In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 19-272V
Filed: August 22, 2025

ROBERT MEYERS,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

Special Master Horner

Ronald Craig Homer, Conway, Homer, P.C., Boston, MA, for petitioner.
James Vincent Lopez, U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

On February 19, 2019, petitioner, Robert Meyers, filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10, *et seq.* (2012) ("Vaccine Act"),[2] alleging that an influenza ("flu") vaccine received on December 16, 2016, caused him to suffer anti-PL7 anti-synthetase syndrome, a form of dermatomyositis. (ECF No. 1.) For the reasons set forth below, I conclude that petitioner is *not* entitled to an award of compensation.

I. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations, including showing that an individual received a vaccination covered by the statute;

[1] Because this document 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 document 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] Within this ruling, all citations to § 300aa will be the relevant sections of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury. In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table. If so, the Table Injury is presumed to have been caused by the vaccination, and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B).

Alternatively, if no injury falling within the Table can be shown, a petitioner could still demonstrate entitlement to an award by instead showing that the vaccine recipient's injury or death was caused-in-fact by the vaccination in question. § 300aa-13(a)(1)(A); § 300aa-11(c)(1)(C)(ii). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321-22 (Fed. Cir. 2010) (quoting *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Human Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006). To successfully demonstrate causation-in-fact, petitioner bears a burden to show: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury. *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005).

In this case, petitioner has alleged that the flu vaccine caused him to suffer anti-PL7 anti-synthetase syndrome. Neither anti-PL7 anti-synthetase syndrome, nor dermatomyositis more broadly, are listed on the Vaccine Injury Table. Accordingly, petitioner must satisfy the above-described *Althen* test for establishing causation-in-fact.

Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. § 300aa-13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2 (alternation in original); *see also Snowbank Enters., Inc. v. United States*, 6 Cl. Ct. 476, 486 (1984) (explaining that mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In finding causation, a program fact-finder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F.3d at 1279-80. However, a petitioner may not receive a Vaccine Program award based solely on her assertions; rather, the petition must be

supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1).

Cases in the Vaccine Program are assigned to special masters who are responsible for "conducting all proceedings, including taking such evidence as may be appropriate, making the requisite findings of fact and conclusions of law, preparing a decision, and determining the amount of compensation, if any, to be awarded." Vaccine Rule 3(b)(1). Special masters must ensure each party has had a "full and fair opportunity" to develop the record. Vaccine Rule 3(b)(2). However, special masters are empowered to determine the format for taking evidence based on the circumstances of each case. Vaccine Rule 8(a); Vaccine Rule 8(d). Special masters are not bound by common law or statutory rules of evidence but must consider all relevant and reliable evidence in keeping with fundamental fairness to both parties. Vaccine Rule 8(b)(1). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." § 300aa-13(b)(1)(A). The special master is required to draw plausible inferences and articulate a rational basis for the decision. *Winkler v. Sec'y of Health & Human Servs.*, 88 F.4th 958, 963 (Fed. Cir. 2023) (citing *Hines ex rel. Sevier v. Sec'y of Health & Human Servs.*, 940 F.2d 1518, 1528 (Fed. Cir. 1991)).

II. Procedural History

This case was initially assigned to another special master and was subsequently reassigned to the undersigned on August 28, 2019. (ECF Nos. 4, 15-16.) Between February 2019 and February 2020, petitioner filed medical records and two affidavits. (ECF Nos. 7-9, 17, 21, 23, 27, 30; Exs. 1-17.) Thereafter, respondent filed his Rule 4(c) Report on May 4, 2020, recommending against compensation. (ECF No. 33.) Specifically, respondent argued that petitioner had not "submitted any medical evidence or an expert report that provides a medical theory showing that the flu vaccine can cause anti-PL7 antisynthetase syndrome and that it did so here." (*Id.* at 14.)

Petitioner then filed an expert report by rheumatologist Samardeep Gupta, M.D., along with supporting medical literature. (ECF Nos. 35-36; Exs. 18-34.) In response, respondent filed an expert report by rheumatologist, Christopher Mecoli, M.D., along with supporting medical literature. (ECF No. 40; Exs. A-B.) Thereafter, petitioner filed a supplemental expert report by Dr. Gupta, as well as an expert report by immunologist, Eric Gershwin, M.D., with accompanying medical literature. (ECF Nos. 49, 51; Exs. 35-41.) Respondent responded in kind with a supplemental expert report by Dr. Mecoli, as well as an expert report by immunologist Stephen Hedrick, Ph.D. (ECF No. 57; Exs. C-E.) Respondent subsequently filed an amended expert report by Dr. Hedrick and supporting medical literature. (ECF No. 59; Ex. F.) The parties exchanged another round of immunology expert reports with supporting medical literature (ECF Nos. 64-66,

68-70, 72-74, 76-79, 81-83, 86, 93; Exs. 42-202, G), before confirming that the case was ripe for an entitlement hearing (ECF No. 94).

On May 23, 2024, an entitlement hearing was scheduled to commence on August 7, 2024. (ECF No. 95.) Prior to the hearing, petitioner filed additional medical records and a supplemental expert report by Dr. Gershwin, along with supporting medical literature. (ECF Nos. 96, 99, 107; Exs. 203-24.) A two-day entitlement hearing was held, commencing on August 7, 2024. (*See* Transcript of Proceeding ("Tr"), at ECF Nos. 122-23.) At the close of the hearing, the parties agreed to forgo post-hearing briefing. (Tr. 277.) Accordingly, this case is now ripe for resolution of entitlement.

III. Factual History

a. Medical Records

Prior to the subject vaccination, petitioner's medical history was significant for a right knee replacement, low back pain, hip pain, degenerative joint disease of the bilateral knees, and gastroesophageal reflux disease. (*See generally* Ex. 3.) Petitioner was admitted to the hospital on April 3, 2016, for chest pain, but he was discharged home the following day after normal evaluation and test results. (Ex. 4, pp. 3-4; Ex. 5.) Notably, petitioner previously received the flu vaccine on December 4, 2014, and December 10, 2015. (Ex. 2, p. 1.) Petitioner received the subject flu vaccine on December 16, 2016. (Ex. 1; ECF No. 102, p. 1.) At the time of vaccination, petitioner was fifty-seven years of age. (ECF No. 102, p. 1.)

Petitioner's first post-vaccination appointment was with his orthopedist, Michael A. Colucci, M.D., on January 17, 2017, for a work-related injury to his right hip and groin. (Ex. 3, pp. 27-28.) There is no mention of rash during this encounter. However, a little over a week later, on January 26, 2017, petitioner reached out to his primary care office and reported a rash on his cheek and both ears that felt warm to the touch as well as swelling in his jaw. (Ex. 2, pp. 405-06.) Petitioner presented to his primary care physician, Michael Krasner, M.D., the following day. (*Id.* at 415.) Dr. Krasner recorded a one-week history of redness and itchiness over the ears and skin on the face that was worse on the left side. (*Id.*) On physical exam, a large patch of erythema and slight scaling were observed. (*Id.* at 416.) Although petitioner denied any known exposures to topical agents, fabrics, or any other contact potential allergens, Dr. Krasner's assessment was contact dermatitis. (*Id.* at 415-16.) A topical steroid cream was prescribed, and petitioner was advised to return if his rash did not resolve within a week. (*Id.* at 416.)

On January 31, 2017, petitioner returned to Dr. Krasner with complaints of sore throat and minimal congestion or cough that had persisted for about four days. (Ex. 2, p. 432.) A physical exam revealed normal tympanic membranes and no lymphadenopathy in the neck, and a rapid strep test was negative. (*Id.* at 433.) Petitioner was diagnosed with a "[s]ore throat, viral pharyngitis," and advised to treat symptomatically. (*Id.*) On February 4, 2017, petitioner called his primary care office,

complaining of persistent gland swelling, sore throat, mouth soreness, and fatigue. (*Id.* at 445.) He denied pain with swallowing, and a self-examination of his throat did not reveal any white spots or exudate. (*Id.*) He was instructed to continue treating symptomatically and to go to urgent care if his symptoms worsened. (*Id.*)

Petitioner presented to Joseph Gasparino, M.D., at his primary care physician's office on February 10, 2017. (Ex. 2, p. 454.) Dr. Gasparino recorded a six-week history of fatigue and sore throat that began after he received the flu vaccine in December. (*Id.*) Within the past two weeks, petitioner also developed chest tightness and a productive cough. (*Id.*) Bilateral, scattered rhonchi was noted on physical exam, and petitioner was diagnosed with bronchitis. (*Id.* at 454-55.) A one-week course of doxycycline[3] was prescribed. (*Id.* at 455.) Petitioner's next primary care appointment was with Dr. Krasner on February 13, 2017. (*Id.* at 472.) During this encounter, he reported slight fevers for the past few days and dry cough that progressed to an intense cough when laying on his right side. (*Id*.) A physical exam was unremarkable, and petitioner was prescribed guaifenesin[4] with codeine to be taken at night, when his symptoms were the most pronounced. (*Id.* at 473.) On February 20, 2017, petitioner underwent a chest x-ray, which revealed "ill-defined pulmonary airspace opacity in the left lower lung lobe, which may represent atelectasis or pneumonia." (*Id.* at 494-95.) Dr. Krasner's assessment was "[s]pasmodic cough following viral infection, suspicious for bronchospasm." (*Id.* at 496.) A physical exam showed patchy, erythematous rash on the buttocks that was slightly pink. (*Id*.) Dr. Krasner recommended a prednisone[5] taper. (*Id*.) Petitioner's cough persisted through the end of February and into March. (*Id.* at 511-13, 537, 539-40.)

On March 6, 2017, petitioner had a follow up appointment with Dr. Krasner. (Ex. 2, p. 556.) During this encounter, petitioner underwent another chest x-ray that revealed "[p]ersistent opacity in left lower lobe is slightly decreased" that "could represent atelectasis or infiltrate." (*Id.* at 553.) Dr. Krasner noted that petitioner's cough had persisted in spite of two courses of antibiotics. (*Id.* at 556.) He also noted that petitioner had developed bilateral lower extremity edema following a five-day prednisone taper. (*Id*.) Petitioner's differential diagnoses included viral pneumonitis and possible edema from prednisone; however, a cardiac etiology was not suspected. (*Id.* at 557.)

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[3] Doxycycline is an orally administered "semisynthetic broad-spectrum antibacterial." *Doxycycline*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=14859 (last visited July 23, 2025).

[4] Guaifenesin is an orally administered expectorant that reduces mucus viscosity. *Guaifenesin*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=2107 (last visited July 23, 2025).

[5] Prednisone is "a synthetic glucocorticoid derived from cortisone, administered orally as an anti-inflammatory and immunosuppressant in a wide variety of disorders." *Prednisone*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=40742 (last visited July 23, 2025).

Petitioner presented to the emergency department at Strong Memorial Hospital on March 12, 2017, with "cough, extremity edema, and rash." (Ex. 2, p. 600.) Petitioner reported a two-month history of an intermittent, minimally productive cough and intermittent, low-grade fevers, as well as a two-week history of intermittent edema in his extremities and an itchy, red rash on his shins and left forearm. (*Id*.) On physical exam, petitioner exhibited rhonchi and rales in the left lower field, swelling in his bilateral wrists and ankles, and an urticarial rash. (*Id.* at 602-03.) It was noted that petitioner had "a known left lower lobe infiltrate, which has been suggestive of pneumonia, but [has] not responded to oral doxycycline or azithromycin." (*Id.* at 603.) The left-sided rales noted on physical exam were consistent with pneumonia in that area. (*Id*.) At this point, the differential diagnoses included "atypical bacterial pneumonia, fungal pneumonia, paraneoplastic syndrome[,] congestive heart failure, lung neoplasm, hepatitis, [and] hypoalbuminemia." (*Id*.) Petitioner was admitted for further evaluation. (*Id.* at 608, 610-12.)

During his hospital stay, petitioner was evaluated by rheumatologist Darren Tabechian, M.D., and his resident Ryan Canissario, M.D. (Ex. 2, pp. 624-30.) Petitioner reported developing soreness over his shoulder blades, which progressed to his neck and was associated with dry mouth and jaw pain, after receiving the flu vaccine in December. (*Id.* at 625.) Dr. Canissario provided a brief description of petitioner's post-vaccination medical history. (*Id*.) Since his last primary care encounter, petitioner had completed a course of azithromycin[6] with no relief and the swelling in his bilateral ankles worsened despite discontinuing prednisone. (*Id*.) Around March 10, 2017, petitioner reportedly began experiencing hand and facial swelling, prompting his hospital visit. (*Id*.) Bitemporal wasting, bibasilar crackles, and edema of distal upper and lower extremities were observed on physical exam. (*Id.* at 627, 629.) Dr. Canissario noted,

> Workup is remarkable for leukocytosis, elevated [creatine kinase], mild transaminitis, hypoalbuminemia, and fibrotic changes on CT chest. The pattern of the patient's edema (hands/feet) is most consistent with capillary leak of unidentified etiology. . . . The mildly elevated [creatine kinase] may be due to myositis, which in turn could explain the elevated AST. Furthermore, there is an association between myositis and interstitial lung disease. His arthralgias seems more consistent with his known [osteoarthritis] (worse in knees and hips, no involvement of previously unaffected joints) than with inflammatory arthritis. . . . Working against an autoimmune etiology is the lack of response of his symptoms to prednisone therapy.

(*Id.* at 629.) Dr. Canissario assessed possible myositis and ordered further testing, including a myositis panel. (*Id*.) After separately evaluating petitioner and reviewing Dr.

[6] Azithromycin is an orally or intravenously administered antibiotic that is used to treat mild to moderate bacterial infections. *Azithromycin*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=5244 (last visited July 23, 2025).

Canissario's exam findings, Dr. Tabechian noted mild erythema of the eyelids that was not consistent with heliotrope and some muscle wasting, as well as coarse rales in the lower lungs and swelling in the lower legs. (*Id*.) Dr. Tabechian observed,

> In the setting of apparent [interstitial lung disease], [the] exam and lab findings point to an inflammatory myopathy . . . with capillary leak. This can be a primary idiopathic process or paraneoplastic in up to 15%. An overlap syndrome: systemic sclerosis with [idiopathic inflammatory myopathy], sarcoidosis, giant cell myositis and possible vaccine induced myositis are other possibilities.

(*Id*. at 629-30.) A rheumatology progress note on March 14, 2017, lists a working diagnosis of idiopathic inflammatory myopathy with interstitial lung disease vs. overlap syndrome. (*Id.* at 648-49.) Petitioner's workup was negative for ANA but positive for anti-Ro antibodies. (*Id.* at 649.) An EMG/NCS on March 16, 2017, revealed "mild muscle membrane irritability in the left deltoid and paraspinals which, although not diagnostic, could represent an early myositis." (*Id.* at 672-74.) Additionally, petitioner's tibial motor and sural sensory responses were low in amplitude, a finding that was of uncertain diagnostic significance but could be secondary to lower extremity edema. (*Id.* at 674.) Petitioner was subsequently discharged on March 17, 2017, and an outpatient muscle biopsy was ordered to confirm his differential diagnoses of dermatomyositis or idiopathic inflammatory myositis. (*Id.* at 611.) On discharge, petitioner's myositis panel results were still pending, and he was started on empiric treatment with prednisone. (*Id.*at 611-12.)

