# In the United States Court of Federal Claims

**OFFICE OF SPECIAL MASTERS**

Filed: December 27, 2024

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| HENRY GAUVIN, | * | |
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| Petitioner, | * | No. 18-480V |
| | * | |
| v. | * | Special Master Young |
| | * | |
| SECRETARY OF HEALTH AND HUMAN SERVICES, | * | |
| | * | |
| Respondent. | * | |

*Ronald Craig Homer*, Conway, Homer, P.C., Boston, MA, for Petitioner.
*Alec Saxe*, U.S. Department of Justice, Washington, DC, for Respondent.

## DECISION ON ENTITLEMENT[1]

On April 2, 2018, Henry Gauvin ("Petitioner") filed a petition for compensation in the National Vaccine Injury Compensation Program ("the Program").[2] Pet., ECF No. 1. Petitioner alleged that the influenza ("flu") and pneumococcal conjugate ("Prevnar 13") vaccines he received on October 31, 2016, caused him to suffer from arthritis. *Id.* at 1.

After carefully analyzing and weighing all the evidence and testimony presented in this case in accordance with the applicable legal standards,[3] I find that Petitioner has failed to provide

[1] Because this Decision contains a reasoned explanation for the action taken in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' 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 ("the Vaccine Act" or "Act"). Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2018).

[3] While I have reviewed all of the information filed in this case, only those filings and records that are most relevant to the Decision will be discussed. *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 he does not explicitly reference such evidence in his decision.") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.*, 527 F. App'x 875, 884 (Fed. Cir. 2013) ("Finding

preponderant evidence that the flu vaccine he received on October 31, 2016, caused his arthritis. Accordingly, Petitioner is not entitled to compensation.

## I. Procedural History

Petitioner filed his petition on April 2, 2018. Pet. Petitioner filed medical records and an affidavit[4] on April 4, 2018. Pet'r's Exs. 1–24, ECF Nos. 8–11. Petitioner filed additional medical records on September 25, 2018. Pet'r's Exs. 26–28, ECF No. 16. Respondent filed his Rule 4(c) report, arguing compensation is not appropriate in this case, on March 7, 2019. Resp't's Rept., ECF No. 23.

On June 19, 2019, Petitioner filed Dr. Samar Gupta's expert report, curriculum vitae ("CV"), and supporting medical literature. Pet'r's Exs. 29–45, ECF Nos. 28–29. On October 17, 2019, Respondent filed Dr. Brendan Antiochos' expert report and CV. Resp't's Exs. A–B, ECF No. 34. Petitioner filed vaccine adverse event reporting system ("VAERS") results and supplemental expert report from Dr. Gupta on December 23, 2019. Pet'r's Exs. 46–47, ECF Nos. 37–38. The following day, Petitioner filed supplemental medical literature. Pet'r's Exs. 48–51, ECF No. 39. Respondent filed a supplemental expert report from Dr. Antiochos and supporting medical literature on March 27, 2020. Resp't's Exs. C, C Tabs 1–2, ECF No. 43. Petitioner filed additional medical records on April 2, 2020, and May 21, 2020. Pet'r's Exs. 52–54, ECF Nos. 44, 48.

Petitioner filed a motion for interim attorneys' fees and costs on June 30, 2020. ECF No. 52. Respondent responded to Petitioner's motion on July 14, 2020. ECF No. 54. On August 31, 2020, Petitioner filed a supplemental expert report from Dr. Gupta and medical literature. Pet'r's Exs. 56–61, ECF No. 56. Respondent filed a supplemental expert report from Dr. Antiochos and medical literature on December 21, 2020. Resp't's Exs. D, D Tab 1, ECF No. 61. Petitioner filed an additional expert report from Dr. Gupta and medical literature on February 11, 2021. Pet'r's Exs. 62–64, ECF No. 62. On May 24, 2021, Respondent filed an additional expert report from Dr. Antiochos. Resp't's Ex. E, ECF No. 64. On June 24, 2021, I issued a decision awarding Petitioner interim attorneys' fees and costs. ECFs No. 65.

On February 10, 2022, an entitlement hearing was scheduled for June 16-17, 2022. ECF No. 70. In April 2022, Petitioner filed his prehearing brief and additional medical records. Pet'r's Prehearing Br., ECF No. 74; Pet'r's Exs. 65–71, ECF No. 72. In May 2022, Respondent filed his prehearing brief and Petitioner filed additional medical records. Resp't's Prehearing Br., ECF No. 78; Pet'r's Exs. 72–73, ECF No. 76. Petitioner filed a prehearing reply brief on June 10, 2022. Pet'r's Prehearing Reply, ECF No. 88. That same day, Respondent filed additional medical literature. Resp't's Exs. A Tabs 1–15, E, ECF Nos. 90–93.

The entitlement hearing was held on June 16, 2022. Min. Entry, docketed June 16, 2022. On November 2, 2022, Petitioner filed additional medical literature and a posthearing brief. Pet'r's

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certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered.").

[4] Petitioner titled this as an affidavit, however, it is not notarized and therefore I will consider it as a declaration.

Exs. 77–78, ECF No. 103; Pet'r's Posthearing Br., ECF No. 105. On January 11, 2023, Respondent filed his posthearing brief. Resp't's Posthearing Br., ECF No. 108. Petitioner filed a posthearing reply brief on February 13, 2023. Pet'r's Posthearing Reply, ECF No. 110.

This matter is now ripe for consideration.

## II. Factual Background

### A. Medical Records

#### 1. Pre-vaccination Medical Records

Petitioner's pre-vaccination medical history is significant for hypertension, insulin dependent diabetes mellitus, obesity, hyperlipidemia, gastroesophageal reflux disease ("GERD"), fatty liver, and anxiety disorder. *See* Pet'r's Ex. 3 at 20, ECF No. 8-3. Petitioner also had a bilateral knee replacement in 2014. *Id.*

#### 2. Vaccination

On October 31, 2016, Petitioner received a flu vaccine during an annual wellness examination. Pet'r's Ex. 1 at 2, ECF No. 8-1. Later that day, Petitioner received the Prevnar 13 vaccine at a Rite Aid Pharmacy. *Id.* at 1–2. Petitioner was 80 years old at the time of vaccination. *See id.*

#### 3. Post-Vaccination Medical Records

On November 2, 2016, Petitioner had an endocrinology appointment. Pet'r's Ex. 4 at 44–45, ECF No. 8-4. No joint paints were noted. *Id.* On November 3, 2016, Petitioner had a podiatry appointment. Pet'r's Ex. 7 at 5, ECF No. 8-7. No joint complaints were noted. *Id.* A physical examination of the lower extremities did not reveal any joint inflammation or abnormalities. *Id.* The diagnosis was peripheral neuropathy.[5] *Id.*

Four days post vaccination, on November 4, 2016, Petitioner had a follow-up appointment for hypertension and hyperlipidemia with Laura Fitzgerald, Nurse Practitioner ("NP"), at Internal Medicine Group. Pet'r's Ex. 3 at 11. At this visit, Petitioner complained of a "sore throat" that started "[after] his flu shot." *Id.* He further complained that he "felt [achy]" after the flu and Prevnar 13 vaccines. *Id.* at 13. Petitioner reported nasal congestion, sinus tenderness, headache, and bothersome ears. *Id.* Petitioner denied joint pain and shortness of breath. *Id.* at 14. Physical examination revealed "right maxillary sinus tenderness." *Id.* Petitioner had normal range of

[5] Peripheral neuropathy or polyneuropathy is "neuropathy of several peripheral nerves simultaneously." *Polyneuropathy*, DORLAND'S MED. DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=40203 (last visited Nov. 18, 2024). Neuropathy is "a functional disturbance or pathologic change in the peripheral nervous system, sometimes limited to noninflammatory lesions as opposed to those of neuritis." *Neuropathy*, DORLAND'S MED. DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=33813 (last visited Nov. 18, 2024).

motion, no pain on motion, and no joint crepitations in all four extremities. *Id.* at 15. Petitioner was diagnosed with acute sinusitis[6] and prescribed azithromycin ("Z-Pak"). *Id.* at 15–16.

One week post vaccination, on November 7, 2016, emergency services were called to Petitioner's home where he was found lying on his den floor. Pet'r's Ex. 13 at 1, ECF No. 9-4. Petitioner stated he "had no strength when he went to stand up and slid himself down the couch to the floor." *Id.* He also stated he "had the flu shot last Tuesday and [had not] been feeling right since [he] saw his doctor on Friday and [his doctor] put him on antibiotics." *Id.*

Petitioner was transported to the emergency department ("ED") at William Backus Hospital where he was evaluated for "a several day history of increasing weakness and peripheral joint aches." Pet'r's Ex. 2 at 269, ECF No. 8-2. Petitioner reported that he received the flu and Prevnar 13 vaccines six days prior, and the day after, he "developed significant joint pain in his extremities" including bilateral knees, ankles, and wrists. *Id.* He reported swelling in these areas as well as redness which had since resolved and feeling malaise and generalized weakness. *Id.* Physical examination was normal. *Id.* at 271. The ED physician ruled out Guillain-Barré syndrome ("GBS") due to a normal neurological examination. *Id.* It was noted that Petitioner may have been "having some postimmunization joint pain." *Id.* Initial lab work was normal except for slightly decreased sodium levels. *Id.* at 271–74. Petitioner was admitted to the hospital with a clinical impression of weakness and hyponatremia. *Id.* at 264, 275. Subsequent labs revealed elevated C-reactive protein ("CRP") of 13.2 (normal range < 0.50) and elevated erythrocyte sedimentation rate ("ESR") of 74 (normal range 0–20). *Id.* at 272–73.

While hospitalized on November 8, 2016, Petitioner saw rheumatologist Dr. Sandeep Varma. *Id.* at 261. Dr. Varma noted Petitioner received the flu and Prevnar 13 vaccines "then ended up developing hand pain and swelling, knee pain and swelling, difficulty ambulating, redness in both hands, left greater than right." *Id.* The "[q]uestion was raised whether this was a reaction to immunization. [Petitioner] [a]lso received Zithromax in case there was an infection, but the joint pains got worse. Both hands started to swell up more. [Petitioner] started to have difficulty ambulating." *Id.* On Sunday, November 6, 2016, "he really felt worse and then was finally brought to the [ED]." *Id.* Dr. Varma also noted that Petitioner had both knees replaced and his ankles bothered him periodically "but it [was] the hands and stiffness that [was] the biggest issue." *Id.* Physical examination revealed severe synovitis[7] in the proximal and distal interphalangeal joints and synovitis in the metacarpophalangeal joints. *Id.* at 262. Petitioner's wrists were tender and swollen. *Id.* The differential diagnosis was "most likely reactive arthritis,[8]

[6] Sinusitis is "inflammation of a sinus, usually a paranasal sinus; it may be purulent or nonpurulent, acute or chronic." *Sinusitis*, DORLAND'S MED. DICTIONARY ONLINE, https://www.dorlandsonline.com /dorland/definition?id=45939 (last visited Nov. 18, 2024).

[7] Synovitis is "inflammation of a synovial membrane; it is usually painful, particularly on motion, and is characterized by a fluctuating swelling due to effusion within a synovial sac." *Synovitis*, DORLAND'S MED. DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=48576 (last visited Nov. 18, 2024). The synovial membrane is "the inner of the two layers of the articular capsule of a synovial joint, composed of loose connective tissue and having a free smooth surface that lines the joint cavity." *Membrana Synovialis Capsulae Articularis*, DORLAND'S MED. DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=88558 (last visited Nov. 18, 2024).

