In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: February 16, 2021

CLAYTON T. COLEMAN,	*	PUBLISHED
	*	
Petitioner,	*	No. 18-352v
	*	
v.	*	Special Master Nora Beth Dorsey
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Ruling on Entitlement; Causation-in-Fact; Influenza ("Flu") Vaccine; Sweet's Syndrome.
	*	
Respondent.	*	
	*	

David A. Tierney, Rawls Law Group, Richmond, VA, for petitioner.
Sarah C. Duncan, U.S. Department of Justice, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

I. INTRODUCTION

On March 7, 2018, Clayton T. Coleman ("petitioner") filed a petition for compensation under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42 U.S.C. § 300aa-10 et seq. (2012).[2] Petitioner alleged that he suffered from Sweet's syndrome

[1] The undersigned intends to post this Ruling on the United States Court of Federal Claims' website. **This means the Ruling 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, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material from public access. Because this published Ruling contains a reasoned explanation for the action in this case, undersigned is required to post it on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services).

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 to -34 (2012). All citations in this Ruling to individual sections of the Vaccine Act are to 42 U.S.C. § 300aa.

and development of arthralgia as the result of an influenza ("flu") vaccination he received on February 3, 2016. Petition at Preamble (ECF No. 1).

After a review of the record as a whole, expert reports and medical literature, briefing by the parties, and for the reasons set forth below, the undersigned finds by preponderant evidence that the petitioner is entitled to compensation.

II. PROCEDURAL HISTORY

Petitioner filed his petition on March 7, 2018, alleging that he suffered from Sweet's syndrome and development of arthralgia caused by a flu vaccine administered to him on February 3, 2016. Petition at Preamble. On March 13, 2018, petitioner filed medical records and affidavits. Petitioner's Exhibits ("Pet. Exs.") 1-13. On November 1, 2018, respondent filed respondent's Rule 4(c) Report. Respondent's Report ("Resp. Rept."), filed Nov. 1, 2018 (ECF No. 12). At that time, respondent was unable to formulate an opinion because the Division of Injury Compensation Programs ("DICP") did not have the opportunity to review the case. Id. at 9.

On February 15, 2019, petitioner filed an expert report with accompanying medical literature. Pet. Exs. 14-31. Petitioner filed additional medical records and a motion to issue subpoena on February 25, 2019. Pet. Exs. 32-35; Pet. Motion ("Mot.") to Issue Subpoena, filed Feb. 25, 2019 (ECF No. 17). The court granted petitioner's motion the next day. Order Granting Mot. to Issue Subpoena dated Feb. 26, 2019 (ECF No. 19).

On July 2, 2019, respondent filed a responsive expert report with accompanying medical literature. Resp. Exs. A-B. Petitioner filed a supplemental expert report on September 18, 2019. Pet. Exs. 36-41.

The case was reassigned to the undersigned on October 1, 2019. Order Reassigning Case dated Oct. 1, 2019 (ECF No. 27). The parties then filed a Joint Status Report on October 24, 2019, requesting a Rule 5 status conference. Joint Status Rept., filed Oct. 24, 2019 (ECF No. 29).

The Rule 5 status conference was held on November 21, 2019. See Rule 5 Order dated Nov. 22, 2019 (ECF No. 30). During the Rule 5 conference, the undersigned concluded that Sweet's syndrome was the proper diagnosis and that her preliminary findings were that "petitioner would likely be able to satisfy all three Althen Prongs if this case proceeds to a hearing." Id. at 2; see Althen v. Sec'y of Health & Hum. Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005). In response to one of petitioner's treating physicians questioning whether petitioner's medication, allopurinol, was a possible trigger, the undersigned directed petitioner to "submit a memorandum and affidavit detailing when he started, discontinued, and resumed his use of allopurinol, along with any adverse symptoms he may have experienced during the interim period." Rule 5 Order at 2. The undersigned encouraged the parties to engage in settlement negotiations. Id. at 3.

On January 6, 2020, petitioner filed his memorandum and affidavit addressing his use of allopurinol and additional medical records. Pet. Exs. 42-44. Petitioner filed additional medical records in February and March 2020. Pet. Exs. 45-46. On April 22, 2020, the parties filed a Joint Status Report indicating that respondent was not interested in settlement and the parties wished to proceed with a Ruling on the Record to determine whether petitioner was entitled to compensation. Joint Status Rept., filed Apr. 22, 2020 (ECF No. 44).

Petitioner filed his motion for a Ruling on the Record on July 6, 2020. Pet. Mot. for Ruling on the Record ("Pet. Mot."), filed July 6, 2020 (ECF No. 48). Respondent filed his response to petitioner's motion on September 4, 2020. Resp. Response to Pet. Mot. ("Resp. Response"), filed Sept. 4, 2020 (ECF No. 49). On November 3, 2020, petitioner filed his reply. Pet. Reply, filed Nov. 3, 2020 (ECF No. 50).

The matter is now ripe for adjudication.

III. ISSUES TO BE DECIDED

The parties dispute causation. Petitioner alleged he has suffered from a variety of symptoms related to Sweet's syndrome which began four days after the administration of the vaccine. Pet. Mot. at 1. Petitioner averred he is entitled to compensation as outlined by the evidence presented in the relevant medical records and expert reports. Id.

Respondent argued petitioner has not satisfied his burden to demonstrate a reliable medical theory causally connecting the flu vaccine to Sweet's syndrome, a "logical" sequence of cause and effect showing that the flu vaccination was the cause of his injury, or an appropriate temporal association between his flu vaccination on February 3, 2016 and his Sweet's syndrome as required under the Althen Prongs. Resp. Response at 2-3.

IV. FACTUAL SUMMARY

A. Sweet's Syndrome

Acute febrile neutrophilic dermatosis—or Sweet's syndrome—is a rare inflammatory skin condition characterized by fever, neutrophilia,[3] tender erythematous,[4] skin lesions (papules, nodules, and plaques), and a diffuse infiltrate consisting predominantly of mature neutrophils.

[3] Neutrophilia is an increase in white blood cells due to inflammation. Neutrophilia, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=33918&searchterm=neutrophilia (last visited Jan. 27, 2021).

[4] Erythema is redness of the skin due to inflammation. Erythema, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=17187 (last visited Jan. 27, 2021).

Pet. Ex. 17 at 1.[5] Fever is the most frequent symptom followed by cutaneous manifestations. Id. at 5. Skin lesions are often distributed asymmetrically, most frequently appearing on the upper extremities, face, and neck. Id. Ocular inflammation is also a common extracutaneous manifestation. Resp. Ex. A, Tab 1 at 6.[6] Arthralgias, malaise, headache, and myalgias are additional symptoms that frequently occur in Sweet's syndrome. Id. Biopsy may be necessary for correct diagnosis. Pet. Ex. 17 at 14.