On March 21, 2017, petitioner had a follow up appointment with Dr. Tabechian. (Ex. 2, p. 928.) Dr. Tabechian relayed petitioner's recent medical history, including his hospitalization and differential diagnosis of an early dermatomyositis variant. (*Id.*) After three days of treatment with prednisone, petitioner reported some improvement in his musculoskeletal symptoms but worsening of his leg swelling. (*Id*.) Petitioner also reported that his cough had largely resolved with the exception of a paroxysm earlier that day. (*Id*.) On physical exam, petitioner had no heliotrope, subtle but improved erythema over the extensor aspects of the fingers, improved swelling, and pitting edema in the lower extremities with underlying chronic stasis changes. (*Id.* at 929.) Dr. Tabechian concluded that his "impression [was] unchanged at this point, mild interstitial lung disease associated with likely inflammatory myopathy." (*Id.* at 930.) Given the residual leg swelling, hypoalbuminemia, and appearance of cachexia, he expressed concern that petitioner's condition was consistent with an "occult malignancy presenting or causing this paraneoplastic autoimmune phenomenon." (*Id*.) Petitioner was continued on prednisone, but based on petitioner's pending serologic evaluation, Dr. Tabechian suggested he "may either initiate IVIG and/or methotrexate, and begin the steroid tapering process" at petitioner's next follow up appointment. (*Id*.) A CT scan of the abdomen and pelvis was ordered to rule out a compressive occlusive process that could explain his persistent swelling. (*Id*.)

Petitioner's muscle biopsy revealed "[m]ild active myopathy with necrotic and regenerating muscle fibers and scattered perimysial perivascular inflammation." (*Id*.) The report clarified that, although not diagnostic, these findings "can be seen with systemic vasculitic processes and early, or partially treated, dermatomyositis." (Ex. 2, p. 965.) During a March 27, 2017 primary care encounter, Dr. Krasner noted "[l]ikely dermatomyositis, with multiple systemic as well as localized signs and symptoms including lower extremity edema[,] hypoalbuminemia, transaminases and [creatine kinase] elevations." (*Id.* at 1039-40.)

Petitioner's next appointment with Dr. Tabechian was on April 14, 2017. (Ex. 2, p. 1155.) During this encounter, Dr. Tabechian recorded that petitioner had tested positive for anti-PL7, an antibody directed against aminoacyl-transfer ribonucleic acid ("tRNA") synthetase, which confirmed his diagnosis of "a variant form of dermatomyositis with a predilection for causing pericardial disease and interstitial lung disease." (*Id*.) Petitioner reported that his rash and swelling had improved, but he recently developed swallowing problems that were believed to represent significant laryngeal reflux, rather than muscle weakness. (*Id.* at 1155-56.) He also reported some improvement in his strength, though it was noted that his strength was only minimally involved. (*Id*.) Lesions in his mouth were suspected to be related to a fungal infection and treated empirically. (*Id.* at 1158.) Petitioner's echocardiogram and CT scan of the abdomen and pelvis were unremarkable; however, his lab results remained abnormal with elevated creatine kinase and transaminases; reduced, but still elevated, c-reactive protein and total protein; and reduced, but stabilized, albumin. (*Id.* at 1156.) Dr. Tabechian assessed slow improvement in petitioner's dermatomyositis. (*Id.* at 1158.) Given the refractory nature of petitioner's c-reactive protein level, Dr. Tabechian decided to supplement his prednisone and azathioprine regimen with IVIG.[7] (*Id*.)

Petitioner received his first IVIG infusion in May of 2017. (Ex. 2, pp. 1279,1286, 1307, 1326, 1385.) At his next rheumatology appointment on May 17, 2017, Dr. Tabechian recorded that petitioner had "tested positive for the PL-7 antisynthetase antibody, confirming our suspicion of an overlap inflammatory muscle disease, dermatomyositis, based on his skin findings at onset, and interstitial lung disease, which has been mild and responded to treatment." (*Id*. at 1385)

On June 16, 2017, petitioner had a follow up appointment with Dr. Tabechian for his dermatomyositis. (Ex. 2, pp. 1463-67.) Petitioner's skin condition remained consistent, despite beginning to taper his prednisone. (*Id.* at 1463.) Although his strength was generally improved, petitioner reported intermittent flares and "persistent weakness in his bilateral forearms/elbows, as well as his thighs." (*Id*.) Petitioner also

[7] IVIG is intravenously administered immunoglobulin, which is "a concentrated preparation containing mostly gamma globulins, predominantly IgG, from a large pool of human donors" that is used in the treatment of primary immunodeficiency disorders. *Immune globulin*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=78973 (last visited July 24, 2025); *Immune globulin intravenous (human)*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=78975 (last visited July 24, 2025); *see also Immunoglobulin*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=24894 (last visited July 24, 2025).

reported "nearly constant numbness of his toes bilaterally" and new onset of numbness in his right foot. (*Id*.) Finally, petitioner reported persistent bloating and gastrointestinal symptoms that he was treating symptomatically. (*Id*.) Dr. Tabechian noted that petitioner's symptoms appeared stable and that his creatine kinase level had plateaued. (*Id.* at 1465-66.) He decided to adjust petitioner's regimen by decreasing his prednisone dosage, which would hopefully help with the gastrointestinal issues, and increasing his azathioprine dosage. (*Id.* at 1466.) Petitioner was continued on IVIG therapy. (*Id*.) However, Dr. Tabechian wanted to monitor petitioner's gastrointestinal issues as dermatomyositis has been associated with malignancy and further intervention may be warranted. (*Id*.) Petitioner's June 28, 2017 labs revealed elevated creatine kinase, resulting in an increase in his IVIG therapy. (*Id.* at 1499, 1516.)

Throughout July of 2017, petitioner continued to receive IVIG infusions and to follow up with Drs. Krasner and Tabechian. (Ex. 2, pp. 1525, 1545, 1557, 1569-70, 1592-94.) On July 3, 2017, petitioner presented to Dr. Krasner with complaints of chest congestion. (*Id.* at 1525.) An EKG was normal, and Dr. Krasner's assessment was congestion without evidence of acute bacterial infection. (*Id*.) On July 19, 2017, petitioner presented for a rheumatology evaluation with Dr. Tabechian. (*Id.* at 1592.) Dr. Tabechian noted that petitioner had experienced functional and chemical improvement with his treatment regimen; however, his condition had deteriorated after steroid tapering. (*Id.* at 1593.) At the time, Dr. Tabechian observed that petitioner's "likelihood of returning to work in a warehouse this year seems low given both his inflammatory and corticosteroid induced muscle weakness." (*Id.* at 1594.)

On August 22, 2017, petitioner had a follow up appointment with Dr. Tabechian, during which petitioner reported persistent muscle involvement and reduced endurance, as well as paresthesias in both feet but particularly in his right foot. (Ex. 2, pp. 1726-28.) However, petitioner denied pulmonary symptoms. (*Id.* at 1726.) Dr. Tabechian's impression was recalcitrant dermatomyositis with anti-PL7 antibodies. (*Id.* at 1728.) He considered adjusting petitioner's treatment regimen, which he had been avoiding due to petitioner's interstitial lung disease. (*Id*.) He decided to consult with the myositis group at Johns Hopkins for advice on petitioner's specific form of dermatomyositis and to taper petitioner's prednisone. (*Id*.) On September 8, 2017, petitioner presented to internist Trevor Litchmore, M.D., pursuant to a referral by the Division of Disability Determination. (Ex. 14, p. 71.) Petitioner reported "generalized muscle weakness in the limbs, fingers, legs, toes and feet." (*Id*.) Dr. Litchmore recorded petitioner's diagnosis as anti-PL-7 syndrome and scoliosis of the thoracolumbar spine. (*Id.* at 74.)

Petitioner continued to receive regular IVIG infusions. (Ex. 2, pp. 1774, 1805, 1893-94, 1915.) During a rheumatology appointment on October 6, 2017, Dr. Tabechian recorded that petitioner had "achieved [a] nice remission now again with [creatine kinase] almost normalizing," though "he certainly does not have functional capacity back." (*Id.* at 1952.) In particular, petitioner complained of "weakness in the left leg with some burning pain that radiates from the buttock down his legs" and localized knee pain. (*Id*.) He also complained of arm and hand weakness and new onset of fasciculations in his bilateral calves. (*Id*.) However, petitioner reported no

cutaneous changes beyond low back acne. (*Id*.) Dr. Tabechian impression was "dermatomyositis, presenting with a capillary leak-like phenomenon, cutaneous changes, weakness, and interstitial lung disease. He is also anti Ro positive." (*Id*. at 1954.) His knee pain was suspected to be related to his degenerative arthritis; however, it was unclear whether his persistent leg weakness and burning pain were related to peripheral muscle or back and nerve compression. (*Id*.) Based on his positive response to therapy, petitioner was to continue IVIG and azathioprine while tapering prednisone. (*Id*.)

On November 10, 2017, petitioner presented to John Orsini, M.D., for left lower back and leg pain. (Ex. 2, p. 2095.) Dr. Orsini noted that petitioner's lower extremity symptoms, particularly his numbness, could not be treated with injection; however, he recommended injection for petitioner's back pain, which he believed was "related to his significant facet arthropathy." (*Id.* at 2098, 2123-47.) On November 20, 2017, petitioner presented to Michael Stanton, M.D., for an EMG/NCS and neuromuscular consultation for his low back and leg pain. (*Id.* at 2199-203.) Dr. Stanton recorded petitioner's history of chronic low back pain and dermatomyositis with interstitial lung disease and noted that petitioner "developed worsening of his low back pain over the last 6 months" that radiates down his left leg after prolonged standing and is associated with numbness and weakness. (*Id*. at 2199.) Petitioner's examination was unremarkable, but with subjective reports of decreased sharp sensation circumferentially below the left knee. (*Id.* at 2200-02.) An EMG revealed no muscle membrane irritability, active myositis, or left-sided lumbosacral radiculopathy. (*Id.* at 2202.) When compared to his prior study, petitioner showed "considerable improvement in the sural sensory response and the tibial motor response on the left side and both sides are symmetric with only mildly reduced sural sensory responses." (*Id*.) Based on the lab and electrodiagnostic results, Dr. Stanton assessed petitioner's myositis as "in remission under combined treatment with IVIG, azathioprine, and prednisone." (*Id*.) Regarding petitioner's back pain, Dr. Stanton observed that an MRI revealed moderate scoliosis with degenerative arthritis, primarily affecting the left-sided neural foramen but without significant central stenosis. (*Id*.) He suggested that petitioner follow up with Dr. Orsini for conservative treatment of his low back pain. (*Id.* at 2203.)

Petitioner had a follow up appointment with Dr. Tabechian on December 1, 2017. (Ex. 2, pp. 2271-73.) Petitioner's condition was being maintained on IVIG, azathioprine, and prednisone, though he remained "quite limited by both his back and corticosteroid side effects." (*Id.* at 2271.) Dr. Tabechian recorded that petitioner's "inflammatory muscle disorder with interstitial lung disease is in remission on treatment" and suggested that he begin tapering prednisone and IVIG. (*Id.* at 2273.) He referred petitioner for a colonoscopy screening given that his muscle disorder can have paraneoplastic effects. (*Id*.) A December 5, 2017 CT scan of petitioner's chest revealed a "[s]table 7 mm right lower lobe pulmonary nodule." (Ex. 17, pp. 9-10.) The impression noted "[m]arked interval improvement in bibasilar lung disease likely representing resolved inflammatory process." (*Id.* at 10.) On December 20, 2017, petitioner had a follow up appointment with Dr. Orsini. (Ex. 2, pp. 2341-45.) Petitioner reported no improvement with injections. (*Id.* at 2341.) Dr. Orsini recommended trying

medial branch blocks with an endpoint of radiofrequency ablation, which petitioner received in January and March of 2018. (*Id.* at 2344, 2442-46; Ex. 7, pp. 227-28.)

Petitioner's treatment continued throughout 2018, 2019, 2020, and 2021. (*E.g.*, Ex. 2, pp. 2470-73, 2486, 2506, 2514, 2543, 2551, 2565-68; *see generally* Exs. 7, 224.) During an April 20, 2018 rheumatology appointment, Dr. Tabechian noted that petitioner had been "in remission now for some time with our current regimen" and that he had "finally achieved better control of his disease." (Ex. 7, pp. 424-26.) On physical exam, Dr. Tabechian observed "very subtle Gottron-like or at least pattern of changes of his fingers." (Ex. 7, p. 424.) In October of 2018, Dr. Tabechian recorded that petitioner was in clinical remission; however, his recurrent ulcers were concerning for dermatomyositis involvement of the esophageal/gastric mucosa, prompting a temporary adjustment in his treatment regimen. (Ex. 13, pp. 270, 273-74.)

On July 20, 2022, petitioner presented to rheumatologist Colin C. Edgerton, M.D., for evaluation of suspected inflammatory myopathy, which petitioner associated with his flu vaccination. (Ex. 204, p. 12.) Dr. Edgerton considered switching petitioner to rituximab as a substitute for IVIG, but petitioner was continued on prednisone and azathioprine. (*Id.* at 16.) In August of 2022, petitioner received his first rituximab infusion, and he began tapering prednisone after receiving his second rituximab infusion in September of 2022. (*Id.* at 6-7, 25, 35.) It was noted that petitioner experienced a good response to rituximab. (*Id.* at 51.) However, after being tapered off prednisone, his creatine kinase levels increased, and he developed active symptoms. (*Id.* at 56.) His symptoms significantly improved once he was restarted on prednisone. (*Id.*) He continues to seek treatment for his dermatomyositis and anti-synthetase syndrome.

b. Affidavit

Petitioner avers that he was "relatively healthy" prior to vaccination, and his "only major health issue was a right knee replacement." (Ex. 10, ¶ 1.) However, after receiving the subject flu vaccine on December 16, 2016, he "developed shoulder blade stiffness and pain," which started on one side, but eventually progressed to both sides and his neck. (*Id.* ¶ 2.) By the end of December 2016, petitioner had developed swollen salivary glands and dry mouth, especially at night. (*Id.* ¶ 3.)

In January 2017, petitioner developed a "deep and prolonged" cough at night when sleeping on his side. (Ex. 10, ¶ 4.) As his cough progressed, he noticed that it was aggravated by laying in any position and somewhat relieved when sitting upright. (*Id.*) Petitioner also began notice that he was feeling fatigued more easily. (*Id.* ¶ 5.) "Simple tasks were becoming very difficult to accomplish because of the muscular weakness [he] was feeling." (*Id.*) Eventually, petitioner's cough began affecting him during the day, prompting a primary care visit. (*Id.* ¶¶ 5-6.) Petitioner's primary care physician prescribed cough medicine, which provided partial relief. (*Id.* ¶ 6.) Because petitioner's symptoms did not resolve, his primary care physician order an x-ray of his chest. (*Id.* ¶ 7.) Based on the results of the x-ray, petitioner avers that he was "incorrectly diagnosed" with pneumonia and prescribed antibiotics. (*Id.*) By March

2017, petitioner had developed swelling in his hands and feet, aching in his knees and elbows, and an itchy rash on his legs, arms, and back. (*Id.* ¶ 8.) His cough, fever, and fatigue persisted. (*Id.*) Petitioner explains, "After extensive testing, I was diagnosed with an inflammatory muscle disorder and I was started on prednisone and later, IVIG infusions." (*Id.* ¶ 9.)