[8] Reactive arthritis is an "acute aseptic arthritis occurring after bacterial infection of the gastrointestinal or genital tracts or other distant site; it is often characterized by lower limb involvement, psoriasiform

which is generalized," or possibly new onset rheumatoid arthritis ("RA"),[9] polymyalgia, or gout.[10] *Id.* Petitioner was started on intravenous ("IV") Solu-Medrol (steroids). *Id.*

On November 9, 2016, Dr. Varma observed that Petitioner was walking, but noted that Petitioner's "left hand still bother[ed] him, which [was] still [] puffier than the right hand." *Id.* at 277. Dr. Varma noted that if Petitioner's immunoglobulin E ("IgE") came "back significantly elevated, or if the anti-histone [came] back significantly positive, consideration of drug-induced inflammatory arthritis that is the immunization that he got could be the underlying etiology." *Id.* at 278. Updated lab results revealed normal rheumatoid factor ("RF"), IgE, and normal (negative) tick-born disease analysis. *Id.* at 214, 267–68, 277. Petitioner's CRP remained elevated at 23 and his ESR was over 88. *Id.* at 260, 277. The plan was to continue steroids at a lower dose. *Id.* at 277.

Petitioner was discharged from the hospital on November 10, 2016. *Id.* at 259–260. The discharge diagnosis was "[a]cute inflammatory arthritis, likely reactive in nature." *Id.* at 259. The discharge summary noted GBS was ruled out but that there was "evidence of arthritis affecting his knees [and] both hands." *Id.* at 260. It also noted that Dr. Varma felt that Petitioner was "likely suffering from a reactive arthritis versus [RA]." *Id.* Petitioner had "improved throughout hospitalization" and was "able to ambulate without any help. Weakness and lethargy ha[d] completely resolved[,] and he [was] discharged home." *Id.*

Two days later, on November 12, 2016, emergency services were again dispatched to Petitioner's home where he was found seated upright, complaining of shortness of breath, "'achy' chest pain/tightness," and a productive cough. Pet'r's Ex. 14 at 5, ECF No. 9-5.

Upon arrival at the ED, Petitioner was evaluated for shortness of breath and malaise. Pet'r's Ex. 2 at 253. Notes indicated "that since his [Prevnar 13] [and] flu shot[s] a couple weeks ago, he ha[d] not felt quite right, and was recently admitted for hyponatremia . . . . [Petitioner] ha[d] become increasingly weak and short of breath over the past 24–48 hours." *Id.* During his prior admission, "he was thought to have reactive arthritis and serum sickness related to recent flu and [Prevnar 13] vaccine[s]." *Id.* at 225. Petitioner was again admitted to the hospital for low-grade fever, pneumonia, tachycardia, hyperglycemia, and respiratory distress. *Id.* During hospitalization, Petitioner was diagnosed with sepsis likely due to health care associated pneumonia. *Id.* at 236. An infectious disease workup by specialist Dr. Michael Rajkumar was unrevealing. *Id.* at 211–13.

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lesions of skin and mucous membranes, and eye lesions, but the defining factor is the temporal relation to infection." *Reactive Arthritis*, DORLAND'S MED. DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=58987 (last visited Nov. 18, 2024). "It usually . . . runs a self-limited but relapsing course. Most patients have increased levels of the histocompatibility antigen HLA-B27." *Id.*

[9] RA is "a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory changes in the synovial membranes and articular structures and by muscle atrophy and rarefaction of the bones. In late stages, deformity and ankylosis develop. The cause is unknown, but autoimmune mechanisms and virus infection have been postulated." *Rheumatoid Arthritis*, DORLAND'S MED. DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=58988 (last visited Nov. 18, 2024).

[10] Gout refers to "a group of disorders of purine metabolism, manifested by . . . recurrent acute inflammatory arthritis induced by crystals of monosodium urate monohydrate." *Gout*, DORLAND'S MED. DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=20868 (last visited Nov. 18, 2024).

Dr. Varma's impression was that Petitioner's fevers "very well could be related to his underlying autoimmune disease." *Id.* at 201. Petitioner was discharged on November 21, 2016, after being treated for suspected pneumonia. *Id.* at 197, 220. His discharge diagnosis was "[r]eactive arthritis versus seronegative [RA] or adult-onset [RA]." *Id.* at 196.

On November 28, 2016, Petitioner saw Dr. Varma for a follow-up of inflammatory arthritis "happening after having the flu shot and [Prevnar 13] shot." *Id.* at 49. During this time Petitioner was in a wheelchair and had "difficulty getting up from his wheelchair." *Id.* Petitioner also reported stiffness in his hands. *Id.* Dr. Varma's impression was inflammatory arthritis "starting after flu shot and [Prevnar 13] shot" and noted it "[v]ery well could be seronegative [RA]." *Id.*

The following day, on November 29, 2016, Petitioner returned to the ED for general weakness, recurrent fever, and cough. *Id.* at 189. After examination and lab workup, it was determined that Petitioner did not need to be admitted to the hospital. *Id.* at 192. The ED physician noted that he had discussed the case with Dr. Varma, who "believe[d] that [Petitioner] ha[d] a fever that [was] secondary to inflammatory[,] not infectious[,] process and he [] had an elevated sedimentation rate." *Id.* The ED clinical impression was "[i]mproving pneumonia with post inflammatory rheumatologic process." *Id.* at 195. Petitioner was sent to a rehabilitation facility. *Id.*

On November 30, 2016, a VAERS form was submitted by the Rite Aid Pharmacy where Petitioner received the Prevnar 13 vaccine. Pet'r's Ex. 11, ECF No. 9-2. The VAERS form stated that Petitioner received the vaccine and was hospitalized three days later for joint pain. *Id.* at 1. The VAERS report noted that Petitioner was "being treated for pneumonia." *Id.* at 1, 118–19, 124.

On December 1, 2016, Petitioner presented to the ED with complaints of weakness. Pet'r's Ex. 2 at 178. He denied fever and any pain except for pain in the right side of his neck. *Id.* Bloodwork showed "critically elevated" lactic acid levels. *Id.* at 172. Petitioner was admitted to rule out sepsis. *Id.* at 182. Petitioner's sepsis workup revealed negative results, and his lactic acidosis was thought to be possibly due to his medication. *Id.* at 165. Petitioner continued to have elevated inflammatory markers. *Id.* Dr. Varma felt Petitioner had had a flare of inflammatory arthritis. *Id.* at 170. Petitioner was discharged three days later, on December 4, 2016, back to the rehabilitation facility. *Id.* at 164.

The next day, on December 5, 2016, Petitioner again presented to the ED and was subsequently admitted to the hospital for high-grade fever and increased cough with shortness of breath. *Id.* at 76, 146. Intake notes indicated Petitioner had "been back and forth between the hospital and the nursing home since mid November and early November he had [two] vaccinations for [flu and] for [Prevnar 13] and since then ha[d] been having intermittent fevers and joint pains as well as joint swelling particularly in his hands." *Id.* at 146. The assessment was "presumed reactive arthritis after [Prevnar 13] vaccine." *Id.* at 147.

During his hospitalization, Petitioner saw Dr. Varma, whose impression was inflammatory arthritis "which started after vaccination and still [] persisted." *Id.* at 117. Petitioner was treated for pneumonia and possible reactive arthritis. *Id.* at 76. Petitioner also saw Dr. Jie Ying for an oncology evaluation. *Id.* at 142. Dr. Ying's history notes included that Petitioner was in his usual

state of health until he "developed profound weakness, fever, shaking chills, pain all over his body, and swollen hands" three days after receiving the flu and Prevnar 13 vaccines. *Id.* Since then, he had multiple hospitalizations and the current conclusion was that Petitioner's "fever and joint pain [was] seronegative inflammatory arthritis, which may be related to the said vaccines." *Id.* Dr. Ying's evaluation found no evidence of malignancy as the cause for Petitioner's constitutional symptoms. *Id.* at 144. His "[c]urrent suspicion" was "inflammatory arthritis that may be related to flu vaccine and [Prevnar 13 vaccine]." *Id.*

At discharge on December 19, 2016, Petitioner's inflammatory markers remained high, but were lower than at the time of admission. *Id.* at 76. Discharge notes reported several lab test results including a high ferritin level, which could also indicate inflammation. *Id.* at 77. Additionally, an extensive infectious disease workup was unrevealing. Petitioner's IgG antibodies for Epstein-Barr virus ("EBV") were positive, but IgM was negative. *Id.* at 76. Likewise, IgG antibodies for parvovirus were positive, but IgM was negative. *Id.* A tuberculosis test and a repeat Lyme test came back negative. *Id.* Petitioner's discharge diagnoses included healthcare-associated pneumonia, inflammatory arthritis, reactive arthritis (seronegative), fever, and sepsis on admission. *Id.* at 75. The plan was to return to the rehabilitation facility and follow up with Dr. Varma. *Id.* at 77.

On December 23, 2016, Petitioner presented to Dr. Varma for a follow-up appointment. *Id.* at 47. Petitioner's physical examination revealed tenderness in his hands, wrists, elbows, shoulders, knees, and ankles. *Id.* The synovitis in his hands had "definitely improved," and his strength was better. *Id.* Dr. Varma stated that Petitioner "[was] actually feeling good" and had "done really well." *Id.* The impression was reactive arthritis and inflammatory arthritis, which "most likely happened after immunization." *Id.* His prednisone was decreased. *Id.* Petitioner saw Dr. Varma again for follow-up on January 27, 2017. *Id.* at 45. Physical examination was the same as his last visit and Dr. Varma noted Petitioner was "looking better." *Id.* He also noted Petitioner's inflammatory markers were stable. *Id.*

On February 6, 2017, Petitioner had a pulmonary follow-up for his healthcare-associated pneumonia. Pet'r's Ex. 15 at 4, ECF No. 9-6. The notes from this visit reported a "severe reaction to [Prevnar 13] vaccine – reactive arthritis." *Id.* The diagnosis was clinically resolved healthcare-associated pneumonia. *Id.* at 5.

A follow-up with Dr. Varma on February 27, 2017, revealed Petitioner's ESR and CRP levels went up since the last visit. Pet'r's Ex. 2 at 42. Petitioner had "[n]o actual joint swelling" but felt "a little sluggish." *Id.* His prednisone was increased. *Id.*

On March 2, 2017, Petitioner consulted with Dr. Scott Stanat at Orthopedic Partners for bilateral knee pain and swelling. Pet'r's Ex. 20, ECF No. 10-2. Dr. Stanat performed a bilateral knee arthrocentesis to rule out infection. *Id.* at 10.

On March 10, 2017, Petitioner presented to the ED with a one-week history of worsening bilateral knee pain and swelling, as well as fever, chills, and shaking since that morning. Pet'r's Ex. 2 at 61. Petitioner also had a fever and reported he could not work due to the pain. *Id.* The ED physician noted Petitioner's history of reactive arthritis to previous vaccination." *Id.* at 68. Dr.

Varma was consulted and noted Petitioner "had similar episodes in the past whenever he trie[d] to taper down the [] steroids." *Id.* at 69. A chest X-ray revealed bibasilar atelectasis and Petitioner's lactic acid levels were elevated. *Id.* at 61. Petitioner was admitted for sepsis and bilateral knee pain. *Id.* The sepsis workup was unrevealing. *Id.* at 52. During hospitalization, IV Solu-Medrol helped, and Petitioner stayed afebrile. *Id.* at 54. Petitioner was discharged on March 13, 2017, with a diagnosis of "[i]nflammatory arthritis status post vaccination." *Id.* at 51.