Sweet's syndrome presentation can be classical (idiopathic), malignancy-associated, or drug-induced. Pet. Ex. 17 at 2. Classical or idiopathic Sweet's syndrome predominantly affects women and may be associated with infection, inflammatory bowel disease, or pregnancy. Id. at 3. Several medications have been associated with drug-induced Sweet's syndrome, especially following the administration of granulocyte-colony stimulating factor. Id. at 4. The pathogenesis of Sweet's syndrome is not well understood, but factors theorized to contribute to the development of this disorder include hypersensitivity reactions, cytokine dysregulation, and genetic susceptibility. Resp. Ex. A, Tab 1 at 4. Studies suggest Sweet's syndrome is probably an immune-complex mediated process. See Pet. Exs. 17, 18,[7] 26.[8]

Skin hypersensitivity[9] is a Sweet's syndrome-associated feature characterized by dermatosis-associated skin lesions appearing at sites of cutaneous trauma. Pet. Ex. 17 at 7. These include the sites where procedures such as biopsies, intravenous catheter placement, vaccination, and venipuncture. Id.; see also Resp. Ex. A, Tab 1 at 6. A hypersensitivity reaction to an eliciting bacterial, viral, or tumor antigen may promote the development of Sweet's syndrome. Pet. Ex. 17 at 13.

B. Summary of Relevant Facts

Petitioner was forty years old when he received a flu vaccine in his left arm on February 3, 2016 during an annual examination conducted by his primary care provider ("PCP"), Dr.

[5] Phillip R. Cohen, Sweet's Syndrome – A Comprehensive Review of an Acute Febrile Neutrophilic Dermatosis, 2 Orphanet J. Rare Diseases 34 (2007).

[6] Joseph F. Merola, Sweet Syndrome (Acute Febrile Neutrophilic Dermatosis): Pathogenesis, Clinical Manifestations, and Diagnosis, UpToDate (2019).

[7] Abu S. M. Giasuddin et al., Sweet's Syndrome: Is the Pathogenesis Mediated by Helper T Cell Type 1 Cytokines?, 39 J. Am. Acad. Dermatology 940 (1998).

[8] Shahzad Raza et al., Insight into Sweet's Syndrome and Associated-Malignancy: A Review of the Current Literature, 42 Int'l J. Oncology 1516 (2013).

[9] Hypersensitivity is a state of altered reactivity in which the body reacts with an exaggerated or inappropriate immune response to what is perceived to be a foreign substance. Hypersensitivity, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=24004&searchterm=hypersensitivity (last visited Jan. 27, 2021).

Derek Einhorn. Pet. Ex. 3 at 2; Pet. Ex. 5 at 12. At the time of vaccination, he was taking allopurinol,[10] sertraline, hydrochlorothiazide, tamsulosin, and sildenafil. Pet. Ex. 5 at 10.

On February 9, 2016, petitioner returned to Dr. Einhorn complaining of a rash and fever and chills. Pet. Ex. 5 at 14-15. Dr. Einhorn noted grouped pustules and vesicles on the right side of his neck and on both wrists and diagnosed petitioner with bullous impetigo.[11] Id. at 14. Dr. Einhorn prescribed Bactrim and Mupirocin topical ointment. Id.

The next day, on February 10, 2016, petitioner presented to dermatologist Dr. Leonard Kerwin at Associated Dermatology. Pet. Ex. 8 at 1. Dr. Kerwin noted a red, painful, itchy, and severe rash present for four days located on petitioner's hand, neck, face, and leg. Id. Petitioner reported that he had received a flu vaccine the week prior. Id. Dr. Kerwin diagnosed a drug eruption. Id. Dr. Kerwin counseled petitioner that drug eruptions may result from any class of medications with the offending agents started 1-2 weeks prior to the eruption. Id. Dr. Kerwin advised petitioner to discontinue Bactrim and prescribed Triacinolone acetonide topical cream, Valtrex, and an injection of celestone. Id.

On February 15, 2016, petitioner returned to Associated Dermatology and presented to Dr. Leonard Cetner. Pet. Ex. 8 at 3. Dr. Cetner reported petitioner was "following up for drug eruption which started 2 days following his flu vaccine." Id. He noted "[p]olycyclic erythematous edematous urticarial plaques and with erythema nodosum-like lesions distributed on the left proximal posterior upper arm, right buttock, and right antecubital skin." Id. at 3, 5-6. Petitioner stated he felt better for 48-72 hours after the celestone injection, but then his rash began to flare again, and he experienced joint aches and tenderness, swelling, and malaise. Id. at 3. Dr. Cetner diagnosed petitioner with worsening unspecified dermatitis, with a differential diagnosis of serum sickness vs. erythema multiforme vs. exanthem vs. parvovirus. Id. Dr. Cetner performed a punch biopsy in the left upper arm. Id. The punch biopsy revealed superficial to mid-dermal perivascular, interstitial, and focally perifollicular dermatitis with neutrophils, scattered eosinophils, and segmental marked papillary dermal edema with no definitive fungal organisms identified. Id. at 8. Primary diagnosis was hypersensitivity reaction, such as drug eruption. Id. Petitioner received another injection of celestone and was advised to see an ophthalmologist for possible eye involvement. Id. at 3-4.

On February 16, 2016, petitioner was seen by ophthalmologist Dr. David Shepherd. Pet. Ex. 9 at 1-2. Dr. Shepherd recorded an auto-immune reaction to flu vaccine leading to eye discharge, red and irritated eyes, and blurry vision. Id. at 1. Dr. Shepherd diagnosed petitioner

[10] Allopurinol is a pharmaceutical treatment for gout and kidney stones. Allopurinol, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=1854&searchterm=allopurinol (last visited Dec. 28, 2020).

[11] Bullous impetigo are skin eruptions which begin as small vesicles that enlarge to form blisters with erythematous rims; the lesions later rupture and form a thin, varnish-like crust. Bullous Impetigo, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=82053&searchterm=impetigo%20bullosa (last visited Feb. 8, 2021).

with dry eye syndrome of the right eye related to flu vaccine reaction and squamous blepharitis of the left lower eyelid. Id. at 2.

Petitioner had a follow up visit with Dr. Kerwin on February 17, 2016, for left proximal posterior upper arm, right buttock, and right antecubital unspecified dermatitis. Pet. Ex. 8 at 7. Dr. Kerwin noted an overall improvement and less joint pain. Id. He also noted petitioner's ophthalmology evaluation was negative. Id. Dr. Kerwin's impression was erythema elevatum diutinum, with associated diagnoses of serum sickness vs. erythema multiforme. Id. Prednisone and valacyclovir were continued. Id. Petitioner then returned to Dr. Kerwin's office on February 18, 2016 complaining of a pain intensity of 6/10, swelling, stiffness, and night sweats. Id. at 13. Dr. Kerwin's assessment remained the same and he administered a Kenalog injection. Id.

On February 25, 2016, petitioner returned to Dr. Kerwin for a follow-up. Pet. Ex. 8 at 12. Petitioner reported pain 4/10. Id. Dr. Kerwin advised petitioner to finish his prednisone prescription, administered another injection of celestone, and referred petitioner to rheumatologist, Dr. Stephen Portney. Id.