Petitioner avers that he continues to undergo infusions, to take multiple immunosuppressants, and to require monthly blood tests. (Ex. 10, ¶ 10.) He describes these interventions as "painful and uncomfortable in different ways, making this regimen emotionally draining." (*Id.*) He continues to suffer from muscle weakness and a lack of endurance. (*Id.*) As a result of his condition, petitioner has been unable to work. (*Id.*) The effect that his condition has had on his ability to perform his duties at work and the cost of his treatment have resulted in financial hardship. (*Id.*) Petitioner worries that he "may never return to the life [he] knew before this disease." (*Id.*)

IV. Expert Opinions

a. Petitioner's Experts

i. Samardeep Gupta, M.D.[8]

Petitioner's expert, Dr. Gupta, submitted two expert reports and provided expert testimony during the entitlement hearing in this case. (Exs 18, 35, Tr. 5.) Dr. Gupta explains that the relevant condition in this case is dermatomyositis or inflammatory myositis as distinct from viral myositis.[9] (Ex. 18, p. 4; Ex. 35, p. 2.) Dermatomyositis is an autoimmune inflammatory condition within the broader category of myopathies,

[8] Dr. Samardeep ("Samar") Gupta received his medical degree from Maharshi Dayanand University in Rohtak, India, before going on to complete residencies in internal medicine and orthopedic surgery at the same university. (Ex. 19, p. 1; Tr. 6.) From there, Dr. Gupta completed an internship in internal medicine at Rush University Medical Center in Chicago, Illinois; an additional residency in internal medicine at Wayne State University in Detroit, Michigan; and a fellowship in rheumatology and immunology at University of Michigan in Ann Arbor, Michigan. (Ex. 19, p. 1; Tr. 6.) He is board certified in internal medicine, as well as rheumatology and immunology, and he maintains an active medical license in Wyoming. (Ex. 19, p. 1; Tr. 6.) Throughout his career, Dr. Gupta has worked as a professor and attending physician at University of Michigan hospitals. (Ex. 19, p. 1; Tr. 6.) He currently holds a position as a clinical associate professor in internal medicine, specifically in rheumatology, at the University of Michigan and VA Ann Arbor Healthcare Systems. (Ex. 19, p. 1; Tr. 6-7.) He also treats patients, including patients with dermatomyositis and other forms of myositis, on a regular basis. (Tr. 7-8.) Dr. Gupta has authored 17 peer reviewed articles, one non-peer reviewed article, and two abstracts. (Ex. 19, pp. 5-6.) He was proffered as an expert in rheumatology without objection. (Tr. 9-10.)

[9] During the hearing, Dr. Gupta explained that viral myositis is the sequela of an infection. (Tr. 19.) Because "true viral myositis" is "a direct effect of the virus particle damaging the muscles," the condition is self-limited with improvement after the immune system eliminates the virus, which typically takes weeks to months, at most. (Tr. 17-19; Ex. 35, p. 2.) Additionally, patients with viral myositis do not exhibit the rash that is characteristic of dermatomyositis, and the CT thorax and muscle biopsy are not consistent with dermatomyositis. (Tr. 17-18; Ex. 35, p. 2.) There is usually scant or no evidence of inflammation, no myositis antibodies, and no lung involvement in viral myositis. (Ex. 35, p. 2.) Ultimately, Dr. Gupta opined that petitioner's clinical course and work up were not consistent with viral myositis. (*Id.*)

which are "a heterogenous group of muscle diseases," meaning that the various subtypes have different clinical manifestations. (Ex. 18, pp. 4-5; Tr. 16-17, 26.) The incidence rate of dermatomyositis has not yet been clearly established (Ex. 18, p. 5; Tr. 21); however, Dr. Gupta opines that this rare disease affects around 10 per 1,000,000 individuals (Ex. 18, p. 5; Tr. 21, 25). He cites the Bohan and Peter Classification Criteria for Dermatomyositis, which supports diagnosis based on (1) exclusion of all other myopathies, (2) symmetric proximal muscle weakness, (3) elevated serum muscle enzymes, (4) abnormal electromyographic findings, (5) abnormal muscle biopsy findings, and (5) skin rash. (Ex. 18, pp. 5-6 (citing Anthony Bohan & James B. Peter, *Medical Progress: Polymyositis and Dermatomyositis (First of Two Parts),* 292 NEJM 344 (1975) (Ex. 21)).) However, he clarified during the hearing that there are no universal diagnostic criteria for dermatomyositis and that "classification criteria," such as the Bohan and Peter criteria, are meant to provide uniformity for research purposes, not for diagnosis, and may result in the exclusion of individuals with dermatomyositis. (Tr. 20-24 (discussing I. E. Lundberg et al., *Diagnosis and Classification of Idiopathic Inflammatory Myopathies*, 280 J. INTERNAL MED. 39 (2016) (Ex. A, Tab 2); Joerg-Patrick Stübgen, *A Review on the Association Between Inflammatory Myopathies and Vaccination*, 13 AUTOIMMUNITY REVS. 31 (2014) (Ex. A, Tab 13; *see also* Ex. F, Tab 7)).)

Dr. Gupta explains that diagnosis in the clinical setting is usually based on consideration of medical history, physical examination, lab testing and biopsy, and response to therapy. (Tr. 21.) The predominant symptoms associated with dermatomyositis are muscle weakness and low muscle endurance, but other associated symptoms include arthritis, skin rash, and heart and lung involvement. (Ex. 18, p. 5.) Although any rash can support diagnosis, the most common rashes include heliotrope rash, Gottron's papules,[10] and a rash around the nails. (Tr. 39-40.) EMG changes, despite tending to be nonspecific, are a helpful indicator of myopathic changes. (Ex. 18, p. 5.) Dr. Gupta denies that there are known risk factors for dermatomyositis (Tr. 27), but he asserts that genetic risk factors, including immune response genes and familial clustering of myositis, are relevant to diagnosis (Ex. 18, p. 5).

The presence of inflammatory antibodies is also relevant to diagnosis and can be suggestive of clinical course. (Tr. 14-15, 26-28.) For instance, the presence of anti-Jo-1, NRA, anti-Ro, and anti-PL7 antibodies denotes autoimmunity, and the presence of anti-PL7 antibodies specifically suggests that the dermatomyositis patient is likely to develop interstitial lung disease. (Tr. 27-28.) While dermatomyositis is strongly associated with malignancy when compared to other autoimmune myopathies (Ex. 18, p. 6), the presence of anti-Ro antibodies suggests that malignancy is less likely (Tr. 29). The most common myositis antibodies are "anti-synthetase autoantibodies directed against aminoacyl-tRNA synthetases," including *inter alia* anti-Jo-1 and anti-PL-7.[11]

[10] Gottron's papules are "discolored lichenoid flat-topped papules" that appear over the knuckles. *Gottron papules*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=96002 (last visited May 12, 2025).

[11] During the hearing, Dr. Gupta clarified that "myositis-specific antibodies" and "myositis-associated antibodies" are essentially the same; the semantic difference stems from whether a lab uses a certain

(Ex. 18, p. 4 (citing Kanneboyina Nagaraju et al., *Inflammatory Diseases of Muscle and Other Myopathies*, in 2 KELLEY AND FIRESTEIN'S TEXTBOOK OF RHEUMATOLOGY 1461 (Gary S. Firestein et al. eds., 10th ed. 2017) (Ex. 20)); Tr. 35.) Diagnosis of myositis based on these antibodies is referred to as anti-synthetase syndrome. (Ex. 18, p. 4.) Anti-synthetase syndrome is a clinically distinct subset of myositis that is characterized by interstitial lung disease, Raynaud's phenomenon,[12] nonerosive symmetric polyarthritis of the small joints, and mechanic's hands.[13] (*Id.* (citing Nagaraju et al., *supra*, at Ex. 20).)

Dr. Gupta opines that petitioner's correct diagnosis is dermatomyositis and, specifically, anti-synthetase syndrome. (Tr. 13, 84; Ex. 35, pp. 2-3.) In coming to this conclusion, Dr. Gupta relies on petitioner's clinical presentation, which included muscle weakness, inflammatory joint swelling, and dry cough consistent with pulmonary fibrosis, as well as his constitutional symptoms, including fatigue, decreased appetite, and diffuse skin rash. (Tr. 11-12; *see also id.* at 38-53 (citing Ex. 2, pp. 410, 415-16, 432-33, 454-55, 496, 554-57, 600-04, 625, 629-30).) The Gottron's papules on petitioner's hands in particular were "highly suggestive of an inflammatory dermatomyositis." (*Id.* at 12.) He further notes petitioner's abnormal CT scan of the lungs that showed interstitial lung disease, as well as an abnormal EMG and muscle biopsy, were consistent with dermatomyositis. (*Id.* at 12-13; *see also id.* at 43-44, 49-50, 53 (citing Ex. 2, pp. 494-95, 689, 970).) Petitioner's lab testing revealed high inflammatory markers (namely, ESR and CRP), electrophoresis, and elevated transaminases, creatine kinase, and platelets. (Tr. 12-13; *see also id.* at 46-47 (citing Ex. 2, pp. 554-57).) These results were consistent with muscle damage and inflammation. (*Id.* at 12-13; Ex. 18, p. 10.) Petitioner had some response to steroids, no response to antibiotics, and good response to disease-modifying or steroid-sparing drugs, suggesting an auto-inflammatory explanation for his condition. (Tr. 13; *see also id.* at 53-54 (citing Ex. 2, p. 1952).) Additionally, Dr. Gupta opines that petitioner tested positive for anti-Ro antibodies, which he explained is a "marker for systemic autoimmunity" and the most common antibody found in inflammatory myopathies. (Ex. 18, p. 9; Tr. 29.) When asked whether he agreed with petitioner's diagnosis of anti-PL7 anti-synthetase syndrome, Dr. Gupta explained, "I'm a clinical person, I'm not a classification person;" therefore, he was willing to agree with a diagnosis of anti-synthetase syndrome despite the lack of anti-Jo-1 antibodies, which are the "hallmark of anti-synthetase." (Tr. 35, 84-85.)

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panel as their group of testing. (Tr. 28-29.) Regardless of the chosen designation, all panels will include anti-PL7, anti-Jo-1, and anti-Ro antibodies in their testing. (*Id.* at 29.)

[12] Raynaud's phenomenon presents as intermittent bilateral ischemia, typically of the fingers and toes but sometimes of the ears and nose, and is associated with severe pallor, paresthesias, and pain. *Raynaud phenomenon*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=97633 (last visited May 12, 2025). The phenomenon, which is usually brought on by cold or emotional stimuli and relieved with heat, is indicative of an underlying disease or anatomical abnormality. *Id.*

[13] Mechanic's hands are "hands with chronic, eczematous skin that is fissured and scaly." *Mechanics hands*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=79997 (last visited May 12, 2025).

Dr. Gupta opines that, even though vaccines are thoroughly tested, "coincidental adverse events . . . that are temporally associated with vaccination" sometimes occur. (Ex. 18, p. 6 (citing Elaine R. Miller et al., *Deaths Following Vaccination*, 33 VACCINE 3288 (2015) (Ex. 23)).) Although Dr. Gupta ultimately defers to Dr. Gershwin's opinion on general causation, he opines that molecular mimicry, whereby the immune response to a foreign substance invokes cross reactivity to a self-protein, could explain how the flu vaccine can cause dermatomyositis. (*Id.* at 6-8 (citing H Orbach & A Tanay, *Vaccines as a Trigger for Myopathies*, 18 LUPUS 1213 (2009); (Ex. 31; *see also* Ex. A, Tab 11)); Tr. 60-61.) Dr. Gupta explains that the fact of post-vaccination adverse events strongly suggests that vaccines "can trigger autoimmunity in a similar way to the infections they are designed to prevent." (Ex. 18, p. 7.) He cites Walker & Jeffrey to support a mechanistic role for molecular mimicry of viral proteins and tRNA synthetases, which targets skeletal muscle. (*Id.* (citing Elaine J. Walker & Peter D. Jeffrey, *Polymyositis and Molecular Mimicry, A Mechanism of Autoimmunity*, 2 LANCET 605 (1986) (Ex. 25; *see also* Ex. F, Tab 11)).) The authors compared two amino acid sequences from *E. coli* that have been identified as autoantigens in myositis with polypeptide sequences taken from a database and found "significant homology between the myositis antigens and the haemagglutinin molecules of two strains of influenza virus, as well as tropomyosin." (*Id.* (discussing Walker & Jeffrey, *supra*, at Ex. 25).) Thus, Dr. Gupta suggests that vaccination can function as part of the "mosaic of autoimmunity," in which the vaccine can prevent autoimmunity (by protecting against infection that could lead to autoimmunity) and "concomitantly induce another autoimmune disease" in a susceptible individual. (*Id.* at 7-8 (citing Bhagirath Singh, *Stimulation of the Developing Immune System Can Prevent Autoimmunity*, 14 J. AUTOIMMUNITY 15 (2000) (Ex. 27)).) Accordingly, some experts suggest that "vaccination administration might not be safe when an autoimmune process is active." (Ex. 35, p. 1 (citing Victoria Furer et al., *2019 Update of EULAR Recommendations for Vaccination in Adult Patients with Autoimmune Inflammatory Rheumatic Diseases*, 79 ANNALS RHEUMATIC DISEASES 39 (2020) (Ex. 38)); Tr. 65.)

Dr. Gupta cites several articles describing dermatomyositis following flu vaccination. (Ex. 18, pp. 8-9 (citing Clodoveo Ferri et al., *Polymyositis Following Pandemic Influenza A (H1N1) and 2009-10 Seasonal Trivalent Vaccines*, 2012 CASE REPS. RHEUMATOLOGY 1 (2012) (Ex. 30; *see also* Ex. F, Tab 5); Ignasi Rodriguez-Pintó & Yehuda Shoenfeld, *Myositis and Vaccines*, *in* VACCINES AND AUTOIMMUNITY 349 (Yehuda Shoenfeld et al. eds., 2015) (Ex. 32); F. M. Jani et al., *Influenza Vaccine and Dermatomyositis,* 12 VACCINE 1484 (1994) (Ex. 33; *see also* Ex. F, Tab 6); Vidya Limaye et al., *Infections and Vaccinations as Possible Triggers of Inflammatory Myopathies*, 56 MUSCLE & NERVE 987 (2017) (Ex. 34)).) However, Dr. Gupta explains that the rarity and heterogenicity of myositis frustrates research efforts to uncover potential causes, especially epidemiologically. (Tr. 22-26 (discussing Lundberg et al., *supra*, at Ex. A, Tab 2; Stübgen, *supra*, at Ex. A, Tab 13).) He describes a study that found approximately 23% of inflammatory myopathy patients had a history of preceding infection or vaccination. (Ex. 18, p. 9 (citing Limaye et al., *supra*, at Ex. 34).) Additionally, the authors noted an increased presence of anti-Ro antibodies in patients

with preceding vaccination when compared to the control group. (Tr. 29-30, 32 (discussing Limaye et al., *supra*, at Ex. 34).) During the hearing, however, Dr. Gupta acknowledged that the study's results were based on responses to questionnaires over an extended period of time (more than 30 years), which could result in recall bias. (*Id.* at 30-32 (discussing Limaye et al. *supra*, at Ex. 34).) He further explained that it was not clear, based on this study, whether the anti-Ro antibodies were pathogenic. (Tr. 33-34; Ex. 18, p. 9.) Dr. Gupta further cites two case reports by Ferri et al. and Jani et al. (Ex. 18, pp. 8-9 (citing Ferri et al., *supra*, at Ex. 30; Jani et al., *supra*, at Ex. 33.) Ferri et al. describes three patients who developed inflammatory myopathy (associated with interstitial lung disease in two cases) following vaccination with pandemic A (H1H1) and seasonal trivalent flu vaccines. (*Id.* (citing Ferri et al., *supra*, at Ex. 30).) Onset in the described cases ranged between five days and one month. (*Id.* at 9 (citing Ferri et al., *supra*, at Ex. 30).) Jani et al. describes a 68-year-old woman who developed dermatomyositis within two weeks of flu vaccination. (*Id.* (citing Jani et al., *supra*, at Ex. 33).) Dr. Gupta opines that these case reports are "suggestive" of a causal relationship, though he acknowledged that he could not make any causal conclusions based on one or two case reports. (Tr. 64-65, 68-72.)