Petitioner returned to Dr. Varma for a follow-up appointment on March 20, 2017. *Id.* at 40. Petitioner denied any fever, chills, or chest pain but did mention that his knees and hands felt stiff, and his hands were swollen. *Id.* Dr. Varma noted that Petitioner's presentation appeared more akin to RA that "[s]tarted after his [Prevnar 13] injection." *Id.*

On April 4, 2017, at another follow-up appointment, Dr. Varma's impression was inflammatory arthritis, most likely RA, that "[m]ay have been triggered by immunization." *Id.* at 38. Petitioner's inflammatory markers were still elevated. *Id.*

Approximately six months post vaccination, on May 15, 2017, Petitioner continued to have swelling, stiffness, and pain in his joints. Pet'r's Ex. 3 at 117.

**B. Petitioner's Declaration**

Petitioner executed a declaration on March 26, 2018. Pet'r's Ex. 24 at 6, ECF No. 11-1. Petitioner averred that prior to the October 31, 2016 flu and Prevnar 13 vaccines, he considered himself "generally healthy." *Id.* at ¶ 1. He stated his diabetes, hypertension, hyperlipidemia, and low back pain were "well-controlled and did not severely affect [his] daily life." *Id.* Additionally, he recovered well from his knee replacements and subsequently went to the gym regularly where he walked on the treadmill and swam. *Id.* at ¶ 2.

The next "several days" after his October 31, 2016 flu and Prevnar 13 vaccines, Petitioner began to feel ill; he was achy, sweating, and felt lethargic. *Id.* at ¶ 4. He also started experiencing pain and swelling in his joints. *Id.* at ¶ 5. Petitioner mentioned some of these symptoms to his primary care physician at a follow-up appointment on November 4, 2016. *Id.* at ¶ 4. Soon, his joint pain worsened, and it became difficult for him to walk. *Id.* at ¶ 6. He also had pain in both wrists, knees, and ankles. *Id.* He stated his hands "were stiff and swollen, and looked like balloons." *Id.*

On November 7, 2016, Petitioner had a fever and was "sweating profusely." *Id.* at ¶ 6. He was transported to the hospital where he saw Dr. Varma. *Id.* at ¶¶ 6–7. Dr. Varma told him he was suffering from arthritis. *Id.* at ¶ 7. In the coming days, Petitioner became sick; while his joint pain "improved a little," he developed a cough, fever, and shortness of breath. *Id.* at ¶ 8. He was hospitalized and continued on steroids. *Id.* at ¶¶ 8–9.

Petitioner reported he continued to be in and out of the hospital and nursing facility with arthritis flares, fevers, and cough. *Id.* at ¶10. He was also hospitalized for suspected sepsis and his steroid dosage was increased. *Id.* Petitioner returned home from the hospital on January 4, 2017, and he had a nurse, occupational therapist, and physical therapist come to his house. *Id.* at ¶ 11.

When Dr. Varma tried decreasing Petitioner's dosage of steroids, Petitioner noticed his joints became stiffer and walking became more difficult. *Id.* at ¶ 12. Accordingly, Dr. Varma told him to increase his dose of steroids. *Id.*

Petitioner ended up going back to the hospital in March 2017 for fever, weakness, and inability to walk. *Id.* at ¶ 13. He averred he also had swollen and painful knees. *Id.* Dr. Varma increased Petitioner's steroids and prescribed additional medication. *Id.* Petitioner continued to see Dr. Varma in the coming months but continued to "suffer stiffness in [his] hands and knees, and tenderness in some of [his] other joints." *Id.* at ¶ 14. He started monthly injections, which he responded well to. *Id.* at ¶¶ 15–16. Whenever he decreased his prednisone, his RA would flare up. *Id.* at ¶16.

In September 2017, Petitioner increased his prednisone dosage. *Id.* at ¶ 17. As of the date Petitioner executed his declaration, Petitioner averred he remains on multiple medications to treat his RA and he still struggles to rise from a seated position. *Id.* While he can walk independently, he still experiences some mobility issues due to knee pain and swelling. *Id.*

## III. Experts

### A. Expert Backgrounds and Qualifications

#### 1. Petitioner's Expert, Samar Gupta, M.D.

Dr. Gupta submitted four expert reports and testified at the entitlement hearing. Pet'r's Ex. 29, ECF No. 28-1; Pet'r's Ex. 47, ECF No. 38-1; Pet'r's Ex. 56, ECF No. 56-1; Pet'r's Ex. 62, ECF No. 62-1; Tr. 3, 9.

Dr. Gupta is board certified in rheumatology and internal medicine. Tr. 10. He completed medical school in India and subsequently completed an internal medicine residency at Wayne State University in Detroit, Michigan, and a rheumatology fellowship at the University of Michigan School of Medicine. *Id.* Dr. Gupta is currently an Associate Professor in the Rheumatology Division at the University of Michigan. *Id.* In this role, he sees patients four days per week and regularly diagnoses RA. Tr. 11. He also has an administrative role as a Clinical Chief at Ann Arbor VA Medical Center where he oversees training and clinical operations. *Id.* Dr. Gupta conducts research surrounding RA. *Id.* He has authored or co-authored several publications. Pet'r's Ex. 55 at 4–5, ECF No. 50-1.

#### 2. Respondent's Expert, Brendan Antiochos, M.D.

Dr. Antiochos submitted four expert reports and testified during the entitlement hearing. Resp't's Ex. A, ECF No. 34-1; Resp't's Ex. C, ECF No. 43-1; Resp't's Ex. D, ECF No. 61-1; Resp't's Ex. E, ECF No. 64-1; Tr. 3, 87.

Dr. Antiochos is board certified in rheumatology. Tr. 89. He received his M.D. from Dartmouth College in Hanover, New Hampshire. *Id.*; Resp't's Ex. B at 1, ECF No. 34-2. Thereafter, he completed an internal medicine residency at Oregon Health & Science University

and a rheumatology fellowship at Johns Hopkins University School of Medicine. Tr. 89; Resp't's Ex. B at 1. Currently, Dr. Antiochos is an Assistant Professor in the Rheumatology Division at Johns Hopkins. Tr. 87–88. He also works in the outpatient and inpatient setting where he works with patients who have something relevant to rheumatology. Tr. 88, 90. Dr. Antiochos also conducts laboratory research "to understand the mechanisms responsible for the development of systemic rheumatic diseases." Resp't's Ex. A at 1. He has authored or co-authored numerous publications. Resp't's Ex. B at 1–3.

### B. Expert Reports and Testimony

#### 1. Petitioner's Expert, Dr. Gupta

##### a. Diagnosis

Dr. Gupta explained that "inflammatory arthritis[11] happens due to an inflammatory reaction to a foreign antigen, such as a component of a bacterial or virus particle." Pet'r's Ex. 62 at 1, ECF No. 62-1. However, he acknowledged the exact etiology of RA is unknown. Tr. 35–36; Pet'r's Ex. 57 at 1, ECF No. 56-2 ("[T]he precise cause of RA remains uncertain.").[12]

Dr. Gupta testified that RA is a chronic inflammatory autoimmune disease that mainly affects the synovial joints of the body, symmetrically. Tr. 16. RA "most typically presents as polyarticular disease and with a gradual onset, but some patients can present with acute onset with intermittent or migratory joint involvement or with monoarticular disease." Pet'r's Ex. 31 at 1, ECF No. 28-3.[13] "Most patients show fluctuation of disease activity over periods lasting weeks to months." *Id.* at 10. The initial clinical onset includes joint involvement such as swelling and pain, which can affect the ability to perform activities of daily living, as well as systemic symptoms. *Id.* In one-third of patients, acute onset is associated with aching, myalgia, fatigue, low-grade fever, weight loss, and depression. *Id.* at 1, 3. Morning stiffness is also common in the insidious onset of RA. *Id.* at 1–2.

A diagnosis of RA can be made when the following clinical features are present: positive RF and/or anti-citrullinated peptide ("anti-CCP"), inflammatory arthritis involving three or more joints, elevated levels of CRP or ESR, duration of symptoms more than six weeks, and other diseases with similar clinical features have been excluded. Pet'r's Ex. 32 at 4, ECF No. 28-4.[14] When symptoms have been present for less than six weeks, they could be "due to an acute viral polyarthritis rather than to RA. The longer the symptoms persist, the more likely the diagnosis of RA becomes." *Id.* at 2. Seronegative RA is the diagnosis when patients have symptoms consistent

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[11] Dr. Gupta noted that inflammatory arthritis and RA are sometimes used interchangeably. Tr. 32.

[12] Gary S. Firestein, *Etiology and Pathogenesis of Rheumatoid Arthritis*, *in* KELLEY AND FIRESTEIN'S TEXTBOOK OF RHEUMATOLOGY 1115 (Gary S. Firestein et al. eds.,10th ed., 2017).

[13] P.J.W. Venables, *Clinical Manifestations of Rheumatoid Arthritis*, UPTODATE https://www.uptodate.com/contents/clinical-manifestations-of-rheumatoid-arthritis (last updated Oct. 12, 2017).

[14] P.J.W. Venables, *Diagnosis and Differential Diagnosis of Rheumatoid Arthritis*, UPTODATE https://www.uptodate.com/contents/diagnosis-and-differential-diagnosis-of-rheumatoid-arthritis (last updated Aug. 23, 2018).

with RA but without the presence of antibodies (RF and anti-CCP) in the blood.[15] *Id.* at 5; Pet'r's Ex. 29 at 5; Tr. 19. Dr. Gupta testified that patients also often have constitutional systems such as fatigue. Tr. 16.

Dr. Gupta testified that Petitioner developed inflammatory arthritis, which was later diagnosed as seronegative RA. Tr. 16. Petitioner's treating rheumatologist Dr. Varma maintained a diagnosis of RA for several years and Dr. Gupta agreed with this diagnosis. Tr. 16, 77. Dr. Gupta reasoned Petitioner had subjective and objective signs of inflammation in his joints including hands, wrists, knees, and feet. Pet'r's Ex. 29 at 4. Petitioner's lab work, including ESR and CRP, indicated systemic inflammation. *Id.*; Tr. 20. Petitioner's response to steroids was also "very consistent with [RA]." Tr. 19; Pet'r's Ex. 29 at 5. For example, Petitioner responded well to Methotrexate, which Dr. Gupta testified is an RA-specific drug. Tr. 20. Additionally, Dr. Gupta opined Petitioner qualifies for an RA diagnosis under the 1987 and 2010 criteria for the classification of RA, determined by a score-based algorithm allotting a certain number of points for the number of joints involved, serology, and duration of symptoms.[16] Tr. 18; Pet'r's. Ex. 29 at 6 (citing Pet'r's Ex. 33 at 5, ECF No. 28-5;[17] Pet'r's Ex. 34 at 6, ECF No. 28-6).[18] Further, Dr. Gupta testified that alternative diagnoses, including reactive arthritis, were ruled out and Petitioner was instead documented as having and treated for seronegative RA. Tr. 30–31.

**b. Causation**

Dr. Gupta opined that RA is an autoimmune condition and he explained autoimmunity generally. Tr. 21. The factors that influence the development of an autoimmune condition, such as inflammatory arthritis, are genetic predisposition ("first hit") and an environmental trigger ("second hit"). Tr. 21–22. He opined infections and vaccinations have been identified as environmental triggers in the development of autoimmunity. Tr. 22; Pet'r's Ex. 29 at 16; Pet'r's Ex. 74 at 1, ECF No. 80-1 ("[T]he onset of rheumatic disease after vaccination signifies that the vaccine may trigger persistent autoimmune response in genetically predisposed individuals.").[19] Dr. Gupta was unable to "tell which individual vaccine could have precipitated [Petitioner's] RA," but opined "the concomitant administration of [f]lu and Prevnar [13] most likely contributed by presenting a high antigenic load." Pet'r's Ex. 29 at 6. According to Dr. Gupta, flu vaccines have been implicated in inflammatory arthritis like RA. *Id.* at 7 (citing Pet'r's Ex. 42 at 2, ECF No. 29-4);[20] Tr. 23.