Petitioner presented to Dr. Einhorn on March 1, 2016 due to his ongoing rash. Pet. Ex. 5 at 16. On exam, petitioner's left ankle had diffused swelling and there were scattered pustules on his neck and on both arms. Id. at 17. Dr. Einhorn noted, "serum sickness reaction following flu shot continue to follow with dermatologist slowly improving. . . . May need to consult with rheum[atology] or immunology if symptoms persist and re other forms of flu vaccine in future." Id.

On March 8, 2016, petitioner presented to rheumatologist Dr. Portnoy. Pet. Ex. 10 at 1-5. Dr. Portnoy reported petitioner "was in his usual health and had an [flu] vaccine February 3, 2016 at the time he had a physical examination. He developed an undocumented fever within the same 24 hours and noted a rash on his posterior neck 2 days later." Id. at 1. "He has received several intramuscular steroid injections which provide 3-5 days of benefit but his pain then recurs." Id. Physical examination revealed tenderness and pain in petitioner's joints and erythematous rashes. Id. at 2-3. Dr. Portnoy's impression concluded, "[h]e's had a rash with biopsy revealing possible hypersensitivity response" that "occurred after a[] [flu] vaccine and I cannot exclude an association with this. Although I cannot exclude serum sickness, some his symptoms occurred fairly soon after the vaccine. I cannot exclude that his rash could be associated with other medication he is currently taking."[12] Id. at 3. Dr. Portnoy advised further serologic studies to evaluate petitioner for underlying autoimmune abnormality and indicated that since petitioner was having significant issues with pain, steroid injections would not be a suitable long-term form of therapy. Id. at 4.

On April 29, 2016, petitioner returned to Dr. Kerwin, whose impressions and therapies remained unchanged. Pet. Ex. 8 at 16. Pain was 8/10. Id. On May 13, 2016, petitioner was seen by dermatologist Dr. Michael Dorman. Id. at 17. Dr. Dorman documented 13% of

[12] Petitioner's medications included allopurinol, tamsulosin, hydrochlorothiazide, and sertraline. Pet. Ex. 10 at 2.

petitioner's body was covered by the rash. Id. Dr. Dorman also noted petitioner was referred to Dr. David Fivenson and that he was going on a trip to Mexico. Id.

On June 21, 2016, petitioner presented to dermatologist Dr. Fivenson. Pet. Ex. 11 at 13-17. Dr. Fivenson noted itchy, painful rash with extreme joint pain. Id. at 15. He reported onset of over three months which occurred after the flu shot. Id. Dr. Fivenson stated, "[a]fter review of the prior medical records available, the patient's history and physical examination, I favor sweet's vs [linear IgA bullous disease] as the likely diagnosis. Skin biopsy and direct immunofluorescence have been suggested/ordered to help establish the diagnosis." Id. at 16. Dr. Fivenson performed a skin punch biopsy. Id. at 17. On June 30, 2016, Dr. Fivenson diagnosed petitioner with acute febrile neutrophilic dermatosis with findings consistent with the clinical impression of Sweet's syndrome. Id. at 12. He instructed petitioner to stop taking allopurinol since it could be a "possible trigger" of his Sweet's syndrome. Id.

On July 22, 2016, Dr. Portney diagnosed Sweet's syndrome by biopsy. Pet. Ex. 10 at 6. On October 14, 2016, Dr. Portney noted, "flu . . . ? Sweet's syndrome." Id. at 7. On October 25, 2016, petitioner presented to Dr. Fivenson who stated "[r]ash has improved but still present on [left] arm and [left] neck." Pet. Ex. 11 at 3. Petitioner followed up with Dr. Portney on April 21, 2017, and Dr. Portney stated his rash and joint pain had resolved. Pet. Ex. 10 at 9-10.

C. Affidavits

1. Petitioner

Petitioner reported he began to feel "feverish" and "achy" on the evening of February 3, 2016, after he received the flu vaccination. Pet. Ex. 1 at 1. He felt worse that weekend and had full body aches and fever as if he "had a severe flu." Id. On February 7, 2016, he noticed a rash spreading on his back and neck. Id. Petitioner presented to Dr. Einhorn on February 9, 2016, and Dr. Einhorn prescribed antibiotics for petitioner's painful and itchy rash that spread to his face. Id. However, the rash spread to petitioner's eyes on February 10, 2016, and Dr. Einhorn referred petitioner to the dermatologist for further evaluation. Id.

Petitioner averred his rash began on his back and quickly spread to his wrists, arms, and shoulders, and onto his face, eyes, and hairline. Pet. Ex. 1 at 1. Petitioner had "severe joint pain in [his] wrists and thumbs." Id. The joint pain spread to petitioner's ankles, legs, back, and shoulders and caused numbness, burning, and tingling sensation in his legs. Id. at 1-2. Petitioner's pain was so intense he could not hold a pen or walk for three months. Id. at 2. Due to this, petitioner was unable to attend his uncle's funeral, and was unable to participate in his normal everyday activities. Id.

After vaccination petitioner stated he could not take his normal trips to the grocery store, help with household chores, or engage in the active lifestyles of his eight children. Pet. Ex. 1 at 2. For example, he could not take his kids to practices or tournaments or participate in group camping and hiking trips. Id. Petitioner reported he was able to continue his work as a Supervising Operator at a power plant with the exception of eight days he took off due to pain. Id. at 3. Petitioner stated his condition slowed the process of obtaining his engineer's license,

but he completed the required testing and is up to date on all required qualifications for his job. Id.

a. Issue Related to Whether or Not Petitioner's Allopurinol Medication Caused or Contributed to Sweet's Syndrome

Petitioner stated in his second affidavit he had taken allopurinol since 2005 for kidney stone prevention. Pet. Ex. 42 at 1. Petitioner averred he stopped taking the medication for almost eight weeks when Dr. Fivenson diagnosed his condition, but has "since resumed taking allopurinol." Id.

In his memorandum, petitioner averred that allopurinol is cited repeatedly as a current or active medication in records from Novidocs, Oakland Orthopedic Surgeons, Associated Dermatology, Newland Medical Associates, and Michigan Institute of Urology between June 2014 and March 2016. Pet. Ex. 43 at 2.

On June 30, 2016, Dr. Fivenson noted, "[s]top allopurinol to see if that is the possible trigger for your Sweet's syndrome." Pet. Ex. 43 at 2; Pet. Ex. 11 at 33. Petitioner stated, Dr. Fivenson's direction is the only mention in the medical record of discontinuation. Pet. Ex. 43 at 2. At petitioner's subsequent follow-ups with Dr. Fivenson, they did not discuss petitioner's discontinuation of allopurinol, the effects of discontinuation, or a resumption of it. Id. at 2-3. Except for the eight weeks after June 30, 2016, when petitioner discontinued taking allopurinol, petitioner resumed taking it, and continues to take it, "with no effect." Id. at 4.

2. Patricia Coleman

Patricia Coleman, petitioner's mother, also submitted an affidavit on petitioner's behalf. Pet. Ex. 2. Ms. Coleman stated after the February 3, 2016 flu vaccination, she observed lesions all over petitioner's body, especially on his face, head, neck, torso, and arms on April 3, 2016. Id. at 1. Ms. Coleman stated petitioner complained of exhaustion and severe joint pain. Id. She said there was no change by May 2016. Id.

