In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 17-1367

Filed: March 26, 2025

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BENJAMIN S. MAXWELL,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

* *

Elizabeth Martin Muldowney, Sands Anderson, PC, Richmond, VA, for Petitioner.
Dorian Hurley, U.S. Department of Justice, Washington, DC, for Respondent.

DECISION DENYING ENTITLEMENT[1]

Shah, Special Master:

On September 28, 2017, Benjamin Maxwell ("Petitioner") filed a petition for compensation under the National Vaccine Injury Compensation Program, 42 U.S.C. § 300aa-10, *et seq*.[2] (the "Vaccine Act" or "Program"). The petition alleges that Petitioner suffered from an inflammatory polyarthropathy and/or rheumatoid arthritis ("RA") caused by an influenza ("flu") vaccination he received on October 5, 2014. Pet. at 1 (ECF No. 1). The petition alternatively alleges that the vaccination significantly aggravated an unnamed preexisting condition. *Id.* Throughout the course

[1] Because this Decision contains a reasoned explanation for the action in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims's website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). This means the Decision will be available to anyone with access to the internet. In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, I agree that the identified material fits within this definition, I will redact such material from public access.

[2] National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755. For ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

of the litigation, Petitioner has clarified that he alleges he developed seronegative RA caused by the subject flu vaccination. *See, e.g.*, Ex. 18 (report of Petitioner's expert, Dr. M. Eric Gershwin).

Upon review of the evidence in this case, I find that Petitioner has failed to preponderantly demonstrate that the flu vaccination in question caused him to develop seronegative RA. The petition is accordingly dismissed.

I. PROCEDURAL HISTORY

After filing the petition, Petitioner filed affidavits and medical records. Exs. 1-17. On June 18, 2018, Respondent filed a Rule 4(c) Report ("Report"), recommending that entitlement be denied. Report at 1 (ECF No. 18).

Petitioner filed an expert report by M. Eric Gershwin, M.D., MACR, MACP, along with Dr. Gershwin's curriculum vitae and medical literature, on October 16, 2018. Exs. 18-26. On February 27, 2019, Respondent filed expert reports from Chester Oddis, M.D., and You-Wen He, M.D., Ph.D., along with their curricula vitae and medical literature. Exs. A & Tabs 1-4, B, C & Tabs 1-13, D.

On March 4, 2019, former Special Master Katherine E. Oler ordered Petitioner to file a second expert report from Dr. Gershwin addressing Dr. Oddis's opinion concerning Petitioner's diagnosis and Dr. He's opinion concerning the appropriate onset for the alleged condition. Petitioner filed a second expert report and literature from Dr. Gershwin addressing these issues. Exs. 29-30. Respondent filed responsive reports from Drs. Oddis and He on August 7, 2019. Exs. E, F.

On August 22, 2019, Special Master Oler held a status conference at which she advised the parties that the issues in dispute appeared to be diagnosis and causation. In Special Master Oler's view, based on the diagnostic criteria for RA, the evidence indicated that diagnosis was appropriate. As such, she encouraged the parties to discuss settlement. ECF No. 37.

Petitioner filed a third expert report and additional literature from Dr. Gershwin on October 15, 2019. Exs. 34-37. Respondent filed responsive expert reports and literature from Drs. Oddis and He on March 6, 2020. Exs. G & Tabs 1-2, H. Petitioner filed a fourth report and an article from Dr. Gershwin on April 3, 2020. Exs. 38-39.

The parties could not informally resolve the case, and it was scheduled for an entitlement hearing. *See* ECF No. 57. On February 1 and April 26, 2022, Petitioner filed additional medical records. Exs. 40-48. Petitioner filed additional literature on August 23, 2022. Exs. 49-52. Prehearing briefs were filed on August 24 and September 8, 2022. ECF Nos. 66, 75.

Special Master Oler conducted an entitlement hearing on September 21, 2022, at which Drs. Gershwin, Oddis, and He testified. After the hearing, the parties filed further expert reports and literature. Exs. 53-62; L-R. The parties filed post-hearing briefs on February 7, April 10, and June 2, 2023. ECF Nos. 85, 86, 88.

Both parties agreed that the record was complete on June 20, 2023. ECF No. 89. This matter is now ripe for adjudication.

II. FACT EVIDENCE

Petitioner served in the Army National Guard. *See* Ex. 1. Prior to the subject vaccination, he had a medical history notable for hernia surgery in 2011; he was also diagnosed with anxiety, major depression, and PTSD. *See* Ex. 5 at 3; Ex. 9 at 1; Ex. 10 at 24, 28, 33, 41. He was 28 years old when he received a flu vaccine on October 5, 2014, during a monthly Army National Guard drill. Ex. 11 at 1. He was attending the University of Idaho at the time. Ex. 1 at 2.

According to his affidavit, executed on September 26, 2017, Petitioner had no immediate reaction to the vaccination. Ex. 1 at 1. But two days later, he woke up with a fever of 102 degrees, along with chills, stiffness, and achiness throughout his body. *Id.* He missed two days of school. *Id.* Four days after the vaccination, the symptoms had subsided except for joint stiffness and achiness. *Id.* Petitioner did not seek medical attention at the time because his symptoms did not limit his mobility and were controlled with ibuprofen. *Id.* By the next week, however, his achiness and stiffness worsened, and he started having pain in both shoulders. *Id.*

Petitioner's wife, Mrs. Tabitha Maxwell, also submitted an affidavit executed September 26, 2017. Ex. 2. Mrs. Maxwell stated that the day after the vaccination, Petitioner was tired but was able to attend classes. *Id.* at 1. The next morning, however, he "woke up with a fever and body aches and was not able to attend school for the next two days because of his symptoms." *Id.* By October 9, 2014, he was feeling better but still complained of discomfort in his right rotator cuff. *Id.*

Petitioner and Mrs. Maxwell stated that later in October 2014, he began experiencing pain in both knees, which prevented him from sleeping in his bed. Ex. 1 at 1; Ex. 2 at 1. By the end of October, his pain precluded him from standing or walking. Ex. 1 at 1. He made an appointment to see his primary care provider ("PCP"). *Id.* at 2.

The medical records show that Petitioner presented to his PCP, Physician's Assistant ("PA") Todd Bledsoe, on November 7, 2014, for pain in all his joints that had been ongoing for the past month. Ex. 13 at 1. He reported the pain "all started after his flu shot" and that he had been in his "usual good state of health" before the vaccination. *Id.* He said two days after he received the vaccine, he developed flu-like symptoms, including fever and body aches. *Id.* His muscle aches resolved, but he continued to have joint aches, which were getting worse. *Id.* He reported having hand and wrist swelling in the morning, with redness in his knuckles and finger joints. *Id.* The symptoms would ease as the day went on. *Id.* He also complained of pain with movement after prolonged immobility of any joint. *Id.* He denied any prior history of these symptoms, but he noted he had a cousin with RA. *Id.*

On exam, Petitioner had no swelling, redness, or warmth in his extremities. Ex. 13 at 1. He had pain with range of motion ("ROM") in all of the joints of his fingers and in his knees, elbows, and hips. *Id.* PA Bledsoe diagnosed Petitioner with polyarthropathy, ordered lab tests, and prescribed ibuprofen 800mg. *Id.* at 2. He provided a note releasing Petitioner from all

military activities until further notice. *Id.*

On November 12, 2014, Petitioner returned to PA Bledsoe to follow up on his lab tests. Ex. 13 at 3. His joint pain was worse. *Id.* His erythrocyte sedimentation rate ("ESR"),[3] antinuclear antibody ("ANA"),[4] and C-reactive protein ("CRP")[5] results were negative. *Id*. at 4-5. His white blood cell ("WBC") count was normal. *Id.* at 4. PA Bledsoe commented that "notably, all his connective tissue panel and inflammatory markers are [negative]." *Id.* at 3. His exam showed no evidence of "swelling, redness, or warmth of the extremities" but revealed pain on ROM of the hands, knees, hips, and elbows. *Id.* at 5. PA Bledsoe diagnosed arthralgia, suspecting Petitioner had experienced an allergic reaction to the flu shot. *Id*. He referred Petitioner to rheumatology and started him on a prednisone taper. *Id.*

In a follow-up appointment on November 19, 2014, Petitioner reported 60% relief of his symptoms with prednisone, but he had pain after prolonged sitting and was unable to attend classes. Ex. 13 at 7. He had discontinued his military training exercises and was in the process of withdrawing from school for the semester. *Id.* An exam showed full ROM in all extremities, with pain in standing up from a prolonged sitting position and mild pain with ROM in his wrists and fingers. *Id.* He was continued on the prednisone taper. *Id.* at 7-8.

On November 25, 2014, 51 days after the vaccination, Petitioner saw rheumatologist Dustin Dinning, D.O. Ex. 14 at 1. He reported bilateral hand pain with sudden onset that was relieved with medications. *Id*. He also reported fatigue, decreased mobility, nocturnal awakening, nocturnal pain, spasms, and swelling. *Id*. On exam, he had swelling in both hands, but no observations of redness or warmth were documented. *Id*. at 3. Dr. Dinning diagnosed inflammatory arthritis, which he suspected was caused either by a virus or the flu

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[3] Erythrocyte sedimentation rate: the rate at which erythrocytes precipitate out from a well-mixed specimen of venous blood, measured by the distance the top of the column of erythrocytes falls in a given time interval under specified conditions; an increase in rate is usually due to elevated levels of plasma proteins, especially fibrinogen and immunoglobulins, which decrease the zeta potential on erythrocytes by dielectric shielding and thus promote rouleau formation. It is increased in monoclonal gammopathy, hypergammaglobulinemia due to inflammatory disease, hyperfibrinogenemia, active inflammatory disease, and anemia. DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=102146&searchterm=erythrocyte+sedimentation+rate (last visited March 19, 2025) ("DORLAND'S").

[4] Antinuclear Antibody: antibodies directed against nuclear antigens; ones against a variety of different antigens are almost invariably found in systemic lupus erythematosus and are frequently found in rheumatoid arthritis, scleroderma (systemic sclerosis), Sjögren syndrome, and mixed connective tissue disease. Antinuclear antibodies may be detected by immunofluorescent staining. Serologic tests are also used to determine antibody titers against specific antigens. DORLAND'S, https://www.dorlandsonline.com/dorland/definition?id=56804&searchterm=antinuclear+antibodies (last visited March 19, 2025).

[5] C-reactive protein: a globulin that forms a precipitate with the somatic C-polysaccharide of the pneumococcus in vitro; it is the most predominant of the acute-phase proteins. DORLAND'S, https://www.dorlandsonline.com/dorland/definition?id=100489&searchterm=C-reactive%20protein (last visited March 19, 2025).

vaccine. *Id.* He ordered additional lab tests, including for cytomegalovirus, Epstein-Barr virus, and parvovirus B19. *Id*. The plan was to continue to slowly wean Petitioner off the prednisone. *Id.*

Petitioner's affidavit said his symptoms continued to worsen during December 2014. Ex. 1 at 3. Mrs. Maxwell stated that, around this time, Petitioner was unable to "do anything more than basic actions such as walking to the bathroom or getting something to eat." Ex. 2 at 2.

On December 31, 2014, Petitioner saw Dr. Dinning. Ex. 14 at 7. Petitioner described his symptoms as "constant," leading Dr. Dinning to suspect he might be developing a chronic inflammatory arthritis, such as RA. *Id.* On exam, Dr. Dinning observed swelling in the bilateral hands, knees, feet, and ankles. *Id.* at 8-9. No redness or warmth of the joints was observed. *Id.* Dr. Dinning noted that Petitioner's lab work showed a negative rheumatoid factor ("RF"). *Id.* at 7. He pondered whether a cyclic citrullinated peptide ("CCP")[6] test would be positive, given the involvement of Petitioner's large joints. *Id.* He diagnosed chronic inflammatory arthritis, prescribed weekly methotrexate injections, and advised Petitioner to continue prednisone. *Id.* at 8.

On January 7, 2015, Petitioner returned to PA Bledsoe. Ex. 13 at 9. His current pain level was 7/10. *Id*. His ROM was slow due to pain. *Id*. That month, he returned to school but was using a cane. Ex. 1 at 3. According to his affidavit, he was unable to type or write due to the inflammation in his hands, and he had to use voice command software to complete assignments. *Id.* at 2. He needed assistance getting to class. *Id.*

On February 10, 2015, Petitioner returned to Dr. Dinning for worsening pain. Ex. 14 at 13. He had swelling in the hands and knees. *Id*. at 15. He was diagnosed with RA, and Humira was added to his medications. *Id.* The same day, Petitioner had x-rays of his bilateral knees and hands, which showed no joint abnormality, soft tissue abnormality, or significant joint effusion. Ex. 8 at 2-5.

On February 18, 2015, Petitioner returned to PA Bledsoe with complaints of lumps on the backs of his knees. Ex. 13 at 11. Petitioner reported he was feeling much better since starting prednisone and methotrexate, with minimal joint pain in the hands and wrists in the morning. *Id.* He was diagnosed with bilateral Baker's cysts[7] of the knee and was instructed to

[6] Cyclic citrullinated peptide: a synthetic, citrulline-containing peptide with a cyclic structure, used in assays for rheumatoid arthritis; the presence of antibodies to this peptide is highly specific for rheumatoid arthritis. DORLAND'S, https://www.dorlandsonline.com/dorland/definition?id=97140&searchterm=cyclic+citrullinated+peptide (last visited March 12, 2025).

