to the theory that in some cases RA symptoms could follow closely after an inciting occurrence. Tr. at 191. But he deemed an "explosive" presentation of symptoms to be uncommon with classic RA, which usually was progressive and insidious, developing "over weeks to months." *Id.* at 123. Dr. Oddis also emphasized that it was highly likely Petitioner possessed the anti-CCP antibodies (which have not otherwise been alleged to have been vaccine-caused) long before vaccination. Oddis Rep. at 4-5. And he did not accept Dr. Wallace's contention that the mere possession of these antibodies placed a person in an elevated inflammatory state, such that the impact of vaccination would increase the likelihood of symptoms onset. Tr. at 173, 176.

Besides disputing RA as the proper diagnosis, Dr. Oddis provided his opinion about some of the other competing or co-diagnoses at issue. He noted that as of July 2016 (and before her RA diagnosis), Ms. Monzon had been diagnosed with PMR (Ex. 3 at 2), but he questioned the validity of the diagnosis. Oddis Rep. at 2. At best, her initial symptoms of neck and leg pain, plus the subsequent one-time ESR elevation, initially appeared consistent with PMR, but Petitioner's age combined with the subsequent finding of a positive anti-CCP ruled that diagnosis out. *Id.* However, he deemed the fibromyalgia diagnosis far more evidentiarily-supported. Oddis Rep. at 5. Petitioner's overall course of symptoms, the physical examination findings, the impression of her treating rheumatologist, and the effectiveness of the fibromyalgia treatments Petitioner received all corroborated its likelihood as an appropriate diagnosis. *Id.*; Tr. at 209.

On cross-examination, Dr. Oddis acknowledged that Ms. Monzon displayed no real RA symptoms pre-vaccination. Tr. at 180-81. He also allowed that there was a possibility that the Tdap vaccine could trigger RA, but he unquestionably did not concede the medical reliability of the contention. *Id.* at 171, 196.

III. Procedural History

This matter commenced with the filing of the Petition on August 4, 2017. On March 15, 2018, Respondent filed a Rule 4(c) report asserting that Petitioner had not established a *prima facie* case and that compensation was not appropriate. Petitioner subsequently filed an expert

report from Dr. Wallace and Respondent filed an expert report from Dr. Oddis. On December 21, 2018, Petitioner filed a supplemental report from Dr. Wallace, and on March 29, 2019, Petitioner filed an additional supplemental report from Dr. Wallace in response to a specific inquiry from the Court regarding the possibility that Petitioner's RA was pre-clinical at the time of vaccination. An entitlement hearing was set for August 21, 2020 and a schedule was set for prehearing briefing. Petitioner filed her prehearing submission on May 5, 2019 and after an unopposed motion for an extension of time was granted, Respondent filed his prehearing submission on July 9, 2020. The July 9, 2020, the entitlement hearing was also rescheduled to February 4, 2021. Some medical records were subsequently filed and then a one-day hearing entitlement hearing took place on February 4, 2021. Petitioner was ordered to file various items of medical literature that were discussed during the hearing and she did so on February 8, 2021. The parties did not elect to file post-hearing briefs, and the matter is now fully ripe for resolution.

IV. Applicable Legal Standards

A. *Petitioner's Overall Burden in Vaccine Program Cases*

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[8] In this case, Petitioner does not assert a Table claim.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344,

[8] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Hum. Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Hum. Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Hum. Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

1352–53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Hum. Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274, 1278 (2005): "(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 proximate temporal relationship between vaccination and injury."

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury.

In discussing the evidentiary standard applicable to the first *Althen* prong, the Federal Circuit has consistently rejected the contention that it can be satisfied merely by establishing the proposed causal theory's scientific or medical *plausibility*. *See Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019); *see also LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) ("[h]owever, in the past we have made clear that simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof." (citing *Moberly*, 592 F.3d at 1322)). Petitioners otherwise always have the ultimate burden of establishing their *overall* Vaccine Act claim with preponderant evidence, regardless of what evidentiary level of evidence on the "can cause" prong is required. *W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted); *Tarsell v. United States*, 133 Fed.