Petitioner moved in with his parents at the end of July 2016. Pet. Ex. 2 at 1. Ms. Coleman reported the lesions were improving as petitioner visited his doctors, but his joint pain and exhaustion did not change. Id. Petitioner and his mother would take walks together, but petitioner's pain necessitated frequent stops and he needed rest for hours after. Id. Ms. Coleman stated petitioner was not out of shape or led a sedentary life prior to vaccination. Id.

Ms. Coleman reported by April 2017, most of petitioner's pain and his skin lesions were gone. Pet. Ex. 2 at 1. She stated petitioner has periodic joint pain, but for the most part is healthy now. Id.

D. Expert Reports

1. Petitioner – Dr. M. Eric Gershwin

a. Background and Qualifications

Dr. Gershwin is a Distinguished Professor of Medicine with the University of California, Davis, where he currently holds a chaired professorship in honor of Jack and Donald Chia. Pet. Ex. 15 at 2. Dr. Gershwin received his undergraduate degree, summa cum laude, from Syracuse University and his medical degree from Stanford. Id. He has an honorary doctorate from the University of Athens, in recognition for his lifetime contribution in immunology and medicine. Id. He has also been awarded the AESKU prize in Autoimmunity in 2008, in recognition of his lifetime contribution in immunology. Id. He is also fellow with the American Association for the Advancement of Science. Id. He is board certified in internal medicine, rheumatology, and allergy and clinical immunology. Id. at 3. Dr. Gershwin authored two expert reports. Pet. Exs. 14, 36.

b. Opinion

i. Diagnosis

In regard to diagnosis, Dr. Gershwin opined that petitioner developed the idiopathic form of Sweet's syndrome. Pet. Ex. 14 at 2. Dr. Gershwin noted there were a number of other diagnoses considered, including viral infection, erythema multiforme, serum sickness, Stevens-Johnson syndrome, and hypersensitivity reaction. Id. at 1. However, Dr. Fivenson ultimately diagnosed Sweet's syndrome as consistent with petitioner's second punch biopsy. Id. at 2.

ii. Althen Prong One: Medical Theory of Causation

Dr. Gershwin opined the mechanism for Sweet's syndrome remains enigmatic, but most likely is due to abnormal cytokine production following vaccination. Pet. Ex. 14 at 2. More specifically, he stated Sweet's syndrome develops as a result of cytokine production and inflammasome activation in a genetically susceptible host, which can lead directly to neutrophilia and the abnormal neutrophil infiltrates within lesions. Pet. Ex. 36 at 2.

Dr. Gershwin opined Sweet's syndrome is an inflammatory syndrome and may likely be due to activation of the inflammasome with an underlying genetic predisposition. Pet. Ex. 36 at 2. He cited Heath and Ortega-Loayza[13] who state, "[t]he exact pathogenesis of Sweet's syndrome is unclear; however[,] . . . findings include an improved understanding of inflammasome activation . . . and genetic contributions." Pet. Ex. 39 at 1. "Mutations in isocitrate dehydrogenase I (IDHI) have been identified as a possible connection to [Sweet's syndrome] pathogenesis." Id. at 6. The authors explained that "IDHI catalyzes reactions leading to alterations in histones and DNA, causing differential gene expression." Id. This suggests the mechanism underlying Sweet's syndrome is the "dysfunctional activation of the inflammasome and IL- 1β pathway." Id. Dr. Gershwin stated vaccination is a stimulator of the immune response, and thus catalyzes inflammasome activation. Pet. Ex. 36 at 2.

[13] Michael Heath & Alex Ortega-Loayza, Insights into the Pathogenesis of Sweet's Syndrome, 10 Frontiers Immunology 1 (2019).

According to Dr. Gershwin, Sweet's syndrome has been previously associated with vaccination. Pet. Ex. 14 at 2. Though, due to the uncommon frequency of Sweet's syndrome following vaccination, epidemiologic studies do not have sufficient power to establish causation. Id. However, Dr. Gershwin did cite a number of different case reports in the medical literature documenting Sweet's syndrome following vaccination. For example, Carpentier et al.,[14] documented a previously healthy 36-year-old woman who received a BCG vaccination in her left arm and ten days later developed Sweet's syndrome lesions on her abdomen and limbs. Pet. Ex. 16. Gunawardena et al.[15] described eighteen case reports of Sweet's syndrome. Pet. Ex. 19. In two of the case reports, patients developed Sweet's syndrome following smallpox vaccination. Id. One patient was a 47-year-old woman who received a secondary smallpox vaccination and three days later developed a fever with itching, redness, and swelling around the vaccination site. Id. at 2. The eruption spread to her chest and both arms and affected her eyes. Id. Another 70-year-old woman developed a fever approximately three days post smallpox vaccination and had erythematous eruptions on her extremities approximately four days later. Id. at 5.

Additionally, Dr. Gershwin cited the article by Jovanoic et al.,[16] who documented a 45-year-old woman who developed Sweet's syndrome 12 hours after flu vaccination. Pet. Ex. 22 at 1. Maddox and Motley[17] similarly found a 36-year-old woman who received a pneumococcal vaccine after an emergency splenectomy developed Sweet's syndrome approximately seven days later. Pet. Ex. 23 at 1. Pedrosa et al.[18] described a 52-year-old man who developed Sweet's syndrome fifteen days after receiving a pneumococcal vaccine. Pet. Ex. 24 at 1. Radeff and Harms[19] documented a case report of a 23-year-old woman who developed Sweet's syndrome 15 days after BCG vaccination. Pet. Ex. 25 at 3. Finally, Tan et al.[20] reported a 46-year-old man with HIV who suffered from an eruption two days after a flu vaccination. Pet. Ex. 30 at 1.

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[14] Olivier Carpentier et al., Sweet's Syndrome After BCG Vaccination, 82 Acta Dermatology Venereology 221 (2002).

[15] D.A. Gunawardena et al., The Clinical Spectrum of Sweet's Syndrome (Acute Febrile Neutrophilic Dermatosis) – A Report of Eighteen Cases, 92 Br. J. Dermatology 363 (1975).

[16] Marina Jovanoic et al., Acute Febrile Neutrophilic Dermatosis (Sweet's Syndrome) After Influenza Vaccination, 52 J. Am. Acad. Dermatology 367 (2005).

[17] P.R. Maddox & R.J. Motley, Sweet's Syndrome: A Severe Complication of Pneumococcal Vaccination Following Emergency Splenectomy, 77 Br. J. Surgery 809 (1990).

[18] Ana Filipa Pedrosa et al., Sweet's Syndrome Triggered by Pneumococcal Vaccination, 32 Cutaneous Ocular Toxicology 260 (2013).

[19] Boris Radeff & M. Harms, Acute Febrile Neutrophilic Dermatosis (Sweet's Syndrome) Following BCG Vaccination, 66 Acta Dermatology Venereology 357 (1986).

[20] Tan et al., Bullous Sweet's Syndrome Following Influenza Vaccination in a HIV-Infected Patient, 45 Int'l J. Dermatology 1254 (2006).