[7] Baker Cyst: a swelling behind the knee, caused by escape of synovial fluid that becomes enclosed in a membranous sac; called also popliteal c. DORLAND'S, https://www.dorlandsonline.com/dorland/definition?id=68277&searchterm=Baker%20cyst (last visited March 12, 2025).

ice the area and return if the pain worsened. *Id.*

On March 11, 2015, Petitioner filed a VAERS report. Ex. 12 at 1. He described the onset of flu-like symptoms beginning October 7, 2015, two days after vaccination. *Id.*

On March 26, 2015, Dr. Dinning completed a Veterans Administration ("VA") disability benefits form stating that Petitioner had experienced the "sudden, explosive onset of joint pain/swelling/stiffness/fever two days after flu vaccination" and had been diagnosed with RA. Ex. 4 at 187-92.

On May 4, 2015, occupational health specialist Laurie Duran at the Naval Medical Center in San Diego had a telephone consultation with Petitioner on behalf of the Defense Health Agency, Immunization Healthcare Branch ("DHA-IHB"). Ex. 4 at 47. Petitioner discussed his medical history and reported that he had experienced mild symptoms with previous vaccinations. *Id.* at 49. He reported that his first cousin and great aunt had been diagnosed with RA. *Id.* Additionally, in February 2015, his brother was diagnosed with arthritis that was attributed to a 2010 exposure to hydraulic fluid. *Id.*

Bloodwork completed May 11, 2015, was positive for Epstein-Barr virus.[8] Ex. 14 at 26.

On June 19, 2015, the DHA-IHB issued a "causality assessment" of Petitioner's case. Ex. 4 at 53. The committee found Petitioner had seronegative RA, which was acquired in the line of duty, but it declared that the relationship between that condition and his flu vaccine was "indeterminate." *Id.* at 54. That same day, Petitioner saw Ms. Duran, who advised that Petitioner should continue to follow with his rheumatologist and also see a military rheumatologist. *Id.* at 53. Ms. Duran noted that Petitioner should approach live vaccines "with caution" in light of the "theoretical risk" of exacerbating his condition. *Id.* at 54.

On June 29, 2015, Petitioner had a follow-up appointment with Dr. Dinning and reported that the severity of his pain had decreased, but he was experiencing joint swelling and fatigue. Ex. 14 at 29. An exam documented swelling in both hands, knees, and ankles. *Id.* at 31. Dr. Dinning increased the Humira dosage. *Id.* at 32.

On August 28, 2015, Petitioner saw PCP Deborah Collins, M.D., for knee stiffness, popping, and "giving out." Ex. 13 at 18. He was using a cane and having difficulty walking. *Id.* He reported pain ranging from 3-8/10 in severity. *Id.* On exam, he had mild tenderness to palpation ("TTP") and crepitus in both knees. *Id.* He had very little ability to bear weight on the right knee. *Id.* at 19. Dr. Collins recommended starting naproxen and obtaining x-rays of the knees, but she suspected that Petitioner more likely had a "soft tissue pathology." *Id.*

On September 4, 2015, Petitioner saw psychologist Jane Barga, Ph.D., for reported

[8] Epstein-Barr virus: a virus of the genus *Lymphocryptovirus* that causes infectious mononucleosis and is associated with Burkitt lymphoma and nasopharyngeal carcinoma. DORLAND'S, Https://www.dorlandsonline.com/dorland/definition?id=80849 (last visited December 20, 2024).

anxiety associated with his RA diagnosis. Ex. 9 at 6.[9]

On September 28, 2015, Petitioner saw orthopedist Steven Pennington, M.D., for bilateral knee pain. Ex. 15 at 1. Petitioner reported that the Humira had eased his symptoms in all joints except his knees. *Id.* He was walking with a cane. *Id.* An MRI of his knee was normal, but his knees were stiff on exam. *Id.* He inquired about the possibility of undergoing a synovectomy (a surgery to address intractable knee pain), but Dr. Pennington did not think that was indicated. *Id.* Dr. Pennington administered a right knee corticosteroid injection. *Id*.

Petitioner's affidavit states that the Army and the VA conducted medical evaluations in November 2015. Ex. 1 at 3. The Army gave Petitioner a 90% disability rating, and the VA gave him an 80% disability rating, which was deemed to be service related. *Id.* Petitioner was placed on the Army's Permanent Disability Retired List, and he medically retired on February 18, 2016. *Id.*

Petitioner saw Dr. Collins on August 4, 2016, to secure a disability letter for his school. Ex. 13 at 26. He reported that his symptoms were much better and controlled with Humira and etodolac (an NSAID used to treat arthritis). *Id.* The diagnosis was RA. *Id*.

Petitioner moved to Tempe, Arizona, in July 2017 to start a graduate degree. Ex. 1 at 3. Shortly thereafter, he developed shingles, which required him to suspend Humira treatment for six weeks. *Id.*

On June 22, 2018, Petitioner saw internist Sriharsha Vajjala, M.D., at Marana Main Health Center in Marana, Arizona, to establish care as a new patient. Ex. 27 at 1. Petitioner reported that he had recently moved to the area and that he had been diagnosed in 2015 with "chronic RA," for which he had been on Humira for the "past [three] years and prednisone as needed." *Id*. His exam was normal. *Id.* at 3. Petitioner stated that he believed his RA medications were losing efficacy, so Dr. Vajjala gave him a rheumatology referral. *Id*.

On July 20, 2018, nearly four years after his vaccination, Petitioner presented to rheumatologist Jeffrey Loomer, M.D. Ex. 28 at 1. He reported that he was diagnosed with seronegative RA in 2014 and had been followed by Dr. Dinning.[10] *Id.* His symptoms would "flare up" every four to six weeks, affecting his knees, wrists, ankles, and elbows. *Id.* He attributed his condition to the flu vaccination, but he was not certain he had RA. *Id*. He reported that he had a "big family history of RA and [ankylosing spondylitis] with [his] brother and three cousins who[] were all diagnosed in [their] late twenties." *Id*. He reported that all of his relatives with RA "started out seronegative then would 'turn' seropositive after 1-2 years after their diagnosis, but [he had] not." *Id*. He requested additional laboratory testing before resuming taking RA medications. *Id*.

[9] Petitioner continued to see a psychologist for his anxiety and his other preexisting mental health issues through December 2015 and again in July 2016. *See generally* Ex. 9.

[10] Petitioner reported that his last appointment with Dr. Dinning was in June of 2017. Ex. 28 at 1. The record before me, however, does not contain any notes from such a visit.

On the day of the visit with Dr. Loomer, Petitioner was "coming out of a flare, which put him down in bed for two days." Ex. 28 at 1. He had not taken the Humira for three weeks due to a rash he had developed. *Id.* A review of systems "(ROS") was positive for fatigue, heartburn, rash, low back pain, joint pain, joint swelling, morning stiffness, neck pain, and muscle pain. *Id*. at 2. A joint exam documented 24 tender joints and 23 swollen joints. *Id.* at 3. Dr. Loomer observed signs of a fungal rash. *Id.* at 2. He ordered lab tests and x-rays of the ankles, chest, feet, hands, wrists, and lumbar and sacroiliac spine. *Id.* at 4. He believed that Petitioner had RA but indicated that he would "take a fresh look at serologies and x-rays to formulate a most accurate diagnosis." *Id*.

Petitioner followed up with Dr. Loomer on August 6, 2018. Ex. 28 at 6. He continued to be off of the Humira, and he felt "no wor[s]e off this medication (it was not working)." *Id.* at 7. His lab results, dated July 21, 2018, were negative for RF, CCP, or elevated ESR or CRP, and were otherwise normal. *Id*. at 12. His hand, wrist, foot, and ankle x-rays were negative for inflammatory changes, and his lumbosacral spine and sacroiliac joints were negative for degenerative or inflammatory changes. *Id*. He complained of abdominal pain. *Id.* at 7. He had mild TTP of the joints on exam. *Id.* at 8. Dr. Loomer assessed seronegative RA, commenting on Petitioner's "strong" family history of the disease. *Id.* at 12. He prescribed sulfasalazine. *Id.*

On August 19, 2018, Petitioner presented to Estela Rutiaga, M.D., at Dove Mountain Urgent Care, complaining of a rash and a flareup of his RA symptoms. Ex. 27 at 15. He had been off of the Humira for the past six weeks. *Id.* He had discontinued use of the sulfasalazine after two days when he developed a rash, and he had discontinued the prednisone due to abdominal pain. *Id*. A ROS was negative for joint pains, muscle weakness, inflammation, tenderness, or swelling. *Id*. at 16. An exam showed mild TTP to the right lower quadrant but was otherwise normal. *Id.* Dr. Rutiaga assessed Petitioner with a rash. *Id.* She advised him to discontinue the sulfasalazine, gave Petitioner a "GI cocktail" in the office, and administered a Kenalog injection for the rash. *Id*.

On August 22, 2018, Petitioner returned to Dr. Loomer after his urgent care visit. Ex. 28 at 14. On exam, Dr. Loomer observed tenderness in 16 joints in Petitioner's elbows, wrists, hands, and knees. *Id.* at 16. Petitioner's ankles were tender and swollen. *Id.* at 17. Dr. Loomer started Petitioner on Simponi Aria infusions. *Id.* at 20.

On August 30, 2018, Petitioner returned to Dr. Loomer sooner than anticipated due to worsening abdominal discomfort and rash. Ex. 28 at 22. Dr. Loomer felt the rash was caused by the sulfasalazine. *Id*. at 27. He prescribed a low dose of prednisone. *Id.*

Petitioner had his first Simponi Aria infusion on September 20, 2018. Ex. 28 at 29. He had a second infusion on October 18, 2018. *Id.* at 32.

Petitioner relocated to New England. On September 19, 2019, he presented to rheumatology fellow Elizabeth Graef, D.O., at Beth Israel Deaconess Medical Center, to establish care. Ex. 45 at 8. He reported "notable improvement" on Simponi Aria, but he was

still experiencing recurrent morning stiffness affecting the metacarpophalangeal joints, proximal interphalangeal joints, and knees. *Id.* at 9. His exam showed no signs of synovitis but did show tenderness in several bilateral metacarpophalangeal joints. *Id.* at 11-12. Dr. Graef opined that Petitioner's history was "somewhat atypical" and commented that she would "consider seronegative spondyloarthropathy though symmetric small joint involvement was more consistent with RA." *Id.* at 12. She referred Petitioner to allergy and immunology for testing. *Id.* at 13.

Dr. Graef's exam was reviewed by attending rheumatologist Robert Shmerling, M.D. Ex. 45 at 14. Dr. Shmerling's impression was "[History] of seronegative RA – details uncertain. Will check xrays, labs . . . consider past fungal exposure given time spent in Arizona, Idaho; vaccination [history] reviewed." *Id.* His plan was to closely follow Petitioner and review his medical records. *Id.*

Petitioner's lab tests from September 19, 2019, were negative for RF or CCP. Ex. 45 at 3, 8. X-rays of the hands and knees were normal. *Id.* at 54.

On September 26, 2019, Petitioner presented to allergist Qura Rashid, M.D., for a consult relating to a possible vaccine allergy. Ex. 45 at 15. Dr. Rashid advised Petitioner that "there is no way to test for [a] [non-IgE] mediated allergic reaction." *Id.* at 18. He recommended that Petitioner receive the intranasal flu vaccine, as he had previously tolerated that formulation of the vaccine. *Id.*

Petitioner resumed Simponi Aria infusions on October 3, 2019, and continued to receive them regularly. *See generally* Ex. 45.

On December 12, 2019, Petitioner saw Drs. Graef and Shmerling. Ex. 45 at 23. Petitioner reported that his breakthrough arthralgias had resolved with the infusions. *Id.* at 24. The only symptom he reported was mild achiness in his hands and knees when outside during cold weather. *Id.* at 25. An exam revealed no synovitis. *Id.* Petitioner was advised to continue the current regimen. *Id.* at 26.

Petitioner had a telephonic appointment with Dr. Graef on April 30, 2020, with complaints that his hands felt stiffer two to three days a week and were worse at the end of the day after extensive typing. Ex. 45 at 34. Dr. Graef concluded that his symptoms were likely due to poor ergonomics while working. *Id.* at 35. She ordered a trial of Voltaren gel. *Id.*

On August 5, 2020, Petitioner saw rheumatology fellow Afroditi Boulougoura, M.D., and attending rheumatologist Kristie Pepper, D.O. Ex. 45 at 41. Petitioner's RA was noted to be in remission, and his treatment plan remained unchanged. *Id.* On November 3, 2020, Petitioner returned to Dr. Boulougoura, reporting a three-week history of pain in his hands and knees with tenderness in the bilateral fourth metacarpophalangeal joints and proximal interphalangeal joints, left wrist, and bilateral knees. *Id.* at 51. His exam showed tenderness of several joints but no synovitis. *Id.* at 53. Repeat labs were normal. *Id.* At that time, the plan was to continue the Simponi Aria infusions every eight weeks, start naproxen and omeprazole, and return for a follow-up in six weeks. *Id.* at 54.

Petitioner's last appointment with Dr. Boulougoura was on February 24, 2021, as he was preparing to move back to Idaho. Ex. 45 at 66. Petitioner was to continue with the treatment plan and was strongly advised to make an appointment with a rheumatologist in Idaho. *Id.*

On September 23, 2021, Petitioner was seen by PCP Amanda Berbert, M.D., at Family Medicine Health Center, seeking a referral to continue the Simponi Aria infusions. Ex. 47 at 11. On October 12, 2021, he returned to Dr. Berbert because he was unable to get a rheumatology appointment until December. Ex. 47 at 5-7. Dr. Berbert noted that Petitioner was due for an infusion on October 8, 2021, and she prescribed prednisone as needed for RA flareups. *Id.*

On November 3, 2021, Petitioner saw rheumatologist Achini Dingman, M.D. Ex. 48 at 25-29, 51-56. He reported increased joint pain involving his hands and knees, noting that he was taking prednisone for the pain. *Id.* at 25-26. An exam was negative for synovitis, but Dr. Dingman observed "notable warmth" with "mild fullness" over the right wrist. *Id.* at 28. Petitioner denied significant pain in the wrists. *Id.* Dr. Dingman administered an intramuscular steroid injection for Petitioner's knee pain. *Id.*

On February 7, 2022, Petitioner presented to Dr. Dingman for a follow-up appointment. Ex. 48 at 1. He was doing well on the Simponi Aria infusions. *Id.* at 3. There are no further relevant treatment records.