Cl. 782, 793 (2017) (noting that *Moberly* "addresses the petitioner's overall burden of proving causation-in-fact under the Vaccine Act" by a preponderance standard).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as 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'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

Medical records and statements of a treating physician, however, do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Veryzer v. Sec'y of Dept. of Health & Hum. Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review denied*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 F. Appx. 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *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 & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must align with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand*, 105 Fed. Cl. 353 (2012), *aff'd*

mem., 503 F. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for rev. denied* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Legal Standards Governing Factual Determinations*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Hum. Servs.*, 3 F.3d 415, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

Medical records that are created contemporaneously with the events they describe are presumed to be accurate and "complete" (i.e., presenting all relevant information on a patient's health problems as of the time of their creation). *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Hum. Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd sub nom. Rickett v. Sec'y of Health & Hum. Servs.*, 468 F. Appx. 952 (Fed. Cir. 2011) (non-precedential opinion). This presumption is based on the linked propositions that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Hum. Servs.*, No. 11-685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Hum. Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Hum. Servs.*, No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also*

Murphy v. Sec'y of Dep't of Health & Hum. Servs., 23 Cl. Ct. 726, 733 (1991) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

There are, however, situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Hum. Servs.*, 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("'[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent'") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Hum. Servs.*, 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Hum. Servs.*, No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *Lalonde v. Sec'y of Health & Hum. Servs.*, 110 Fed. Cl. 184, 203-04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 594–96 (1993). *See Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999)). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been

subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)); *see also Isaac v. Sec'y of Health & Hum. Servs.*, No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for rev. denied*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. Appx. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs.*, 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

Expert opinions based on unsupported facts may be given relatively little weight. *See Dobrydnev v. Sec'y of Health & Hum. Servs.*, 556 F. Appx. 976, 992–93 (Fed. Cir. 2014) ("[a] doctor's conclusion is only as good as the facts upon which it is based") (citing *Brooke Group Ltd. v. Brown & Williamson Tobacco Corp.*, 509 U.S. 209, 242 (1993) ("[w]hen an expert assumes

facts that are not supported by a preponderance of the evidence, a finder of fact may properly reject the expert's opinion")). Expert opinions that fail to address or are at odds with contemporaneous medical records may therefore be less persuasive than those which correspond to such records. *See Gerami v. Sec'y of Health & Hum. Servs.*, No. 12-442V, 2013 WL 5998109, at *4 (Fed. Cl. Spec. Mstr. Oct. 11, 2013), *aff'd*, 127 Fed. Cl. 299 (2014).

D. *Consideration of Medical Literature*

Both parties filed medical and scientific literature in this case, but not every filed item factors into the outcome of this decision. While I have reviewed all the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case—just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.,* 527 F. Appx. 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

E. *Consideration of Comparable Special Master Decisions*

In reaching a decision in this case, I have considered other decisions issued by special masters (including my own) involving similar injuries, vaccines, or circumstances. I also reference some of those cases in this Decision, in an effort to establish common themes, as well as demonstrate how prior determinations impact my thinking on the present case.

There is no error in doing so. It is certainly correct that prior decisions from different cases do not *control* the outcome herein.[9] *Boatmon v. Sec'y of Health & Hum. Servs.,* 941 F.3d 1351, 1358–59 (Fed. Cir. 2019); *Hanlon v. Sec'y of Health & Hum. Servs.*, 40 Fed. Cl. 625, 630 (1998). Thus, the fact that another special master reasonably determined elsewhere, on the basis of facts not in evidence in this case, that preponderant evidence supported the conclusion that vaccine X caused petitioner's injury Y does not compel me to reach the same conclusion in *this* case. Different actions present different background medical histories, different experts, and different items of medical literature, and therefore can reasonably result in contrary determinations.

However, it is *equally* the case that special masters reasonably draw upon their experience in resolving Vaccine Act claims. *Doe v. Sec'y of Health & Hum. Servs.,* 76 Fed. Cl. 328, 338–39

[9] By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Hum. Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Hum. Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014). Special masters are also bound within a specific case by determinations made by judges of the Court of Federal Claims after a motion for review is resolved.