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[15] Seropositive RA is the diagnosis when RF and anti-CCP are present. Tr. 19. The pathogenesis is the same for both seropositive and seronegative RA. Tr. 74.

[16] Dr. Gupta testified that some kinds of arthritis resolve in less than six weeks. Tr. 18.

[17] Frank C. Arnett et al., *The American Rheumatism Association 1987 Revised Criteria for the Classification of Rheumatoid Arthritis*, 31 ARTHRITIS RHEUMATISM 315 (1988).

[18] Daniel Aletaha et al., *2010 Rheumatoid Arthritis Classification Criteria*, 62 ARTHRITIS RHEUMATISM 2569 (2010).

[19] Gurjot Basra et al., *Rheumatoid Arthritis and Swine Influenza Vaccine: A Case Report*, 2012 CASE REPTS. RHEUMATOLOGY 785028.

[20] Normi Bruck et al., *Transient Oligoarthritis of the Lower Extremity Following Influenza B Virus Infection: Case Report*, 8 PEDIATRIC RHEUMATOLOGY (2010).

To explain how vaccinations lead to the development of autoimmunity and RA, Dr. Gupta proposed several mechanisms, with the most prominent being molecular mimicry and nonspecific immune system activation. Pet'r's Ex. 29 at 6–7; *see also* Pet'r's Ex. 74 at 2 ("Vaccine-triggered autoimmune reactions can involve two different processes: 'antigen specific' in which vaccine products share epitope mimicry and 'antigen nonspecific' in which the vaccine activates autoreactive T cells that release cytokines.").

Dr. Gupta testified that molecular mimicry is the most accepted mechanism for autoimmune disease and inflammatory arthritis.[21] Tr. 26, 46. "Molecular mimicry is one mechanism by which infectious agents (or other exogenous substances) can trigger an immune response against autoantigens." Pet'r's Ex. 29 at 7. "A susceptible host acquires an agent that has antigens that are immunologically similar to the host antigens but differ sufficiently to induce an immune response when presented to T cells." *Id.* The immune system then mistakenly attacks its own tissue. Tr. 21, 23, 54, 69. When this occurs, it can cause damage to tissues, such as synovial tissues, and start the inflammatory process in joints. Tr. 25.

Next, Dr. Gupta described the immune complex theory and its relation to molecular mimicry. Tr. 24, 69. He wrote that immune complexes are "a combination of the viral antigens and the antibodies induced by the antigen." Pet'r's Ex. 29 at 7. In molecular mimicry, not only are the antibodies trying to kill the virus, "it's also targeting the similar . . . peptide sequence in the synovium. [I]t's a combination of things, so not only [is] our immune system [] attacking directly the synovium, but it is also could be attaching to the virus particle and those virus particles with the antibody, which is immune complex." Tr. 69. The body is supposed to get rid of those immune complexes. Tr. 69–70. But in certain cases, instead of the body getting rid of the immune complexes, "they go on to go deposit on the synovium and they attach there and [the] body can't get rid of it." Tr. 70. Dr. Gupta testified "those are the abnormal immune complexes causing inflammation in the joints or inflammation in the blood vessels." *Id.*; *see also* Tr. 24 (explaining immune complexes can settle into joint tissue and start an inflammatory abnormal reaction that results in perpetual synovial inflammation and arthritis). Dr. Gupta opined molecular mimicry works in tandem with the immune complex theory which expedites and perpetuates the process. *Id.* In other words, the body is not identifying the correct antigen to attach to the antibody, and at the same time, the body is unable to dispose of immune complexes. *Id.*

Dr. Gupta also described the mechanism of polyclonal activation of B cells and how it is implicated in the development of autoimmune rheumatologic disease.[22] Tr. 26–27; Pet'r's Ex. 29 at 7. He opined all three of the mechanisms can work in concert in the development of autoimmunity. Tr. 27.

[21] Dr. Gupta testified there are some models of inflammatory arthritis that are similar to RA and "we take our ideas [for the pathogenic mechanisms of RA] from there." Tr. 46. Molecular mimicry is the most accepted theory in that regard. *Id.*

[22] While Dr. Gupta implicated polyclonal activation of B cells, his primary mechanism focused on molecular mimicry and immune complexes. Therefore, I will not discuss this mechanism in depth.

Relevant to flu specifically, Dr. Gupta cited Sun et al.[23] which found the flu virus "shares some peptide sequence" with synovial tissue. Tr. 26. Dr. Gupta admitted he did not find homogenous peptides from the flu vaccine. Tr. 60. But he extrapolated the homology from the virus to the vaccine and opined "there could be a homology between the vaccine containing the virus particles and the peptide sequence in the synovium of the joint." *Id.* He admitted it is unknown whether the homologous peptide chain from the flu virus is actually present in the vaccine. *Id.*; *see also* Pet'r's Ex. 62 at 1 (stating the vaccines at issue are not live but, without providing specifics, stating they do share components of the original bacteria or virus). Dr. Gupta cited Giat and Lidar[24] which discussed that infectious agents have been suggested as triggering RA. Pet'r's Ex. 38, ECF No. 28-10. In relation to vaccinations, the authors stated that "since immunizations tend to mimic infectious agents, they are able to initiate an autoimmune process in a similar manner." *Id.* at 2. But Dr. Gupta did not explain how the vaccinations at issue here, can mimic infectious agents.

However, he cited case reports for the proposition that vaccination, including flu vaccination, has been implicated in the development of inflammatory arthritis. Tr. 31; Pet'r's Ex. 56 at 1 (citing Pet'r's Ex. 58, ECF No. 56-3 (describing a 44-year-old female who developed a flu-like illness as well as pain, stiffness, and swelling in the hands, wrists, ankles, and knees three days after a flu vaccine and was diagnosed with RA for fulfilling five of the seven criteria);[25] Pet'r's Ex. 74 (describing a 33-year-old female who experienced transient joint pain one week after a seasonal flu vaccine and one month later, after receiving an H1N1 vaccine, developed more severe joint pain one week later (eventually diagnosed as RA for fulfilling most of the criteria)); Pet'r's Ex. 59, ECF No. 56-4 (describing six patients with joint symptom onset (eventually diagnosed with RA) one to 20 days following hepatitis B vaccination, but concluding a causal relationship between the two cannot be easily established)).[26]

Medical literature explains that RA usually develops gradually "but some patients can present with acute onset with intermittent or migratory joint involvement." Pet'r's Ex. 31 at 1, 3 (describing "progressive joint damages"); *see also* Pet'r's Ex. 32 at 2 ("[T]he longer the symptoms persist, the more likely the diagnosis of RA becomes."). In some patients, the onset of RA is episodic "with several joint areas being affected sequentially for hours to days, alternating with symptom-free periods that may last from days to months." Pet'r's Ex. 31 at 2. These patients have similar predisposing genetic risk factors as patients with the typical presentation of RA. *Id.*

Dr. Gupta acknowledged that typical or classic RA develops over months or years. Tr. 47; Pet'r's Ex. 57 at 2 ("The initiation of RA begins years before the onset of clinical symptoms.").

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[23] Jian Sun et al., *Superior Molecularly Altered Influenza Virus Hemagglutinin Peptide 208-317 Inhibits Collagen-Induced Arthritis by Inducing CD4+ Treg Cell Expansion*, 64 ARTHRITIS & RHEUMATISM 2158 (2012).

[24] Eitan Giat & Merav Lidar, *Vaccinations in Rheumatoid Arthritis*, *in* VACCINES AND AUTOIMMUNITY 233 (Yehuda Shoenfeld et al. eds., 1st ed. 2015).

[25] M.A. Brown & J.V. Bertouch, *Rheumatic Complications of Influenza Vaccination*, 24 AUSTL. NZ J. MED. 572 (1993). This is also cited as Pet'r's Ex. 41, ECF No. 29-3, and Resp't's Ex. A, Tab 7, ECF No. 95-6.

[26] J.F. Maillefert et al., *Rheumatic Disorders Developed After Hepatitis B Vaccination*, 38 RHEUMATOLOGY 978 (1999).

But according to Dr. Gupta, RA is a disease of dysregulation in innate and adaptive immunity which is why in atypical cases it may begin quickly, days after an inciting injury such as vaccination, and continue to evolve over weeks. Pet'r's Ex. 56 at 1; *see also* Tr. 47–48. He testified that immune-mediated reactions can occur from a few days to several months of the "second hit." Tr. 30. Whereas the genetic component (the "first hit") begins years before the onset of clinical symptoms. Pet'r's Ex. 57 at 2.

The first hit "involves certain specific genes that can lead to the production of pathogenic antibodies that bind to modified proteins, help break tolerance, and lead to autoreactivity." *Id.* "It is likely that the earliest phases are marked by repeated environmental stress, either through toxic exposures or activation of innate immunity." *Id.* Dr. Gupta explained that not all patients who are predisposed to RA will develop the clinical disease unless the second hit occurs. Tr. 54. The second hit is marked by repeated environmental toxic exposure or the activation of innate immunity. Pet'r's Ex. 57 at 1–2 ("Innate immune responses such as complement activation or Toll-like receptor activation can contribute to the initiation and perpetuation of synovial inflammation."). He testified the timing of the second hit is different for each particular insult. Tr. 54, 57. For example, a slow insult such as continued smoking may cause RA to develop insidiously. Tr. 57. But in this case, Dr. Gupta testified, the second hit was different in that the vaccination "reciprocat[ed] it very quickly," in part because of molecular mimicry. Tr. 58–59. He added that while the insult here is different than regularly seen in individuals that would develop RA more gradually, it is shown in the case reports that even after four to five days, "we can see the viral antigen in the synovial tissue homing in." *Id.*

After the hearing, Petitioner filed additional medical literature to help explain how a process that usually takes months to years to develop could happen in a matter of days. *See* ECF No. 103. Dr. Gupta did not file a supplemental expert report explaining these articles.

Tanaka et al.[27] studied collagen-induced arthritis ("CIA"), with similarities to RA in both cause and pathology, in a mouse model of RA. Pet'r's Ex. 77 at 1, ECF No. 103-1. They discussed the importance of inflammatory mediators/cells in the development of clinical disease, including proinflammatory cytokines, such as TNF-α, IL-1β, IL-6 and IL-17, that induce and amplify inflammation and subsequent tissue destruction in the joint synovium. *Id.* at 1–2. In this study, Type II collagen-immunized mice were injected with lipopolysaccharide ("LPS"), a bacterial toxin known to accelerate CIA.[28] *Id.* at 1. Testing for proinflammatory cytokines demonstrated increased levels of TNF-α just six hours after LPS injection, with levels returning to baseline on day three (after the onset of arthritis by day three) and increasing again on day six in parallel with the further development of arthritis. *Id.* at 3. Increased levels of IL-6 and other proinflammatory cytokines were also demonstrated on day one. *Id.* Testing of joint synovium demonstrated infiltration of leukocytes, proliferation of synovial cells and edema on day one, reaching maximum and sustained levels from day three to day seven. *Id.* Manifestation of clinical disease, specifically paw swelling, was observed on day two, reaching its peak on day seven, then declining until day 17. *Id.* The authors compared the clinical symptoms in the study to human RA. *Id.* at 7. The authors concluded

[27] Shinji Tanaka et al., *Lipopolysaccharide Accelerates Collagen-Induced Arthritis in Association with Rapid and Continuous Production of Inflammatory Mediators and Anti-Type II Collagen Antibody*, 57 MICROBIOLOGY IMMUNOLOGY 445 (2013).