III. EXPERT EVIDENCE

A. Pre-Hearing Expert Reports

1. Eric Gershwin, M.D., MACR, MACP: First Expert Report

Dr. Gershwin submitted five reports in this case. Ex. 18 ("First Gershwin Rep."); Ex. 29 ("Second Gershwin Rep."); Ex. 34 ("Third Gershwin Rep."); Ex. 38 ("Fourth Gershwin Rep."); Ex. 53 ("Fifth Gershwin Rep."). He also testified at the entitlement hearing. Tr. at 7-95, 163-67.

Dr. Gershwin earned his M.D. from Stanford University in 1971 and is board certified in internal medicine, rheumatology, and allergy/clinical immunology. Tr. at 8; Ex. 19 ("Gershwin CV") at 1-2. He is a Master of the American College of Rheumatology and a Master of the American College of Physicians, the highest clinical honors a rheumatologist/internal medicine specialist can receive in the United States. Tr. at 11; Gershwin CV at 1. He is currently the Jack and Donald Chia Professor of Medicine and a Distinguished Professor of Medicine at the University of California, Davis. Tr. at 8; Gershwin CV at 1. He serves as the editor-in-chief for *Clinical Reviews in Allergy*, *Reviews in Autoimmunity*, *Autoimmunity Reviews*, and the *Journal of Autoimmunity*, and as an ad hoc editor for numerous other publications. Gershwin CV at 5-7. He has written and edited 1,000 peer-reviewed experimental papers, several hundred book chapters and book reviews, and at least 50 books. Tr. at 910.

Dr. Gershwin concluded that Petitioner suffered from seronegative RA. First Gershwin Rep. at 1. RA is "an inflammatory arthropathy that leads to significant inflammation, and, if unresponsive, joint destruction and reduction in physical function." *Id.* at 2. The disease affects women over men at a ratio of at least 4-5:1. *Id.* at 1. In men, RA is most often seen in those with a history of smoking. *Id.* at 2. Severe periodontal disease is also a risk factor. *Id.* at 3. In 80-90% of patients, serology will eventually be positive for antibodies to RF and/or CCP antigens. *Id.* at 2. It is unusual to see a male, non-smoking, seronegative RA patient without any history of periodontal disease. *Id.* at 2-3.

The diagnosis of RA includes blood testing and examination for synovitis, or swelling of the synovium. First Gershwin Rep. at 2. Patients often respond to drugs that inhibit a pro-inflammatory cytokine response. *Id.* at 3. Here, Petitioner showed evidence of joint swelling and responded to anti-inflammatory treatments, but he had neither a positive RF nor antibodies to CCP, so the proper diagnosis was seronegative RA. *Id.* at 1-3.

Dr. Gershwin disavowed a causal connection between seropositive RA and vaccination. First Gershwin Rep. at 2. He stated that, if Petitioner had been seropositive, he would not have offered an opinion supporting vaccine causation. *Id*. However, seronegative RA "should be considered a distinct clinical pathologic entity." *Id*; Firestein & McInnes, *Immunopathogenesis of Rheumatoid Arthritis*, 46 IMMUNITY REV. 183, 185 (2017) (Ex. 20) ("Firestein & McInnes"). Specifically, the environmental risks, disease severity, and overall clinical outcome are different for seropositive and seronegative RA patients. First Gershwin Rep. at 2. Genetic factors likely account for these differences. *Id.*

Dr. Gershwin noted that "[t]here is considerably less epidemiology on seronegative disease following vaccination and, in fact, there is no significant power calculations that I am aware of for the presence of seronegative [RA] in a young, non-smoking male following influenza vaccination." First Gershwin Rep. at 2. Nonetheless, he opined that there was a reliable mechanistic theory linking seronegative RA and the flu vaccination. *Id.* These patients experience "intense cellular infiltrates" that result from activation of both the innate and adaptive immune responses. *Id.* The innate response would "include activation of cytokines and complement and the adaptive response would include an immune response to self-proteins." *Id.* The initial RA presentation (within 48 hours) would result from the innate response, while the adaptive response would follow and perpetuate the disease. *Id.*

> Whether or not B cells are producing antibody or only acting as antigen-presenting cells, and/or producers of inflammatory cytokines, is also less clear. What is clear, however, is that patients are treated and often respond to drugs that inhibit a pro-inflammatory cytokine response and this indeed is the treatment that has been given to [Petitioner].

Id. at 2-3.

Dr. Gershwin concluded that Petitioner developed an acute inflammatory arthritis 48 hours after his flu vaccination, which was caused by an innate immune cell activation due to the vaccine and subsequently evolved into seronegative RA. First Gershwin Rep. at 3.

2. Chester V. Oddis, M.D.: First Expert Report

Dr. Oddis submitted four reports in this case. Ex. A ("First Oddis Rep."); Ex. E ("Second Oddis Rep."); Ex. G ("Third Oddis Rep."); Ex. R ("Fourth Oddis Rep."). He also testified at the entitlement hearing. Tr. at 96-136.

Dr. Oddis earned his M.D. from Pennsylvania State University College of Medicine, where he also completed his residency in internal medicine. Tr. at 97; Ex. B ("Oddis CV") at 1. He is board certified in internal medicine and rheumatology. Tr. at 97; Oddis CV at 3. In 1987, he completed a fellowship in rheumatology at the University of Pittsburgh, where he currently serves as a Professor of Medicine in the Division of Rheumatology and Clinical Immunology. Tr. at 97; Oddis CV at 1-2. Outside of teaching, Dr. Oddis performs clinical research and maintains a clinical practice, spending half his time seeing patients with a variety of conditions, from autoimmune diseases like myositis to rheumatological diseases. Tr. at 98-99. He sees about 40-45 RA patients monthly, fewer than 10% of whom are seronegative. Tr. at 99-100. He has published about 150 peer-reviewed articles. *Id.* at 101; Oddis CV at 4-13.

Dr. Oddis opined that Petitioner did not have seronegative RA. First Oddis Rep. at 3. At the time of his initial presentation in November 2014, his lab results were "completely normal." *Id.* Additionally, his musculoskeletal exam revealed no joint swelling. *Id.* Consistent with these observations, the initial diagnosis was polyarthropathy, indicating joint pain, not polyarthritis, which would have signified an inflammatory condition. *Id.* When Petitioner was seen by rheumatologist Dr. Dinning in late November 2014, he still had no objective lab evidence of any inflammatory condition. *Id.* Petitioner's ESR and CRP findings were normal to low-normal, which is "distinctly unusual in a patient with RA." *Id.* The only evidence of any joint abnormality was swelling of the hands, which was repeated in a template form in Dr. Dinning's notes. *Id.*

Dr. Oddis commented that there were "other peculiar findings in this patient." First Oddis Rep. at 3. When Petitioner saw PCP Dr. Collins on August 28, 2015, he complained of his knee "popping out" and reported an 8/10 pain level, but he had a normal exam and was assessed with a "likely soft tissue pathology," which was inconsistent with RA. *Id.* at 2-3. When he saw orthopedist Dr. Pennington on September 28, 2015, he was using a cane and asked about a synovectomy, but his examination was normal. *Id.* at 3; Ex. 15 at 1. Dr. Oddis concluded that Petitioner experienced "a subjective over-reaction to pain which likely forced the hand of the rheumatologist to pursue a treatment approach that was more aggressive than was clinically indicated." First Oddis Rep. at 4. He was not surprised that Petitioner responded to RA therapies, noting that there was a documented placebo response in the clinical trials. *Id.*; Azais et al, *Meta-Analysis of The Clinical Efficacy of The Placebo Effect from Tumour-Necrosis-Factor Inhibitors to Treat Rheumatoid Arthritis After Methotrexate Failure*, 2 J. RHEUMATIC DISEASES & TREATMENT 1, 4 (2016) (Ex. A, Tab 1) ("Azais"); Abdullah, *Placebo Effect in The Treatment of Rheumatoid Arthritis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials*, SCI. ABSTRACTS 263, 263 (2015) (Ex. A, Tab 2) ("Abdullah").

Dr. Oddis disagreed with Dr. Gershwin's statement that seronegative RA patients can become positive for RF and CCP antibodies over time. First Oddis Rep. at 4. To the contrary, the prevailing view is that "autoantibody positivity actually develops ***before*** the clinical manifestations of RA," which is referred to as "preclinical" RA. *Id.* (emphasis in original); Deane & El-Gabalawy, *Pathogenesis and Prevention of Rheumatic Disease: Focus on Preclinical RA and SLE*, 10 NATURE REV.'S RHEUMATOLOGY 212, 212 (2014) (Ex. A, Tab 3) ("Deane & El-Gabalawy"); Deane, *Preclinical Rheumatoid Arthritis (Autoantibodies): An Updated Review*, 16 CURRENT RHEUMATOLOGY REP.'S 1, 1 (2014) (Ex. A, Tab 4) ("Deane").

Dr. Oddis opined that if Petitioner's inflammatory response was as intense as Dr. Gershwin described, he "would have expected elevated inflammatory markers." First Oddis Rep. at 4. These were never observed. *Id.* Dr. Oddis also disagreed with Dr. Gershwin's theory of how Petitioner developed acute inflammatory polyarthritis 48 hours after vaccination, as Petitioner never had an acute polyarthritis and, in particular, presented in November 2014 with a normal examination and laboratory findings. *Id.*

3. You-Wen He, M.D., Ph.D.: First Expert Report

Dr. He submitted three reports in this case. Ex. C ("First He Rep."); Ex. F ("Second He Rep."); Ex. H ("Third He Rep."). He also testified at the entitlement hearing. Tr. at 136-62.

Dr. He received his medical degree in China from the Fourth Military Medical University and his Ph.D. from the University of Miami School of Medicine. Tr. at 138-39; Ex. D ("He CV") at 1. He has been a Professor of Immunology in the Department of Immunology at Duke University Medical Center since 2000. Tr. at 137; He CV at 1. About 80-85% percent of his work is focused on research, with the remaining time spent on teaching and consultations. Tr. at 137. He also serves as a Principal Investigator in four clinical trials testing cancer immunotherapies. Tr. at 137-38. He has published more than 135 peer-reviewed articles. *Id.* at 138; He CV at 8-15.

Dr. He deferred to Dr. Oddis on Petitioner's diagnosis and focused his report on causation. First He Rep. at 2. He defined RA as a chronic inflammatory autoimmune disease primarily affecting joints. *Id.*; Firestein & McInnes at 183; Klareskog et al., Rheumatoid arthritis, 373 LANCET 659, 659 (2009) (Ex. C, Tab 2) ("Klareskog"). The disease can take many years to develop. First He Rep. at 4. A major feature of RA is the development of autoantibodies to immunoglobin and anti-citrullinated proteins, which are the autoimmune responses considered to cause self-destructive damage in RA. First He Rep. at 2. Seropositive patients have detectable RF and CCP antibodies, while patients without detectable amounts of these substances are classified as seronegative. *Id.*; Pratt & Isaacs, *Seronegative Rheumatoid Arthritis: Pathogenetic and Therapeutic Aspects*, 28 BEST PRACTICE & RES. CLINICAL RHEUMATOLOGY 651, 651-52 (2014) (Ex. C, Tab 3) ("Pratt"). Only a small fraction of RA patients are seronegative. First He Rep. at 2.

Dr. He explained that although the etiology of RA is still unclear, genetic predisposition and environmental factors are considered the probable root causes. First He Rep. at 2; Firestein & McInnes at 183; Klareskog at 659; Pratt at 653. There are also differences in the genetic

backgrounds, risk factors, and clinical courses for seronegative and seropositive RA patients. First He Rep. at 3, 5; Pratt at 653. Identified risk factors for RA include "certain human MHC haplotypes, some epigenetic markers, smoking, microbiota," and female sex. *Id.* at 2. However, microbes and smoking are established risk factors for seropositive RA only, not seronegative RA. *Id*. at 5.

Dr. He opined that there is no causal relationship between either serotype of RA and the flu vaccine. First He Rep. at 3. Population-based studies showed that "different influenza vaccines did not enhance the incidence of [RA]." *Id.*; Kurland et al., *Lack of Association of Swine Flu Vaccine and Rheumatoid Arthritis*, 59 MAYO CLINIC PROC. 816, 820 (1984) (Ex. C, Tab 4) ("Kurland"); Bardage et al., *Neurological and Autoimmune Disorders After Vaccination Against Pandemic Influenza A (H1N1) With a Monovalent Adjuvanted Vaccine: Population Based Cohort Study in Stockholm, Sweden*, BMJ 1, 4-5 (2011) (Ex. C, Tab 5) ("Bardage"). Studies also found the flu vaccine was safe for RA patients. First He Rep. at 3.

Dr. He disagreed with Dr. Gershwin's theory that innate immune cell activation alone could lead to RA. First He Rep. at 6. Rather, the development of RA is gradual, beginning with citrullination of host proteins, which leads to the presentation of antigens, activation of T lymphocytes, and production of antibodies that recognize self-proteins. *Id.* at 2. This autoimmune response induces synovial inflammation and produces inflammatory cytokines, such as TNF, IL-1, IL-6, and IL-8, which cause tissue damage. *Id.* at 2-3. "Thus, the treatment based on blockage of inflammatory cytokines is effective to relieve symptoms and reduce tissue damage." *Id.* at 3. Both innate and adaptive cellular responses are involved in the process. *Id.* at 4.