(2007) ("[o]ne reason that proceedings are more expeditious in the hands of special masters is that the special masters have the *expertise and experience to know the type of information that is most probative of a claim*") (emphasis added). They would therefore be remiss in ignoring prior cases presenting similar theories or factual circumstances, along with the reasoning employed in reaching such decisions. This is especially so given that special masters not only routinely hear from the same experts in comparable cases but are also repeatedly offered the *same* items of medical literature regarding certain common causation theories. It defies reason and logic to obligate special masters to "reinvent the wheel", so to speak, in each new case before them, paying no heed at all to how their colleagues past and present have addressed similar causation theories or fact patterns. It is for this reason that prior decisions can have high persuasive value—and why special masters often explain how a new determination relates to such past decisions.[10] Even if the Federal Circuit does not *require* special masters to distinguish other relevant cases (*Boatmon,* 941 F.3d at 1358), it is still *wise* to do so.

ANALYSIS

I. Overview of RA's Treatment in Vaccine Program

Since both testifying experts are rheumatologists with demonstrated experience in diagnosing and treating RA, and both spoke at length about its characteristics (and largely concurred in so doing), little more needs to be said about it herein. Overall, RA is "a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory changes in the synovial membranes and articular structures and by muscle atrophy and rarefaction of the bones. In late stages deformity and ankylosis develop. The cause is unknown, but autoimmune mechanisms and virus infection have been postulated." *Dorland's Illustrated Medical Dictionary*, 157 (32nd. ed. 2012); Q. Guo et al., *Rheumatoid Arthritis: Pathological Mechanisms and Modern Pharmacologic Therapies*, 6 Bone Research 15 (2018), filed as Ex. 17 on June 22, 2018 (ECF No. 19-6) ("Guo"). Clinical manifestations include arthralgia, swelling, redness, and limited range of motion. Guo at 1.

Program petitioners asserting RA as a vaccine injury have in a few circumstances obtained entitlement awards. *See, e.g.*, *H.J. v. Sec'y of Health & Hum. Servs.*, No. 11-301V, 2015 WL 6848357 (Fed. Cl. Spec. Mstr. Nov. 6, 2015) (petitioner established that her immune system was predisposed to autoimmune diseases such as RA, and that the Tdap vaccine significantly

[10] Consideration of prior determinations is a two-way street that does not only inure to the benefit of one party. Thus, I would likely take into account the numerous decisions finding no association between vaccination and autism when confronted with a new claim asserting autism as an injury and have informed such claimants early in the life of their case that the claim was not viable for just that reason. But I would *also* deem a non-Table claim asserting GBS after receipt of the flu vaccine as not requiring extensive proof on *Althen* prong one "can cause" matters, for the simple reason that the Program has repeatedly litigated the issue in favor of petitioners.

aggravated her pre-existing RA); *Campbell v. Sec'y of Health & Hum. Servs.*, 97 Fed. Cl. 650 (2011) (petitioner successfully demonstrated that the flu vaccine could cause RA). However, it is not a class of claim that is guaranteed to succeed. *See, e.g.*, *Suliman v. Sec'y of Health & Hum. Servs.*, No. 13-993V, 2018 WL 6803697 (Fed. Cl. Spec. Mstr. Nov. 27, 2018) (dismissing petition and denying entitlement for claim alleging Tdap vaccination caused Petitioner to develop polymyalgia rheumatica and/or myositis); *Bean-Sasser v. Sec'y of Health & Hum. Servs.*, No. 13-326V, 2016 WL 1649355 (Fed. Cl. Spec. Mstr. April 5, 2016) (denying entitlement to Petitioner alleging hepatitis B vaccine caused her to manifest symptoms of rheumatoid arthritis approximately 11 hours later).

Indeed, I recently denied entitlement in a case where a petitioner alleged that he developed RA following receipt of the flu vaccine. *Hock v. Sec'y of Health & Hum. Servs.*, No. 17-168V, 2020 WL 6392770 (Fed. Cl. Spec. Mstr. Sept. 30, 2020). As I explained in *Hock*, other than the *Campbell* decision noted above I could identify no cases finding that *any* vaccine could cause either the development of rheumatoid factor or anti-CCP antibodies associated with RA's chronicity.[11] Indeed, given what is known about RA (and in particular the fact that the presence of the antibodies closely associated with it often long precede onset of RA symptoms), it is highly unlikely a vaccine could *either* cause these autoantibodies to develop in a medically-reasonable timeframe, or spark an autoimmune process dependent upon them, such that a vaccine administered close in time to appearance of RA symptoms could be deemed causal. *See also Olson v. Sec'y of Health & Hum. Servs.*, No. 13-439V, 2017 WL 3624085 at *5 (Fed. Cl. Spec. Mstr. July 14, 2017 (HPV vaccine not causal of RA), *mot. for review den'd*, 2017 WL 6809589 (Fed. Cl. Dec. 14, 2017), *aff'd*, 758 Fed. App'x. 919 (Fed. Cir. 2018).