Dr. Gupta opines that the subject flu vaccine more likely than not caused petitioner's dermatomyositis. (Tr. 65.) Dr. Gupta observes that there was no evidence of myositis and petitioner had normal transaminase and a normal chest x-ray prior to vaccination. (Ex. 18, p. 10; Tr. 36-38.) He suggests that the change in composition in the flu vaccine from year to year could explain why petitioner did not develop symptoms when he received prior flu vaccinations in 2014 and 2015. (Ex. 35, p. 2.) At the same time, Dr. Gupta opines that petitioner's past flu vaccinations could have left him "primed" to develop dermatomyositis upon subsequent vaccination. (*Id*.) Based on review of petitioner's medical records, Dr. Gupta opines that his clinical course was more consistent with an evolving dermatomyositis than with an infectious process followed by an autoimmune process. (Tr. 56-57.) Dr. Gupta additionally suggests that petitioner's treating physicians opined that the vaccine could be a possible cause of petitioner's condition. (Ex. 18, p. 10 (citing Ex. 2, pp. 624-30).)

Regarding alternative causes, Dr. Gupta explains that some viral symptoms, including reactive swollen lymph nodes, myalgias, fatigue, cough, low-grade fever, and fatigue, are also symptoms of inflammatory myopathies. (Ex. 35, p. 3 (citing Dana P. Ascherman et al., *Classification, Epidemiology, and Clinical Features of Inflammatory Muscle Disease*, *in* RHEUMATOLOGY 1293 (Marc C. Hochberg et al. eds., 7th ed. 2019) (Ex. 41)).) However, he opines that there was no evidence of infection throughout petitioner's clinical course. (Tr. 56-57.) Although certain cancers have been associated with inflammatory myopathies, Dr. Gupta explains that petitioner "underwent a full work up of age-appropriate subclinical cancer detection" and was never diagnosed with cancer. (Ex. 35, pp. 2-3 (citing Lara Dani et al., *Overall and Site-Specific Cancer Before and After Diagnosis of Idiopathic Inflammatory Myopathies: A Nationwide Study 2002–2016*, 51 SEMINARS ARTHRITIS & RHEUMATISM 331 (2021) (Ex. 40)).) He further explains that patients with cancer associated myositis rarely have myositis autoantibodies. (*Id*. (citing Fahad Khan et al., *Paraneoplastic Musculoskeletal Syndromes*, 46 RHEUMATIC

DISEASES CLINICS N. AM. 577 (2020) (Ex. 22)).) As relevant here, the presence of anti-PL7 and anti-Ro antibodies has been associated with lower incidence of cancer. (Tr. 28-29.)

Finally, Dr. Gupta opines that there is a temporal relationship between petitioner's flu vaccination and the development of his inflammatory myositis. (Ex. 18, p. 10; *see also* Ex. 35, p. 3.) Dr. Gupta explains that it is generally accepted that an immune mediated response can occur several days to months following the triggering event. (Ex. 18, p. 10.) Petitioner "experienced the onset of myositis symptoms approximately six weeks post-vaccination," which is within that medically accepted time frame. (*Id.*; Tr. 56.) Accordingly, Dr. Gupta opines that, "[g]iven the strong temporal association, documented associations between vaccination and development of autoimmune diseases like myopathy, biologically plausible mechanisms, and lack of alternative cause, it is more likely than not that the vaccination he received precipitated inflammatory myositis." (Ex. 18, p. 10.)

ii. M. Eric Gershwin, M.D., M.A.C.R., M.A.C.P.[14]

Dr. M. Eric Gershwin submitted three expert reports and provided expert testimony during the entitlement hearing in this case. (Exs. 36, 194, 206, Tr. 91.) Dr. Gershwin begins with an in-depth overview of molecular mimicry and autoimmune diseases generally. (Ex. 36.) He explains that, although clinically diverse, all autoimmune diseases "share common immunopathogenic mechanisms and risk factors," and that autoimmunity occurs when the immune system, which "is designed to protect us from the outside world," instead attacks the self. (Ex. 36, p. 4 (citing Juan-Manual Anaya, *The Autoimmune Tautology*, 12 ARTHRITIS RSCH. & THERAPY 147 (2010) (Ex. 46)); Tr. 102-03.) Autoimmune diseases are characterized by the activation of B and T-cells against self-antigens, and molecular mimicry has been proposed as a likely mechanism of disease. (Ex. 36, pp. 4, 10 (citing George K Bertsias et al., *Therapeutic Opportunities in Systemic Lupus Erythematosus: State of the Art and Prospects for the New Decade*, 69 ANNALS RHEUMATIC DISEASE 1603 (2010) (Ex. 108); Peter K. Gregersen

[14] Dr. M. Eric Gershwin received his medical degree from Stanford University, before going on to complete an internship and residency at Tufts New England Medical Center. (Ex. 37, pp. 1-2; Tr. 91.) From there, he worked as a clinical associate in immunology at the National Institutes of Health, followed by a professor of rheumatology and allergy at the University of California Davis School of Medicine. (Ex. 37, pp. 1-2; Tr. 91.) While at the University of California Davis School of Medicine, Dr. Gershwin has maintained several positions, including Director of the Special Immunology Diagnostic Laboratory, Directory of the Allergy-Clinical Immunology Program, and Chief of the Division of Rheumatology/Allergy and Clinical Immunology. (Ex. 37, pp. 1-2.) In 2003, Dr. Gershwin was elevated to position as a Distinguished Professor of Medicine in the Division of Rheumatology/Allergy and Clinical Immunology at the University of California Davis School of Medicine. (*Id.* at 1.) He is board certified in internal medicine with a subspecialty in rheumatology, as well as in allergy and clinical immunology, and he maintains an active medical license in California. (*Id.* at 2; Tr. 92.) Dr. Gershwin's major area of research is autoimmune disease, including the relationship between genetic predisposition and the environment. (Tr. 94.) He has authored 72 books and monographs, 164 book chapters, 1039 experimental papers, 40 reviews, and 5 letters to the editor. (Ex. 37, pp. 9-139.) Dr. Gershwin was proffered as an expert in immunology and rheumatology without objection. (Tr. 95.)

et al., *The Shared Epitope Hypothesis: An Approach to Understanding the Molecular Genetics of Susceptibility to Rheumatoid Arthritis*, 30 ARTHRITIS & RHEUMATISM 1205 (1987) (Ex. 109); Diane Mathis et al., *β-Cell Death During Progression to Diabetes*, 414 NATURE 792 (2001) (Ex. 110))), Tr. 100-01, 115-16.) Both infections and vaccinations have been associated with autoimmune disease. (Ex. 36, pp. 4-8.) By way of example, Dr. Gershwin notes that molecular mimicry has been implicated as a mechanism underlying how infectious agents and vaccination can cause Guillain-Barré syndrome ("GBS"). (*Id.* at 4-5 (citing Yhojan Rodríguez et al., *Guillain-Barré Syndrome, Transverse Myelitis and Infectious Diseases*, 15 CELLULAR & MOLECULAR IMMUNOLOGY 547 (2018) (Ex. 49); Nortina Shahrizaila & Nobuhiro Yuki, *Guillain-Barré Syndrome Animal Model: The First Proof of Molecular Mimicry in Human Autoimmune Disorder*, J. BIOMEDICINE & BIOTECHNOLOGY, 2011, at 1 (Ex. 50); Nobuhiro Yuki, *Ganglioside Mimicry and Peripheral Nerve Disease*, 35 MUSCLE & NERVE 691 (2007) (Ex. 56); Claudia Vellozzi et al., *Guillain-Barré Syndrome, Influenza, and Influenza Vaccination: The Epidemiologic Evidence*, 58 CLINICAL INFECTIOUS DISEASE 1149 (2014) (Ex. 57)).)

Dr. Gershwin opines that there is epidemiological and experimental evidence to support a mechanistic role for molecular mimicry in autoimmunity. (Ex. 36, pp. 7, 15.) He discusses several different murine models. (*Id.* at 15-17.) For example, Nachamkin et al. inoculated mice with the 1976 swine flu vaccine and found that the inoculated mice developed anti-GM1 antibodies, which "play a central role in the pathogenesis of GBS and are a prime example of the role of molecular mimicry." (*Id.* at 16 (citing Irving Nachamkin et al., *Anti-Ganglioside Antibody Induction by Swine (A/NJ/1976/H1N1) and Other Influenza Vaccines: Insights into Vaccine-Associated Guillain-Barré Syndrome*, 198 J. INFECTIOUS DISEASES 226 (2008) (Ex. 145); Rodríguez et al., *supra*, at Ex. 49).) In another example, Evans et al. developed transgenic mice that expressed the nucleoprotein or glycoprotein of lymphocytic choriomeningitis virus ("LCMV") as a self-protein in oligodendrocytes and subsequently inoculated the mice with a LCMV strain. (*Id*. (citing Claire F. Evans et al., *Viral Infection of Transgenic Mice Expressing a Viral Protein in Oligodendrocytes Leads to Chronic Central Nervous System Autoimmune Disease*, 184 J. EXPERIMENTAL MED. 2371(1996) (Ex. 146)).) After an initial infection, the mice developed peripheral damage but there was no central nervous system ("CNS") involvement; however, after a second infection, the mice developed chronic CNS inflammation, loss of myelin, and clinical motor dysfunction. (*Id*. (citing Evans et al., *supra*, at Ex. 146).) Dr. Gershwin opines that "[t]his model provides experimental evidence of molecular mimicry in the development of autoimmunity in the CNS." (*Id.*) Dr. Gershwin also provides a table detailing which autoimmune diseases have been associated with various infections and vaccines in the literature. (*Id.* at 18-21.) Although Dr. Gershwin advocates for the use of murine models, he acknowledged during the hearing that "it's often a leap of faith between the murine immune system and the human immune system, particularly in autoimmunity." (Tr. 119.) He recognized that that there is no epidemiologic proof of a relationship between the flu vaccine and anti-synthetase syndrome, specifically. (*Id.* at 131, 134.) Dr. Gershwin provides four criteria for proving molecular mimicry in a "perfect world"; however, it would be difficult to meet

these criteria "in real world practice."[15] (*Id.* at 110-11; Ex. 36, pp. 7-9.) He explains that murine models do not account for gender bias or the six biases for anti-synthetase syndrome, and that they simply recapitulate disease. (Tr. 120-21.) Dr. Gershwin acknowledges that "there is no disease in the mouse that entirely mimics human dermatomyositis and especially anti-synthetase syndrome." (*Id.* at 119-20.) Nonetheless, Dr. Gershwin opines that the theory of molecular mimicry is generally accepted by the scientific community and has been implicated in a variety of diseases. (*Id.* at 121-22.)

Dr. Gershwin opines that the most commonly reported type of molecular mimicry underlying autoimmune disease involves "common or similar native or glycosylated amino acid sequences or epitopes shared between the microorganisms or environmental agents and its host." (Ex. 36, p. 9 (quoting Lisa K. Peterson & Robert S. Fujinami, *Molecular Mimicry*, *in* AUTOANTIBODIES (Yehuda Shoenfeld et al. eds., 2d ed. 2007) (Ex. 90)); Tr. 112-14.) However, Dr. Gershwin suggests that our understanding of molecular mimicry has moved away from the understanding that molecular mimicry "is defined strictly on the basis of linear amino acid sequence." (Ex. 194, p. 1; Ex. 36, pp. 5-7.) Dr. Gershwin explains that, although mimicry has been historically based on "simple homology" between primary amino acid sequences, identification of epitopes has been difficult due to the reality that "the immune response is generally multidimensional." (Ex. 36, pp. 22-23.) "[B]ecause those epitopes are not linear, because they depend on secondary structure, amino acids, because they depend on tertiary structure of how proteins may fold, there's increasing attempts at using computational analysis to try and define what epitopes are." (Tr. 109-10.) During the hearing, Dr. Gershwin introduced the concept of peptides in three-dimensional origami-like structures, in which "residues that are not directly next to each other in a flat surface . . . become close to each other three dimensionally."[16] (*Id.* at 108.) He opines that the linear type of molecular mimicry involving a three-dimensional origami-like analysis is the most likely mechanism underlying dermatomyositis, specifically. (*Id.* at 114-15.)

Dr. Gershwin explains that T-cell receptors can recognize very small portions of antigens with heptapeptides being the optimal length by which some antigens will be recognized. (Ex. 36, p. 10 (citing Philip A. Reay et al., *Use of Global Amino Acid Replacements to Define the Requirements for MHC Binding and T Cell Recognition of Moth Cytochrome* c *(93-103)*, 152 J. IMMUNOLOGY 3946 (1994) (Ex. 111); Francesco Sinigaglia & Juergen Hammer, *Rules for Peptide Binding to MHC Class II Molecules*, 102 ACTA PATHOLOGICA MICROBIOLOGICA ET IMMUNOLOGICA SCANDINAVICA 241 (1994) (Ex. 112); Kai W. Wucherpfennig et al., *Structural Requirements for Binding of an*

[15] They are: (1) similarity between a host epitope and an epitope of an environmental agent; (2) detection of antibodies or T-cells that cross-react with both epitopes in patients; (3) an epidemiologic link between exposure and development of the disease; and (4) reproduction of such autoimmunity in an animal model. (Ex. 36, p. 7.)

[16] During the hearing, Dr. Gershwin also discussed the concept of "origami vaccines" as a recent innovation in cancer/vaccine research and development. (Tr. 259.) He explained that he raised this concept as a general principle of antibodies that recognizes the importance of how the three-dimensional structure is folded, as well as how the immune response is so variable. (*Id.* at 262-64.)

Immunodominant Myelin Basic Protein Peptide to DR2 Isotypes and for Its Recognition by Human T Cell Clones, 179 J. EXPERIMENTAL MED. 279 (1994) (Ex. 113)); Tr. 108, 116.) T-cell receptor specificity for specific MHC bearing peptides is known as "MHC restriction." (Ex. 36, p. 10 (citing Reay et al., *supra*, at Ex. 111; Sinigaglia & Hammer, *supra*, at Ex. 112; Wucherpfennig et al., *supra*, at Ex. 113).) Dr. Gershwin explains that this phenomenon, coupled with the fact that "even a small substitution can dramatically affect binding," illustrates the enormous degree of genetic variation in humans. (Tr. 116-18 (discussing Reay et al., *supra*, at Ex. 111).) He further explains that, while there are "critical residues" that are necessary for T-cell recognition and binding, there is "a certain degree of plasticity in other residues." (Ex. 36, p. 10.) This is due to the fact that T-cell receptors that bind to antigen peptides on MHC molecules screen only some amino acid side chains on both the presenting peptides and the MHC molecules. (Ex. 194, p. 3.) Because not all amino acids are directly perceived, a single T-cell may recognize a variety of different antigens with the same receptor, a phenomenon known as "polyspecificity." (*Id.*; Ex. 36, p. 10 (citing Anup Vatti et al., *Original Antigenic Sin: A Comprehensive Review*, 83 J. AUTOIMMUNITY 12 (2017) (Ex. 95); James Harbige et al., *New Insights into Non-Conventional Epitopes as T Cell Targets: The Missing Link for Breaking Immune Tolerance in Autoimmune Disease?*, 84 J. AUTOIMMUNITY 12 (2017) (Ex. 114); Alexandra Punn et al., *Immune Recognition and Response to the Intestinal Microbiome in Type 1 Diabetes*, 71 J. AUTOIMMUNITY 10 (2016) (Ex. 115); Kai W. Wucherpfennig et al., *Polyspecificity of T Cell and B Cell Receptor Recognition*, 19 SEMINARS IMMUNOLOGY 216 (2007) (Ex. 116)).)