In response to Dr. Matloubian's report, Dr. Gershwin cited Cohen and Kurzrock,[21] to explain that Sweet's syndrome is a rare disease characterized by the presence of fever, elevated neutrophil count, painful red papules, nodules, and plaques. Pet. Ex. 36 at 2 (citing Pet. Ex. 38). Cytokines directly or indirectly play a role in the etiology of lesions on the skin and because the syndrome is systemic, lesions do not always appear at the site of vaccination as would be expected if it was an allergic response. Pet. Ex. 36 at 2.

Dr. Gershwin stated that the medical literature provides support that a patient's genetic susceptibility influences the immune response to flu vaccination. Pet. Ex. 36 at 2. The Castrucci[22] article found that preexisting immunity affects flu vaccine responsiveness in host bodies. Pet. Ex. 40 at 1. The article stated, "[p]olymorphisms of any of the involved genes in the molecular interactions within the immune-system reflect the high variability between individuals to respond efficiently to vaccines." Id. at 3. Forero et al.[23] emphasized, "[t]he host innate immune response to [flu] virus is a key determinant of pathogenic outcomes and long-term protective immune response against subsequent exposures." Pet. Ex. 41 at 1.

iii. Althen Prong Two: Logical Sequence of Events

Dr. Gershwin opined that there is a logical sequence of cause and effect here. Pet. Ex. 36 at 2. Sweet's syndrome is associated with certain medications and drugs, infections, autoimmune diseases, neoplasia, and pregnancy. Pet. Ex. 14 at 2. However, Dr. Gershwin stated there is no evidence that petitioner had an autoimmune disease, nor evidence that he had an antecedent infection, used a drug thought to stimulate Sweet's syndrome, or had underlying neoplasia. Id. Dr. Gershwin asserted "[t]he vaccination [wa]s the only known immune stimulus found in this case." Pet. Ex. 36 at 2. Petitioner had no other underlying predisposing factors that could be attributed to his development of Sweet's syndrome. Pet. Ex. 14 at 3.

Petitioner was diagnosed with the idiopathic form of Sweet's syndrome, which has previously been associated with vaccination. Pet. Ex. 14 at 2. Dr. Gershwin opined that genetic susceptibility, which has been reported with Sweet's syndrome, is most likely what happened in petitioner. Id. Petitioner most likely had abnormal cytokine production following vaccination, which then led to the development of his Sweet's syndrome. Id. In summary, Dr. Gershwin opined "[petitioner] is an example of a very rare event in a genetically susceptible host following cytokine production to a vaccine." Id. at 3.

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[21] Phillip R. Cohen & R. Kurzrock, Sweet's Syndrome Revisited: A Review of Disease Concepts, 42 Int'l J. Dermatology 761 (2003).

[22] Maria R. Castrucci, Factors Affecting Immune Responses to the Influenza Vaccine, 14 Hum. Vaccines & Immunotherapeutics 637 (2018).

[23] Adriana Forero et al., Evaluation of the Innate Immune Responses to Influenza and Live-Attenuated Influenza Vaccine Infection in Primary Differentiated Human Nasal Epithelial Cells, 35 Vaccine 6112 (2017).

In regard to whether allopurinol played a causal role in petitioner's illness, Dr. Gershwin stated petitioner was taking allopurinol May 7, 2014, and continued it without interruption until June 2016. Pet. Ex. 36 at 1. Petitioner resumed taking it in August 2016. Id. Dr. Gershwin opined it is unlikely that allopurinol caused petitioner's Sweet's syndrome. Id. Case reports demonstrate that symptoms most commonly occur shortly after beginning the medication. Id. In Polimeni et al.,[24] Sweet's syndrome occurred eight days after allopurinol initiation. Pet. Ex. 37 at 2. In contrast, Dr. Gershwin stated petitioner had taken allopurinol for at least two years before the onset of his rash. Pet. Ex. 36 at 1.

iv. Althen Prong Three: Proximate Temporal Relationship

Dr. Gershwin reported petitioner's flu vaccination was on February 3, 2016 and his rash was noted on February 7, 2016. Pet. Ex. 36 at 1; Pet. Ex. 1 at 1. Petitioner presented to Dr. Einhorn on February 9, 2016 for evaluation of his rash. Pet. Ex. 14 at 1. Therefore, Dr. Gershwin opined, there is a proximate temporal relationship of four days between vaccination and injury. Pet. Ex. 36 at 2.

2. Respondent – Dr. Mehrdad Matloubian

a. Background and Qualifications

Dr. Mehrdad Matloubian is a Clinical Professor at the University of California, San Francisco. Resp. Ex. A at 1. He received his undergraduate degree, summa cum laude, his medical degree, and his Ph.D in virology from University of California, Los Angeles. Id. Dr. Matloubian completed his fellowship, residency, and post-doctoral fellowship at University of California, San Francisco. Id. He is board-certified in internal medicine and rheumatology. Id. at 2. He has an active rheumatology practice and is an associate director of the Molecular Medicine Consult Service. Id. at 3. Dr. Matloubian authored one expert report. Resp. Ex. A.

b. Opinion

i. Diagnosis

As for diagnosis, Dr. Matloubian stated, "even though at first [petitioner's] treating physicians considered entities such as serum sickness, erythema multiforme, and erythema elevatum diutinum, he was eventually diagnosed with Sweet['s] syndrome based on a second biopsy and discussion at a dermatology grand rounds."[25] Resp. Ex. A at 4-5. Petitioner's rheumatologist could not find any evidence of an inflammatory arthritis or an associated autoimmune disease. Id. at 5. Petitioner's rash completely resolved, did not recur, and there was no evidence of joint inflammation while off immunosuppressive therapy. Id. Therefore, Dr.

[24] G. Polimeni et al., Allopurinol-Induced Sweet's Syndrome, 2 Int'l J. Immunopathology Pharmacology 329 (2016).

[25] In his report, Dr. Matloubian primarily used the wording "Sweet syndrome." However, for consistency purposes, the undersigned will use "Sweet's syndrome."

Matloubian agreed with the diagnosis of Sweet's syndrome based on the pathologic findings of petitioner's skin biopsy as well as his eventual response to therapy. Id.

ii. Althen Prong One: Medical Theory of Causation

Dr. Matloubian disagreed with Dr. Gershwin that the flu vaccine could cause Sweet's syndrome as a result of elevated cytokine production in a genetically susceptible host. Resp. Ex. A at 6. He opined that Dr. Gershwin's theory was speculative and based on only general assertions regarding genetic susceptibility. Id. Dr. Matloubian also asserted that Dr. Gershwin did not provide any persuasive medical literature beyond a few case reports of rare occurrences of Sweet's syndrome in temporal association with immunization. Id.