II. The Evidence Best Supports Preclinical RA as the Proper Diagnosis

The Vaccine Act provides a framework permitting petitioners to seek compensation for a vaccine-related "illness, disability, injury, or condition." 42 U.S.C. §§ 300aa-11(c)(1)(C), (c)(1)(D)(i). In many cases, determining the nature of the alleged injury is critical to the claim's resolution (especially if causation theories depend on the alleged injury having occurred). *Broekelschen*, 618 F.3d at 1346 ("identifying the injury is a prerequisite to the [causation] analysis"). Here, I must determine as a preliminary matter whether Petitioner's preferred diagnosis of RA is preponderantly established, or if (as Respondent maintains) the evidence supports the conclusion that she more likely suffered from preclinical RA.

Petitioner was able to offer a number of reliable evidentiary items supportive of the RA diagnosis. In particular, she had some common (if nonspecific) presenting symptoms, like joint pain. She could point to a positive anti-CCP antibody test result, as well as the fact that this result encouraged her primary rheumatologic treater to embrace RA as the proper diagnosis, and to prescribe RA-oriented medical treatments that had some efficacy. And some of Petitioner's other

[11] *H.J.* involved a claim of significant aggravation, which has not been asserted herein.

initial treaters—i.e., those who saw her in the first two to three months post-onset—allowed for the possibility that her RA-like symptoms were in reaction to vaccination (although I do not see compelling treater support associating vaccination with RA *specifically*).

At the same time, however, the record when reviewed in its totality casts doubt on the accuracy of the initial RA diagnosis (which I note was arrived at within four months of Petitioner's first post-vaccination symptoms complaints). As Dr. Oddis points out, Petitioner's RA never fully manifested—in particular because she never experienced any progression in symptoms or swelling of joints (a symptom particularly significant to RA's diagnosis, as Dr. Wallace admitted). First Wallace Rep. at 2. Dr. Wallace's attempts to downplay the absence of swelling by attributing it to effective treatment were not persuasive either, as he (i) admitted that these treatments only control symptoms but "do not stop the underlying progression of the disease" (Wallace Rep. at 2), and (ii) Dr. Oddis convincingly established through a *total* record review (including many medical records he had not possessed at the time of his written report) that even after cessation of *all* RA-specific treatment, Petitioner's RA-like symptoms did not recur or progress. Tr. at 147; Ex. 38 at 3 (six months after stopping all RA related medication Petitioner still had no clinical or lab evidence of disease activity).

Dr. Oddis also persuasively noted that at no point in Petitioner's 15-month care by Dr. Lopez (from June 2016 through August 2017), was "there ever a description of any clinical features of RA" (i.e., descriptions of clinical symptoms of any joint swelling or synovitis). Oddis Rep. at 3. And Dr. Lopez's diagnosis seems to have relied heavily on the positive anti-CCP antibody test. Oddis Rep. at 3-4; Ex. 6 at 4, 7-10; Ex. 10 at 171-72. The fact that these antibodies are highly associated with RA does not mean, as Dr. Oddis explained, that an RA diagnosis can be based primarily upon a positive antibody test result—especially in light of the newer classification of preclinical RA.