Identification and evaluation of T-cell receptors has proven to be difficult for several reasons. (Ex. 36, pp. 13-14.) First, Dr. Gershwin opines that it is unlikely that a blood sample obtained at a single time interval could observe the complete diversity of T-cell receptors without consideration of other factors including age, viral infections, vaccinations, and immunosuppressive processes. (*Id*. (citing Keith Naylor et al., *The Influence of Age on T Cell Generation and TCR Diversity*, 174 J. IMMUNOLOGY 7446 (2005) (Ex. 135); Dirk Meyer-Olson et al., *Limited T Cell Receptor Diversity of HCV-Specific T Cell Responses Is Associated with CTL Escape*, 200 J. EXPERIMENTAL MED. 307 (2004) (Ex. 136); H. Höhn et al., *Longitudinal Analysis of the T-Cell Receptor (TCR)-VA and -VB Repertoire in CD8$^+$ T Cells from Individuals Immunized with Recombinant Hepatitis B Surface Antigen*, 129 CLINICAL & EXPERIMENTAL IMMUNOLOGY 309 (2002) (Ex. 137); Paolo A. Muraro et al., *T Cell Repertoire Following Autologous Stem Cell Transplantation for Multiple Sclerosis*, 124 J. CLINICAL INVESTIGATION 1168 (2014) (Ex. 138)).) He describes a study by Warren et al. that found only 35% identity in two samples from the same subject taken within a week. (*Id.* at 13 (citing René L. Warren et al., *Exhaustive T-Cell Repertoire Sequencing of Human Peripheral Blood Samples Reveals Signatures of Antigen Selection and a Directly Measured Repertoire Size of at Least 1 Million Clonotypes*, 21 GENOME RSCH. 790 (2011) (Ex. 134)).) Second, Dr. Gershwin opines that current research techniques are either insufficient or "technically challenging." (*Id.* at 14 (discussing Daniel J. Laydon et al., *Estimating T-Cell Repertoire Diversity: Limitations of Classical Estimators and a New Approach*, PHILOSOPHICAL TRANSACTIONS ROYAL SOC'Y LONDON. SERIES B BIOLOGICAL SCIS., Aug. 2015, at 1 (Ex. 130); Ulf G. Wagner et al., *Perturbation of the T Cell Repertoire in*

Rheumatoid Arthritis, 95 PROC. NAT'L ACAD. SCIS. 14447 (1998) (Ex. 140); Michiaki Koga et al., *CDR3 Spectratyping Analysis of the T Cell Receptor Repertoire in Guillain-Barré and Fisher Syndromes*, 141 J. NEUROIMMUNOLOGY 112 (2003) (Ex. 141); Yoh Matsumoto et al., *CDR3 Spectratyping Analysis of the TCR Repertoire in Myasthenia Gravis*, 176 J. IMMUNOLOGY 5100 (2006) (Ex. 142)).) Third, even if T-cell receptor configuration can be depicted, the functional role of the configuration in antigen recognition is hard to prove, given T-cell receptor polyspecificity. (*Id*. (citing Laydon et al., *supra*, at Ex. 130).)

Dr. Gershwin agrees with Dr. Gupta's opinion regarding the two-hit theory, which requires both a genetic predisposition and an environmental trigger.[17] (Tr. 96.) He emphasizes that environmental factors are "critical" and opined that, while dermatomyositis has been associated with infection, statins, and underlying cancer, the flu vaccine is the only relevant environmental factor at issue in this case.[18] (*Id.* at 96-97, 105-06, 115, 143-44.) Dr. Gershwin explains that the flu vaccine likely "unmasked" the underlying dermatomyositis, "either by bystander activation or by a boost or a molecular mimic, but that it would have been the environmental factors that moved him from a preclinical to a clinical phase."[19] (*Id.* at 126.) Regarding a genetic predisposition, Dr. Gershwin opines that an "extraordinary number" of genetic susceptibilities can exist, and that the entire T-cell receptor repertoire must be characterized in order to fully understand the molecular mechanisms involved in host genetic susceptibility, a feat which seems impossible at this time. (Ex. 36, p. 13 (citing Laydon et al., *supra*, at Ex. 130); Tr. 140-42.) Dr. Gershwin explains that no specific genetic testing exists in either

[17] Although host genetics and the "magnitude" of homology are relevant considerations in understanding autoimmune pathology (Ex. 36, pp. 4-8; Tr. 107), "the fact that up to 99.7% of bacterial heptapeptides are shared between microbes and humans suggests that such molecular identity . . . cannot be the sole etiology in autoimmunity." (Ex. 36, pp. 5-6 (citing Brett Trost et al., *No Human Protein Is Exempt from Bacterial Motifs, Not Even One*, 1 SELF NONSELF 328 (2010) (Ex. 52); Matthew F. Cusick et al., *Molecular Mimicry as a Mechanism of Autoimmune Disease*, 42 CLINICAL REVS. ALLERGY & IMMUNOLOGY 102 (2012) (Ex. 59); Darja Kanduc, *Quantifying the Possible Cross-Reactivity Risk of an HPV16 Vaccine*, 8 J. EXPERIMENTAL THERAPEUTICS & ONCOLOGY 65 (2009) (Ex. 77)); Tr. 107; *see also* Ex. 36, p. 6 (citing Matthias Hardtke-Wolenski et al., *The Influence of Genetic Predisposition and Autoimmune Hepatitis Inducing Antigens in Disease Development*, 78 J. AUTOIMMUNITY 39 (2017) (Ex. 72); Wen-Tao Ma et al., *Development of Autoantibodies Precedes Clinical Manifestations of Autoimmune Diseases: A Comprehensive Review*, 83 J. AUTOIMMUNITY 95 (2017) (Ex. 73); Haijing Wu et al., *Epigenetic Regulation in B-Cell Maturation and Its Dysregulation in Autoimmunity*, 15 CELLULAR & MOLECULAR IMMUNOLOGY 676 (2018) (Ex. 74)) ("[O]ther factors in addition to homology itself are necessary for triggering autoimmunity.").)

[18] Dr. Gershwin explains that statins are another environmental agent and have been associated with dermatomyositis. (Tr. 96-97, 105, 124, 137-38, 147.) He explains that statins can induce a spectrum of myopathies from minor aches and pains to severe necrotizing myositis. (*Id.* at 261-62.) However, Dr. Gershwin is critical of Dr. Mecoli's opinion regarding statins because, in his opinion, "there was a lot of warning, a lot of signals" of potential muscle issues related to statins before necrotizing myositis was described. (*Id.* at 262.)

[19] Dr. Gershwin also references adjuvants as a factor affecting immune response (Ex. 36, pp. 5, 7, 9); however, he acknowledged during the hearing that the subject vaccine did not contain any adjuvant and that his causal opinion does not depend on an adjuvant (Tr. 108-09).

a clinical or research setting that could have identified a genetic predisposition in petitioner. (Tr. 99-100, 141-42.) That said, Dr. Gershwin opines that the presence of anti-Ro antibodies indicates a genetic predisposition. (*Id.* at 126.)

During the hearing, Dr. Gershwin acknowledged that his causal opinion was not based on any specifically identified homology between components of the flu vaccine and the host target antigen. (Tr. 131.) He explains that identifying such homology "is a research question that would be virtually impossible to answer [and] might be different between people." (*Id*.) He further acknowledges that he has not identified any homology between the subject vaccine and tRNA synthetase, explaining that "you could give me a lab and a giant budget, and it still could not be reasonably done," and that his causal opinion could, in theory, apply to any vaccine. (*Id.* at 131, 136-37.) In his opinion, the condition is too rare for epidemiology to ascertain any association between dermatomyositis and vaccination, and there has been no evidence apart from case reports to support an association between myositis and infection. (*Id.* at 131-34, 137.) He notes that case reports have "linked" myositis and a variety of vaccines, explaining that "[i]t may not be that that there's any one vaccine or any one infection, but, rather, they're all involved in unmasking to take someone with a genetic predisposition and adduce disease." (*Id.* at 134-37.)

Dr. Gershwin ultimately opines that petitioner's December 16, 2016 flu vaccine more likely than not caused his dermatomyositis. (Tr. 128.) He agrees with Dr. Gupta's opinion that there is a logical temporal association between the subject vaccination and onset of petitioner's dermatomyositis and emphasized that petitioner's cough and rash represent the initial onset of his anti-synthetase syndrome. (*Id.* at 126-28.) He further notes that there was no evidence of malignancy of infection that could otherwise explain petitioner's onset. (*Id.* at 127.)

b. Respondent's Experts

i. Christopher A. Mecoli, M.D., M.H.S.[20]

Respondent's expert, Dr. Christopher Mecoli, submitted two expert reports and provided expert testimony during the entitlement hearing in this case. (Exs. A, C; Tr. 149.) Although Dr. Mecoli agrees with petitioner's experts that petitioner was properly diagnosed with dermatomyositis, he opines that "PL7 positive anti-synthetase syndrome is the most accurate term to use when describing his condition." (Ex. A, p. 6; Tr. 158, 160.) However, he acknowledges that dermatomyositis and anti-synthetase syndrome are not mutually exclusive entities and that it is possible for the same patient to meet the diagnostic criteria for both conditions. (Tr. 157-58.) He explains that dermatomyositis and anti-synthetase syndrome are multi-system inflammatory conditions that fall under the larger umbrella of idiopathic inflammatory myositis, which is a group of disorders that affects the muscle, joints, lungs, and skin. (Ex. A, p. 6 (citing Jiří Vencovský et al., *Idiopathic Inflammatory Myopathies*, 45 RHEUMATIC DISEASE CLINICS N. AM. 569 (2019) (Ex. A, Tab 1); I.E. Lundberg et al., *Diagnosis and Classification of Idiopathic Inflammatory Myopathies*, 280 J. INTERNAL MED. 39 (2016) (Ex. A, Tab 2); Gabriela A. Cobos et al., *Dermatomyositis: An Update on Diagnosis and Treatment*, 21 AM. J. CLINICAL DERMATOLOGY 339 (2020) (Ex. A, Tab 3)); Tr. 156-57.) While myositis generally consists of muscle inflammation and achiness, dermatomyositis specifically features a "characteristic rash" that may present over several different areas of the body. (Tr. 156; Ex. A, p. 6.) Dermatomyositis can be diagnosed through medical history, physical examination, bloodwork, MRI, EMG, pulmonary and cardiac testing, and skin/muscle biopsy. (Ex. A, p. 6 (citing Vencovský et al., *supra*, at Ex. A, Tab 1; Lundberg et al., *supra*, at Ex. A, Tab 2; Cobos et al., *supra*, at Ex. A, Tab 3).) Dr. Mecoli further explains that a subset of patients with anti-synthetase syndrome may test positive for autoantibodies, such as PL-7, which can inform their treatment.[21] (Tr. 157-58, 160, 164-65.) In the instant case, Dr. Mecoli opines that petitioner "had a pretty typical presentation" of anti-synthetase syndrome with proximal muscle weakness,

[20] Dr. Christopher Mecoli received his medical degree from Rutgers University, New Jersey Medical School, before going on to complete an internship and residency at the University of Pennsylvania, as well as rheumatology fellowship at Johns Hopkins Hospital. (Ex. B, p. 1; Tr. 149-50.) From there, Dr. Mecoli accepted clinical appointments as an attending physician at Johns Hopkins Hospital and Johns Hopkins Bayview Medical Center, as well as academic appointments as Director of Research Operations in the Johns Hopkins Myositis Center, Director of Myositis Precision Medicine Center Initiative, and an instructor in the Division of Rheumatology at Johns Hopkins University. (Ex. B, p. 1; Tr. 150-52.) In 2019, he was elevated to Assistant Professor of Medicine in the Division of Rheumatology at Johns Hopkins University. (Ex. B, p. 1; Tr. 150, 152.) Dr. Mecoli is board certified in internal medicine and rheumatology, and he maintains an active medical license in Maryland. (Ex. B, p. 5; Tr. 150.) His clinical care has focused in part on idiopathic inflammatory myopathies or myositis, and he regularly treats patients with idiopathic inflammatory myopathies, including anti-synthetase syndrome, while his research focuses on understanding the relationship between cancer and myositis and directly involves all forms of myositis, including anti-synthetase syndrome. (Tr. 150-55.) He has published 24 original research publications, 7 invited review articles, a book chapter, a case report, and an editorial. (Ex. B, pp. 1-3; Tr. 154.) Dr. Mecoli was proffered as an expert in rheumatology without objection. (Tr. 155.)

[21] Dr. Mecoli distinguishes "myositis-associated" antibodies and "myositis-specific" antibodies. (Tr. 164-65.)

inflammatory arthritis, interstitial lung disease, rash, elevated muscle biomarkers, and a PL-7 positive antibody test. (*Id.* at 160.)

While the cause of idiopathic inflammatory myopathies is currently unknown, some possibilities include "genetic predisposition, infectious agents (bacteria and viruses), medications, ultraviolet light, and cancer." (Ex. A, p. 7 (citing C. Thompson et al., *The Pathogenesis of Dermatomyositis*, 179 BRIT. J. DERMATOLOGY 1256 (2018) (Ex. A, Tab 4); Brittany L. Adler & Lisa Cristopher-Stine, *Triggers of Inflammatory Myopathy: Insights into Pathogenesis*, 25 DISCOVERY MED. 75 (2018) (Ex. A, Tab 5)); Tr. 157.) Dr. Mecoli explains that we know even less about the causal mechanism underlying anti-synthetase syndrome. (Tr. 161,166.) Although he agrees that molecular mimicry is a logical theory of causation in the right context, he expresses skepticism regarding its application in the context of this case, explaining that there is no evidence that the human immune system cross-reacts with components of the flu vaccine, resulting in development of idiopathic inflammatory myositis or damage to human muscle, lungs, or skin. (Ex. A, p. 7; Ex. C, pp. 1-2; Tr. 162, 176.) Dr. Mecoli asserts that sequence homology between viral sequences and tRNA synthetases cannot on its own support molecular mimicry as a causal mechanism for autoimmunity. (Ex. C, p. 2; Ex. A, pp. 8-9.) He also notes that Dr. Gershwin provided four criteria described as "ideal" to establish evidence of molecular mimicry, and that none of the criteria are met in this case. (Ex. C, pp. 2-3.) Specifically, Dr. Mecoli notes that (1) there is no documented homology between the flu vaccine and the host epitope; (2) there is no evidence of immune system cross-reactivity between components of the flu vaccine and the affected tissue; (3) there is no epidemiologic support for an association between idiopathic inflammatory myopathy and the flu vaccine; and (4) there have been no models demonstrating that the flu vaccine can induce a clinical phenotype of idiopathic inflammatory myopathy. (*Id*.) Regarding Dr. Gershwin's opinion that dermatomyositis is too heterogenous to detect a signal in larger studies, Dr. Mecoli raises two points. (Tr. 162-64.) First, he notes that there are other examples of rare outcomes following common exposures that have been detected epidemiologically. (*Id.* at 163-64.) For instance, there has been an epidemiologic association between statins and necrotizing myositis, although the incidence rate is on par with anti-synthetase syndrome. (*Id.* at 163.) Second, the lack of epidemiology does not mean that other studies showing no association should be disregarded. (*Id*.; Ex. C, p. 3.)