[28] Petitioner did not explain how LPS compares to a vaccine.

that LPS "induces arthritis in [collagen injected]-immunized mice and that the onset of that arthritis is preceded by rapid and continuous production of inflammatory mediators and anti-CII antibody." *Id.* at 8. They further conclude, "[i]t is possible that the rapid and continuous production of inflammatory mediators and autoantibodies is the mechanism by which infections exacerbate RA." *Id.* at 9; *see also* Pet'r's Ex. 61 at 8, ECF No. 56-6 (finding that chronic inflammation in RA "may result from persistent viral antigens").[29]

Hayden et al.[30] examined cytokine responses after flu infection. Pet'r's Ex. 78 at 1, ECF No. 103-2. They measured "the levels of IL-1beta, IL-2, IL-6, IL-8, IFN-alpha, TGF-beta, and TNF-alpha in nasal lavage fluid, plasma, and serum obtained serially from 19 volunteers experimentally infected with [flu] A/Texas/36/91 (H1NI) and correlated these levels with various measures of infection and illness severity." *Id.* at 1. The authors found that levels of IL-6 and TNF-α were found in nasal fluid and plasma circulation by day two, with TNF-α peaking by day three in plasma circulation and day four in nasal fluid. *Id.* Petitioner's brief argued the seasonal flu vaccine is typically comprised of flu A and flu B variants and that the 2015-2016 seasonal flu vaccine included the flu A H1N1 variant involved in Hayden et al. Pet'r's Posthearing Br. at 11–12 (citing Pet'r's. Ex. 64 at 14, ECF No. 62-3).

According to Dr. Gupta, Petitioner experienced the onset of joint symptoms, attributable to his inflammatory arthritis, approximately five to seven days post vaccination. Tr. 19; Pet'r's Ex. 29 at 8. Petitioner received the subject vaccines on October 31, 2016. *See* Tr. 28. Shortly after vaccination, Petitioner had several doctor appointments, including the November 4, 2016 primary care visit, in which he did not complain of joint pain nor were objective signs of joint inflammation or swelling observed on examination. *Id.* It was not until November 7, 2016, that Petitioner presented to the ED with swelling and pain in multiple joints and objective signs of inflammation. Tr. 29. At that time, a diagnosis of inflammatory arthritis was made. *Id.* Based on these records, Dr. Gupta concluded that Petitioner's subjective joint complaints started five to seven days post vaccination, and objective evidence of inflammatory arthritis was recorded seven days post vaccination (November 7 ED presentation). *Id.*

Applying the factors that influence the development of an autoimmune condition, Dr. Gupta implied that Petitioner had been predisposed to RA all his life, "and then he got this environmental trigger or viral component and then it precipitated his [RA] quickly. Tr. 54–55. He posited that if Petitioner did not suffer an insult or second hit, he may not have developed the clinical presentation of RA. Tr. 55.

Dr. Gupta described Petitioner's case of RA as one of "explosive onset." Pet'r's Ex. 29 at 4; Tr. 47. However, because "immune-mediated responses can occur several days up to a couple of months following a triggering event," Dr. Gupta opined Petitioner's onset is within a medically acceptable timeframe. Pet'r's Ex. 29 at 8; Pet'r's Ex. 56 at 1.

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[29] E.R. Walker et al., *Ultrastructural Study of Avian Synovium Infected with an Arthrotropic Reovirus*, 20 ARTHRITIS & RHEUMATISM 1269 (1977).

[30] F.G. Hayden et al., *Local and Systemic Cytokine Responses During Experimental Human Influenza A Virus Infection. Relation to Symptom Formation and Host Defense*, 101 J. CLINICAL INVESTIGATION 643 (1998).

Lastly, Dr. Gupta opined there is no alternative cause for Petitioner's RA. Regarding infection, Dr. Gupta explained that while Petitioner had a "very slightly low white [blood cell] count," prior to vaccination, "people are not predisposed to infection unless they drop significantly more than [Petitioner's] white [blood cell] count." Tr. 49; *see* Pet'r's Ex. 2 at 335 (showing low white blood cell count from September 23, 2016), 337 (showing low white blood cell count from October 29, 2016). Moreover, Petitioner was worked up by infectious disease specialists and no infection was found. Tr. 49. As to the bacterial sinusitis Petitioner was diagnosed with on November 4, 2016, four days post vaccination, Dr. Gupta disagreed with this diagnosis. Tr. 83. He reasoned that a fever is usually associated with bacterial sinusitis and that was not present in this case. Tr. 80. Additionally, a white blood cell count would be expected to be higher with bacterial sinusitis. *Id.* He explained Petitioner's symptoms that day were nonspecific and there was no sign of infection. Tr. 79, 82. While Petitioner was prescribed antibiotics that day, Dr. Gupta maintained that even if the antibiotics cleared up a hypothetical infection, that hypothetical infection still could not cause Petitioner's RA because if a bacteria clears up so quickly with antibiotics, it would not be able to mount an immune reaction because an infection must persist for "some days" to mount that kind of reaction. Tr. 66; *see also* Tr. 61(discussing the same reasons for why sepsis cannot be the trigger).

### 2. Respondent's Expert, Dr. Antiochos

#### a. Diagnosis

Dr. Antiochos defined RA as "an inflammatory disease, . . . an immune-mediated disease characterized by inflammation in and around the joints." Tr. 96. It is a condition "where the immune system is abnormally activated in joints." *Id.* While there are risk factors for RA, Dr. Antiochos opined that no specific cause for RA has been identified. Tr. 97–98, 112. He explained the symptoms of RA build gradually, usually "over weeks to months." Tr. 98; 112, 118. Dr. Antiochos also described reactive arthritis which he contrasted with RA in that reactive arthritis is "linked to a specific infection which is then identified." Tr. 117.

According to Dr. Antiochos, Petitioner has a form of inflammatory arthritis.[31] Tr. 99, 114; Resp't's Ex. A at 4. He conceded that over time, Petitioner met the classification criteria for RA. Tr. 116. He added, "[t]here is clear documentation of clinical signs of inflammatory arthritis in a pattern consistent with RA." Resp't's Ex. A at 2; *see also* Tr. 108. For example, Petitioner's symptoms lasted for several months which satisfies the symptom duration criterion. Resp't's Ex. A at 2. He opined, however, that while Petitioner "may satisfy classification criteria for RA, there are some elements of [Petitioner's] presentation that are worth noting, as they do not fit well with a diagnosis of [RA]." *Id.* at 3, 9; Tr. 114. For example, Dr. Antiochos noted that while the tempo of RA can vary from patient to patient, Petitioner's "explosive" onset is not typical for RA. Tr. 99. Further he noted the first several months of Petitioner's clinical course were also "quite unusual" for RA, including septic physiology,[32] hypotension, and frequent hospitalization. Tr. 99, 101–02; Resp't's Ex. A at 3. "These elements of [Petitioner's] case raise concern respect to the diagnosis

[31] Dr. Antiochos explained that Dr. Varma sometimes used the term reactive arthritis and sometimes used the term RA to describe Petitioner's condition. Tr. 109. Dr. Antiochos opined that Dr. Varma was approaching Petitioner "therapeutically as someone with an inflammatory arthritis." *Id.*

[32] Dr. Antiochos acknowledged that septic arthritis was eventually ruled out. Tr. 118.

of RA." Resp't's Ex. A at 3. Dr. Antiochos considered giant cell arteritis, antisynthetase syndrome and Still's disease as alternate diagnoses, but did not opine any of these as Petitioner's more likely than not diagnosis. *Id*. at 3–4. Instead, he proposed that "most rheumatologists would note that [Petitioner's] course includes elements that fit with these more highly inflammatory conditions, as opposed to RA." *Id.* at 4.

**b. Causation**

Dr. Antiochos understood Dr. Gupta's causation theory to rely on the temporal relationship, between the vaccination and onset of symptoms, and molecular mimicry. Tr 104; Resp't's Ex. A at 3–4. He agreed that the pathogenesis of rheumatic disease "likely involves multiple 'hits' to the immune system, separated in time." Resp't's Ex. D at 2. But he opined the pathogenesis is still complex. *Id.* Deane[33] wrote that "the long period of autoimmunity prior to the onset of clinically-apparent RA suggests that the genes and environmental factors that influence RA are acting years prior to the first swollen joint." Resp't's Ex. D, Tab 1 at 8, ECF No. 61-2. And "since these factors have not been well studied in preclinical RA, it is as of yet unclear if these environmental factors trigger RA-related autoimmunity, or propagate it." *Id.*

Dr. Antiochos conceded that molecular mimicry is "one of the theories that's been put forth as possibly playing a role in rheumatic diseases" and is "widely discussed" in the rheumatology community. Tr. 106–07, 130. However, he opined there is no evidence that the flu and/or Prevnar 13 vaccinations could cause RA via molecular mimicry or any other mechanism. *See* Tr. 107, 114; Resp't's Ex. A at 7, 9. He explained that molecular mimicry would not work as the mechanism here because it does not fit the timeline of events. Tr. 120. Molecular mimicry involves the adaptive immune system and to fully engage that process, meaning "respond to a new stimulus and develop a de novo autoimmune disease," Dr. Antiochos testified that would take weeks rather than a couple of days. Tr. 130, 132–33. Additionally, he stated that an individual's immune system is involved long before they develop clinical symptoms of RA. Tr. at 131–32.

Further, Dr. Antiochos explained that in a viral infection, the "replicating virus activates the immune system, causing recruitment of immune cells and expression of inflammatory mediators at the site of viral replication." Resp't's Ex. D at 2. Thus, while he would expect antiviral immunity to occur rapidly, he opined that is not the case here because the vaccines given were not live and thus not capable of replication. *Id.*

During the hearing, Dr. Antiochos was questioned about the studies he referenced and how many of them involved an exacerbation of diseases after vaccination. Tr. 127. He acknowledged that many do involve exacerbation, but explained that some studies, such as Bengtsson et al.[34] studied whether vaccines can cause new onset RA. *Id.* (citing Resp't's Ex. A, Tab 9, ECF No. 95-8); *see also* Resp't's Ex. E at 2. Bengtsson et al. conducted a large population-based epidemiological investigation and found no increased risk for RA after vaccination. Resp't's Ex.

[33] Kevin D. Deane, *Preclinical Rheumatoid Arthritis (Autoantibodies): An Updated Review*, 16 CURRENT RHEUMATOLOGY REPS. 419 (2014).

[34] Camilla Bengtsson et al., *Common Vaccinations Among Adults Do Not Increase the Risk of Developing Rheumatoid Arthritis: Results from the Swedish EIRA Study*, 69 ANNALS RHEUMATIC DISEASES 1831 (2010).

A, Tab 9 at 1. Dr. Antiochos used other large-scale studies like Bengtsson et al. to support his position and relied heavily on epidemiological evidence to conclude vaccinations do not cause RA. He testified that epidemiological studies are the standard for "definitively establishing a relationship between any exposure and disease." Tr. 124. He admitted this means scientific certainty. *Id.*

Dr. Antiochos preferred this epidemiological evidence over isolated case reports in forming his opinions. *Id.*; Resp't's Ex. D at 1 (opining "[c]ase reports do not undermine [epidemiological] studies" and "do not prove causality between any given exposure and the development of a disease"); Resp't's Ex. E at 2. Brown and Bertouch explained that while flu vaccination is associated with myalgia, only case reports exist involving association with rheumatic diseases. Pet'r's Ex. 58 at 1. They explained that while case reports, often relying on close temporal relationships between vaccination and the onset of rheumatic diseases, suggest a causal relationship, they do not prove it. *Id.* But the authors noted that resolution of rheumatic conditions within nine months of vaccinations is more consistent with a vaccine reaction than an idiopathic autoimmune disease. *Id.* Dr. Antiochos added that if we accept case reports over epidemiologic studies to prove causation between an exposure and an outcome such as Dr. Gupta, then we could conclude that "absolutely anything that [Petitioner] ingested, breathed, or touched on October 31, 2016, was the cause of his arthritis." Resp't's Ex. E at 1.