Overall, although Petitioner's diagnosis contentions have some evidentiary support, I find the evidence preponderates in favor of the preclinical RA diagnosis favored by Respondent. The presence of the anti-CCP antibodies is a significant factor in diagnosing RA, but it is alone not enough. And while Dr. Lopez (relying on Petitioner's presenting symptoms and the antibody test results) might reasonably have initially thought that an RA diagnosis was appropriate, the longer medical history—which shows not only no swelling or synovitis ever developing, but also an eventual cessation of Petitioner's initial symptoms despite stopping treatment—is more consistent with preclinical RA. It is not uncommon in the Program to find that initial treater views as to the nature of a disease or its cause are later supplanted as more medical evidence comes in. *See Deshler v. Sec'y of Health & Hum. Servs.*, No. 16-1070V, 2020 WL 4593162, at *21 (Fed. Cl. Spec. Mstr. July 1, 2020) (treater speculation that petitioner's GBS was caused by vaccine not corroborated by subsequent record evidence); *Harrington v. Sec'y of Health & Hum. Servs.*, No. 15-572, 2018 WL 1125831, at *11 (Fed. Cl. Spec. Mstr. Jan. 19, 2018) (entire record did not corroborate initial treater suspicions that petitioner had experienced GBS).

As a result, and although I have attempted to give Dr. Lopez's diagnosis as much credence as possible, Petitioner's complete presentation as reflected by the record is less consistent with full RA than the preclinical version outlined by Dr. Oddis.[12]

III. Petitioner Did Not Preponderantly Show the Tdap Vaccine Can Cause RA

Because I have determined that Petitioner more likely than not never experienced classic RA as alleged, the matter could be dismissed due to Petitioner's failure to prove her alleged injury.[13] However, even if in fact she had suffered from RA as contended, Petitioner's claim would still falter on her *Althen* prong one showing. While she was able to offer some reliable *general* evidence about a possible association between *other* vaccines and RA, or links between the Tdap vaccine and parallel conditions such as reactive arthritis, the evidence was not sufficiently preponderant in linking the Tdap vaccine to RA itself.

Petitioner's expert has *not* argued that her anti-CCP antibodies came into being as a result of vaccination (and reliable science does not support such a contention). Tr. at 104-05.[14] Instead, Dr. Wallace posited that the initial, innate response to the vaccine had sparked Petitioner's presenting joint pain. Thus, he specifically maintains that her RA was in some form *already occurring as of the time of vaccination*, and that "once an autoimmune process as a result of vaccination is underway, it is entirely possible for it to manifest as RA, since RA is characterized by systemic inflammation[.]" Wallace First Rep. at 4. In effect, something about vaccination's immune-stimulative role prompted a pathologic setting that would encourage a person's other RA risk factors, like the preexisting anti-CCP antibody, to begin to cause the synovial damage associated with RA. Tr. at 52, 62-63.

Because the record shows Petitioner experienced pain so close in time to vaccination, the innate immune response by definition would have to be implicated, since it is understood that the

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[12] By contrast, the record in this case *does* support the finding that Petitioner suffers from fibromyalgia, as admitted by Respondent's expert. Petitioner does not, however, allege that her fibromyalgia was vaccine-cased—and even if she had, such a claim would not succeed, since she has offered no expert support for the "can cause" aspect of such a putative claim. *See also Morris v. Sec'y of Health & Hum. Servs.*, No. 12-415V, 2016 WL 3022141, at *12-13 (Fed. Cl. Spec. Mstr. April 1, 2016) (petitioner's expert did not establish that myositis/fibromyalgia could be caused by the Tdap vaccine). I have located no other reasoned Vaccine Program decisions finding that the Tdap vaccine caused fibromyalgia. In addition, Petitioner was not diagnosed with fibromyalgia until October 3, 2016, but it has not been demonstrated that her course from vaccination to that point (with an onset two days post-vaccination) was reflective of what a person experiencing vaccine-caused fibromyalgia would likely encounter. Certainly, the initial symptoms she encountered that *were* possibly vaccine-related were deemed more representative of RA than fibromyalgia, further diminishing any possible association between her later fibromyalgia diagnosis and her vaccination.

[13] Petitioner has not alleged preclinical RA could be or was vaccine-caused, and Dr. Wallace did not argue or demonstrate that the Tdap vaccine could cause a person to enter into such a preclinical state.

[14] At most, Dr. Wallace allowed that it the timing of development of the anti-CCP antibodies could not be ascertained one way or another, since no pre-vaccination testing for them ever occurred. Third Wallace Rep. at 2.

secondary, adaptive response does not occur in such a short timeframe. *See, e.g.*, *Hock*, 2020 WL 6392770, at *5 (discussing difference in timing for innate versus adaptive response). But this theory was under-substantiated, with little reliable evidence offered that would corroborate it. How would the limited inflammation that vaccination is expected to cause, as part of its inherent immune-stimulative purpose, interact with those factors *known* to be pathogenic in RA, like the anti-CCP antibodies, to produce symptoms? How would the process in turn become chronic? Such questions were hardly answered by Petitioner's causation theory.