Regarding the literature presented by petitioner, Dr. Mecoli explains that the review by Segal and Shoenfeld describes the theoretical framework of vaccine-induced autoimmunity via molecular mimicry but ultimately focuses on a proposed role for adjuvants, an issue that is not relevant in this case as the subject flu vaccine does not contain any adjuvants. (Ex. A, p. 8 (citing Yahel Segal & Yehuda Shoenfeld, *Vaccine-Induced Autoimmunity: The Rule of Molecular Mimicry and Immune Crossreaction*, 14 CELLULAR & MOLECULAR IMMUNOLOGY 1 (2018) (Ex. 24); Prescribing Information, AFLURIA, Influenza Vaccine: Suspension for Intramuscular Injection: 2019-2020 Formula [hereinafter Vaccine Package Insert] (Ex. 28)).) Moreover, the study did not make any causal conclusions. (*Id*. (quoting Segal & Shoenfeld, *supra*, at Ex. 24, p. 7).) He also highlights that the Walker and Jeffrey paper, which petitioner presented as

identifying homology between several viral proteins and the sequences of two tRNA synthetases, included an acknowledgement by the authors that identification of sequence homology does not demonstrate cross-reaction between the viral protein and tRNA synthetase. (*Id.* at 8-9 (citing Walker & Jeffrey, *supra*, at Ex. 25).) Dr. Mecoli notes that Vadalà et al. found that there was insufficient evidence to support a causal relationship between the flu vaccine and a list of adverse events. (*Id.* at 9 (citing Maria Vadalà et al., *Vaccination and Autoimmune Diseases: Is Prevention of Adverse Health Effects on the Horizon?*, 8 EPMA J. 295 (2017) (Ex. 26)).) Further, the paper by Singh argues that vaccination decreases the likelihood of autoimmunity. (*Id*. (citing Singh, *supra*, at Ex. 27).) Although petitioner cites a chapter on myositis and vaccines that describes several case reports of post-vaccination myositis, Dr. Mecoli notes that the authors also cite several studies finding no association between the flu vaccine and myositis. (*Id*. (citing Rodriguez-Pintó & Shoenfeld, *supra*, at Ex. 32; Ellen M. Kurland et al., *Lack of Association of A/NJ/76 (Swine Flu) Vaccine and Polymyositis*, 4 NEUROEPIDEMIOLOGY 125 (1985) (Ex. A, Tab 8); Chazan Bibiana et al., *Influenza Vaccine Does Not Produce Myopathy in Patients Taking Statins*, 51 J. FAM. PRAC. 986 (2002) (Ex. A, Tab 9)).) Dr. Mecoli explains that case reports can support a temporal relationship and trigger more robust investigation but are insufficient on their own to establish causation. (Tr. 177-78; Ex. A, p. 9 (citing Ferri et al., *supra*, at Ex. 30).) Finally, Dr. Mecoli addresses the Limaye et al. study that analyzed over 600 adults with idiopathic inflammatory myopathies. (Ex. A, p. 10 (citing Limaye et al., *supra*, at Ex. 34).) He suggests that the study methodology, which included a study period of over 20 years and required participants to respond to a mailed questionnaire, likely created bias. (*Id.*; Tr. 171-72.) Additionally, the article found no causal relationship between vaccination or infection and idiopathic inflammatory myopathy. (Ex. A, p. 10 (citing Limaye et al., *supra*, at Ex. 34).) In sum, Dr. Mecoli concludes that "there are too many inherent limitations in these studies to draw any meaningful conclusions with regard to causality." (*Id.*) Dr. Mecoli explains that the recommendation against vaccinating patients with active autoimmune inflammatory rheumatic disease is a precaution based on the lack of data regarding the efficacy and safety of vaccines during active disease. (Tr. 193-94.)

By contrast, Dr. Mecoli asserts that the relevant literature does not support causality between vaccination and idiopathic inflammatory myopathy. (Ex. A, pp. 10-11 (citing Carla G S Saad et al., *Immunogenicity and Safety of the 2009 Non-Adjuvanted Influenza A/H1N1 Vaccine in a Large Cohort of Autoimmune Rheumatic Diseases*, 70 ANNALS RHEUMATIC DISEASES 1068 (2011) (Ex. A, Tab 10)).) He cites a literature review by Orbach and Tanay, which he describes as "the best evidence that we had available to us on this issue." (Tr. 168-69; Ex. A, p. 11 (citing Orbach & Tanay, *supra*, at Ex. A, Tab 11).) The authors described case reports of myositis following various vaccinations but also cited studies where no association between vaccination and dermatomyositis was found. (Tr. 194; Ex. A, p. 11 (citing Orbach & Tanay, *supra*, at Ex. A, Tab 11; Richard K. Winkelmann, *Influenza Vaccine and Dermatomyositis*, 320 LANCET 495 (1982) (Ex. A, Tab 12)).) After a thorough review of the literature investigating increased incidence of dermatomyositis after mass vaccination programs, the authors determined that there is no statistically significant signal for any form of myositis. (Tr.

168-69; Ex. A, p. 11 (discussing Orbach & Tanay, *supra*, at Ex. A, Tab 11).) Dr. Mecoli further cites a more recent literature review describing several case reports linking inflammatory myopathies and vaccinations, which he opines supports a "possible," but not a more likely than not, causal relationship between vaccines and autoimmune disease. (Ex. A, p. 11 (citing Stübgen, *supra*, at Ex. A, Tab 13); Tr. 167, 195-96.) Finally, Dr. Mecoli conducted his own literature review, replicating the search criteria utilized by Stübgen for the period following publication of that paper, and found no additional evidence implicating the flu vaccine in the pathogenesis of dermatomyositis or anti-synthetase syndrome. (Ex. A, p. 11; Tr. 168.)

Although Dr. Mecoli does not go so far as to argue that there is preponderant evidence of an alternative cause for petitioner's condition, he opines that petitioner's overall clinical picture casts some doubt on a causal role for the vaccine. (Tr. 175, 191.) Dr. Mecoli notes that petitioner presented with symptoms that are consistent with a viral process, including sore throat, swollen lymph nodes/glands, rash, malaise, myalgias, fatigue, cough, and fever, and that petitioner's treaters suspected an underlying viral process, such as viral pharyngitis or viral bronchitis. (Ex. A, pp. 7-8; Tr. 174-75, 190-91.) However, Dr. Mecoli also recognizes that anti-synthetase syndrome patients often develop a "prodrome clinical syndrome" that can include symptoms that resemble infection, and that no specific infection was identified. (Tr. 174, 190.) He suggests that petitioner could have suffered from "a viral infection that then segued into an actual autoimmune form of myositis." (*Id.* at 175.) Additionally, Dr. Mecoli explains that cancer has been causally associated with myositis. (Ex. A, p. 8; Tr. 173-74, 163-64.) Although he acknowledges that cancer is found less frequently in patients who produce autoantibodies, such as PL-7, he asserts that it is "still hypothesized to be causally related." (Ex. A, p. 8 (citing Khan et al., *supra*, at Ex. 22; Iago Pinal-Fernandez et al., *A Longitudinal Cohort Study of the Anti-Synthetase Syndrome: Increased Severity of Interstitial Lung Disease in Black Patients and Patients with Anti-PL7 and Anti-PL12 Autoantibodies*, 56 RHEUMATOLOGY 999 (2017) (Ex. A, Tab 6); Liubing Li et al., *Analysis of Myositis Autoantibodies in Chinese Patients with Cancer-Associated Myositis*, J CLINICAL LAB ANALYSIS e23307 (2020) (Ex. A, Tab 7)); Tr. 189.) Dr. Mecoli also acknowledges that cancer-associated dermatomyositis must be detected within three years before or after a dermatomyositis diagnosis and that no malignancy has ever been clinically detected in petitioner's case. (Tr. 188.) He suggests the possibility of "subclinical cancers" that may not be detected through routine testing or cancer that was eradicated by the immune system before becoming clinically detectable but caused sufficient damage that "the immune system no longer relies on the cancer to actually drive the dermatomyositis." (Ex. A, p. 8 (citing Adler & Cristopher-Stine, *supra*, at Ex. A, Tab 5); Tr. 173-74, 189-90.)

Dr. Mecoli ultimately concludes that petitioner's experts have presented a "theoretical construct" of how molecular mimicry may lead to autoimmune disease generally, but they have not submitted sufficient evidence to support molecular mimicry as a causal mechanism to explain dermatomyositis or anti-synthetase syndrome following flu vaccination. (Ex. C, p. 3.) He explains that a specific cause cannot be identified in the majority of dermatomyositis patients. (Tr. 172-73.) In this case, Dr.

Mecoli does not believe that petitioner's vaccination more likely than not contributed to the development of dermatomyositis or anti-synthetase syndrome. (*Id.* at 178-79; Ex. A, p. 12; Ex. C, p. 3.) He asserts that his opinion is bolstered by the fact that petitioner received flu vaccines in 2014 and 2015 without issue. (Ex. A, pp. 8, 12.)

ii. Stephen M. Hedrick, Ph.D.[22]

Dr. Stephen M. Hedrick submitted two reports and provided expert testimony during the entitlement hearing in this case.[23] (Exs. F, G; Tr. 201.) Dr. Hedrick agrees that petitioner suffered from anti-synthetase syndrome that was temporally associated with his vaccination. (Ex. F, p. 1; Tr. 213, 253.) However, he disputes petitioner's causal showing, asserting that Drs. Gupta and Gershwin rely on "case reports and their own understanding of immunology and the processes within" to support their theory. (Tr. 214.)

Dr. Hedrick observes that petitioner's experts invoke the theory of molecular mimicry to explain why he developed anti-synthetase syndrome following vaccination. (Ex. F, p. 2.) He provides an overview of molecular mimicry, noting that the process has been "exceedingly difficult to demonstrate." (Ex. F, pp. 2, 4 (citing Robert S. Fujinami & Michael B. A. Oldstone, *Amino Acid Homology Between the Encephalitogenic Site of Myelin Basic Protein and Virus: Mechanism for Autoimmunity*, 230 SCIENCE 1043 (1985) (Ex. F, Tab 2); N. R. Rose & I. R. Mackay, *Molecular Mimicry: A Critical Look at Exemplary Instances in Human Diseases*, 57 CELLULAR & MOLECULAR LIFE SCIS. 542 (2000) (Ex. F, Tab 13)).) Dr. Hedrick acknowledges one exception, in which rabbit myelin basic protein was shown to incite a T-cell response that cross-reacted with human myelin basic protein, resulting in demyelinating autoimmune disease. (Ex. F, p. 4 (citing Thiravat Hemachudha et al., *Myelin Basic Protein as an Encephalitogen in Encephalomyelitis and Polyneuritis Following Rabies Vaccination*, 316 NEJM 369 (1987) (Ex. F, Tab 14)).) However, molecular mimicry is typically demonstrated through singular case studies noting temporality between vaccination and

[22] Dr. Stephen M. Hedrick received his Ph.D. in molecular biology and biochemistry from the University of California, Irvine. (Ex. E, p. 1, Tr. 202.) He went on to complete a post-doctoral fellowship in immunology at the National Institutes of Health. (Ex. F, p. 1; Tr. 202.) From there, Dr. Hedrick accepted a faculty position as an assistant professor in the Department of Biology at the University of California, San Diego, where he taught immunology and virology, as well as classes in pandemics and epidemiology. (Ex. E, p. 1; Ex. F, p. 1; Tr. 202.) During his tenure, he served as Chair of both the Department of Biology and the Division of Biological Sciences in the Department of Molecular Biology. (Ex. E, p. 1; Ex. F. p. 1.) He was elevated to Distinguished Professor in 2007. (Ex. E, p. 1; Tr. 202.) Additionally, Dr. Hedrick ran a research laboratory at the University of California, San Diego, for around 40 years. (Tr. 203.) In that capacity, he investigated T cell immunology, including T cell development, T cell recognition, T cell memory response to viruses, molecular biology underlying T cell response, and the persistence of memory in T cell response. (*Id.* at 203-04; Ex. F, p. 1.) He has authored 174 publications, given lectures on immunology, and worked in an editorial capacity on relevant journals. (Ex. E, pp. 2-11; Tr. 204-06.) Dr. Hedrick was proffered as an expert in immunology without objection. (Tr. 206.)

[23] Respondent initially submitted Dr. Hedrick's expert report marked Exhibit D (ECF No. 57); however, he later filed an amended expert report by Dr. Hedrick marked Exhibit F (ECF No. 59). In his subsequent report, Dr. Hedrick made five substantive corrections to his prior report. (*Id.*) Exhibit F and accompanying medical literature, rather than Exhibit D, are summarized herein.

disease onset, as well as animal studies requiring "contrived" sets of conditions not found in human vaccine populations. (*Id*.; *see also* Tr. 245-50 (discussing Robert S. Fujinami et al., *Molecular Mimicry, Bystander Activation, or Viral Persistence: Infections and Autoimmune Disease*, 19 CLINICAL MICROBIOLOGY REVS. 80 (2006) (Ex. G, Tab 4); Michael B. Bracken, *Why Animal Studies Are Often Poor Predictors of Human Reactions to Exposure*, 102 J. ROYAL SOC'Y MED. 120 (2008) (Ex. 208)).) For example, to achieve a loss of tolerance in one study, the mouse pancreas was genetically altered from birth to express an actual viral protein from lymphocytic choriomeningitis virus, and then mice were injected with the "highly proliferative" lymphocytic choriomeningitis virus, resulting in diabetes from the immune destruction of pancreatic islet cells. (Ex. F, p. 4 (citing Pamela S. Ohashi et al., *Ablation of "Tolerance" and Induction of Diabetes by Virus Infection in Viral Antigen Transgenic Mice*, 65 CELL 305 (1991) (Ex. F, Tab 15); Michael B. A. Oldstone et al., *Virus Infection Triggers Insulin-Dependent Diabetes Mellitus in a Transgenic Model: Role of Anti-Self (Virus) Immune Response*, 65 CELL 319 (1991) (Ex. F, Tab 16)).) Dr. Hedrick explains that this set of conditions "has no resemblance to human beings vaccinated with influenza hemagglutinin protein." (*Id.*; Tr. 248.) Although he ultimately agrees there are accepted examples of molecular mimicry as a mechanism of autoimmunity, he contends that these examples feature infections, not vaccinations. (Ex. G, p. 4.) He opines that infection elicits a more potent inflammatory response when compared to vaccination, especially where, as here, the vaccine does not contain an adjuvant. (Tr. 218-20.)

Dr. Hedrick asserts that Dr. Gershwin has failed to explain how the flu vaccine can induce high-affinity anti-synthetase-specific antibodies via molecular mimicry. (Ex. G, p. 1.) Anti-synthetase syndrome patients develop antibodies to one of several distinct tRNA synthetases. (Ex. F, p. 1; Tr. 226-27.) Dr. Hedrick emphasizes that tRNA synthetases are "multi-domain proteins with a wide variety of functions unrelated to protein synthesis," but each synthetase has a specificity for a different amino acid. (Ex. F, pp. 1-2 (citing Wing-Sze Lo et al., *Human tRNA Synthetase Catalytic Nulls with Diverse Functions*, 345 SCI. MAG. 328 (2014) (Ex. F, Tab 1)); Tr. 250.) Because they are secreted or transported out of the cell, synthetases are accessible to induce an antibody response, though the reason they are a target of autoimmunity is unknown. (Ex. F, pp. 1-2.) Dr. Hedrick explains that molecular mimicry in this case would depend on induction of an antibody with specificity for a sequence of amino acids in the flu vaccine that cross-reacts with a similar sequence found in threonyl-tRNA synthetase. (Ex. F, p. 3; Tr. 225-27 (citing Chuan V. Dang et al., *Myositis Autoantibody Reactivity and Catalytic Function of Threonyl-tRNA Synthetase*, 2 FASEB J. 2376 (1988) (Ex. F, Tab 8)).) Anti-synthetase syndrome has specificity for the "native 3-dimensional structure of threonyl-tRNA synthetase" and autoantibodies do not recognize the unfolded, denatured tRNA-synthetase protein sequence. (Ex. F, p. 3; Tr. 225-29 (citing Dang et al., *supra*, at Ex. F, Tab 8).) Dr. Hedrick opines that this is significant because the antibody response is "almost certainly induced by the native protein or an entire domain of the native protein." (Ex. F, p. 3.) The flu vaccine "more or less" consists of a single protein; however, although Dr. Hedrick agrees that molecular mimicry can involve tertiary protein structures, he opines that the flu protein does not have the necessary native structure regardless of sequence homology. (Tr. 221, 226, 252; Ex. F, p. 3.)