In this case, Petitioner's ESR and CRP levels were normal, indicating that there was no systemic inflammation. First He Rep. at 4. The lack of systemic inflammation made it unlikely that activation of innate immunity alone was the cause of his severe joint pain. *Id.* at 5. Moreover, the onset of Petitioner's symptoms within 48 hours was inconsistent with an adaptive immune reaction causing severe tissue damage. *Id.* at 4. In a typical immune response, the initiation of innate immune response is rapid, occurring within the first three days of vaccination. *Id.* The adaptive immune response then takes between 7-15 days, as the anti-joint tissue T lymphocytes and B cell-produced autoantibodies take time to develop and induce tissue damage. *Id.* at 4-5. For flu vaccines specifically, it would take two to four weeks to develop detectable anti-influenza antibodies. *Id.* at 4. Given the time needed for an adaptive immune response, Petitioner's acute onset of symptoms could not have been induced by the flu vaccine. *Id.* at 5.

4. Dr. Gershwin's Second Expert Report

In response to Dr. Oddis, Dr. Gershwin noted that in 2018, a second rheumatologist, Dr. Loomer, agreed with Petitioner's seronegative RA diagnosis. Second Gershwin Rep. at 1; Ex. 28. In fact, none of Petitioner's treating physicians questioned the initial RA diagnosis assigned by Dr. Dinning. Second Gershwin Rep. at 2. Furthermore, Dr. Dinning observed synovitis following the vaccination, supporting the RA diagnosis. *Id.*; Ex. 14 at 2-3. Also, Petitioner's negative CRP and ESR tests did not rule out a RA diagnosis; instead, those tests reflected the relative mildness of his condition. Second Gershwin Rep. at 2.

Dr. Gershwin agreed with Dr. Oddis that RA antibodies can develop before clinical symptoms in seropositive RA, but a patient with seronegative RA will not develop detectable autoantibodies. Second Gershwin Rep. at 2; Venables, *Diagnosis and Differential Diagnosis of Rheumatoid Arthritis*, UPTODATE 1, 3 (2018) (Ex. 30) ("Venables") (noting that both the RF and anti-CCP antibody tests "are negative on presentation in up to 50 percent of patients and remain negative during follow-up in 20 percent of patients with RA").

Responding to Dr. He on the question of onset, Dr. Gershwin pointed out that they agreed that the "initiation of an innate immune response is rapid, occurring within the first [three] days," with the adaptive immune response trailing later. Second Gershwin Rep. at 2. Petitioner's clinical course indicates he had an initial, rapid innate response. *Id.* However, Dr. Gershwin could not point to evidence of an adaptive immune response because Petitioner had seronegative RA, which is a complex disease that is not fully understood. *Id.* at 2-3. Nonetheless, the innate immune response was what initially triggered Petitioner's disease. *Id.*

5. Dr. Oddis's Second Expert Report

In his second report, Dr. Oddis again explained that Petitioner's initial exam in November 2014 "never documented joint swelling, and, as previously summarized, [Petitioner] has never once had elevated inflammatory markers commonly seen with RA." Second Oddis Rep. at 1. Later, when Petitioner saw Dr. Loomer in July 2018, he complained of a recent flare of his arthritis that rendered him bedridden for two days. *Id.* at 2-3. However, extensive lab testing at that time was completely normal, despite the fact that his blood was "drawn at a time when [Petitioner] was *completely off all medications for [RA] for several weeks*." *Id.* at 1 (emphasis in original). Dr. Oddis could not recall any of his RA patients with normal lab results being bedridden. *Id.* at 2-3. Furthermore, four years after the onset of Petitioner's symptoms, he continued to have negative RF and anti-CCP autoantibodies, and every musculoskeletal examination by Dr. Loomer was negative for swelling of the joints. *Id.*at 1; Ex. 28 at 8, 16, 23, 35.

Dr. Oddis questioned the relevance of Petitioner's family history of RA, because it was unverified and because a family history is only relevant in patients with seropositive RA. Second Oddis Rep. at 2. He pointed out that the Venables article, which discussed seronegative RA, noted that the diagnosis requires that the patient exhibit characteristics of RA, which Petitioner never had. *Id.*; Venables at 7. In Dr. Oddis's opinion, Petitioner consistently exhibited a subjective over-reaction to pain and had a chronic pain syndrome, not RA. Second Oddis Rep. at 2.

6. Dr. He's Second Expert Report

Dr. He opined that, for RA to develop, both the innate and adaptive immune systems would need to be activated. Second He Rep. at 2. Activation of innate immunity would exhibit as acute inflammation and disappear in a few days. *Id.* Activation of adaptive immunity would take "much longer than the 2 days that was exhibited in [Petitioner's] disease course." *Id.* An autoimmune response to the joints would not occur without subsequent development of autoreactive adaptive antibody and/or T lymphocyte responses. *Id.* Because Petitioner's T lymphocytes were not assayed, it is unknown whether he had such a response. *Id.* Dr. Gershwin's complete reliance on activation of innate response was not scientifically sound and not supported

by the literature. *Id.*

7. Dr. Gershwin's Third Expert Report

Dr. Gershwin reiterated that two qualified rheumatologists agreed with the seronegative RA diagnosis and treated Petitioner for that condition. Third Gershwin Rep. at 1. He acknowledged that Petitioner did not have positive inflammatory markers and might have had an overreaction to his pain, but that did not necessarily obviate the RA diagnosis. *Id.*

Dr. Gershwin disagreed with Dr. He that innate immunity was not an essential component of RA. Third Gershwin Rep. at 1. Indeed, it is impossible to develop an adaptive immune response without an innate immune response. *Id*. Also, Dr. Gershwin pointed to "multiple studies reflecting that effector cells and molecules of the innate immune system are locally recruited into the synovium, as evidenced by macrophage expression of TNFalpha, IL-1 and IL-6." *Id.*; Gierut et al., *Innate Immunity and Rheumatoid Arthritis*, 36 RHEUMATIC DISEASE CLINICS N. AM. 271, 271 (2010) (Ex. 35) ("Gierut"); Firestein, *Evolving Concepts of Rheumatoid Arthritis*, 423 NATURE 356, 360 (2003) (Ex. 36) ("Firestein"); Hong et al., *Arthritis Critically Dependent on Innate Immune System Players*, 16 IMMUNITY 157, 157-58 (2002) (Ex. 37) ("Hong").

8. Dr. Oddis's Third Expert Report

Dr. Oddis pointed out that, because Petitioner had normal inflammatory markers over the course of his then six-year diagnosis, the articles discussing innate immunity leading to an inflammatory state were irrelevant. Third Oddis Rep. at 1.

Dr. Oddis responded to Special Master Oler's September 4, 2019 Order, in which she stated her preliminary opinion that Petitioner's condition satisfied the American College of Rheumatology's criteria for RA ("ACR Criteria"). Third Oddis Rep. at 1; Aletaha & Smolen, *2010 Rheumatoid Arthritis Classification Criteria*, 62 ARTHRITIS & RHEUMATISM, 2569, 2569 (2010) (Ex. G, Tab 1) ("Aletaha"). Dr. Oddis disagreed, explaining that the classification criteria were used in clinical trials and were not appropriate for diagnosing an individual patient. Third Oddis Rep. at 1; *see* Aletaha at 2572.

Furthermore, regardless of the intended use of the ACR Criteria, Dr. Oddis explained that Petitioner would not meet the standards to enter a clinical trial based on the criteria. Third Oddis Rep. at 2. In fact, Petitioner would only score a "1" based on the duration of his symptoms, given his normal lab results and lack of joint inflammation. *Id.*; *see* Aletaha at 2574.

9. Dr. He's Third Expert Report

Dr. He reiterated his position that the innate immune response alone would not be sufficient to cause RA. Third He Rep. at 2. RA, as he described, is a chronic disease, which evolves slowly, involving both an innate and an adaptive immune cellular response. *Id*. Two days is insufficient for the initiation of the adaptive immune cellular response; therefore, the subject vaccine is not a plausible cause of Petitioner's condition. *Id*. at 3.

10. Dr. Gershwin's Fourth Expert Report

Dr. Gershwin agreed with Dr. He's statement that an adaptive immune response could not occur within 2 days. Fourth Gershwin Rep. at 1. However, Dr. He based his opinion "on the presence of a typical adaptive immune response in seropositive [RA]," but since Petitioner was seronegative, this opinion was irrelevant. *Id.*; Firestein at 358.

Dr. Gershwin also disagreed with Dr. Oddis's suggestion that Petitioner had a psychosomatic illness. Fourth Gershwin Rep. at 1-2. He opined that the medical records did not support such an alternative diagnosis, and he reiterated that Petitioner's treating physicians diagnosed and treated Petitioner for seronegative RA. *Id.* at 2.

B. Expert Testimony

1. Dr. Gershwin's Testimony

Dr. Gershwin opined that Petitioner was correctly diagnosed with seronegative RA. Tr. at 14-15. The onset of Petitioner's symptoms was abrupt, suggesting that there was an environmental factor that triggered the condition. *Id*. Also, Petitioner experienced morning stiffness, pain, and swelling of his joints in a distribution compatible with RA. *Id*. at 15, 18-19, 26, 71; Ex. 4 at 384-86 (December 7, 2015 visit); Ex. 14 at 1-2 (November 25, 2014 visit); 7-12 (December 31, 2014 visit); 29-32 (June 29, 2015 visit). On at least one exam, he had swelling in multiple joints, but not in the distal interphalangeal joints ("DIP joints"),[11] which is noteworthy because in RA those joints remain disease-free. Tr. at 15, 20-23, 26; Ex. 28 at 1-5 (July 20, 2018 visit). Erythema,[12] another characteristic of RA, was also documented.[13] Tr. at 21-23, 26, 69; Ex. 13 at 1-2 (November 7, 2014 visit); Ex. 14 at 1-2. The treating physicians uniformly believed Petitioner had seronegative RA, and that diagnosis was confirmed by a military review panel. Tr. at 15, 53, 67. He was prescribed steroids and biologics, common RA therapies. *Id.* at 15-16. The treating physicians would not have prescribed these therapies absent a definitive RA diagnosis. *Id.* at 29.

Dr. Gershwin differentiated between seropositive and seronegative RA, stating that the serotypes are likely different diseases, with seropositive RA characterized by the presence of antibodies against proteins like CCP, fibrinogen, vimentin, alpha-enolase, and RF, in contrast to seronegative RA. Tr. at 31-32, 51-52, 77-78. The treatment protocols for seronegative and

[11] DIP joint: the interphalangeal joint located distally on any digit. DORLAND'S, https://www.dorlandsonline.com/dorland/definition?id=83515&searchterm=DIP+joint (last visited March 19, 2025).

[12] Erythema: a redness of the skin produced by congestion of the capillaries. DORLAND'S, https://www.dorlandsonline.com/dorland/definition?id=17187 (last visited March 19, 2025).

[13] Dr. Gershwin admitted on cross examination that the medical record in question documented a general finding of skin "redness" without specifying that the finding applied to the joints; he assumed that was what was meant. Tr. at 58-59; *see* Ex. 14 at 2.

seropositive RA may be similar. *Id.* at 32.

Petitioner met the published diagnostic criteria for RA. Tr. at 16; Kay & Upchurch, *ACR/EULAR 2010 Rheumatoid Arthritis Classification Criteria*, 51 RHEUMATOLOGY 1, 1 (2012) (Ex. 52) ("Kay"). A rheumatologist would not need to determine a patient met these criteria to diagnose RA in the clinical setting. Tr. at 16. Nonetheless, Petitioner satisfied the criteria because he had symptoms across multiple, symmetric joints, while sparing the DIP joints.[14] *Id.*; Kay at 4 (Table 2).

Further, although Petitioner's ESR and CRP levels were normal, that would not rule out a diagnosis of RA.[15] Tr. at 23-24, 73. Instead, they signified that his disease was mild. *Id.* at 24, 54, 75. Moreover, because Petitioner was treated with biologics and steroids, his signs, symptoms, and inflammatory markers were likely suppressed to some extent. *Id.* at 15-16, 23-26. These treatments also helped alleviate Petitioner's condition, further supporting the diagnosis. *Id.* at 26-28; *see* Ex. 15 at 1 (September 28, 2015 visit); Ex. 28 at 1-5 (July 20, 2018 visit). Dr. Gershwin did not believe Petitioner's response to these treatments was a mere placebo reaction. Tr. at 26.

Dr. Gershwin testified that RA is caused by a combination of genetic and environmental factors. Tr. at 29-30, 63. The flu vaccine can cause seronegative RA in a genetically predisposed person through the innate immune response. *Id.* at 40-45. After vaccination, there is an initial innate immune response. *Id.* at 35-39; Firestein at 356; Hervé et al., *The How's and What's of Vaccine Reactogenicity*, 4 NPJ VACCINES 1, 2 (2019) (Ex. 49) ("Hervé"). As part of that response, cytokines and prostaglandins are released and can activate the innate immune cells in the synovium. Tr. at 34-35; Hervé at 2-4; *see* Tu et al., *A Tale of Two Immune Cells in Rheumatoid Arthritis: The Crosstalk Between Macrophages and T Cells in the Synovium*, 12 FRONTIERS IMMUNOLOGY 1, 1 (2021) (Ex. 51) ("a variety of immune cells are involved in the pathogenesis of RA [], including cells from the innate immune system"). This causes the local production of inflammatory factors and "[c]ould amplify innate cytokine expression to promote disease." Tr. at 38. Innate immunity is sufficient to trigger an inflammatory disease like seronegative RA. *Id.* at 44, 48-51. Although adaptive autoimmunity also likely develops as part of the natural history of seronegative RA, the host tissues against which those autoantibodies or cytotoxic T cells are directed have not been identified. *Id.* at 77.