Dr. Wallace invested heavily in Wang, maintaining that it established a scientifically-reliable connection between vaccines and RA. Wang at 756. However, as discussed above, only *two* of the studies included in Wang bear on the Tdap vaccine—Bengtsson and Ray—with a third, Verstraeten, turning out not to involve tetanus-containing vaccines at all. *See* Wang at 765. And review of these articles revealed no statistically significant association between exposure to the vaccine and development of RA. Ray at 6592, 6595; *see also* Verstraeten at 6637 (finding nothing to suggest unusual patters of autoimmune disorder following exposure to AS04 adjuvanted vaccines). Thus, although I credit Petitioner's arguments about weaknesses in Respondent's preferred article Bengtsson (which at least facially rebuts the alleged Tdap-RA association), this does not change the fact that *Petitioner's own literature* offered for the opposite contention was no more persuasive. And Dr. Wallace's expertise did not extend to the field of epidemiology or immunology, such that his personal testimony could fill holes that literature (which is of course *not* required to prevail) did not.

Dr. Wallace has also placed great weight on individual case reports—and even ignoring the fact that this class of evidence generally receives less weight in the Program,[15] the case reports filed herein were similarly unhelpful because they were factually distinguishable. Kaul, for example, involved a recurrence of *reactive arthritis* after a booster dose of tetanus toxoid. As Dr. Oddis explained at hearing, however, reactive arthritis is not the same as RA, and the patient in Kaul actually had demonstrated preexisting arthritis that was worsened by a vaccine. Tr. at 169. The Maillefert case report also involved reactive arthritis—not RA—with no long-term evidence of persistent synovitis. Tr. at 171. And Jawad, which was written more than thirty years ago (before the significance of anti-CCP antibodies was understood), relied on outdated RA criteria. Tr. at 170.

Dr. Wallace's proposed mechanisms were similarly not preponderantly substantiated.[16] First, he referenced molecular mimicry (a perennial concept in Vaccine Program cases), arguing that an autoimmune disorder like RA could be mediated by a cross reaction between antibodies

[15] *See, e.g.*, *Campbell,* 97 Fed. Cl. at 668 (case reports "do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value").

[16] The concept that an anamnestic immune response explained Petitioner's alleged autoimmune vaccine reaction was insufficiently substantiated to any degree in light of Petitioner's own circumstances, and too vaguely-supported to assist Petitioner's causation theory.

produced in response to a vaccine's antigens and self tissue structures that resemble or "mimic" those same antigens. First Wallace Rep. at 3, 4. But the vagueness and omissions in the presentation of this aspect of his opinion were too numerous to count. *What* about the Tdap antigens would cross-react with the relevant joint tissues, and where? What evidence establishes that an intercurrent inflammatory process of any kind (brought on by a wild infection or vaccine) might interact with separate RA risk factors, and how might this happen? And was there some other cross-reactive antibody created by the vaccine that would contribute to the pathologic development of RA, in addition to the anti-CCP antibodies?

I have repeatedly noted in other cases that petitioners cannot simply refer to molecular mimicry as a mechanistic explanation for certain autoimmune disease processes and expect that to suffice as preponderant support for their "can cause" showing. *See, e.g.*, *McKown v. Sec'y of Health & Hum. Servs.*, No. 15-1451V, 2019 WL 4072113 at *50 (Fed. Cl. Spec. Mstr. July 15, 2019) (citing *Devonshire v. Sec'y of Health & Hum. Servs.*, No. 99-031V, 2006 WL 2970418, at *15 (Fed. Cl. Spec. Mstr. Sept. 2006), *aff'd*, 76 Fed. Cl. 452 (2007) ("[b]ut merely chanting the magic words "molecular mimicry" in a Vaccine Act case does not render a causation theory scientifically reliable, absent *additional evidence* specifically tying the mechanism to the injury and/or vaccine in question.") (emphasis in original)). Dr. Wallace's embrace of this mechanism, without support from reliable evidence or his own personal experience in studying the concept, amounted to just such an insufficient showing.