Thus, Dr. Hedrick suggests that sequence homology, if any, between flu hemagglutinin and tRNA synthetase would be limited to a short stretch of amino acids that would not be recognized by relevant antibodies, and even if the linear sequences had sufficient homology, it is unlikely that the flu vaccine would be folded such that it could mimic the natural antibody. (Tr. 230-31.)

Setting aside these basic disagreements with the theory of molecular mimicry as applied in this case, Dr. Hedrick notes that anti-synthetase syndrome is often associated with anti-Ro antibodies, though the presence of these antibodies does not seem to affect the clinical characteristics of the disease. (Ex. F, p. 4.) The anti-Ro antibodies "recognize TRIM21, an E3-ubiquitin ligase," and "bind to a specific protein domain of the Ro52 protein in the region bordered by amino acids 126 and 252." (*Id*. (citing S. A. Rutjes et al., *Anti-Ro52 Antibodies Frequently Co-Occur with Anti-Jo-1 Antibodies in Sera from Patients with Idiopathic Inflammatory Myopathy,* 109 CLINICAL EXPERIMENTAL IMMUNOLOGY 32 (1997) (Ex. F, Tab 12)).) Dr. Hedrick performed a BLAST search of this polypeptide, filtering for influenza A and influenza B proteins, but found no significant homologies. (*Id.*) He performed an additional BLAST search of this polypeptide, filtering for flu hemagglutinin, and again found no significant homologies. (*Id*.)

Dr. Hedrick criticizes a study cited by petitioner as purporting to show similarities between tRNA synthetase and flu hemagglutinin. (Ex. F, pp. 3-4 (citing Walker & Jeffrey, *supra*, at Ex. F, Tab 11).) The 1986 paper compared two tRNA synthetase enzymes taken from *E. coli* bacteria with the 3600 protein sequences found in the National Biomedical Research Foundation protein sequence database. (*Id.* at 3 (citing Walker & Jeffrey, *supra*, at Ex. F, Tab 11); Tr. 233-34.) Dr. Hedrick opines that the paper was published at a time when there were few known protein sequences, whereas there are now millions of known sequences. (Ex. F, pp. 3-4; Tr. 233, 235.) He further criticizes the authors' use of "informatics techniques that would not be considered appropriate in the current scientific literature, namely the use of bacterial tRNA synthetase amino acid sequence[s] as a surrogate for the human enzyme, the equation of related but distinct amino acids, and most notably the 'alignment' of discontinuous amino acid sequences." (Ex. F, p. 4 (citing Walker & Jeffrey, *supra*, at Ex. F, Tab 11); Tr. 234-35.) Relevant here, the authors investigated various viral proteins, not components of the flu vaccine, and the two types of synthetase identified in this paper are histidyl tRNA synthetase and alanyl tRNA synthetase, neither of which reacts to anti-PL7 antibody. (Tr. 235-37.)

Dr. Hedrick emphasizes that he could not find a single study, using more modern search techniques, that validated the Walker & Jeffrey article. (Ex. F, p. 4.) He cites more recent papers by Miller et al. (1990) and Martin et al. (1995), in which the authors concluded that the relevant inciting antigen is the human tRNA synthetase, not a small peptide cross-reaction. (Tr. 231-32; Ex. F, p. 3 (citing Frederick W. Miller et al., *The Role of an Autoantigen, Histidyl-tRNA Synthetase, in the Induction and Maintenance of Autoimmunity*, 87 PROC. NAT'L. ACAD. SCIS. USA 9933 (1990) (Ex. F, Tab 9); Alberto Martin et al., *Epitope Studies Indicate that Histidyl-tRNA Synthetase is a Stimulating*

Antigen in Idiopathic Myositis, 9 FASEB J. 1226 (1995) (Ex. F, Tab 10)).) Although these papers deal with a different antibody (anti-Jo antibodies, rather than anti-PL7 antibodies) and a different tRNA synthetase (histidyl-tRNA synthetase, rather than threonyl-tRNA synthetase), Dr. Hedrick opines that the authors' conclusions bolster his opinion that these autoantibodies do not recognize short amino acid sequences. (Tr. 231-32; Ex. F, p. 3.) Therefore, Dr. Hedrick concludes that, in order "[f]or a high-affinity antibody response to occur, antigen-specific, reactive, follicular helper T cells must be induced and these T cells have to react with components of the same molecular complex that is bound by tRNA-synthetase-specific B cells." (Ex. G, p. 1.) This reaction can occur either "if the T cell peptide epitope is contained in the same protein that is bound by the B cell antibody receptor" of "if the peptide epitope recognized by the T cell forms a molecular complex with that which is bound by the B cell—in this case tRNA-synthetase." (*Id*.) Dr. Hedrick acknowledges that a single T cell can recognize different peptides, but he submits that any suggestion that a single T cell can recognize more than a million different peptides is a "gross exaggeration." (*Id.* at 5.)

Dr. Hedrick opines that one would expect a rise over the background incidence of autoimmune disorders following mass vaccine administration if vaccines elicited a cross-reactive T-cell response leading to autoimmunity. (Ex. F, p. 2; Ex. G, p. 5.) As an example, more than 450 million doses of the seasonal flu vaccine were administered between 2016-2021; however, there are only two Vaccine Adverse Event Reporting System ("VAERS") reports of dermatomyositis or anti-synthetase syndrome following flu vaccination during this time interval. (Ex. F, pp. 2-3; Tr. 221-23.) While Dr. Hedrick agrees that the actual annual incidence rate of inflammatory myopathy is unknown, an incidence rate of 2 per 480 million vaccinees (based on an estimated 80 million annual flu vaccinations over the course of 6 years) is still less than the proposed incidence rate of 1-10 per million cases of inflammatory myopathy annually. (Ex. F, p. 3; Tr. 222-23.) Despite recognizing that VAERS is a voluntary reporting system and not expected to be comprehensive, he contends the fact that there are so few VAERS reports supports his position that there is no evidence of a relationship between autoimmune myositis and flu vaccination. (Ex. F, p. 3; Tr. 254-55.) Thus, although myositis has been reported following vaccination to many different infectious agents, Dr. Hedrick contends that there is no evidence of a causal role for molecular mimicry in this case. (Ex. F, p. 3 (citing Arie Altman et al., *HBV Vaccine and Dermatomyositis: Is There an Association?*, 28 RHEUMATOLOGY INT'L 609 (2008) (Ex. F, Tab 3); W. Ehrengut, *Dermatomyositis and Vaccination*, 1 LANCET 1040 (1978) (Ex. F, Tab 4); Ferri et al., *supra*, at Ex. F, Tab 5; Jani et al., *supra*, at Ex. F, Tab 6; Stübgen, *supra*, at Ex. F, Tab 7).) He suggests that the temporal relationship between vaccination and myositis is merely coincidental. (Tr. 223.)

Finally, Dr. Hedrick agrees that autoimmunity is based on a combination of genetic and environmental factors. (Tr. 243-44.) However, he asserts that there is no evidence that petitioner had a genetic susceptibility. (*Id.* at 243.) Accordingly, Dr. Hedrick accepts that there was a temporal relationship between petitioner's vaccination and onset of his condition; however, he disputes that petitioner's myositis was caused by the flu vaccine. (Ex. F, p. 4; Ex. G, p. 6.)

V. Analysis

As discussed above, petitioner's burden of proof in a cause-in-fact claim is to meet the three-part *Althen* test, which includes (1) a general theory of causation implicating the vaccine as a cause of the alleged condition, (2) a logical sequence of cause and effect implicating the vaccination as a cause of petitioner's own condition, and (3) appropriate timing of onset based on the theory of causation. 418 F.3d at 1278. In this case, the parties present issues with respect to all three *Althen* prongs. However, for the reasons discussed below, petitioner's inability to meet his burden under *Althen* prong one is dispositive.

a. Petitioner has not met his burden of proof under *Althen* prong one

Under *Althen* prong one, petitioner must provide a "reputable medical theory," demonstrating that the subject vaccine can cause the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (quoting *Pafford v. Sec'y of Health & Human Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004)). Such a theory must only be "legally probable, not medically or scientifically certain." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioner may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *See Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1325-26 (Fed. Cir. 2006)). However, "[a] petitioner must provide a 'reputable medical or scientific explanation' for [her] theory. While it does not require medical or scientific certainty, it must still be 'sound and reliable.'" *Boatmon v. Sec'y of Health & Human Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019) (citation omitted) (quoting *Knudsen*, 35 F.3d at 548-49).

Petitioner argues that the flu vaccine can be shown to cause dermatomyositis via the concept of molecular mimicry, as discussed by both of his experts. (ECF No. 116, pp. 23-24; *see also* Tr. 60-61 (Dr. Gupta identifying molecular mimicry as the basis for his opinion as to general causation); *Id.* at 99 (Dr. Gershwin characterizing molecular mimicry as the mechanism "most likely at play here.") There is no dispute that petitioner suffered from a form of dermatomyositis known as anti-synthetase syndrome, that dermatomyositis is an autoimmune condition, or that molecular mimicry is one viable explanation for at least some autoimmune conditions. Importantly, however, these points present only an initial starting premise from which vaccine causation may then be substantiated. Molecular mimicry "is a generally accepted scientific principle, [but] mere invocation of the scientific term does not carry a petitioner's burden in a Program case." *Deshler v. Sec'y of Health & Human Servs*., No. 16-1070V, 2020 WL 4593162, at *20 (Fed. Cl. Spec. Mstr. July 1, 2020) (citing *Forrest v. Sec'y of Health & Human Servs.*, No. 14-1046V, 2019 WL 925495, at *3 (Fed. Cl. Spec. Mstr. Jan. 28, 2019)).

To that point, Dr. Gershwin cited four criteria for demonstrating molecular mimicry "in a perfect world." (Ex. 36, pp. 7-9; Tr. 110-11.) They are: (1) similarity between a host epitope and an epitope of an environmental agent; (2) detection of antibodies or T-cells that cross-react with both epitopes in patients; (3) an epidemiologic link between exposure and development of the disease; and (4) reproduction of such autoimmunity in an animal model. (Ex. 36, p. 7.) While I do not suggest that petitioner must satisfy the four "ideal" criteria referenced by Dr. Gershwin for establishing molecular mimicry or demonstrate scientific certainty to prove causation in this case, prior cases have expressed with regard to the application of molecular mimicry that "[t]he line must be drawn somewhere between speculation and certainty." *Brayboy v. Sec'y of Health & Human Servs.*, No. 15-183V, 2021 WL 4453146, at *19 (Fed. Cl. Spec. Mstr. Aug. 30, 2021); *Datte v. Sec'y of Health & Human Servs.*, No. 18-2V, 2025 WL 1565894, at *15 (Fed. Cl. Spec. Mstr. May 9, 2025) (rejecting similar criteria proposed by respondent's expert as tantamount to requiring that petitioner establish scientific certainty). Without requiring direct, testable evidence, petitioner must still demonstrate cross-reactive potential affecting the health and productivity of the relevant bodily tissue. *Brayboy*, 2021 WL 4453146, at *19; *see, e.g.*, *Arredondo v. Sec'y of Health & Human Servs.*, No. 18-1782V, 2023 WL 8181138, at *26-29 (Fed. Cl. Spec. Mstr. Oct. 31, 2023) (finding that petitioner had preponderantly shown that the influenza vaccine can cause Bell's palsy via molecular mimicry based on Dr. Steinman's identification of influenza vaccine components that could initiate the development of antibodies that could cross-react with peripheral nerve myelin and trigger an autoimmune response, as supported by the cited medical literature); *Smith v. Sec'y of Health & Human Servs.*, No. 08-864V, 2016 WL 2772194, at *15-18 (Fed. Cl. Spec. Mstr. Apr. 18, 2016) (finding that petitioner had preponderantly shown that the hepatitis B vaccine can cause multiple sclerosis via molecular mimicry between components of the vaccine and myelin oligodendrocyte protein, as recognized in the cited medical literature). *But see Salmins v. Sec'y of Health & Human Servs.*, No. 11-140V, 2014 WL 1569478, at *11-14 (Fed. Cl. Spec. Mstr. Mar. 31, 2014) (concluding that, given the nature of GBS, petitioner had preponderantly demonstrated that the HPV vaccine can cause GBS via molecular mimicry despite the absence of any demonstration of homology and cross-reaction). Thus, the critical question is what, if any, evidence supports invocation of the concept of molecular mimicry in this case.

Dr. Gershwin opines that molecular mimicry based on linear homology involving a three-dimensional origami-like analysis is the most likely mechanism to explain dermatomyositis following flu vaccination. (Tr. 114-15.) He explains that T-cell receptors can recognize small portions of antigens and, although there are "critical residues" necessary for T-cell recognition, there is "a certain degree of plasticity in other residues." (Ex. 36, p. 10.) Thus, he asserts that a single T-cell has the capacity to recognize a variety of different antigens in a phenomenon known as polyspecificity. (*Id.* (citing Wucherpfenning el al., *supra*, at Ex. 116); Ex. 194, p. 3.) However, without more, this lacks specificity to the disease process at issue. In that regard, Dr. Gershwin contends that research into the identification of T-cell receptors has proven to be quite difficult and that such identification is beyond the scope of his investigation in this case. (Ex. 36, pp. 13-14 (citing Laydon et al., *supra*, at Ex. 130; Tr. 131.) Moreover, even if

one were able to identify the relevant T-cell receptor configuration, Dr. Gershwin contends that proving the functional role of the T-cell receptor would be burdensome, given the polyspecificity of T-cell receptors. (Ex. 36, p. 14 (citing Laydon et al., *supra*, at Ex. 130).) Ultimately, however, *none* of the four criteria advanced by Dr. Gershwin himself for establishing molecular mimicry have been demonstrated. Moreover, Dr. Gershwin acknowledged that his proposed theory is so vague as to be potentially applicable to any vaccine. (Tr. 136-37.)

Dr. Gupta cites a study by Walker & Jeffrey, which "described data on tRNA synthetases in myositis that strongly supports that a mechanism of myositis is the molecular mimicry of viral proteins" and suggested "a rationale for skeletal muscle being the target." (Ex. 18, p. 7; Tr. 61-62 (discussing Walker & Jeffrey, *supra*, at Ex. 25).) However, Dr. Hedrick disputes the reliability of this paper, arguing that the paper utilized outdated research methods and was written at a time when there were few known protein sequences. (Ex. F, pp. 3-4; Tr. 233-35 (discussing Walker & Jeffrey, *supra*, at Ex. F, Tab 11).) He emphasizes that he could not locate a more recent study, using modern research methods, to validate the study's conclusions. (Ex. F, p. 4.) Dr. Hedrick further disputes the relevance of this study, noting that the authors investigated various viral proteins, rather than components of the subject flu vaccine, and identified two types of synthetases, neither of which have been proven to react to anti-PL7 antibodies. (Tr. 235-37 (discussing Walker & Jeffrey, *supra*, at Ex. F, Tab 11).) He instead cites a study by Dang et al. showing that the autoantibody in dermatomyositis only has specificity for the native three-dimensional structure of threonyl-tRNA synthetase and cannot recognize the "unfolded, denatured tRNA-synthetase protein sequence." (Ex. F, p. 3 (citing Dang et al., *supra*, at Ex. F, Tab 8); Tr. 225-29.) In response, Dr. Gershwin argues that the literature offered by Dr. Hedrick in rebuttal of Walker & Jeffrey is also dated and relies on affinity purification, a technique that does not capture the entire repertoire of autoantibodies. (Tr. 256-58.) He further reiterates his argument that the three-dimensional nature of antigens is imperative to the discussion of molecular mimicry. (*Id.* at 264.) However, Dr. Gershwin did not substantively dispute Dr. Hedrick's critique of the Walker & Jeffrey paper. Dr. Gershwin acknowledges that he has not provided any other evidence identifying any homology between the subject flu vaccine and tRNA synthetase (or indeed any homology at all). (*Id.* at 131.) Moreover, Dr. Mecoli contends that, even accepting the authors' identification of sequence homology, the paper does not support cross-reactive potential between the viral protein and tRNA synthetase. (Ex. A, pp. 8-9.)