Dr. Gershwin commented that shortly after vaccination, Petitioner exhibited signs of fever and body, joint, and muscle aches, which grew progressively worse. Tr. at 32-33, 45; Ex. 13 at 2. This was a sign that the resident innate cells already in Petitioner's synovium had begun to activate. Tr. at 43-45, 81. The fever and polyarthralgias evolved over multiple visits and with no other preexisting evidence of RA. *Id.* at 41-42, 81. Further, the onset of Petitioner's symptoms two

[14] On cross examination, Dr. Gershwin was shown an article he co-authored discussing the diagnostic parameters of RA. Tr. at 68; Greenspan & Gershwin, IMAGING IN RHEUMATOLOGY: A CLINICAL APPROACH 1, 93 (2018) (Ex. L) ("Greenspan & Gershwin"). Dr. Gershwin testified that these criteria reinforced his diagnosis of Petitioner. Tr. at 69-71; Greenspan & Gershwin at 3, 5.

[15] Dr. Gershwin explained that Petitioner's normal ESR and CRP results would result in the deduction of points on the ACR classification scale, but that would not rule out an RA diagnosis. Tr. at 91.

days after vaccination was medically acceptable, because innate immune responses can occur within a few hours. *Id*. at 45.

On cross examination, Dr. Gershwin agreed that Petitioner's blood tests did not show signs of inflammation at any time, even when he was not being treated with biologic therapies. Tr. at 54-57, 59-62; Ex. 13 at 2 (November 7, 2014 visit), 5-6 (November 12, 2014 visit); Ex. 28 at 2, 9-13 (July 20, 2018 visit). Additionally, Petitioner's imaging studies did not show signs of erosion, effusions, synovitis, or other characteristics of RA. Tr. at 76. However, in Dr. Gershwin's opinion, these facts did not exclude an RA diagnosis. Tr. at 57, 73.

Under questioning by Special Master Oler, Dr. Gershwin clarified that in general, he did not believe that seropositive RA could be vaccine caused. Tr. at 82. The serotype was important because there is a clearly defined preclinical phase in seropositive RA, whereas there is no evidence of such a stage in seronegative RA. *Id.* at 83.

Dr. Gershwin testified that although Petitioner lacked the expected imaging changes one would see in progressive, untreated RA, he was taking biologics and steroids, which were used to prevent joint destruction. Tr. at 84-85, 93-94. This explains why he experienced swelling and pain but had no imaging showing any type of synovial erosion. *Id*. at 85, 94. Furthermore, some RA patients do not experience joint erosions. *Id*. at 85.

Special Master Oler inquired about Petitioner's July 20, 2018 visit with rheumatologist Dr. Loomer, who noted:

> Known diagnosis of RA and strong [four-year] history of Humira use which most recently has been minimally effective. . . Based on our clinical and historical finding today, we do believe patient has autoimmune condition (RA), but we will take a fresh look at serologies and [x-rays] to formulate a most accurate diagnosis.

Ex. 28 at 4. Dr. Gershwin did not believe this record indicated doubt about the RA diagnosis; instead, he believed Dr. Loomer wished to confirm the diagnosis was accurate, because using biologics without a clear diagnosis was below the standard of care. Tr. at 87.

Special Master Oler asked how the innate immune response could lead to a chronic disease. Tr. at 87-88. Dr. Gershwin explained that the innate immune response initiated the disease process, and the adaptive response followed with autoantibodies, which are not identified in patients with seronegative RA. *Id*. Although the perpetuation of the disease required an adaptive response, the innate immune response would not disappear; it would simply have continued with the production of inflammatory mediators. *Id.* at 88. Here, Petitioner's reaction occurred after two days, which was "highly consistent with an immune response." *Id.* at 83.

2. Dr. Oddis's Testimony

Dr. Oddis testified that RA involves the symmetric onset of inflammation affecting the small joints of the hands and feet, usually in association with elevated inflammatory markers and

the presence of RF and/or anti-CCP antibody positivity. Tr. at 109-10. ESR and CRP are markers for inflammation. *Id.* at 118-19. The cause of RA is unknown, but there is typically a genetic predisposition along with an environmental insult, such as an infection, which together trigger an inflammatory response. *Id.* at 116-17. The flu vaccine has never been identified as a risk factor for either seropositive or seronegative RA. *Id*. at 117.

There are key differences between seropositive and seronegative RA patients. Tr. at 110-11. Seropositive patients normally have more overt and serious symptoms of swelling and inflammation in their synovia, along with abnormal lab tests. *Id.* at 110. Seropositive and seronegative RA are similarly treated with potent biologic agents and steroids, making it critically important to ensure that a seronegative RA patient actually has the disease:

> If you're going to call somebody seronegative [RA], you better make doggone sure that that's the diagnosis, and it helps to follow these patients over time so that there is [sic] more objective manifestations of an inflammatory state, because, as I said, if you are going to call it seronegative [RA], you are going to use the medications that we have available, which means they are going to be aggressively treated with steroids and some point, maybe low dose, maybe higher dose, along with immunosuppressive drugs, along with biologic agents that target particular cytokines that are indicated in the pathogenesis of [RA], be it seronegative or seropositive.

Id. at 110-11. To diagnose seronegative RA, one would consider clinical exams of the small joints of the hands and feet, lab tests for inflammatory markers, and imaging. *Id.* at 115-16.

According to Dr. Oddis, the classification criteria for RA were intended to be used in clinical trials to ensure participants truly have that diagnosis. Tr. at 112. There is a significant placebo effect with treatments tested in clinical trials. *Id.* As such, to avoid distortion of clinical trial results, it is critical to measure participants against the RA criteria to ensure they actually have RA. *Id.*

Dr. Oddis testified that, after considering Petitioner's overall clinical course, he did not agree with the diagnosis of seronegative RA. Tr. at 104. Within 48 hours of his flu vaccination, Petitioner did have some acute symptoms of joint aches and pains. *Id.* at 106. His lab tests, however, did not show any evidence of inflammation over the course of eight years. *Id.* Although he had intermittent treatment with biologics and steroids, which might have affected his lab findings, it is still significant that his results were consistently normal over his eight-year course. *Id.* Furthermore, Petitioner's first rheumatologist, Dr. Dinning, appears to have "plugged" abnormal exam findings into a template record, suggesting that these observations were not actually made during multiple visits. *Id.* at 107. Also, when Petitioner saw the second rheumatologist, Dr. Loomer, on July 20, 2018, Dr. Loomer documented 47 swollen or tender joints – indicative of "a lot of inflammation" – but Petitioner's ESR and CRP remained normal, showing an "undetectable" level of inflammation, in tests taken the next day. *Id.* at 108-09. Dr. Oddis

concluded: "I don't see this in seronegative [RA], I don't see this in seropositive [RA], I don't see this in any disorder where there is concomitant inflammation." *Id.* at 109.

Also notable was Petitioner's report during the July 2018 visit that a flare-up caused him to stay bedridden for two days. Tr. at 123. "[V]ery rarely does a patient [of Petitioner's age] put themselves in bed." *Id*. Further, Petitioner was not convinced he had RA even after four years of treatment. *Id.* at 123-24. This belief was "the reverse of what we normally see these days," making Dr. Oddis "very skeptical of that history." *Id.* at 124.

Apart from disputing the diagnosis, Dr. Oddis did not believe that there was a reliable theory for how the flu vaccine could cause seronegative RA. Tr. at 125. The flu vaccine was not known to cause, exacerbate, or induce any form of RA. *Id*. at 117. Furthermore, although Petitioner might have had normal, transient symptoms in the days after the vaccination, there was no evidence in the medical records that he had an ongoing inflammatory response consistent with seronegative RA. *Id.* at 127. Finally, the 2-day timeframe was inappropriate for the development of seronegative RA. *Id.* at 126-27.

On cross examination, Dr. Oddis was asked to provide an alternative diagnosis for Petitioner, but he was unable to conclusively opine on this. Tr. at 131-32. Petitioner's actions were overdramatic. *Id.* At his visit with orthopedist Dr. Pennington, he was using a cane for reported knee inflammation but had a normal examination. *Id.* at 131. Also, despite the normal examination, Petitioner made the unusual request for an aggressive operative procedure known as synovectomy, which is used for uncontrolled inflammation in the knee joint. *Id.* at 131-32.

Dr. Oddis acknowledged that elevated ESR and CRP are not required to make a diagnosis of seronegative RA; instead, those measurements are part of the classification criteria for the disease. Tr. at 132.

Responding to Special Master Oler, Dr. Oddis testified that the biologic and steroidal treatments Petitioner took might have suppressed inflammation, but "over a period of six to eight years, never having an elevated inflammatory marker at a time when the joints are visibly noted to be abnormal, would be distinctly unusual in my opinion." Tr. at 134. Additionally, if the treatments were effectively suppressing Petitioner's inflammatory markers, he would have expected Petitioner's physical symptoms, such as swelling, to correspondingly abate, but that was not seen. *Id.*

3. Dr. He's Testimony

Dr. He testified that RA is a chronic, systemic autoimmune inflammatory disorder, for which the etiology is unknown. Tr. at 141-42. The pathogenesis for the seropositive and seronegative serotypes is the same, but the bloodwork of seronegative RA patients does not contain RF or anti-CCP factors.[16] *Id.* at 142, 144-45; Firestein at 357 (Fig. 1). There is no reputable theory as to how the flu vaccine can cause either form of RA. Tr. at 153, 159. There are no epidemiologic studies or case reports supporting such a theory. *Id.* at 146. To the contrary, "the

[16] Dr. He explained that there are other autoantibodies that might be detected in seronegative RA, such as anti-MDA, anti-MAA, and anti-AIAT. Tr. at 143.

evidence is very extensive . . . to show . . . unequivocally that influenza vaccine – there is no relation between influenza vaccine and RA." *Id.* at 147.

Dr. He opined that it would be impossible for innate immune activation alone to cause seronegative RA, based on the pathways that drive RA development. Tr. at 148-49. If the innate immune system alone is activated after vaccination, the patient might suffer two to three days of fever and discomfort, which will then dissipate. *Id.* at 151. But RA is mediated by antibodies, and it also requires the activation of T lymphocytes, which attack joint tissue. *Id.* at 150. Those could not be produced and cause damage within 48 hours, as alleged here. *Id.* at 149. A full-blown autoimmune response would take seven to ten days. *Id.* at 153.

Finally, Dr. He agreed with Dr. Oddis that Petitioner's ESR and CRP levels remained normal, and he had no evidence of joint damage, suggesting there was not an abnormal activation of his immune system. Tr. at 148, 156.

On cross, Dr. He acknowledged that a two-day timeframe would be sufficient for activation of the innate immune response. Tr. at 160. He also claimed that newer literature has discussed a "preclinical" phase of seronegative RA. *Id.* at 160-61.

4. Dr. Gershwin's Rebuttal Testimony

On rebuttal, Dr. Gershwin testified that he was skeptical of the notion that there is a preclinical phase of seronegative RA. Tr. at 163. This is because a preclinical phase is characterized by the presence of antibodies without clinical symptoms, but there are no detectable antibodies in seronegative RA. *Id.*

Dr. Gershwin disagreed with Dr. He that RA symptoms could not manifest without an adaptive immune response. Tr. at 164. He noted that the innate immune response is powerful, and the drugs used to treat RA fight the cytokines that are produced by that response. *Id.* at 164-65. The evidence here indicates that Petitioner experienced an innate immune response within two days of vaccination, after which the adaptive immune response facilitated the continuation of disease. *Id.* at 166.

C. Post-Hearing Expert Reports

1. Dr. Oddis's Fourth Expert Report

Dr. Oddis continued to disagree with the seronegative RA diagnosis, noting that the identification of a preclinical biomarker in seronegative RA "has absolutely nothing to do with whether [Petitioner] has seronegative RA." Fourth Oddis Rep. at 1. He found the most recent literature filed by Dr. Gershwin "irrelevant" to his testimony. *Id.*

2. Dr. Gershwin's Fifth Expert Report

In his final report, Dr. Gershwin discussed literature filed by Dr. He after the hearing. *See* Exs. M-Q. He opined that these papers failed to support the notion of a preclinical biomarker of

seronegative RA. Fifth Gershwin Rep. at 1-3. Several of them explicitly concerned seropositive RA or patients who had RA symptoms and thus were not in a "preclinical" phase of the disease. *Id.* at 1-2. Furthermore, the literature supported Dr. Gershwin's view that the innate immune system could largely drive the development of RA. *Id.* at 3 (referencing paper stating that the immunopathology of seronegative RA "is greatly driven by synovial stromal and myeloid cells, with minor involvement of adaptive immune cells"); *see* Li et al., *ACPA-Negative Rheumatoid Arthritis: From Immune Mechanisms to Clinical Translation*, 83 EBIOMEDICINE 1, 1, 6 (2022) (Ex. M) ("Li")).

IV. APPLICABLE LAW

A. Petitioner's Burden in Vaccine Program Cases

Under the Vaccine Act, a petitioner may prevail in one of two ways. First, he may show that he suffered a Table injury within the time provided in the Table. § 11(c)(1)(C)(i). "In such a case, causation is presumed." *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006); *see* § 13(a)(1)(B). Second, where the alleged injury is not listed in the Table, he may demonstrate that he suffered an "off-Table" injury that was caused-in-fact by his vaccination. § 11(c)(1)(C)(ii).

For both Table and non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. § 13(a)(1). 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 v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1322 n.24 (Fed. Cir. 2010); *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). The 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, 1352 (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 the opinion of a competent physician. § 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. Secretary of Health and Human Services*. 418 F.3d 1274 (Fed. Cir. 2005). *Althen* requires a petitioner to establish by preponderant evidence that the vaccination caused his injury "by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id.* at 1278.