Dr. Matloubian opined that the pathogenesis of Sweet's syndrome is not known, but he agreed that it is thought to be an immune-mediated illness. Resp. Ex. A at 8. Dr. Matloubian referenced the Sweet's syndrome literature review authored by Joseph Merola, stating that Sweet's syndrome involves the recruitment of neutrophils to the skin and responds to immunomodulating agents, such as steroids. Id. (citing Resp. Ex. A, Tab 1 at 4). Dr. Matloubian stated that because cytokines are involved in all aspects of the immune system and responses, their dysregulation has been postulated to play a role in pathogenesis of Sweet's syndrome. Id. However, the exact mechanism that leads to recruitment of neutrophils to the skin, and what leads to cytokine dysregulation, is not understood. Id. Additionally, in regard to the role of cytokine dysregulation in association with vaccination, Dr. Matloubian cited the 2011 IOM committee report[26] which found "no evidence that directly or indirectly supports the oversecretion of cytokines as an operative mechanism" related to vaccination. Id. (citing Resp. Ex. A, Tab 2 at 12).

After reviewing Dr. Gershwin's cited case reports on the occurrence of Sweet's syndrome in association with immunization, Dr. Matloubian concluded that none of the reports provided any insight on a possible mechanism. Resp. Ex. A at 6. Dr. Matloubian stated that Carpentier et al. and Maddox and Motley documented onset after administration of the BCG and pneumococcal vaccines, but he believed these to be flawed comparisons because the components of these vaccines are fundamentally different than the components of the flu vaccine. Id. (citing Pet. Exs. 16, 23). The BCG and pneumococcal vaccines consist of specific types of bacterium while the flu vaccine is composed of a virus with protein antigens. Id.

Additionally, Dr. Matloubian noted that Carpentier et al., Gunawardena et al., and Radeff and Harms case reports indicate Sweet's syndrome lesions appeared at the site of vaccination, suggesting that there might have been an infectious process in the development of the disease. Resp. Ex. A at 6-7 (citing Pet. Exs. 16, 19, 25). Dr. Matloubian stated that the Gunawardena et al. case report complicates a supposed direct causal relationship with the vaccine component itself by documenting a co-existing infectious agent at the site of vaccination. Id (citing Pet. Ex. 19).

[26] Comm. to Rev. Adverse Effects of Vaccines, Inst. of Med., Adverse Effects of Vaccines: Evidence and Causality (Kathleen Stratton et al. eds., 2011).

Dr. Matloubian opined that "[d]espite hundreds of millions of [flu] vaccines administered annually worldwide for decades, the medical literature has only a handful of case reports of an association with Sweet['s] syndrome." Resp. Ex. A at 7. Further, Dr. Matloubian stated the case reports provided by Dr. Gershwin associating Sweet's syndrome with the flu vaccine provide little support for Dr. Gershwin's proposed mechanism of causation. Id. First, Jovanovic et al. documented skin lesions that occurred within 12 hours after flu immunization and also occurred at the site of vaccination. Pet. Ex. 22 at 1. Dr. Matloubian stated the rapidity of onset of symptoms and lesions within hours makes it unlikely that it was due to vaccine-specific T cell and antibody responses. Resp. Ex. A at 7. Tan et al. also described an HIV positive man who developed Sweet's syndrome two days after a flu vaccination. Id. (citing Pet. Ex. 30). The authors noted that Sweet's syndrome in general has been associated with the HIV infection itself, thus making it difficult to reach a conclusion regarding causality due to the flu vaccination. Id. (citing Pet. Ex. 30 at 3).

Dr. Matloubian also opined that the time of onset recorded in the various case reports cited by Dr. Gershwin does not "encompass one unifying immunologic mechanism for how a vaccine component can lead to Sweet['s] syndrome." Resp. Ex. A at 7. The reported timeframe for onset of lesions after any vaccination in the articles range from as early as 12 hours post-vaccination to 15 days. Id.

Additionally, Dr. Matloubian found that petitioner's article by Philip Cohen contradicted Dr. Gershwin's theory of causation. Resp. Ex. A at 7-8 (citing Pet. Ex. 17). Cohen stated there is "a bona fide association between Sweet's syndrome probably exists with" cancer, infections, inflammatory bowel disease, medications, and pregnancy. Pet. Ex. 17 at 9. However, the author described the association between vaccination and development of Sweet's syndrome as "remains to be established." Id. at 13 tbl.7. With regard to vaccination and other conditions named in the article, the author wrote, "indeed, the detection of that condition in an individual with Sweet's syndrome may merely represent a coincidental occurrence." Id. at 10. Thus, opined Dr. Matloubian, "experts who write on the pathogenesis of Sweet['s] syndrome regard the reported rare associations between vaccinations and Sweet['s] syndrome as more likely coincidental rather than causal." Resp. Ex. A at 8.

iii. Althen Prong Two: Logical Sequence of Events

Dr. Matloubian opined that Dr. Gershwin's theory of logical sequence of cause and effect was speculative based on the fact he did not provide any evidence of petitioner's genetic susceptibility. Resp. Ex. A at 6. Dr. Gershwin attributed the rare occurrence of Sweet's syndrome in the petitioner to "a rare event in a genetically susceptible host" without providing any information about the petitioner's genetic susceptibility. Id.

Dr. Matloubian stated that many of Dr. Gershwin's case reports detailing Sweet's syndrome reactions after BCG and pneumococcal vaccinations were unrelated to petitioner's case because petitioner received the flu vaccine. Resp. Ex. A at 6. Further, Dr. Matloubian noted that some of petitioner's case reports, Carpentier et al., Gunawardena et al., and Radeff and

Harms, indicated that Sweet's lesions appeared at the site of vaccination, which he asserted did not occur in petitioner's case.[27] Id. at 6-7.

Additionally, Dr. Matloubian highlighted that the Gunawardena et al. authors noted that there was a "seasonal bias" in their case series of Sweet's syndrome with half of them occurring "during the months of January and February." Resp. Ex. A at 8 (citing Pet. Ex. 19 at 6). Coincidentally, Dr. Matloubian opined "the petitioner developed his Sweet['s] syndrome in February, which is consistent with the seasonal bias observed by the authors of this paper." Id. The concept of seasonality of a disease is highly suggestive of "a possible unrecognized and potentially difficult to diagnose infectious cause." Id. Dr. Matloubian reinforced that in 70% of the cases of Sweet's syndrome the cause is unknown. Id.

Dr. Matloubian reiterated that there is no clarity on the pathogenesis of Sweet's syndrome, and therefore, Dr. Gershwin's opinion that the petitioner developed the disease after the flu vaccine because of his "bad genes and bad luck" is speculative. Resp. Ex. A at 8. After a review of petitioner's medical records, Dr. Matloubian stated "[t]here is no indication in the petitioner's personal medical history or family history that he has a propensity to a dysregulated immune response to vaccinations or infections." Id. Without further evidence of petitioner's genetic makeup in his medical history, Dr. Matloubian stated that neither he nor Dr. Gershwin can state what predisposed petitioner to developing Sweet's syndrome. Id. Petitioner's personal and family history showed no autoinflammatory or autoimmune diseases, and his medical records demonstrated he had no prior adverse responses to infections or vaccines. Id. at 9. Dr. Matloubian opined, "[t]aken together, these observations do not support a genetic susceptibility or propensity in the petitioner to have exaggerated cytokine responses to immunizations, especially with an inactivated, non-adjuvanted [flu] vaccine." Id.