Dr. Wallace also suggested that an adjuvant contained in the Tdap vaccine to boost its immunogenicity could have instigated Petitioner's immune response. Wallace Rep. at 5. The risk of an abnormal response, he argued, was heightened for individuals with certain genetic predispositions. *Id.* Dr. Wallace thus embraced what has been deemed the "ASIA" theory—a mechanistic concept that has never been deemed medically reliable in prior decisions. *Id.* at 3; *Pearson v. Sec'y of Health & Hum. Servs.*, No. 17-489, 2019 WL 1150044 at *11 (Fed. Cl. Spec. Mstr. Feb. 7, 2019) (discussing lack of reliability of ASIA theory); *Morris v. Sec'y of Health & Hum. Servs.*, No. 12-415V, 2016 WL 3022141, at *12 (Fed. Cl. Spec. Mstr. Apr. 1, 2016) (same). When asked about the ASIA theory at hearing, Dr. Wallace was unable to do more than personally vouch for its persuasiveness. Tr. at 107. Given Dr. Wallace's lack of immunologic expertise, plus the insufficiently-reliable proof offered herein to establish that a vaccine adjuvant could spark a pathologic autoimmune process, I do not find that this mechanism was preponderantly established as an alternative reasonable explanation for how the Tdap vaccine produced RA for Petitioner.

IV. The Remaining *Althen* Prongs Have Not Been Satisfied

Besides the above, Petitioner has not presented preponderant evidence to satisfy the second *Althen* prong, which requires a Vaccine Act claimant to establish a logical explanation of how the vaccine actually caused injury under the relevant facts. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992).

First, and as already discussed, the medical record does not reflect RA disease progression instigated by vaccination—particularly because that record best supports a preclinical RA diagnosis. Petitioner's overall course of symptoms does not reveal the movement toward classic RA (i.e., from initial pain to swelling and synovitis later) that would be expected for an RA diagnosis. And as Dr. Oddis persuasively established, the proposed RA diagnosis was undercut significantly by the fact that Petitioner's symptoms did not recur even after being taken off RA-oriented treatments. Indeed (and although I make no finding in this regard), Respondent's expert made compelling and unrebutted points about the extent to which Petitioner's course could be better understood as associated with her later-diagnosed fibromyalgia—a condition Petitioner has not alleged to be vaccine-caused in this case.

Second, I cannot conclude from this record that (outside of the temporal relationship discussed below) the Tdap vaccine played anything more than a transient role in Petitioner's post-vaccination symptoms, however they might be understood. Unquestionably, preponderant evidence supports the conclusion that Petitioner experienced a number of nonspecific symptoms close-in-time to vaccination that were reasonably thought by some treaters potentially to be associated with her prior vaccination.[17] But that same record also establishes that (a) Petitioner's subsequent RA diagnosis predominantly turned on the anti-CCP antibody findings (which are not vaccine-attributable), and (b) her subsequent course was ultimately inconsistent with classic RA. There is also limited evidence of ongoing, measurable inflammation consistent with Dr. Wallace's theory. At best, Petitioner did possess certain biomarkers revealing inflammation in the summer of 2016 – but she the record does not reveal their persistence or recurrence, even after she was taken off RA-specific medication.

What remains is a temporal association between receipt of the Tdap vaccine and some immediate, transient symptoms. But an acute and monophasic serum-sickness type-reaction attributable to vaccination is not equivalent to the chronic vaccine-induced injury alleged in this case. Ex. 2 at 52-54 (Petitioner diagnosed with a mild reaction to Tdap, cervicalgia and lumbago that "[s]tarted after recent daily [sic] vaccination, likely adverse effect, flu like reaction"); *Hock*, 2020 WL 6392770, at *25 (petitioner did not preponderantly establish he had RA beginning a day after vaccination; his symptoms were instead far more consistent with a transient, reactive arthritis brought on by serum sickness that, even if vaccine-induced, resolved within two months). Nor is it compelling that Ms. Monzon's symptoms had not manifested pre-vaccination, or that no other explanations exist for her symptoms, as Dr. Wallace seems to assume. First Wallace Rep. at 4. It is well established Program precedent that "evidence showing an absence of other causes does not meet petitioners' affirmative duty to show actual or legal causation." *Grant*, 956 F.2d at 1149.