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, a petitioner 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 548-49; *Bunting v. Sec'y of Health & Hum. Servs.,* 931 F.2d 867, 873 (Fed. Cir. 1991).

A petitioner 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). Despite their expertise, special masters are not empowered by statute to conclusively resolve what are complex 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. However, this does not negate or reduce a petitioner's ultimate burden to establish his entitlement to damages by preponderant evidence. *W.C. v. Sec'y of Health & Hum. Servs*., 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted).

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 (stating that "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 because 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). However, the existence of medical records and/or statements of treating physician views does not require the special master to adopt their conclusions *per se*. § 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) ("[T]here 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 also be weighed against other, contrary evidence in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Hum. Servs*., 100 Fed. Cl. 742, 749 (2011) (it was 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); *Caves v. Sec'y of Health & Hum. Servs*., No. 06-522V 2011 WL 1935813, *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 Fed. App'x 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.* Thus, 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 also be consistent with the theory for how the relevant vaccine can cause the alleged 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 on other grounds*, 105 Fed. Cl. 353 (2012), *aff'd without op.,* 503 F. App'x 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), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. Law Governing Analysis of Fact Evidence

The process for making factual determinations in Vaccine Program cases begins with analyzing the medical records, which are required to be filed with the petition. §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." §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 413, 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 based on a rational analysis).

Medical records created contemporaneously with the events they describe are generally trustworthy, because they "contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions," where "accuracy has an extra premium." *Kirby v. Sec'y of Health & Hum. Servs.*, 997 F.3d 1378, 1382 (Fed. Cir. 2021) (citing *Cucuras*, 993 F.2d at 1528). Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *See generally Lowrie v. Sec'y of Health & Hum. Servs.*, No. 03-1585V, 2005 WL 6117475 at *19 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are often 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 Health & Hum. Servs.*, 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. U.S. 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.")).

However, there are situations in which compelling oral testimony could be more persuasive than written medical 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) ("[L]ike 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 ("Written records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent.") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, the special master should assess each witness's credibility when determining the weight their

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).

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 deciding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony, a rational analysis must be explicated. *Burns*, 3 F.3d at 417.

C. Analysis of Expert Testimony

Establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of his or her 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 Pharm., 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 in other federal judicial proceedings. Those factors are employed by judges to exclude evidence that is unreliable and potentially confusing to a jury. In Vaccine Program cases, the factors are generally used to assess the reliability and weight of scientific evidence. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("[U]niquely 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 persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 743.

Respondent frequently offers one or more experts of his own 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). 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)). A "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly*, 592 F.3d at 1324. Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis special masters must employ in Vaccine Program cases. *Id.* 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) ("[T]his 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").

D. Consideration of Medical Literature

Finally, although this decision discusses some but not all the medical literature in detail, I have reviewed and considered all the medical records and literature submitted in this matter. *See Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though [s]he does not explicitly reference such evidence in h[er] decision."); *Simanski v. Sec'y of Health & Hum. Servs.*, 115 Fed. Cl. 407, 436 (2014) ("[A] Special Master is 'not required to discuss every piece of evidence or testimony in her decision.'") (citation omitted), *aff'd*, 601 F. App'x 982 (Fed. Cir. 2015).

V. ANALYSIS

A. Diagnosis

As a threshold matter, a petitioner must establish that he suffered the injury for which he seeks compensation. *Broekelschen*, 618 F.3d at 1346. "The function of a special master is not to 'diagnose' vaccine-related injuries, but instead to determine 'based on the record as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the [petitioner]'s injury.'" *Andreu*, 569 F.3d at 1382 (quoting *Knudsen*, 35 F.3d at 549). "Although the Vaccine Act does not require absolute precision, it does require the petitioner to establish an injury – the Act specifically creates a claim for compensation for 'vaccine-related injury or death.'" *Stillwell v. Sec'y of Health & Hum. Servs*., 118 Fed. Cl. 47, 56 (2014) (quoting 42.U.S.C. § 300aa-11(c)). Accordingly, the Federal Circuit has concluded that it is "appropriate for the special master to first determine what injury, if any, [is] supported by the evidence presented in the record" before applying a causation analysis pursuant to *Althen. Lombardi v. Sec'y of Health & Hum. Servs*., 656 F.3d 1343, 1351-53 (Fed. Cir. 2011).

Petitioner alleges he developed seronegative RA. Respondent disputes this diagnosis. Ultimately, it is not necessary to resolve whether Petitioner proved he has seronegative RA, because even assuming he did, he failed to prove his flu vaccination could have or did cause that condition.

B. *Althen* Prong One

In the context of the Program, "to establish causation, the standard of proof is preponderance of evidence, not scientific certainty." *Langland v. Sec'y of Health & Hum. Serv.*, 109 Fed. Cl. 421, 441 (Fed Cir. 2013). Petitioner's burden under *Althen*'s first prong is to provide a medical theory causally connecting the vaccination and the injury. *Id.* This theory must be sound and reliable. *Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019). For the reasons discussed below, even assuming the appropriate diagnosis for Petitioner was seronegative RA, I conclude that Petitioner has not provided a sound and reliable medical theory causally connecting the flu vaccine to that condition.

1. Seronegative Rheumatoid Arthritis

RA is an inflammatory disease of the joints. *See* First Gershwin Rep. at 2; *see also, e.g.*, Firestein & McInnes at 183 (noting that RA is the "most common inflammatory arthropathy" and is thought to be immune mediated); Aletaha at 2570 ("RA is a chronic inflammatory disease characterized by joint swelling, joint tenderness, and destruction of synovial joints[.]"); Klareskog at 659 (RA is a "systemic, inflammatory, autoimmune disorder"). Dr. Oddis testified that RA is characterized by "the symmetric onset of an inflammatory arthritis, [mainly] affecting the small joints of the hands and the feet, usually in association with elevated inflammatory markers and the presence of rheumatoid factor and/or anti-CCP antibody positivity." Tr. at 109-10. To diagnose RA, a clinician will consider exam findings concerning the small joints of the hands and feet, lab tests, and imaging. *Id.* at 115-16 (Dr. Oddis's testimony); *see also* First Gershwin Rep. at 2 (noting that diagnosis of RA includes "determination of whether synovitis . . . is present . . . [and] testing for both rheumatoid factor and antibodies to CCP."). In evaluating the joints, the key signs of inflammation to look for are swelling, warmth, redness, and pain. *See* Greenspan & Gershwin at 3. With respect to lab tests, RF and CCP are found in seropositive RA, but are undetectable in seronegative disease. First Gershwin Rep. at 2; Tr. at 31-32; 109-10. Also, ESR and CRP are markers for inflammation and are usually elevated in RA, although levels might decrease with treatment. Tr. at 23-24, 118-19; *see also, e.g.*, Venables at 7 ("Normal acute phase reactants [e.g., ESR/CRP] may occur in untreated patients with RA, but such findings are very infrequent."). Treatment for RA typically includes the use of Disease-Modifying Antirheumatic Drugs ("DMARDs"), including methotrexate, sulfasalazine, hydroxychloroquine, leflunomide, and glucocorticoids, and/or tumor necrosis factor ("TNF") blockers like infliximab, etanercept, and adalimumab (Humira). *See* Klareskog at 666-67; *see also* Aletaha at 2571 (noting that the optimal use of these treatments has "dramatically enhanced the success of RA management").

As the experts agreed, the etiology of RA is not well understood, but the disease is commonly believed to be caused by a combination of genetic and environmental factors. *See* Tr. at 29-30 (Dr. Gershwin); 116-17 (Dr. Oddis); 141-42 (Dr. He). The experts noted that the female sex, cigarette smoking, and periodontal disease are risk factors for RA. *See* First Gershwin Rep. at 1-3; First He Rep. at 5. Additionally, silica dust, mineral oils, and other airway exposures are considered potential environmental risk factors. Klareskog at 661; *see also id.* (Table 2) (identifying genetic and environmental factors associated with seropositive and seronegative RA); Haville et al., *Pre-RA: Can early diagnosis lead to prevention?*, 36 BEST PRAC. & RSCH. CLINICAL RHEUMATOLOGY 1, 4 (Table 1) (2022) (Ex. 56) ("Haville").

Seronegative RA is thought to be clinically and pathogenetically distinct from seropositive disease. *See, e.g.,* Firestein & McInnes at 185 (stating that "meta-analyses of patients with [seronegative RA] show some differences from [seropositive RA] disease, consistent with the idea that 'seronegative RA' should be considered a distinct clinical pathologic entity"); Aletaha at 2578 (seropositive and seronegative patients "have been shown to differ from a pathogenetic, clinical, and prognostic perspective"); Klareskog at 660 ("growing evidence shows that the disease consists of at least two subsets, with different causes and severity . . . increasingly the separation is made on the basis of presence or absence of antibodies to citrullinated protein antigen (ACPA), sometimes referred to as anti-CCP (cyclic citrullinated peptide)"); Li at 1 (seropositive and seronegative RA are "two distinct disease entities with differential underlying pathophysiology").

2. Causation Theory[17]

Dr. Gershwin opined that the scientific evidence would not support a claim that the flu vaccine can cause *seropositive* RA. *See* First Gershwin Rep. at 2. As discussed below, this position is borne out by the epidemiologic evidence in the record concerning flu vaccine and "RA" broadly. Dr. Gershwin contended, however, that seronegative RA is a distinct entity from seropositive RA, with different environmental risk factors and a different expected clinical course than seropositive RA. *See* First Gershwin Rep. at 2. Thus, he came to a different conclusion concerning whether the flu vaccine can cause seronegative RA.

Dr. Gershwin admitted that "we know very little about the earliest events in the development of either seropositive or seronegative patients." First Gershwin Rep. at 2. He opined, though, that seronegative RA is initially driven by a pathogenic innate immune response in the synovial tissue. Tr. at 40. Dr. Gershwin elaborated, stating that, in seronegative RA specifically, the pathogenic innate immune response is characterized by the innate immune system's *ongoing* production of inflammatory mediators, as well as a pathogenic adaptive immune response. He testified:

> Well, the innate immune response starts this disease off, and the innate immune response is required for an adaptive response. The adaptive response, if seronegative, will include autoantibodies that have yet to be identified, but people believe they exist, and some people have shown them to exist using phased display systems and to include cytotoxic T cells.
>
> If you think of a clock, you've got two cog wheels. Innate immunity is a cog on the left. Adaptive is a cog on the right. The innate

[17] I note that Dr. Gershwin's theory was described in a very short and cursory manner. In his first report, Dr. Gershwin dedicated approximately one page of his two-page report (excluding the list of cited medical literature and letterhead) to his causation theory. First Gershwin Rep. at 2-3. Dr. Gershwin filed four more reports that did not elaborate on his causation theory, totaling seven pages. *See* Second, Third, Fourth, and Fifth Gershwin Reps. This lack of detail lessened the persuasiveness of his opinions. *See Dotson v. Sec'y of Health & Hum. Servs.*, No. 17-637V, 2025 WL 354801, at *28 (Fed. Cl. Spec. Mstr. Jan. 10, 2025) (criticizing Dr. Gershwin's theories for lack of "sufficient development").

> immunity turns and starts the adaptive response. So the perpetuation of the disease requires an adaptive response, *but the innate immune response doesn't disappear, and we continue to see production of inflammatory mediators by the innate response*.

Tr. at 87-88 (emphasis added). The Li article further explained that, in seronegative RA, fibroblast-like synoviocytes in the synovium secrete a variety of cytokines, chemokines, and pro-angiogenic factors to "recruit immune cells to perpetuate joint inflammation." Li at 5.

Dr. Gershwin cited to a number of pieces of medical literature to support his broad theory. I note that many of the papers address RA generally; Li was one of the few that discussed the pathogenesis of seronegative RA. In the Gierut paper, the authors described the contributions of innate immune system components, concluding that "[i]nnate immunity, with macrophages playing a central role, is critically important in the pathogenesis of RA." Gierut at 14. Similarly, the Firestein paper proposed that RA involves activation of the innate immune response "by stimulating dendritic cells, macrophages, fibroblasts and mast cells," which then migrate into the synovium, creating an opportunity for an adaptive immune response in individuals with genetic susceptibility. Firestein at 359 (Fig. 3); *see also* Edilova et al., *Innate Immunity Drives Pathogenesis of Rheumatoid Arthritis*, 44 BIOMEDICAL J. 172, 173 (2021) (Ex. 50) ("Edilova") ("Various innate immune cells including monocytes, macrophages and dendritic cells are involved in inflammatory responses seen in RA patients as well as in driving the activation of the adaptive immune system, which plays a major role in the later stages of the disease.").

Concerning the potential role of the flu vaccine in causing this pathogenic immune response, Dr. Gershwin opined that vaccination can cause the release of cytokines and prostaglandins into the blood, which can in turn activate innate immune cells, including in the synovium. Tr. at 34-35. Dr. Gershwin submitted the Hervé paper to support this opinion. In Hervé, the authors explained that vaccines contain antigens that are recognized as potential pathogens by circulating immune cells. Hervé at 2. This stimulates the innate immune system to produce cytokines and chemokines, activate complement, and signal for cellular recruitment. *Id.* These substances can enter the bloodstream and cause systemic side-effects such as fever, fatigue, and headache. *Id.* The Hervé authors stated that studies of non-adjuvanted vaccines[18] "consistently described a slight and short-lived increase in inflammatory mediators in blood following vaccination, in particular, an increase in CRP and IL-6. The level and kinetics of the inflammatory markers depended on the type of vaccine used and the population studied." *Id.* at 4. With respect to the flu vaccine, the Hervé paper cited a study that found the non-adjuvanted seasonal flu vaccine produced a "mild and transient increase in circulating IL-6 and TNF-α" in pregnant women. *Id.*

Hervé is inadequate to substantiate Petitioner's claim that the seasonal flu vaccine can cause an *abnormal, ongoing* innate immune reaction leading to pathogenic inflammation of the synovium, as is believed to occur in seronegative RA. Nothing in Hervé suggests that the flu vaccine can cause an abnormal inflammatory innate response, particularly an ongoing one. At best, Hervé reports only that the vaccine produces *transient and mild* systemic inflammation. In fact, none of the literature in the record addresses any potential mechanistic connection between

[18] The subject vaccine in this case was non-adjuvanted. *See* Tr. at 36.

the flu vaccine and a pathogenic innate immune response leading to (and perpetuating) seronegative RA.