Although raised as an issue in the case, Dr. Matloubian did not take a position about petitioner's allopurinol medication. He did not state whether it was more likely than not that allopurinol caused or contributed to Sweet's syndrome.

iv. Althen Prong Three: Proximate Temporal Relationship

Dr. Matloubian noted there are some discrepancies in the medical records regarding the onset of petitioner's rash. Resp. Ex. A at 4. Based on petitioner's affidavit, he developed fever and body pain within 12 hours after vaccination and then noted a rash four days after his immunization. Id.; see Pet. Ex. 1 at 1. Petitioner first documented his rash when he saw Dr. Einhorn on February 9, 2016, however, the date of onset for the rash was not noted. Resp. Ex. A at 4. Dr. Kerwin and Dr. Portney documented that the rash began three days after vaccination. Id. However, on his February 15, 2016 visit, Dr. Cetner stated that the rash started "2 days following his flu vaccine." Id.; Pet. Ex. 8 at 3. Dr. Matloubian opined petitioner developed Sweet's syndrome within approximately four days of his February 3, 2016 flu vaccination.

[27] Dr. Matloubian's statement appears to be erroneous. The medical records show that petitioner received the flu vaccination in the left arm on February 3, 2016. Pet. Ex. 3 at 2. On February 15, 2016, Dr. Cetner documented skin lesions on the left upper arm. Pet. Ex. 8 at 3. Therefore, it appears that petitioner did have skin lesions on the left upper arm, the site of vaccination.

V. DISCUSSION

A. Standards for Adjudication – Causation

The Vaccine Act was established to compensate vaccine-related injuries and deaths. 10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Hum. Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, petitioner must prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Hum. Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). The received vaccine, however, need not be the predominant cause of the injury. Shyface, 165 F.3d at 1351. A petitioner who satisfies this burden is entitled to compensation unless respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B).

B. Causation Theory

To receive compensation under the Program, petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that he received, or (2) that he suffered an injury that was actually caused by vaccination. See §§ 13(a)(1)(A) and 11(c)(1); Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1319-20 (Fed. Cir. 2006). Petitioner must show 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 (quoting Shyface, 165 F.3d at 1352-53).

Because petitioner does not allege that he suffered a Table injury, he must prove that the vaccine he received caused his injury. To do so, he must establish, by preponderant evidence: (1) a medical theory causally connecting the vaccine and injury ("Althen Prong One"); (2) a logical sequence of cause and effect showing that the vaccine was the reason for the injury ("Althen Prong Two"); and (3) a showing of a proximate temporal relationship between the vaccine and injury ("Althen Prong Three"). § 13(a)(1); Althen, 418 F.3d at 1278.

The causation theory must relate to the injury alleged. Thus, petitioner must provide a reputable medical or scientific explanation for his theory, although the explanation need only be "legally probable, not medically or scientifically certain," it must be "sound and reliable."

Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1360 (Fed. Cir. 2019); Knudsen v. Sec'y of Health & Hum. Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioner cannot establish entitlement to compensation based solely on assertions. Rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether petitioner is entitled to compensation, the special master shall consider all material contained in the record, including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' offered experts and rule in petitioner's favor when the evidence weighs in his favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in petitioner's favor).

C. Analysis

1. Althen Prong One: Medical Theory of Causation

Under Althen Prong One, petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu, 569 F.3d at 1375; Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by a "sound and reliable" medical or scientific explanation. Boatmon, 941 F.3d at 1359; see also Knudsen, 35 F.3d at 548; Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioner relies upon a medical opinion to support her theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen v. Sec'y of Health & Hum. Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better than the soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

Here, the undersigned finds that petitioner has shown by preponderant evidence a sound and reliable theory that a flu vaccination can cause Sweet's syndrome, and therefore, petitioner has satisfied the first Althen prong. This finding is based on petitioner's expert's opinions, medical literature, case reports, and previous Program cases.

Petitioner's theory, as proffered by Dr. Gershwin, is that Sweet's syndrome can manifest due to abnormal cytokine production following vaccination. More specifically, he stated Sweet's syndrome develops as a result of cytokine production and inflammasome activation in a genetically susceptible host. Dr. Matloubian agreed with the proposed auto-immune mechanism, but he opined that the specific pathogenesis of Sweet's syndrome is not known. Dr. Matloubian referenced the literature stating that Sweet's syndrome involves the recruitment of neutrophils to the skin and responds to immunomodulating agents. Therefore, both experts identify the same

mechanism reflecting the current state of knowledge regarding the pathogenesis of Sweet's syndrome.

This mechanism is supported by medical literature authored by Heath and Ortega-Loayza and by Joseph Merola. Heath and Ortega-Loayza state "[t]he exact pathogenesis of Sweet's syndrome is unclear; however[,] . . . findings include an improved understanding of inflammasome activation . . . and genetic contributions." Pet. Ex. 39 at 1. The authors add that "[m]utations in isocitrate dehydrogenase I (IDHI) have been identified as a possible connection to [Sweet's syndrome] pathogenesis." Id. at 6. "IDHI catalyzes reactions leading to alterations in histones and DNA, causing differential gene expression," which suggests the mechanism underlying Sweet's syndrome is the "dysfunctional activation of the inflammasome and IL- 1β pathway." Id. Dr. Gershwin stated vaccination is a stimulator of the immune response, and thus catalyzes inflammasome activation.

Further, Dr. Gershwin established that Sweet's syndrome has been previously associated with vaccination. While case reports cannot establish causation, they do provide some evidence of causation. Dr. Gershwin cited a number of case reports in the medical literature documenting Sweet's syndrome following vaccination. In regard to Sweet's syndrome following flu vaccination, Dr. Gershwin cited the article by Jovanoic et al., documenting a 45-year-old woman who developed Sweet's syndrome 12 hours after flu vaccination, and Tan et al., who reported a 46-year-old man with HIV who suffered from Sweet's syndrome two days after flu vaccination.

Although this condition is rare, the Program has previously awarded compensation to a petitioner in a Sweet's syndrome case associated with flu vaccination. See Cagle v. Sec'y of Health & Hum. Servs., No. 16-693V, 2018 WL 5929378, at *1 (Fed. Cl. Spec. Mstr. Oct. 17, 2018). While Program case law is not binding, the undersigned takes note of past decisions in favor of petitioners.

While Dr. Matloubian asserted that Dr. Gershwin's theory of susceptibility to Sweet's syndrome due to genetic predisposition was speculative, this theory is supported by the medical literature. Castrucci found that preexisting immunity affects flu vaccine responsiveness in hosts bodies, stating "[p]olymorphisms of any of the involved genes in the molecular interactions within the immune-system reflect the high variability between individuals to respond efficiently to vaccines." Pet. Ex. 40 at 3. Additionally, Forero et al. emphasized "[t]he host innate immune response to [flu] virus is a key determinant of pathogenic outcomes and long-term protective immune response against subsequent exposures." Pet. Ex. 41 at 1. The fact that the specific nature of petitioner's genetic susceptibility is not known does not defeat his claim as the state of scientific knowledge has not yet reached this degree of expertise. Under these circumstances, where medical knowledge as to genetic susceptibility is unknown because it is not yet tested for, it would be a harsh result to penalize petitioner for failure to prove a specific genetic predisposition. In short, scientific certainty is not required. Boatmon, 941 F.3d at 1359; see also Knudsen, 35 F.3d at 548. The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly, 592 F.3d at 1322 n.2. Proof of medical certainty is not required. Bunting, 931 F.2d at 873.