When discussing the relationship between risk and causation, Dr. Antiochos testified that he is more inclined to give credence to chronic risk factors in rheumatic disease, such as smoking, rather than acute factors, such as infection or vaccination, because "there's more information on those available." Tr. 135.

As to timing in relation to vaccination, Dr. Antiochos opined Petitioner's onset of his inflammatory arthritis was "very rapid," between one and seven days after receiving the vaccines. Tr. 109; Resp't's Ex. A at 9. He believed that the medical records were inconsistent as to onset reporting and may suggest an even shorter timeframe of one to three days after vaccination. Tr. 109; Resp't's Ex. A at 5; Resp't's Ex. D at 1. When Petitioner presented to the ED on November 7, 2016, history indicated that Petitioner had the flu and Prevnar 13 vaccines and the "following day," developed joint pain. Resp't's Ex. A at 5 (quoting Pet'r's Ex. 2 at 270). Upon admission to the hospital later that day, notes indicated that Petitioner developed joint pain two days after the vaccinations. *Id.* (citing Pet'r's Ex. 2 at 265). And upon evaluation from oncology, Dr. Yang documented that Petitioner's onset was three days after vaccination. *Id.* at 5–6 (citing Pet'r's Ex. 2 at 143). Dr. Antiochos wrote that three different physicians documented an onset of one to three days post vaccination and opined this timeframe would be "less consistent" with the mechanism proposed by Dr. Gupta. *Id.* at 6; Resp't's Ex. C at 3 n.1 (opining this timeframe is inconsistent with a "'reactive' mechanism theory implicating the vaccines as a cause of [] [P]etitioner's inflammatory arthritis").

Finally, Dr. Antiochos pointed out that leukopenia was identified in Petitioner's lab results two days before vaccination. Resp't's Ex. A at 4, 9. Additionally, he noted Petitioner's white blood cell count was low prior to vaccination. *Id.* at 4. According to Dr. Antiochos, this raises the "possibility of an infection precipitating [Petitioner's] presentation." *Id.* at 9. However, he did not opine this alternative cause as more likely than not.

## IV. Applicable Legal Standards

To receive compensation under the Vaccine Act, a petitioner must demonstrate either that: (1) the petitioner suffered a "Table injury" by receiving a covered vaccine and subsequently developing a listed injury within the time frame prescribed by the Vaccine Injury Table set forth at § 300aa-14, as modified by 42 C.F.R. § 100.3; or (2) that the petitioner suffered an "off-Table injury," one not listed on the Table, as a result of him receiving a covered vaccine. *See* § 300aa-11(c)(1)(C); *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1319–20 (Fed. Cir. 2006). In this case, Petitioner must prove by preponderant evidence that he suffered a Table injury or that his injury was caused-in-fact or significantly aggravated by a Table vaccine.

### A. Causation

To establish causation-in-fact, a petitioner must demonstrate by a preponderance of the evidence that the vaccine was the cause of the injury. § 300aa-13(a)(1)(A). A petitioner is required to prove that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321–22 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)).

In the seminal case of *Althen v. Sec'y of Health & Hum. Servs.*, the Federal Circuit set forth a three-pronged test used to determine whether a petitioner has established a causal link between a vaccine and the claimed injury. *See* 418 F.3d 1274, 1278–79 (Fed. Cir. 2005). The *Althen* test requires petitioners to set forth: "(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. To establish entitlement to compensation under the Program, a petitioner is required to establish each of the three prongs of *Althen* by a preponderance of the evidence. *Id.* "[C]lose calls regarding causation are resolved in favor of injured claimants." *Id.* at 1280. Further, evidence used to satisfy one prong of the test may overlap to satisfy another prong. *Capizzano*, 440 F.3d at 1326.

Under the first prong of *Althen*, a petitioner must offer a scientific or medical theory that answers in the affirmative the question: "can the vaccine[] at issue cause the type of injury alleged?" *Pafford v. Sec'y of Health & Hum. Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004), *mot. for rev. den'd*, 64 Fed. Cl. 19 (2005), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2006). 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 theory must only be "legally probable, not medically or scientifically certain." *Id.* at 548–49. Petitioners are not required to identify "specific biological mechanisms" to establish causation, nor are they required to present "epidemiologic studies, rechallenge[] the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities." *Capizzano*, 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280). Scientific and "objective confirmation" of the medical theory with additional medical documentation is unnecessary. *Althen*, 418 F.3d at 1278–81; *see also Moberly*, 592 F.3d at 1322. However, as the

Federal Circuit has made clear, "simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof." *LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) (citing *Moberly*, 592 F.3d at 1322). Indeed, the Federal Circuit has "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." *Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, (Fed. Cir. 2019) (citing *Moberly*, 592 F.3d at 1322 and *LaLonde*, 746 F.3d at 1339). Rather, "[a] petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case." *Moberly*, 592 F.3d at 1322. In general, "the statutory standard of preponderance of the evidence requires a petitioner to demonstrate that the vaccine more likely than not caused the condition alleged." *LaLonde*, 746 F.3d at 1339.

Furthermore, 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 claim. *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357,1361 (Fed. Cir. 2000). The Supreme Court's opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.* requires that courts determine the reliability of an expert opinion before it may be considered as evidence. 509 U.S. 579 (1993). However, in the Vaccine Program, the *Daubert* factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66–67 (2010) ("[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."); *see also 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)). Under *Daubert*, the

> 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 are "meant to be helpful, not definitive." *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 151 (1999). The factors do not "constitute 'a definitive checklist or test'" and may be applied differently depending on the facts of a particular case. *Id.* at 150 (quoting *Daubert*, 509 U.S. at 593).

"In short, the requirement that an expert's testimony pertain to 'scientific knowledge' establishes a standard of evidentiary reliability." *Daubert*, 509 U.S. at 590 (citation omitted). Thus, for Vaccine Act claims, 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. 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 v. Sec'y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 743 (2009) (quoting *Gen.*

*Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)); *see also D'Tiole v. Sec'y of Health & Hum. Servs.*, No. 15-085V, 2016 WL 7664475, at *24 (Fed. Cl. Spec. Mstr. Nov. 28, 2016) (stating that the Vaccine Act "require[s] a chain of reliable propositions supporting [a] petitioner's theory[]").

Under the second prong of *Althen*, a petitioner must prove that the vaccine actually did cause the alleged injury in a particular case. *See Pafford*, 2004 WL 1717359, at *4; *Althen*, 418 F.3d at 1279. 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; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner does not meet this obligation by showing only a temporal association between the vaccination and the injury; instead, the petitioner "must explain *how* and *why* the injury occurred." *Pafford*, 2004 WL 1717359, at *4 (emphasis in original). The special master in *Pafford* noted petitioners "must prove [] both that her vaccinations were a substantial factor in causing the illness . . . and that the harm would not have occurred in the absence of the vaccination." *Id.* (citing *Shyface*, 165 F.3d at 1352). A reputable medical or scientific explanation must support this logical sequence of cause and effect. *Hodges v. Sec'y of Health & Hum. Servs.*, 9 F.3d 958, 961 (Fed Cir. 1993) (citation omitted). Nevertheless, "[r]equiring epidemiologic studies . . . or general acceptance in the scientific or medical communities . . . impermissibly raises a claimant's burden under the Vaccine Act and hinders the system created by Congress . . . ." *Capizzano*, 440 F.3d at 1325–26. "[C]lose calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F.3d at 1280.

In Program cases, contemporaneous medical records and the opinions of treating physicians are favored. *Capizzano*, 440 F.3d at 1326 (citing *Althen*, 418 F.3d at 1280). Indeed, when reviewing the record, a special master must consider the opinions of treating physicians. *Capizzano*, 440 F.3d at 1326. This is because "treating physicians are likely to be in the best position to determine whether 'a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" *Id.* In addition, "[m]edical records, in general, warrant consideration as trustworthy evidence. The records contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium. These records are also generally contemporaneous to the medical events." *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). However, there is no "presumption that medical records are accurate and complete as to all of the patient's physical conditions." *Kirby v. Sec'y of Health & Hum. Servs.*, 997 F.3d 1378, 1383 (Fed. Cir. 2021) (finding that a special master must consider the context of a medical encounter before concluding that it constitutes evidence regarding the absence of a condition). While a special master must consider these opinions and records, they are not "binding on the special master or court." § 300aa-13(b)(1). Rather, when "evaluating the weight to be afforded to any such . . . [evidence], the special master . . . shall consider the entire record . . . ." *Id.*

In determining the accuracy and completeness of medical records, special masters will consider various explanations for inconsistencies between contemporaneously created medical records and later given testimony. The Court of Federal Claims has identified four such explanations for explaining inconsistencies: (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. *La Londe v. Sec'y of Health & Hum. Servs.*, 110 Fed. Cl. 184, 203 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014).

To satisfy the third *Althen* prong, a petitioner must establish a "proximate temporal relationship" between the vaccination and the alleged injury. *Althen*, 418 F.3d at 1281. This "requires preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). Typically, "a petitioner's failure to satisfy the proximate temporal relationship prong is due to the fact that onset was too late after the administration of a vaccine for the vaccine to be the cause." *Id.* However, "cases in which onset is too soon" also fail this prong; "in either case, the temporal relationship is not such that it is medically acceptable to conclude that the vaccination and the injury are causally linked." *Id.*; *see also Locane v. Sec'y of Health & Hum. Servs.*, 685 F.3d 1375, 1381 (Fed. Cir. 2012) ("[If] the illness was present before the vaccine was administered, logically, the vaccine could not have caused the illness.").

Although a temporal association alone is insufficient to establish causation, under the third prong of *Althen*, a petitioner must also show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d at 1278. The special master cannot infer causation from temporal proximity alone. *See Thibaudeau v. Sec'y of Health & Hum. Servs.*, 24 Cl. Ct. 400, 403–04 (1991); *see also Grant*, 956 F.2d at 1148 ("[T]he inoculation is not the cause of every event that occurs within the ten[-]day period . . . [w]ithout more, this proximate temporal relationship will not support a finding of causation." (quoting *Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1983))).

A petitioner who satisfies all three prongs of the *Althen* test has established a prima facie showing of causation. *Hammitt v. Sec'y of Health & Hum. Servs*., 98 Fed. Cl. 719, 726 (2011). A petitioner who demonstrates by a preponderance of the evidence that he suffered an injury caused by vaccination is entitled to compensation unless the respondent can demonstrate by a preponderance of the evidence that the injury was caused by factors unrelated to the vaccination. *See Althen*, 418 F.3d at 1278; *Knudsen*, 35 F.3d at 547. In such a case, the government must not merely prove the existence of an alternative cause, but that such an alternative actually caused the injury. *Knudsen*, 35 F.3d at 549. Consequently, when and if the petitioner establishes a prima facie case, the burden then shifts to the government to prove that an alternative cause, unrelated to the administration of the vaccine, was the "sole substantial factor" in causing the alleged injury. *de Bazan*, 539 F.3d at 1354; *see also Hammitt*, 98 Fed. Cl. at 726 (explaining that the respondent's burden is to show that the "factor unrelated" was the "sole substantial factor" in causing the injury). Additionally, a factor unrelated "may not include 'any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness or condition.'" § 300aa-13(a)(2); *see also Doe v. Sec'y of Health & Hum. Servs.*, 601 F.3d 1349 (Fed. Cir. 2010) (stating that an idiopathic diagnosis cannot be a "factor unrelated," as it is idiopathic).