Another component to Dr. Gershwin's theory was that the innate immune system attacks the synovium/joints, yet he did not articulate how this happens. First Gershwin Rep. at 2. He testified: "[Petitioner has] got these resident cells in his synovium, and they are activated by virtue of a genetic predisposition, and he gets the inflammation that was described 48 hours later." Tr. at 42. But Dr. Gershwin did not explain how the flu vaccine activates the synovial cells.

Also, Petitioner admittedly did not propose what the pathogenic *adaptive* immune response in seronegative RA might be, even though Dr. Gershwin acknowledged that such a response would be necessary to produce the disease. Dr. Gershwin testified that the role of the adaptive immune system is unknown in seronegative RA. Tr. at 43-44, 77, 87-88. Thus, even accepting that seronegative RA is initially driven by an abnormal innate immune response, and even accepting that the flu vaccine induces some innate immune response, Petitioner failed to produce reliable evidence of a link between the flu vaccine and a pathogenic, ongoing innate response, or the abnormal adaptive immune response, that purportedly causes seronegative RA.

3. Epidemiologic Data

Epidemiologic evidence is not required to prove a Vaccine Act case. It is appropriate, however, for a special master to consider such evidence as part of the overall assessment of the case. *See Druery v. Sec'y of Health & Hum. Servs*., No. 17-1213V, 2023 WL 5094088, at *17 (Fed. Cl. July 11, 2023), *mot. for rev. den'd,* 169 Fed. Cl. 557 (2024) (observing that "[n]othing in *Althen* or *Capizzano* requires the Special Master to ignore probative epidemiological evidence that undermines petitioner's theory.") (quoting *D'Tiole v. Sec'y of Health & Hum. Servs.*, 726 F. App'x 809, 811 (Fed. Cir. 2018)). "Although *Althen* and *Capizzano* make clear that a claimant need not produce medical literature or epidemiological evidence to establish causation under the Vaccine Act, where such evidence is submitted, the Special Master can consider it in reaching an informed judgment as to whether a particular vaccination likely caused a particular injury." *Andreu*, 569 F.3d at 1379; *see also Tullio v. Sec'y of Health & Hum. Servs.*, No. 15-51V, 2019 WL 7580149, *5-8 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), *aff'd*, 149 Fed. Cl. 448 (2020) (in a case alleging a flu vaccination caused RA, discussing at length the proposition that it is appropriate for a special master to consider and give weight to relevant epidemiologic studies, even if they are not dispositive of *Althen* prong one).

Petitioner did not submit any epidemiologic data relating to a potential association between flu vaccination and seronegative RA. Dr. Gershwin acknowledged that there is "considerably less epidemiology on seronegative disease following vaccination," suggesting that it would be difficult to conduct a sufficiently powered study to provide a reliable result for patients like Petitioner. First Gershwin Rep. at 2 ("[T]here is no significant power calculations that I am aware of for the presence of seronegative rheumatoid arthritis in a young, non-smoking male following influenza vaccination.").[19] Petitioner also did not identify any case reports describing seronegative RA following flu vaccination.

[19] This claim is not entirely persuasive. The literature showed that RA is the most common inflammatory arthropathy and affects about 0.5-1% of the total population. Firestein & McInnes at 1; Firestein at 356.

Respondent submitted several epidemiologic studies concerning RA generally and flu vaccination. These studies did not differentiate between seropositive and seronegative RA patients, and they assessed different flu vaccines than the one at issue here, so they are not entirely on point in assessing the particular claim advanced here. Nonetheless, they clearly reported no causal association between any type of RA and any type of flu vaccine, and Dr. Gershwin did not dispute their findings or methodologies.

a. *Kurland*

In Kurland, published in 1984, the investigators performed three separate analyses. First, they studied the incidence of RA following the 1976 swine flu vaccination campaign in patients from the Mayo Clinic who had been diagnosed with RA between 1976 and 1980. Kurland at 818. Of the patients living in Minnesota (the Mayo Clinic's location), 66% had been vaccinated against the swine flu. *Id.* Patients living in adjacent states had a swine flu vaccination rate of 54%. *Id.* A comparison of the rates of RA in various time periods before and after vaccination showed no increase in the risk of RA following vaccination. *Id.*

Second, the Kurland investigators considered the rates of RA in 682,000 U.S. Army servicemembers who had received the swine flu vaccine in the fourth quarter of 1976. Kurland at 818-19. The investigators found no significant increase in the risk of RA after vaccination in this population. *Id.* at 819.

Third, the investigators reviewed other studies of the swine flu vaccine and rheumatologic disorders, including RA. Kurland at 819-20. Again, none of those studies found a significantly increased risk of developing RA or flareups of symptoms following the vaccination. *Id.* The authors stated:

> We can conclude from the review of the available literature that RA has not been associated with past influenza vaccination programs, including the national swine flu vaccination program of 1976. . . . We conclude from the epidemiologic and clinical data that no evidence indicates that the swine flu vaccine is a risk factor for new or existing cases of RA.

Id. at 820.

b. *Bardage*

The Bardage study, published in 2011, evaluated the effects of the H1N1 swine flu vaccine (developed in response to the 2009 H1N1 swine flu pandemic), considering a variety of potential associations, including with RA. Bardage at 1. More than one million patients from a Swedish

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Of that group, about 10-20% have seronegative RA. Firestein & McInnes at 8. This likely represents a fairly large potential dataset of patients, even if one further narrows it to young, non-smoking males. Still, neither party provided any epidemiologic data specifically evaluating a potential association between flu vaccination and seronegative RA.

health database were included in the analysis. *Id.* at 2. The investigators found no significantly increased risk of RA following H1N1 vaccination compared to controls, either during the first 45 days following vaccination or during the period thereafter. *Id.* at 4, 9 (Table 2).

c. Studies of flu vaccination in RA patients

Respondent also submitted a number of studies evaluating the effects of flu vaccination in already-diagnosed RA patients. Each of these studies found that flu vaccination was safe and/or was not significantly associated with clinical exacerbations of RA, providing additional reassuring evidence. *See* Herron et al., *Influenza Vaccination in Patients With Rheumatic Diseases*, 242 JAMA 53 (1979) (Ex. C, Tab 6) ("Herron") (administration of the seasonal flu vaccine to patients with RA did not result in a significantly increased risk of symptom flareup); Del Porto et al., *Influenza vaccine administration in patients with systemic lupus erythematosus and rheumatoid arthritis*, 24 VACCINE 3217 (2006) (Ex. C, Tab 7) ("Del Porto") (no significant difference in clinical activity of RA in patients versus controls following seasonal flu vaccination); Ori Elkayam, *Safety and efficacy of vaccination against influenza in patients with rheumatoid arthritis*, 13 CLINICAL & DEV. IMMUNOLOGY 349 (2006) (Ex. C, Tab 8) ("Elkayam") (literature review showed that the flu vaccine "does not induce clinical exacerbation of RA"); Elkayam et al., *Efficacy and Safety of Vaccination Against Pandemic 2009 Influenza A (H1N1) Virus Among Patients With Rheumatic Diseases*, 63 ARTHRITIS CARE & RSCH. 1062 (2011) (Ex. C, Tab 9) ("Elkayam II") (study finding that vaccination with an adjuvanted H1N1 flu vaccination was safe in RA patients); Saad et al., *Immunogenicity and safety of the 2009 non-adjuvanted influenza A/H1N1 vaccine in a large cohort of autoimmune rheumatic diseases*, 70 ANN RHEUM DIS 1068 (2011) (Ex. C, Tab 10) ("Saad") (no moderate or severe side effects of seasonal flu vaccination in patients with autoimmune rheumatic diseases, including RA); Milanovic et al., *Influenza Vaccination in Autoimmune Rheumatic Disease Patients*, 229 TOHOKU J. EXP. MED. 29 (2013) (Ex. C, Tab 11) ("Milanovic") (administration of seasonal flu vaccine to RA patients did not result in any exacerbation of disease); Milanetti et al., *Safety and immunogenicity of co-administered MF59-adjuvanted 2009 pandemic and plain 2009–10 seasonal influenza vaccines in rheumatoid arthritis patients on biologicals*, 177 THE J. OF TRANSLATIONAL IMMUNOLOGY 287 (2014) (Ex. C, Tab 12) ("Milanetti") (study of adjuvanted H1N1 flu vaccine in RA patients showed no significant increase in disease activity; a slight increase in activated interferon-γ, TNF-α, or IL-17A-secreting T cells was observed a one month post-vaccination, followed by a reduction in such cells by six months post-vaccination).

In sum, Petitioner successfully showed that seronegative RA is a distinct clinical entity from seropositive RA and that it is characterized at least in part by a pathogenic innate immune response. But he failed to provide any relevant clinical data on this question, and the epidemiologic evidence in the record does not support the claim that the vaccine significantly increases the risk of developing RA generally. Also, the mechanistic evidence Petitioner supplied did not adequately substantiate that the flu vaccine could cause the abnormal innate immune response in the joints that is thought to drive seronegative RA. Further, Petitioner provided no reliable evidence at all concerning the potential pathogenic adaptive immune response in seronegative RA, nor how the flu vaccine could cause that response. Thus, after careful review of the record, I conclude that Petitioner has not presented preponderant evidence in the form of a sound and reliable theory that the flu vaccine can cause seronegative RA.

C. *Althen* Prong Two

Under *Althen*'s second prong, a petitioner must "prove a logical sequence of cause and effect showing that the vaccination was the reason for the injury." *Althen*, 418 F.3d at 1278. The sequence of cause and effect must be "'logical' and legally probable, not medically or scientifically certain." *Andreu*, 569 F.3d at 1380 (quoting *Knudsen*, 35 F.3d at 548-49). A petitioner is not required to show "epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." *Capizzano*, 440 F.3d at 1325. Instead, circumstantial evidence and reliable medical opinions may be sufficient to satisfy the second *Althen* prong. *Id.* Further, special masters are expected to consider the views of treating doctors. *Id.* at 1326. Such views are often persuasive because the doctors have direct experience with the patient whom they are diagnosing -- but they are not necessarily dispositive of the causation question. *See McCulloch v. Sec'y of Health & Hum. Servs.*, No. 09-293V, 2015 WL 3640610, at *20 (Fed. Cl. Spec. Mstr. May 22, 2015).

The medical records indicate that PA Bledsoe and Dr. Dinning both initially suspected Petitioner's presentation had a vaccine and/or viral cause. These suspicions were recorded very early in Petitioner's course and before he was formally diagnosed with RA or tested for objective signs of inflammatory disease. When PA Bledsoe initially saw Petitioner on November 7, 2014, he wrote that he suspected Petitioner suffered an "allergic" reaction to the vaccine. Ex. 13 at 5. He did not diagnose Petitioner with RA, though; instead, he diagnosed arthralgia. *Id.* Also, when Dr. Dinning first saw Petitioner on November 25, 2014, he suspected his "inflammatory arthritis" had either a viral cause or was "associated with flu vaccine." Ex. 14 at 3. Again, however, at that time Dr. Dinning had not yet diagnosed Petitioner with RA or completed additional lab testing. When Dr. Dinning first diagnosed Petitioner with RA on February 10, 2015, he did not repeat his suspicion that the condition was caused by the flu vaccine, though he did reference the temporal relationship between the vaccination and the onset of symptoms in the disability form completed March 26, 2015. *See id.* at 14; Ex. 4 at 187-92. Overall, these preliminary statements are not persuasive evidence of vaccine causation.

Moreover, other aspects of the record are unsupportive of the proposition that there is a logical connection between the vaccine and Petitioner's condition, and these factors outweigh the initial suspicions of the treating providers. Most notably, Petitioner's imaging and bloodwork *never* showed any indication of inflammation throughout his eight-year course, belying the argument that he experienced a vaccine-induced, ongoing inflammatory reaction, as Dr. Gershwin contended. Petitioner's x-rays over the span of four and a half years were always unremarkable. Ex. 8 at 2-5 (February 10, 2015 x-rays of hands and knees); Ex. 28 at 12 (August 6, 2018 x-rays of hands, feet, wrists, ankles, lumbosacral spine, and sacroiliac joint); Ex. 45 at 54 (September 19, 2019 x-rays of hands and knees). Also, the biomarkers used to assess inflammation, ESR and CRP, were consistently normal, or even low-normal. Significantly, this was true even during periods when Petitioner was not undergoing any kind of treatment for RA that might have masked inflammation. When Petitioner was seen by PA Bledsoe for his joint pain (and before he began any treatment for RA), his ESR and CRP levels were measured and were normal. Ex. 13 at 3-4. Similarly, when he first saw Dr. Loomer on July 20, 2018, he reported that he had discontinued his Humira treatment for the previous three weeks due to a fungal rash. Ex. 28 at 1. But despite

this pause in treatment, bloodwork done the next day showed an "undetectable" CRP level and a normal ESR level. Ex. 28 at 12. Dr. Oddis testified:

> So at a time when this patient has 47 tender or swollen joints, he's got absolutely no evidence of any inflammation in his – in his blood, and if you go through the entire period of this patient's presentation with many different physicians, you will never find an elevated inflammatory marker, and not only are they normal, they are well within the normal range. In fact, they are in the low normal and sometimes undetectable range.
>
> I don't see this in seronegative rheumatoid arthritis, I don't see this in seropositive rheumatoid arthritis, I don't see this in any disorder where there is concomitant inflammation.