For all of these reasons, undersigned finds that petitioner has provided preponderant evidence of a sound and reliable causal theory, satisfying Althen Prong One.

2. Althen Prong Two: Logical Sequence of Cause and Effect

Under Althen Prong Two, petitioner must prove by a preponderance of the evidence that there is a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." Capizzano, 440 F.3d at 1324 (quoting Althen, 418 F.3d at 1278). "Petitioner must show that the vaccine was the 'but for' cause of the harm . . . or in other words, that the vaccine was the 'reason for the injury.'" Pafford, 451 F.3d at 1356 (internal citations omitted).

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting Althen, 418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528. The petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, petitioner may satisfy his burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

In regard to Althen Prong Two, the undersigned finds petitioner provided preponderant evidence that the February 3, 2016 flu vaccination caused his Sweet's syndrome. This finding is based primarily on the records and opinions of petitioner's treating physicians, Dr. Gershwin's expert opinion, and the supportive case reports.

Petitioner's medical records establish that prior to his flu vaccination, he did not have any dermatological problems. One week after his flu shot, petitioner presented to Dr. Kerwin on February 10, 2016, who diagnosed petitioner with a drug eruption. On February 15, 2016, petitioner presented to Dr. Cetner. Dr. Cetner noted "[p]olycyclic erythematous edematous urticarial plaques and with erythema nodosum-like lesions distributed on the left proximal posterior upper arm, right buttock, and right antecubital skin." Pet. Ex. 8 at 3. Dr. Cetner performed a punch biopsy and the primary diagnosis was hypersensitivity reaction. Dr. Shepherd recorded an auto-immune reaction to flu vaccine on February 16, 2016. On March 1, 2016, petitioner was evaluated by Dr. Einhorn who noted, "serum sickness reaction following flu shot. . . . May need to consult with rheum[atology] or immunology if symptoms persist and re other forms of flu vaccine in future." Pet. Ex. 5 at 16. Petitioner presented to rheumatologist Dr. Portnoy on March 8, 2016. Dr. Portnoy's impression was "rash with biopsy revealing possible hypersensitivity response," which "occurred after a[] [flu] vaccine and I cannot exclude an association with this. Although I cannot exclude serum sickness, some his symptoms occurred fairly soon after the vaccine. I cannot exclude that his rash could be associated with other medication he is currently taking." Pet. Ex. 10 at 3. On October 14, 2016, Dr. Portney noted, "flu . . . ? Sweet's syndrome." Id. at 7.

In summary, these treating physicians questioned whether there was an association between petitioner's flu vaccination and his Sweet's syndrome.

Petitioner's clinical course is similar to case reports filed by petitioner's expert. Jovanoic et al. and Tan et al. documented reports of Sweet's syndrome following flu vaccination. Jovanoic et al. describe a 45-year-old woman who developed classical Sweet's syndrome 12 hours after flu vaccination. Pet. Ex. 22 at 1-2. The patient developed erythematous papules on her legs 12 hours after vaccination, and two days later, the lesions became tender. She then developed erythematous plaques on the injection site on the left arm, back, face, arms, and legs, and a flu-like syndrome with fever. Id. at 2. Tan et al. report a 46-year-old man diagnosed with HIV two years prior and previously in good health who suffered from an eruption two days after a flu vaccination. Pet. Ex. 30 at 1. The patient presented to his physician with a fever and multiple indurated red plaques with bullae and necrosis at the site of vaccination. Id. The authors found "[t]he patient had no apparent triggers for [Sweet's syndrome] other than the [flu] vaccination." Id. at 2.

Like the patients in these two case reports, petitioner had no dermatological conditions prior to flu vaccine administration. Following vaccination in his left arm, petitioner developed a fever and felt as if he had a severe flu the evening after vaccination. Four days later he noticed a rash spreading on his back and neck. By February 15, 2016, Dr. Cetner, a dermatologist, noted lesions distributed on petitioner's left upper arm—the site of vaccination. Therefore, based on a review of the medical records, it appears that petitioner did have lesions at the site of vaccination consistent with case reports.

Further, there is no evidence to suggest that petitioner's Sweet's syndrome was caused by an alternative cause or factor unrelated to vaccination. In his work-up, Dr. Cetner ruled out varicella zoster-virus, other associated viruses, and associated fungal organisms. Pet. Ex. 8 at 4, 9, 11, 21. Petitioner also did not have any identified autoimmune disorders. In regard to allopurinol, Dr. Gershwin stated petitioner was taking allopurinol two years prior to vaccination and continued it without interruption until June of 2016. Dr. Gershwin opined it is unlikely that allopurinol caused petitioner's Sweet's syndrome because case reports demonstrate that symptoms most commonly occur shortly after beginning a new medication. Of note, Dr. Matloubian did not attribute petitioner's rash and symptoms to another cause.

With regard to the second Althen prong, the undersigned finds there is preponderant evidence to support a logical sequence of cause and effect showing the February 3, 2016 flu vaccination to be the cause of petitioner's Sweet's syndrome. See Althen, 418 F.3d at 1278.

3. Althen Prong Three: Proximate Temporal Relationship

Althen Prong Three requires petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That term has been equated to mean a "medically acceptable temporal relationship." Id. The petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disease'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). The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen Prong One). Id.; Koehn v. Sec'y of Health & Hum. Servs., 773 F.3d 1239, 1243 (Fed. Cir. 2014); Shapiro v. Sec'y of Health & Hum. Servs., 101 Fed. Cl. 532, 542 (2011), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 503 F. App'x 952 (Fed. Cir. 2013).

Based on medical records, affidavits, both expert reports, and a review of the record as a whole, the undersigned finds the onset of petitioner's Sweet's syndrome occurred approximately three to four days after vaccination. Petitioner received the flu vaccination February 3, 2016 and presented to Dr. Einhorn on February 9, 2016 for evaluation of a rash. On February 10, Dr. Kerwin noted a red, painful, itchy, and severe rash present for four days. The timing of onset shows a proximate temporal relationship between vaccination and injury, and is consistent with the case reports of Sweet's syndrome injuries described after vaccination. The temporal association is appropriate given the mechanism of injury. Thus, petitioner has satisfied the third Althen prong.

VI. CONCLUSION

Based on the record as a whole, medical records, affidavits, and the petitioner's expert opinions, the undersigned finds there is preponderant evidence to satisfy all three Althen prongs and to establish petitioner's February 3, 2016 flu vaccination caused his Sweet's syndrome. Thus, the undersigned finds petitioner has established by preponderant evidence that he is entitled to compensation. A separate damages order will issue.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master