## V. Discussion

### A. Diagnosis

As Federal Circuit precedent establishes, in certain cases it is appropriate to determine the nature of an injury before engaging in the *Althen* analysis. *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1346 (Fed. Cir. 2010). Here, the parties dispute diagnosis, and so it is appropriate to first resolve that issue.

I find that Petitioner has presented preponderant evidence that he suffered from RA for the purpose of his causation-in-fact claim. Petitioner's treating physicians maintained a diagnosis of inflammatory arthritis for years. *See, e.g.*, Pet'r's Ex. 2 at 259 (The November 10, 2016 discharge diagnosis was acute inflammatory arthritis, "likely reactive in nature"), 34 (assessing Petitioner with inflammatory arthritis, most likely RA in 2017), 36 (same), 38 (same). Dr. Varma noted in April of 2018 that Petitioner had "underlying inflammatory arthritis in the distribution of rheumatoid [that] started after vaccination". Pet'r's Ex. 26 at 443, ECF No. 16-1. I find Dr. Varma's diagnosis persuasive and reliable as he was Petitioner's treating rheumatologist. Notably, he considered alternative diagnoses, but maintained a diagnosis of RA for years. Moreover, the expert rheumatologists in this case agreed Petitioner has a form of inflammatory arthritis. Both experts agreed with Dr. Varma that Petitioner has signs consistent with RA, although Dr. Antiochos described the presentation as atypical.

Furthermore, Petitioner meets the diagnostic criteria and classification for RA. A diagnosis of seropositive RA can be made when the following clinical features are present: positive RF and/or anti-CCP, inflammatory arthritis involving three or more joints, elevated levels of CRP or ESR, duration of symptoms more than six weeks, and other diseases with similar clinical features have been excluded. A diagnosis of seronegative RA can be made when the same clinical features are present but without positive RF and anti-CCP. It is undisputed that the type of RA at issue is seronegative as Petitioner did not have positive RF and/or anti-CCP.

Here, Petitioner met all of the factors for a seronegative RA diagnosis. Petitioner had subjective and objective signs of inflammation in his joints including his hands, wrists, knees, and feet. Petitioner's lab work, including elevated ESR and CRP, indicated systemic inflammation. Diseases with similar clinical features were excluded by treating physicians. *See* Pet'r's Ex. 2 at 271 (ruling out GBS), 262 (considering polymyalgia and gout but not maintaining those as diagnoses), 249 (dropping reactive arthritis from the differential diagnoses), 182 (revealing a negative sepsis workup). And Petitioner's symptoms have lasted for more than six weeks. Dr. Gupta added that Petitioner's response to steroids and RA-specific drugs is also persuasive in finding a diagnosis of RA. *See* Tr. 19–20; Pet'r's Ex. 29 at 5.

Dr. Antiochos agreed Petitioner's presentation satisfied classification criteria for RA. The features that he characterized as atypical included the tempo of onset, septic physiology, and Petitioner's frequent hospitalization. While the diagnosis factors include symptomology present for six weeks, there is no filed literature that includes the tempo of onset of RA. The literature merely states that the longer the symptoms are present, the more easily a diagnosis of RA can be made. Petitioner's symptoms ultimately did last for well over six weeks. Onset of Petitioner's RA

is discussed more in prong three. As to the septic physiology, Dr. Antiochos agreed that septic arthritis was ruled out as a diagnosis. Lastly, none of the filed literature excluded RA as a diagnosis when there were frequent hospitalizations. Dr. Antiochos opined that it was unusual without support for his conclusion. I find this unpersuasive to overcome the other factors met in this case. After consideration of the medical record and the expert's analysis, I find that Petitioner presented preponderant evidence that he suffered from RA.

### B. *Althen* Prongs

#### 1. *Althen* Prong One – Medical Theory

Drs. Gupta and Antiochos agreed that RA, a form of inflammatory arthritis, is an autoimmune disease. They also agreed that molecular mimicry can be a reliable causation theory for some autoimmune diseases. Dr. Gupta opined that in Petitioner's case, molecular mimicry is the primary mechanism but added that it works in concert with the immune complex theory. He explained that in some circumstances, the body is unable to identify the correct antigen to attach to the antibody (molecular mimicry) and at the same time, the body is unable to dispose of immune complexes (immune complex theory) and therefore can result in attacking and depositing on the synovial tissues. According to him, these mechanisms work together to result in a faster immune response process.

Petitioner did not provide peptide homology for his molecular mimicry theory. Dr. Gupta did not identify a relevant peptide from the flu vaccine that could cause a cross reaction. He instead identified a peptide chain from a flu virus that could potentially cross-react with the body and extrapolated homology to the flu vaccine. He also admitted that it is unknown whether the peptide chain that shares a homologous peptide chain from the flu virus is actually present in the vaccine. *See* Tr. 60; Pet'r's Ex. 62 at 1. Program petitioners sometimes present homologies between vaccine components and human tissues, but such is not required to present preponderant support for a theory of molecular mimicry. However, there must be some form of preponderant evidence that a cross reaction between the vaccine and body part at issue can occur. Indeed, "Petitioners cannot simply invoke the concept of molecular mimicry and call it a day. . . . Rather, they need to offer *reliable* and persuasive medical or scientific evidence of some kind . . . that suggests the vaccine components could interact with self structures as maintained." *Johnson v. Sec'y of Health & Hum. Servs.*, No. 14-254V, 2018 WL 2051760, at *26 (Fed. Cl. Spec. Mstr. Mar. 23, 2018). Other cases in the Program where petitioners' experts unsuccessfully identified the relevant proteins and affected body systems have failed because the disease pathogenesis was not consistent with the identified immune response. *See Jewell v. Sec'y of Health and Hum. Servs.*, No. 11-138V, 2016 WL 5404165 (Fed. Cl. Spec. Mstr. Aug. 29, 2015) (petitioners failed to prove that cytokine activity is capable of impacting the brain's 5-HT system in the ways proposed by petitioners' experts); *see also Dougherty v. Sec'y of Health and Hum. Servs.*, No. 15-1333V, 2018 WL 3989519 (Fed. Cl. Spec. Mstr. July 5, 2018) (finding petitioner failed to provide evidence that antibodies reacting to hypocretin-2 receptors would only damage these receptors if located in a limited region in the brain, despite their widespread presence in other regions of the body).

Petitioners filed post-hearing studies that discussed the upregulation of several proinflammatory cytokines in response to LPS, a bacterial toxin that has been connected to

arthritis. Dr. Gupta did not explain how LPS is comparable to either of the vaccines that Petitioner received or why a murine reaction can illustrate vaccine-induced RA in humans. In fact, Dr. Gupta did not provide any context for the additional literature that was filed. Petitioner's biological mechanism must include a but-for causation theory that begins with vaccination and ends with disease. Petitioner's theory begins with an environmental trigger that Dr. Gupta identified as the vaccine in this case, but he did not provide evidence that this "trigger" causes pathological cross-reactivity to occur (molecular mimicry) or that immune complexes are settling in synovial tissue to cause chronic arthritis. Indeed, there is little, if any, discussion by Dr. Gupta of how the chronic and slowly progressive nature of RA is consistent with the acute nature of cross-reactivity. He described Petitioner's presentation as an explosive symptom onset but did not contextualize that distinction in his discussion of disease progression.

Dr. Gupta relied on case reports to try to show an association between vaccination and RA. None, however, discussed mechanisms for how a vaccine can cause RA. Respondent's expert Dr. Antiochos opined there is no evidence of the flu and/or Prevnar 13 vaccines causing RA. First, he disagreed with extrapolating evidence from flu virus to flu vaccine because the vaccines in this case were not live and thus not capable of the same responses as a replicating virus. I agree with Dr. Antiochos here in that there is not preponderant evidence of how the vaccines at issue have the same effect on the body as a self-replicating, live virus. Additionally, Petitioner did not explain how the flu vaccine is synonymous to another identified analogy, a bacterial infection. Dr. Antiochos further took issue with Dr. Gupta relying entirely on case reports. Dr. Antiochos expressed a preference for epidemiological studies, and noted the absence of any study that found causal associations between vaccinations and RA. However, petitioners need not and are not expected to present epidemiological evidence for a claim to be successful.

There are several reasoned Vaccine Program cases that have discussed the association of vaccination to RA.[35] However, most denied entitlement. *See, e.g.*, *Bean-Sasser v. Sec'y of Health & Hum. Servs.*, No. 13-326V, 2016 WL 1649355 (Fed. Cl. Spec. Mstr. April 5, 2016) (denying entitlement to a petitioner alleging the hepatitis B vaccine caused her to manifest symptoms of RA approximately 11 hours later); *Hock v. Sec'y of Health & Hum. Servs.*, No. 17-168V, 2020 WL 6392770 (Fed. Cl. Spec. Mstr. Sept. 30, 2020) (denying entitlement because petitioner did not preponderantly establish he had RA beginning one day after vaccination; his symptoms were instead far more consistent with a transient, reactive arthritis brought on by serum sickness that, even if vaccine-induced, resolved within two months); *Moran v. Sec'y of Health & Hum. Servs.*, No. 16-538V, 2021 WL 4853544 (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).

I have previously denied entitlement in a flu/seropositive RA case. *Parker v. Sec'y of Health & Hum. Servs.*, No. 14-979V, 2019 WL 3425297 (Fed. Cl. Spec. Mstr. June 24, 2019). While I found molecular mimicry could explain how the flu vaccine can cause the development of RA, I found petitioner failed to meet *Althen* prongs two and three. *Id.* at *28–29. Petitioner in that case identified a specific viral antigen that is present in the flu vaccine and then identified the human autoantigen collagen with a similar structure that could cross react. *Id.* at *25–27. This case differs from *Parker*, because here, Petitioner does not explain how cross-reaction could occur.

[35] While decisions of other special masters are not binding, they provide helpful guidelines in understanding the specific contours of causal theories involving how a vaccine might result in RA.

Also comparable to the case at bar is *McGuiness*, in which the petitioner alleged the Prevnar 13 vaccine caused him to develop seronegative RA two weeks post vaccination. *McGuinness v. Sec'y of Health & Hum. Servs.*, No. 17-0954V, 2021 WL 5292343 (Fed. Cl. Spec. Mstr. Oct. 20, 2021). Dr. Gupta was also the expert for petitioner in that case. In *McGuiness*, Dr. Gupta proposed molecular mimicry as a theory for how the Prevnar 13 vaccine can cause RA. *Id.* at *4. Dr. Gupta also described an alternative mechanism for causation—nonspecific activation of the immune system. *Id.* at *5. He did not discuss immune complexes. He did not identify any homology and relied mainly on case reports. *Id.* at *4–5. The special master denied compensation for failing to satisfy all three *Althen* prongs. *Id.* at *20.