[17] Although the records do in some places indicate that Petitioner's primary treater, Dr. Lopez, also associated the Tdap vaccine with her subsequent symptoms, many appear simply to document Petitioner's own statements attributing her symptoms to the vaccine based on the temporal relationship, rather than Dr. Lopez's independent conclusion. *See, e.g.*, Ex. 2 at 35-38, 53-55, 74-77; Ex. 10 at 171; Ex. 11 at 10.

Finally, Petitioner has not established that a two-day onset for vaccine-caused RA was medically acceptable. As is often the case, concurrent consideration of the proof offered in support of the first and third *Althen* prongs may be required in assessing if this prong is satisfied, given the close relationship between the two. *See, e.g., de Bazan*, 539 F.3d at 1352 (the explanation for what is a medically acceptable timeframe for injury onset must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement)); *Shapiro v. Sec'y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 Fed. App'x. 952 (Fed. Cir. 2013).

As previously discussed, Petitioner's prong one showing has not been preponderantly established—and this greatly diminishes the likelihood she could demonstrate that a two-day onset based on such a theory is also medically acceptable. Moreover, Dr. Wallace's contentions about a rapid autoimmune process brought on by a vaccine, thereby encouraging other pathologic contributors to RA (specifically the anti-CCP antibodies) to swing into action, was not corroborated with sufficient independent evidence to even conclude this *would occur at all*, let alone within 48 hours of vaccination. Indeed, it is contrary to what is known about RA's disease course generally to find that it would more often than not progress so rapidly after trigger, even if the possibility is there (for the *plausibility* of fast onset is not equivalent to a *preponderant* showing). Thus, although Dr. Oddis conceded RA might present acutely, it has not been shown *in this case* that the Tdap vaccine could trigger initial clinical manifestations of RA in so short a timeframe.

I again note that the record *does* support the conclusion that Petitioner experienced some kind of post-vaccination reaction. A two-day timeframe for such a non-specific reaction is medically acceptable. *Keja v. Sec.'y of Health & Hum. Servs.,* No. 17-1511, 2021 WL 1736816, at *20 (Fed. Cl. Spec. Mstr. Apr. 2, 2021) (serum sickness reaction to vaccine could manifest within a day of vaccination); *Hock*, 2020 WL 6392770, at *25 (one-day post-vaccination transient reaction). But Petitioner does not claim to have experienced an unspecified reaction as her injury—she asserts that it was the onset of classic RA, that persisted thereafter for a year or more (and could one day recur).[18] Onset of RA in such a short timeframe has not been demonstrated to be medically reasonable.

[18] Even if Petitioner's claim had been narrowed to the allegation that she experienced a nonspecific vaccine reaction, manifesting as pain in her joints and elsewhere, that persisted over time but turned out to be distinct from RA or fibromyalgia, I would not be able to conclude on this record that the vaccine was responsible for the chronicity of Petitioner's symptoms. Dr. Wallace for his part did not so contend either, or devote any of his testimony or reports to this alternative possible claim.

CONCLUSION

The Vaccine Act permits me to award compensation only if a petitioner alleging a "non-Table Injury" can show by medical records or competent medical opinion that the injury was more likely than not vaccine-caused. Petitioner was unable to offer a scientific theory supported by sufficient proof of how the Tdap vaccine specifically could trigger RA or a preclinical version of it, nor did she establish it did so in her case.

I greatly sympathize with Petitioner's medical suffering, and deem it beyond question that post-vaccination she experienced a medical turn for the worse. Moreover, she reasonably and in good faith has questioned whether the Tdap vaccination could have played a role in her health problems. And the record does support the conclusion that she experienced some post-vaccine reaction—I simply cannot conclude that this reaction was RA. There is insufficient evidence to support an award of compensation, and I must therefore **DISMISS** this claim.

In the absence of a timely-filed motion for review (see Appendix B to the Rules of the Court), the Clerk shall enter judgment in accordance with this decision. [19]

IT IS SO ORDERED.

s/Brian H. Corcoran
Brian H. Corcoran
Chief Special Master

[19] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by filing a joint notice renouncing their right to seek review.