Tr. at 109. These facts strongly pull against the theory that Petitioner suffered an ongoing inflammatory response to the flu vaccine, as posited by Dr. Gershwin. *See also* First He Rep. at 5 (opining that the lack of systemic inflammation made it unlikely that an abnormal innate immune response caused Petitioner's joint symptoms).

As such, I conclude that Petitioner has not presented preponderant evidence in support of *Althen's* second prong.

D. *Althen* Prong Three

The timing prong contains two parts. First, a petitioner must establish the "timeframe for which it is medically acceptable to infer causation," and second, he must demonstrate that the onset of the disease occurred in this period. *Shapiro*, 101 Fed. Cl. at 542-43.

The record reflects, and the parties agree, that Petitioner experienced flu-like symptoms two days after vaccination. ECF No. 85 ("Petitioner's Post-Hearing Brief") at 17-18; ECF No. 86 ("Respondent's Post-Hearing Brief") at 29. The question is whether those symptoms represented the onset of seronegative RA, and whether a two-day timeframe for development of initial symptoms is medically appropriate.

Dr. Gershwin posited that Petitioner's seronegative RA was initially caused by an abnormal innate response triggered by the flu vaccine. He further opined that two days was an appropriate timeframe for an innate immune reaction to a vaccination. Tr. at 45-46. At some later point, the abnormal activation of the innate immune response in turn activated an (unknown) adaptive response that led to Petitioner's chronic RA. *Id.* at 88. Dr. Gershwin did not present an opinion on when the adaptive response would initiate, but I do not believe that level of specificity was required in light of the mechanistic theory he proposed, which, as noted, relied on an *ongoing* innate immune response occurring to some extent in parallel with the adaptive response.

Respondent did not refute the proposition that two days would be a medically acceptable timeframe for an innate immune response. Dr. He, in fact, admitted this. Tr. at 160. Dr. He instead focused his opinion on whether an *adaptive* immune response could manifest in this time;

he maintained that two days was not a medically acceptable timeframe for that response. First He Rep. at 4; Second He Rep. at 2; Tr. at 150.

Given Respondent's failure to refute Dr. Gershwin's point, I conclude that Petitioner has met *Althen* prong three based on the record before me and the causation theory he advanced. But since he has failed to satisfy either prong one or prong two, his overall claim for relief must be denied.[20] *Grant v. Sec'y of Dep't of Health & Hum. Servs*., 956 F.2d 1144, 1148 (Fed. Cir. 1992) ("a proximate temporal association alone does not suffice to show a causal link between the vaccination and the injury."); *see also Althen*, 418 F.3d at 1278.

E. Other Rheumatoid Arthritis Cases

Although the decisions of other special masters are not binding in this case, they are instructive. I note that Program petitioners asserting RA as a vaccine injury, including seronegative RA, have mostly failed.

1. Cases involving seronegative RA

Cases alleging seronegative RA as a vaccine injury have been uniformly disfavored in the Program. In *Seivwright*, the petitioner alleged that a flu vaccination caused her to develop seronegative RA. *Seivwright v. Sec'y of Health & Hum. Servs.*, No. 19-1398V, 2023 WL 3197267,

[20] Dr. He testified that some literature supports the existence of a preclinical biomarker for seronegative RA. Tr. at 160-61. He filed several papers purportedly showing this. Exs. M-Q. The identification of a preclinical marker might suggest a genetic cause of seronegative RA and also would raise the possibility that Petitioner's condition began before his vaccination. However, as Dr. Gershwin pointed out, several of the papers submitted by Dr. He concerned studies in patients already diagnosed with arthritis, so they did not concern a putative preclinical biomarker. Fifth Gershwin Rep. at 1-2; *see* Pratt et al., *A CD4 T cell gene signature for early rheumatoid arthritis implicates interleukin 6-mediated STAT3 signalling, particularly in anti-citrullinated peptide antibody-negative disease*, 71 ANN. RHEUM. DIS. 1374, 1374 (2011) (Ex. P) ("Pratt"); Anderson et al., *IL-6-driven STAT signalling in circulating CD4+ lymphocytes is a marker for early anticitrullinated peptide antibody-negative rheumatoid arthritis*, 75 ANN. RHEUM. DIS. 466, 466 (2014) (Ex. Q) ("Anderson"). Another study, using a proprietary assay, identified a protein signature for seronegative RA in a Native American population consisting of first-degree relatives of RA patients. O'Neil et al., *Association of a Serum Protein Signature With Rheumatoid Arthritis Development*, 73 ARTHRITIS & RHEUMATOLOGY, 78, 78 (2020) (Ex. O) ("O'Neil"). Dr. Gershwin acknowledged that the study was "potentially exciting but only illustrate[d] a genetic predisposition to develop disease," which would not preclude vaccine causation. Fifth Gershwin Rep. at 2. He also pointed out that the proteins identified in the study were involved in the innate immune system, purportedly supporting his causal theory. *Id.*

Although at least some of the literature filed by Dr. He supported the hypothesis that a biomarker for seronegative RA might be identified in patients who have not yet developed the disease, the data on that topic appear to be nascent. More fundamentally, it is unknown whether Petitioner had any such biomarker or a genetic predisposition to RA; thus, it is speculative to infer that Petitioner's condition was genetic and/or predated the vaccination. The only clinical evidence I have showed an onset of symptoms beginning two days after vaccination, and Dr. Gershwin's opinion that a two-day onset of innate immunity was medically appropriate was unrefuted. Thus, I still conclude on this record that Petitioner satisfied *Althen* prong three.

at *1 (Fed. Cl. Spec. Mstr. May 2, 2023). She offered expert opinion from Dr. Gershwin; Respondent offered a responsive opinion from Dr. Oddis. *Id.* The special master issued a tentative finding that the petitioner was unlikely to prove entitlement to compensation. *Id.* He specifically rejected Dr. Gershwin's theory of causation "involving somatic changes invoking the adaptive immune system" and cytokine-driven inflammation. *Id.* at *2. He further noted that special masters had "consistently rejected a theory based upon cytokines." *Id.* (citing *Hock v. Sec'y of Health & Hum. Servs.*, No. 17-168V, 2020 WL 6392770, at *29 (Fed. Cl. Spec. Mstr. Sept. 30, 2020); *Olson v. Sec'y of Health & Hum. Servs.*, No. 13-493V, 2017 WL 3624085, at *20 (Fed. Cl. Spec. Mstr. July 14, 2017), *mot. for rev. den'd*, 758 F. App'x 919 (Fed. Cir. 2018)). He granted the petitioner's motion to voluntarily dismiss her claim. *Id.* at *3.

Tullio is also instructive. There, the petitioner's RA diagnosis was seronegative because he did not have detectable anti-CCP antibodies. 2019 WL 7580149, at *2. But unlike here, he had elevated ESR and CRP levels, signifying that he was experiencing inflammation. *Id.* The petitioner's experts articulated a theory based on an abnormal adaptive immune response, opining that the flu vaccine could cause RA through molecular mimicry, resulting in an attack on the collagen within the joints. *Id.* at *5. The special master concluded that the petitioner had failed to preponderantly prove that pathogenic molecular mimicry between the flu vaccine and collagen could cause RA. *Id.* at *22. The special master also examined substantial epidemiologic data showing no causal association between the flu vaccine and RA. *Id.* at *9-11.

In *C.P.*, the special master rejected a causation theory of seronegative RA based on molecular mimicry between an unknown tissue and the flu vaccine. *C.P. v. Sec'y of Health & Human Servs.*, No. 14-917V, 2019 WL 5483621, at *29 (Fed. Cl. Spec. Mstr. Aug. 21, 2019). The petitioner also failed to present a reliable causation theory based on a vaccine-driven T cell response in the synovium. *Id.* at *26. Molecular mimicry theories of flu vaccine-caused seronegative RA were also rejected in *Gauvin* and *McGuinness*. *Gauvin v. Sec'y of Health & Hum. Servs.* No. 18-480V, 2024 WL 5346729 (Fed. Cl. Spec. Mstr. Dec. 27, 2024); *McGuinness v. Sec'y of Health & Hum. Servs.*, No. 17-954V, 2021 WL 5292343 (Fed. Cl. Spec. Mstr. Oct. 20, 2021).

2. Cases involving similar causation theories

As noted above, theories of vaccine-caused RA based on cytokine response have been rejected. *Seivwright*, 2023 WL 3197267, at *2. In *Hock*, the Chief Special Master rejected the petitioner's theory that the flu vaccine caused him to develop seropositive RA. 2020 WL 6392770, at *1. The petitioner's expert offered the theory the vaccine elicits the secretion of proinflammatory cytokines, which can then build up over time and cause RA. *Id.* at *5-6. That process, the expert opined, is followed by bystander activation of autoreactive cells, along with molecular mimicry between the vaccine components and autoantibodies, leading to tissue damage. *Id.* The Chief Special Master concluded that the petitioner had failed to substantiate this theory with scientific evidence showing how this process occurs or the role of the flu vaccine in triggering it. *Id.* at *26.

In *Olson*, the petitioner alleged an HPV vaccine caused her to develop RA. 2017 WL 3624085, at *19. Her causation theory centered on the claim that the alum used as an adjuvant in the vaccine was associated with the production of inflammatory cytokines. *Id.* at *20. The Chief

Special Master noted that the petitioner had failed to demonstrate "that cytokine upregulation allegedly resulting from vaccine administration is *itself* a trigger for RA, rather than either a byproduct or subsequent component of the disease." *Id.* (emphasis in original). She also failed to establish that the alum adjuvant was causally associated with RA or a similar autoimmune disease. *Id.* "The articles referencing the general capacity of alum to stimulate inflammasomes, or the possibly pathogenic role of over-stimulation of inflammasomes," were insufficient to support this theory. *Id.* at *21.

3. Cases involving seropositive RA

There are also several cases involving seropositive RA purportedly caused by vaccines in which entitlement has been denied. *See, e.g.*, *Wilson v. Sec'y of Health & Hum. Servs.*, No. 17-1264V, 2023 WL 9053671, at *12 (Fed. Cl. Spec. Mstr. Dec. 7, 2023) (dismissing petitioner's claim that she suffered from seropositive RA as a result of the flu vaccine); *Clark v. Sec'y of Health & Hum. Servs.*, No. 17-1553V, 2023 WL 4897284, at *28-32 (Fed. Cl. Spec. Mstr. June 16, 2023) (concluding that the flu vaccine did not significantly aggravate or exacerbate petitioner's RA, along with other associated injuries); *Moran v. Sec'y of Health & Hum. Servs.*, No. 16-538V, 2021 WL 4853544, slip. op., at 23-24 (Fed. Cl. Spec. Mstr. Oct. 4, 2021) (denying entitlement for a petitioner asserting the flu vaccine caused him to develop symptoms of RA after three days); *Monzon v. Sec'y of Health & Hum. Servs.*, No. 17-1055V, 2021 WL 2711289, at *21-23 (Fed. Cl. Spec. Mstr. June 2, 2021) (denying entitlement for a petitioner alleging Tdap vaccine caused her to develop RA after 10 days); *Bean-Sasser v. Sec'y of Health & Hum. Servs.*, No. 13-326V, 2016 WL 1649355, at *9-11 (Fed. Cl. Spec. Mstr. April 5, 2016), (denying entitlement to a petitioner alleging the hepatitis B vaccine caused her to manifest symptoms of RA approximately eleven hours later), *aff'd*, 127 Fed. Cl. 161 (2016).

Lastly, I have identified only two cases alleging RA as a vaccine injury in which entitlement was granted, and only one involving the flu vaccine. In *Campbell*, the court vacated the special master's denial of a claim that the flu vaccine caused seropositive RA. *Campbell v. Sec'y of Health & Hum. Servs.*, 97 Fed. Cl. 650, 673-74 (2011). The court found that the petitioner had proven the biologic plausibility of a theory that molecular mimicry and/or immune complexes could cause RA following flu vaccination and had submitted case reports and review articles supporting that theory. *Id.* at 673. The court also relied on the "strong temporal proximity between the vaccination and the onset of her symptoms, and the statements of her treating physicians[.]" *Id.* Federal Circuit decisions, however, have clarified that the proper burden of proof is preponderance, not biologic plausibility. *See Boatmon*, 941 F.3d at 1360 ("We have consistently rejected theories that the vaccine only 'likely caused' the injury and reiterated that a 'plausible' or 'possible' causal theory does not satisfy the standard.") (citing *Moberly*, 592 F.3d at 1322). Thus, to the extent it applies a plausibility standard for satisfaction of *Althen* prong one, *Campbell* is unpersuasive. It is also distinct from this case, in that it involved seropositive RA. 97 Fed. Cl. at 654; *see also H.J. v. Sec'y of Health & Hum. Servs.*, No. 11-301V, 2015 WL 6848357, at *9, 12 (Fed. Cl. Spec. Mstr. Nov. 6, 2015) (finding the petitioner had shown she was predisposed to RA by virtue of having preclinical RA and "overlap syndrome," and that the Tdap vaccine she received caused her RA).

VI. CONCLUSION

Upon careful evaluation of all the evidence submitted in this matter, including the medical records, the testimony, the experts' opinions, and the medical literature, I conclude that Petitioner has not shown by preponderant evidence that he is entitled to compensation under the Vaccine Act. **His petition is therefore DISMISSED. The clerk shall enter judgment accordingly.**[21]

IT IS SO ORDERED.

s/ Jennifer A. Shah
Jennifer A. Shah
Special Master

[21] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by each filing (either jointly or separately) a notice renouncing their right to seek review.