But some Program cases have found petitioners successful in RA claims. *See e.g., H.J. v. Sec'y of Health & Hum. Servs.*, No. 11-301V, 2015 WL 6848357 (Fed. Cl. Spec. Mstr. Nov. 6, 2015) (finding petitioner established that her immune system was predisposed to autoimmune diseases such as RA, and that the Tdap vaccine significantly aggravated her pre-existing RA). In *Campbell v. Sec'y of Health & Hum. Servs.*, the Court of Federal Claims found the petitioner had successfully demonstrated that the flu vaccine could cause RA. 97 Fed. Cl. 650 (2011). The petitioner in *Campbell* received a flu vaccine and started to experience limb pain and other symptoms three days later. *Id* at 653. The Court overturned the special master's denial of entitlement, finding that a causation theory of molecular mimicry[36] leading to a cross-reaction manifesting as seropositive RA was plausible, and thus (because there was also treater support for the conclusion that the vaccine related to the injury) reliable. *Id.* at 664. This has limited persuasiveness regarding the science it relied upon as well as the evidentiary standard it employed because subsequent determinations by the Federal Circuit in *Boatmon* and *Moberly* clarified that mere plausibility does not satisfy reliability or establish preponderance pursuant to the first prong of *Althen*.

It is important to note that much of the evidence presented by Petitioner here only involved the flu vaccination. Petitioner alleged that the flu and Prevnar 13 vaccinations caused his arthritis. Without medical or expert evidence of the vaccines working in tandem or simultaneously, there is no articulated scenario where, for example, the combination of the two vaccines prompts some pathogenic response. Consequently, I cannot find that Petitioner has satisfied his burden that the Prevnar 13 vaccine is wholly or partly responsible for his arthritis without a biological mechanism that speaks specifically to the Prevnar 13 vaccine.

At the conclusion of the hearing in this case, I noted on the record that Dr. Gupta had presented a plausible theory that "could work." Tr. 137. However, I explained that the rapid onset in this case is inconsistent with both experts' opinion that this disease usually develops gradually. Additionally, I noted that Dr. Gupta's mechanism is well supported as it relates to the rheumatological process of RA. However, he did not, during the hearing, and has not subsequently, explained an immunological pathology that starts with the flu or Prevnar 13 vaccines and ends with RA. Ultimately, Petitioner had provided some evidence, but not preponderant evidence, i.e. that it is more likely than not, that one or both of Petitioner's vaccines caused his condition. Petitioner was given an opportunity to close that gap post hearing, but the articles provided were

[36] Petitioner's expert in *Campbell* also proposed the theory of immune complexes. *Campbell*, 97 Fed. Cl. at 659–60.

not analogous to this case or instructive to vaccine-induced RA. And Dr. Gupta provided no additional context for this evidence. Therefore, Petitioner is in the same position as he was post hearing with evidence of possibility and not probability.

Therefore, after consideration of the evidence, I do not find that Petitioner has presented preponderant evidence of a sound and reliable explanation that the flu vaccine can cause RA. He has failed to meet his burden pursuant to *Althen* prong one.

### 2. *Althen* Prong Three – Temporal Relationship

A discussion of *Althen* prong two turns to some extent on the question of onset of Petitioner's arthritis. Therefore, I address *Althen* prong three before moving to *Althen* prong two.

Because *Althen* prong three coincides with *Althen* prong one, Petitioner's inability to meet his burden demonstrating how the flu and/or Prevnar 13 vaccines can cause RA effectively precludes him from being able to meet his burden under the third *Althen* prong. Thus, because I found that Petitioner did not offer a sound and reliable theory of causation, he cannot demonstrate that his condition arose in a medically acceptable timeframe pursuant to that theory. Nonetheless, Petitioner's showing with respect to the third *Althen* prong is still deficient.

Dr. Gupta opined that the breakdown of Petitioner's immune tolerance, the response to that breakdown, and the manifestation of that immune attack that resulted in the clinical presentation of joint pain, occurred over a period of five to seven days. Dr. Antiochos commented on the medical records suggesting a shorter timeframe of one to three days after vaccination. For the reasons discussed below, I find preponderant evidence that Petitioner's RA started as early as three days post vaccination.

Petitioner received the vaccines on October 31, 2016. Petitioner reported to emergency services on November 7, 2016, that he had not been feeling right since the previous Friday (November 4). He presented with subjective complaints of joint pain and there were also objective observations of inflammation, including elevated ESR and CRP. Petitioner was evaluated for a self-reported "several day history" of weakness and joint aches. Pet'r's Ex. 2 at 269. When Petitioner first saw Dr. Varma on November 8, 2016, it was reported that Petitioner's joint pain got worse on Sunday, November 6. Accordingly, it is logical to find Petitioner's onset was prior to November 6. This timeframe is also consistent with his initial account at the ED where he characterized it as several days. Several days before November 7, 2016, would be approximately November 3 or 4.

Prior to Petitioner's trip to the ED, Petitioner presented to his primary care office on November 4, 2016, with complaints of achiness. While the experts did not explicitly discuss this, the medical literature includes aching, myalgia, and fatigue in the clinical onset of RA. *See, e.g.*, Pet'r's Ex. 31 at 1, 3. This further supports a finding that Petitioner's RA started as early as three days post vaccination. The next question is whether there is "preponderant proof that the onset of symptoms occurred within a time frame for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." *de Bazan*, 539 F.3d at 1352.

It is undisputed between the parties' experts that there are two factors involved in the development of an autoimmune disease such as RA: a genetic predisposition ("first hit") and an environmental trigger ("second hit"). And it is undisputed that the genetic component is likely present long before, even years before, the clinical manifestations of the disease. As to the second hit, Dr. Gupta opined immune-mediated responses can occur from a few to several days after a triggering event. Dr. Antiochos opined molecular mimicry involves the adaptive immune system and requires more than a couple of days to activate. *See* Tr. 132–33.

While Dr. Gupta attempted to explain how a second hit such as vaccination can produce a response faster than a second hit such as smoke exposure, the medical literature suggests that it is the continuous, persistent exposure that can lead to RA. *See, e.g.*, Pet'r's Ex. 77 at 9 (concluding "[i]t is possible that the rapid and continuous production of inflammatory mediators and autoantibodies is the mechanism by which infections exacerbate RA"); Pet'r's Ex. 61 at 8 (noting that chronic inflammation in RA "may result from persistent viral antigens"). Here, Petitioner received the vaccines and there is no evidence of continuous exposure. Despite mentioning that Petitioner had received flu vaccinations in the past, Dr. Gupta did not explain how receiving a subsequent vaccination can lead to the clinical presentation of RA days later, consistent with the medical literature.

The post-hearing literature filed in this case did not complement Petitioner's prong three position. Tanaka et al. showed manifestation of clinical disease on day two, peaking on day seven, post injection. Hayden et al. found increased levels of IL-6 and TNF-α by day two, with TNF-α peaking by day three, post H1N1 infection. However, as stated earlier, these articles are not analogous to this case or instructive to flu vaccine-induced RA.

Other Program cases have found a matter of days to be too short to be a medically acceptable timeframe for the onset of RA post vaccination. *Moran*, 2021 WL 4853544, at *34 (finding three days too short for a molecular mimicry theory); *see also Monzon v. Sec'y of Health & Hum. Servs.*, No. 17-1055V, 2021 WL 2711289, at *24 (Fed. Cl. June 2, 2021). In *Parker*, I found petitioner failed to satisfy the third *Althen* prong because petitioner's expert inconsistently opined on the onset. *Parker*, 2019 WL 3425297, at *27–28. He ultimately concluded with an onset of one day post vaccination which I found too short to be medically appropriate with the proposed mechanism. *Id.* at * 28–29.

I find the temporal association is not medically appropriate given the mechanism of injury. Dr. Gupta did not explain how his suggested five to seven days is an acceptable timeframe for his theory, let alone how a shorter timeframe of three days post vaccination can be acceptable. Accordingly, Petitioner has failed to meet his burden as to the third *Althen* prong.

### 3. *Althen* Prong Two – Actual Causation

The strongest evidence in this case of actual causation comes from Petitioner's physicians, mainly his treating rheumatologist, Dr. Varma. Petitioner's treating physicians related Petitioner's arthritis back to his vaccinations. *See, e.g.*, Pet'r's Ex. 2 at 278 (Dr. Varma considering "drug-induced inflammatory arthritis that is the immunization that he got could be the underlying

etiology"), 261 (Dr. Varma questioning whether Petitioner's symptoms were a reaction to immunization), 222–23 (noting Petitioner was in his usual state of health until he received the flu and Prevnar 13 vaccines), 214 (describing Petitioner as a patient who ended up with inflammatory arthritis after vaccines), 142 ("The final conclusion of this extensive workup was that his fever and joint pain is seronegative inflammatory arthritis, which may be related to the said vaccines."), 144 ("Current suspicion is inflammatory arthritis that may be related to flu vaccine and [Prevnar 13 vaccines]."), 47 (Dr. Varma assessing Petitioner with inflammatory arthritis most likely related to immunization), 38 (same), 65 (noting "reactive arthritis related to previous vaccination").

Despite the fact that Dr. Varma articulated a belief that vaccination might be related to Petitioner's arthritis, he did not state how or why it could have been the cause. Rather, these statements appear to be based on the proximity and temporal association between vaccination and Petitioner's arthritis. A "treating physician's recognition of a temporal relationship does not advance the analysis of causation." *Isaac v. Sec'y of Health & Hum. Servs.*, No. 08-601V, 2012 WL 3609993, at *26 (Fed. Cl. Spec. Mstr. July 30, 2012), *aff'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 Fed. App'x 999 (Fed. Cir. 2013). And a temporal relationship between a vaccine and an injury, standing alone, does not constitute preponderant evidence of vaccine causation. *Veryzer v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 344, 356 (2011) (explaining that a "temporal relationship alone will not demonstrate the requisite causal link and that petitioner must posit a medical theory causally connecting the vaccine and injury."), *aff'd*, 475 Fed. App'x 765 (Fed. Cir. 2012).

Dr. Gupta supplemented Dr. Varma's statements by noting how Petitioner was in his regular state of health prior to vaccinations and did not have any joint issues. Dr. Gupta also opined that molecular mimicry, in concert with immune complexes, could produce an immune response ultimately leading to RA in this case. But he did not explain how Petitioner's clinical presentation is consistent with vaccine-induced RA or a continued autoimmune response. He described Petitioner's presentation as explosive in the context of symptom onset but did not continue that distinction in his discussion of disease progression. Further, because Dr. Gupta did not persuasively articulate prong one, it follows that prong two cannot be established.

Lastly, while discussed in depth, no alternative cause was found for Petitioner's RA. Dr. Antiochos raised the fact that Petitioner's white blood cell count was elevated prior to vaccination and that leukopenia was identified in Petitioner's lab results prior to vaccination. According to Dr. Antiochos, this raised "the possibility of an infection precipitating [Petitioner's] presentation." Resp't's Ex. A at 4, 9. However, he did not opine this alternative cause as more likely than not, and the evidence does not support that conclusion. Moreover, Dr. Gupta effectively rebutted Dr. Antiochos's statement that an infection could be the trigger in this case, in part by noting that an infectious disease workup was unrevealing. While Dr. Gupta's discussion regarding a potential infection addresses any argument for a known alternative cause, it does not address the lack of preponderant evidence to articulate the vaccine causation theory and satisfy the second *Althen* prong. *de Bazan*, 539 F.3d at 1351–52.

Overall, I find preponderant evidence of a logical sequence of cause and effect lacking, and thus, Petitioner has failed to meet his burden for the second *Althen* prong.

## VI. Conclusion

After a careful review of the record, Petitioner has failed to prove by preponderant evidence that Petitioner's RA was caused by his October 31, 2016 flu or Prevnar 13 vaccinations. Accordingly, I **DENY** Petitioner's claim and **DISMISS** his petition.[37]

**IT IS SO ORDERED.**

s/Herbrina D. Sanders Young
Herbrina D. Sanders Young
Special Master

[37] Pursuant to Vaccine Rule 11(a), entry of judgment is expedited by the parties' joint filing of a notice renouncing the right to seek review.