Dr. Gupta also cites Limaye et al. to support the presence of anti-Ro antibodies as a signal with respect to whether a patient with inflammatory myopathy has a history of preceding infection or vaccination. (Ex. 18, p. 9 (citing Limaye et al., *supra*, at Ex. 34); Tr. 29-30, 32.) However, Dr. Gupta acknowledged during the hearing that a pathologic role for anti-Ro antibodies in the development of dermatomyositis has not been established. (Tr. 33-34, 36, 79-80.) Dr. Mecoli persuasively opines that the study found no causal relationship between vaccination and inflammatory myopathy. (Ex. A, p. 10.) Moreover, the reliability of the study is questionable for two reasons. First, in response to the undersigned's questioning, Dr. Gupta acknowledges that the study

methodology presents the potential for recall bias. (Tr. 31-32.) Specifically, Dr. Gupta confirmed that data collection was based on questionnaire responses by the patients themselves or their general practitioners with the possibility that some of these questionnaires were completed decades after the events at issue. (*Id.* at 30-32.) Studies relying on similar methodology have been afforded less weight by other special masters in prior cases. *See DeVaughn v. Sec'y of Health & Human Servs.*, No. 22-832V, 2025 WL 758128, at *20 (Fed. Cl. Spec. Mstr. Feb. 10, 2025); *Johnson v. Sec'y of Health & Human Servs.*, No. 14-254V, 2018 WL 2051760, at *24 (Fed. Cl. Spec. Mstr. Mar. 25, 2018) (criticizing a study's use of a population of subjects that voluntarily sought treatment as "too self-selected to draw conclusions from correlations observed with respect to that population"); *Evanson v. Sec'y of Health & Human Servs.*, No. 90-775V, 1991 WL 179085, at *4 (Fed. Cl. Spec. Mstr. Aug. 28, 1991) (criticizing a study that necessarily relied on self-reporting). Respondent's experts' opinions further reinforce the unreliability of the study's methodology. (Ex. A, p. 10; Tr. 171-72.) Second, even setting aside the possibility of bias in the methodology, the study results were unclear with respect to the proposed temporal relationship to vaccination. Results included reports of vaccination up to 24 weeks, with a median of 10 weeks, prior to muscle biopsy rather than onset of the condition. (Limaye et al., *supra*, at Ex. 34, p. 2.) While actual onset is unclear, this reported timeframe extends beyond what petitioner's experts otherwise identified as being an appropriate period for an autoimmune condition to develop following a triggering event. (Tr. 59-60, 128).

Relying on the rarity and heterogenicity of dermatomyositis, petitioner's experts acknowledge that epidemiology and large-scale studies have thus far failed to detect any significant signal following vaccination. (Tr. 22-26; 131-34, 137.) However, they cite several case reports describing dermatomyositis following vaccination. For instance, Ferri et al. described one patient who developed polydermatomyositis one week after receiving the influenza A (H1N1) vaccine.[24] (Ferri et al., *supra*, at Ex. 30, p. 2.) Another case report by Jani et al. described a case of dermatomyositis within two weeks following flu vaccination. (Jani et al., *supra*, at Ex. 33, p. 1.) Dr. Gupta opines that these case reports are "suggestive" of a causal relationship. (Tr. 64-65, 68-72.) While case reports are not entirely without evidentiary value, they are not strong evidence without more. *E.g.*, *Crutchfield v. Sec'y of Health & Human Servs.*, No. 09-0039V, 2014 WL 1665227, at *19 (Fed. Cl. Spec. Mstr. Apr. 7, 2014) (noting that "single case reports of Disease X occurring after Factor Y . . . do not offer strong evidence that the *temporal* relationship is a *causal* one—the temporal relationship could be pure random chance"), *aff'd*, 125 Fed. Cl. 251 (2014); *see also Paluck v. Sec'y of Health & Human Servs.*, 104 Fed. Cl. 457, 475 (2012) (indicating that case reports "do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value. . . [but] the fact that case reports can by their nature only present indicia of causation does not deprive them of all evidentiary weight" (quoting *Campbell v. Sec'y of Health & Human Servs.*, 97 Fed. Cl. 650, 668 (2011))), *aff'd*, 786 F.3d 1373 (Fed. Cir. 2015)). Respondent's experts caution against overreliance on case reports in light of literature finding no association between vaccination and idiopathic inflammatory

[24] Ferri et al. also described two patients who suffered polymyositis complicated by interstitial lung disease following flu vaccination. (Ferri et al., *supra*, at Ex. 30, pp. 1-2.)

myopathy. (Ex. A, pp. 10-11.) Dr. Mecoli notes that Rodriguez-Pintó & Shoenfeld described case reports of post-vaccination myositis, as well as several studies finding no association between the flu vaccine and myositis. (*Id.* at 9 (citing Rodriguez-Pintó & Shoenfeld, *supra*, at Ex. 32).) He also cites Orbach & Tanay, which described case reports of post-vaccination myositis, but specifically concluded that "there is no statistically significant evidence in the literature for an increase in the incidence of [dermatomyositis] or [polymyositis] after any massive vaccination program, whether prospective or retrospective, and no meta-analyses have been published to date." (*Id.* at 11 (quoting Orbach & Tanay, *supra*, at Ex. A, Tab 11, p. 1); Tr. 168-69, 194.) In another literature review, a possible causal link between immunization and inflammatory myopathy was suggested; however, there was insufficient proof of a definitive causal relationship. (Stübgen, *supra*, at Ex. A, Tab 13.) Thus, when examining the literature holistically, it is apparent that a causal link between the flu vaccine and dermatomyositis has not been substantiated despite the existence of some case reports.

Moreover, I am not persuaded by petitioner's experts' arguments that dermatomyositis is too rare to be detected by large-scale studies. Dr. Mecoli opines that studies have detected epidemiologic signals in other comparable circumstances. (Tr. 163-64.) By way of example, Dr. Mecoli points to the epidemiologic association between statins and another form of myositis known as immune-mediated necrotizing myopathy. (*Id.* at 163.) In response, Dr. Gershwin contends that statins have been shown to induce a spectrum of myopathies and, as a result, there were more opportunities to detect signals. (*Id.* at 261-62.) However, Dr. Gershwin ultimately agrees that necrotizing myopathy, as cited by Dr. Mecoli, is a severe and clinically distinct condition when compared to routine symptoms of myopathy due to statins. (*Id.* at 275-76.) He does not otherwise explain why dermatomyositis or anti-synthetase syndrome, which have a similar incidence rate to necrotizing myopathy (*see id.* at 163), are too rare to be detected epidemiologically.

Although petitioner need not present epidemiology in order to meet his burden under *Althen* prong one, *Andreu*, 569 F.3d at 1378-79 (citing *Capizzano*, 440 F.3d at 1325-26), it is also true that "[n]othing in *Althen* or *Capizzano* requires the Special Master to ignore probative epidemiological evidence that undermines petitioner's theory," *D'Tiole v. Sec'y of Health & Human Servs.*, 726 F. App'x 809, 811 (Fed. Cir. 2018). A review paper by Stübgen discussed two types of studies that are less affected by the issues that petitioner's experts assert undermine the feasibility of large-scale study of dermatomyositis in the general population. (Stübgen, *supra*, at Ex. A, Tab 13.) First, retrospective studies have found that vaccination is not an important trigger for dermatomyositis. (*Id.* at 3.) Second, a prospective study determined that the flu vaccine has no short-term effect on the disease course of patients already suffering dermatomyositis.[25] (*Id.* at 6.)

[25] Dr. Gupta contends that the possibility of vaccine-caused disease flare is the reason for the EULAR's recommendation against vaccination during active disease (Tr. 65). However, Dr. Mecoli opines that there is no data to suggest that vaccination during active disease is harmful and that the EULAR's recommendation is an extra precaution due to the lack of data. (*Id.* at 193-94.) Dr. Gershwin ultimately acknowledges that there have been no studies demonstrating that patients with dermatomyositis

Given all of the above, petitioner has not substantiated a role for molecular mimicry in this case. Dr. Gupta's testimony that it is unclear whether the antibodies proposed as causal, namely, anti-Ro or anti-PL7 antibodies, are pathogenic only further undermines petitioner's attempts to invoke molecular mimicry in this case. (Tr. 32-33, 80.) Moreover, petitioner's experts submit that a wide range of genetic and environmental factors have been implicated in autoimmunity. (*E.g.*, Ex. 18, p. 5; Tr. 77-79, 137-38.) Dr. Hedrick emphasizes that, in most cases, there are no known genetic or environmental factors to explain onset of dermatomyositis. (*Id.* at 243.) Dr. Gupta further acknowledges that, given its idiopathic nature, in "most of the cases of dermatomyositis, anti-synthetase, we don't know why it happens. The immune system takes a turn for the worse for some reason, and we try to find some insult . . . . It could be environment. It could be just people getting old, I guess. I don't know." (*Id.* at 37.) Regarding age as a relevant factor, Dr. Gupta suggests a peak incidence of inflammatory myopathy in adults between the ages of 40 and 50 (Ex. 18, p. 5), and Dr. Mecoli extends this period, stating that "40 to 60 is the sweet spot age where we expect patients to develop this condition in adults" (Tr. 179). Petitioner was 57 years old at the time of vaccination (Ex. 2, p. 1), and Dr. Gershwin opines that "it's not uncommon to develop a dermatomyositis at that age" (Tr. 146).

Prior cases in which petitioners have alleged dermatomyositis caused-in-fact by a flu vaccine have led to mixed results. *Ballard v. Sec'y of Health & Human Servs.*, No. 19-1600V, 2025 WL 1454111 (Fed. Cl. Spec. Mstr. Apr. 23, 2025) (Special Master Roth granting entitlement); *Hunt v. Sec'y of Health & Human Servs.*, No. 20-1455V, 2024 WL 3173262 (Fed. Cl. Spec. Mstr. May 23, 2024) (the undersigned denying entitlement); *McDaniel v. Sec'y of Health & Human Servs*., No. 17-1322V, 2023 WL 4678688 (Fed. Cl. Spec. Mstr. June 26, 2023) (Special Master Dorsey denying entitlement); *Ulysse v. Sec'y of Health & Human Servs*., No. 15-451V, 2022 WL 2115248 (Fed. Cl. Spec. Mstr. May 19, 2022) (Chief Special Master Corcoran granting entitlement); *Whelan v. Sec'y of Health & Human Servs*., No. 16-1174V, 2019 WL 1061473 (Fed. Cl. Spec. Mstr. Jan. 28, 2019) (Chief Special Master Corcoran denying entitlement). *Ballard* and *Hunt* were decided on substantially the same evidence as presented here, with the exception that Dr. Gershwin's causal theory in those cases placed more emphasis on interferon-mediated inflammation leading to autoimmunity. *See Ballard*, 2025 WL 1454111, at *17, *21; *Hunt*, 2024 WL 3173262, at *8. The special master in *Ballard* was particularly persuaded by Dr. Gershwin's interferon theory,[26] which she found supported vaccine

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experience flares following flu vaccination. (*Id.* at 133.) Dr. Gershwin also asserts that breaking tolerance in the first instance is not the same as perpetuating disease. (Tr. 133.)

[26] Specifically, the *Ballard* special master found that

> Dr. Gershwin provided a sound and reliable theory that environmental triggers activate the immune system of a genetically predisposed person, which involves both the hyperactivation of the innate immune system, specifically in producing type 1 [interferons] which in turn produce B cell autoantibodies, and dysregulation of the adaptive immune system to begin a feedforward loop of sustained inflammation.

causation when coupled with respondent's expert's insufficient rebuttal to Dr. Gershwin's causal opinion. 2025 WL 1454111, at *21. However, other than citing case reports and invoking the unsubstantiated possibility of molecular mimicry, petitioner's experts in this case have not otherwise articulated any basis for concluding that the flu vaccine can cause dermatomyositis. *See Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl. 706, 743 (2009) (noting that special masters are not required to accept an expert's conclusions "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" (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997))).

Accordingly, petitioner has not carried his burden of preponderantly showing that the flu vaccine can cause anti-synthetase syndrome, a subset of dermatomyositis, under *Althen* prong one.

b. *Althen* prong one is dispositive

Because I have concluded that petitioner has not demonstrated that the flu vaccine likely can cause dermatomyositis, it is not necessary to address in detail whether the vaccine did so in this particular case. Given the outcome regarding *Althen* prong one, by definition it likely did not. Thus, I do not separately reach *Althen* prongs two and three in this decision. *Trollinger v. Sec'y of Health & Human Servs.*, 167 Fed. Cl. 127, 142 (2023) (affirming the Chief Special Master's dismissal based on a dispositive finding that petitioner had not satisfied *Althen* prong one). However, I note briefly that the evidence regarding *Althen* prongs two and three is not so robust as to otherwise influence the analysis under *Althen* prong one.

There is no dispute that petitioner suffered from dermatomyositis or that onset of his condition was temporally associated with vaccination. (*E.g.*, Ex. 18, p. 10; Ex. F, p. 1; Tr. 59, 127-28, 213, 253.) And, indeed, petitioner's experts' opinion that a logical sequence of cause and effect implicates the flu vaccine is similarly limited to (1) a "strong temporal association" with the onset of petitioner's dermatomyositis, and (2) the lack of an alternative cause. (Ex. 18, p. 10.) However, "[a]lthough probative, neither a mere showing of a proximate temporal relationship between vaccination and injury, nor a simplistic elimination of other potential causes of the injury suffices, without more, to meet the burden of showing actual causation." *Althen*, 418 F.3d at 1278 (citing *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1149 (Fed. Cir. 1992)). Apart from the timing of onset, petitioner has not presented any particular aspect of his own medical history as significant evidence favoring vaccine causation. Petitioner does note the presence of anti-Ro antibodies; however, as discussed *supra*, petitioner's experts have not substantiated a pathogenic role for these antibodies.

2025 WL 1454111, at *21. She cites as support for her conclusion medical literature that was not filed in the instant case. Here, Dr. Gershwin's theory is limited to contending that dermatomyositis is an autoimmune condition, and autoimmune conditions have, in some instances, been shown to be caused by molecular mimicry.

Notably, there are only a few instances in the medical records where petitioner's vaccination was mentioned as part of his relevant medical history. (Ex. 204, p. 12; Ex. 2, pp. 625, 628-29, 970.) During petitioner's initial rheumatology evaluation, Dr. Tabechian listed "possible vaccine induced myositis" as among the wide differential diagnosis at that time. (Ex. 2, pp. 628-29.) However, this is tentatively phrased and no similar assessment is included in subsequent records.[27] Petitioner is otherwise characterized as suffering from idiopathic inflammatory myopathy with interstitial lung disease. (*Id.* at 611; 648-49.) It appears from the record that the vaccination was only implicated due to its temporal proximity to onset of petitioner's symptoms and petitioner eventually tested positive for anti-PL7 antibodies, which otherwise confirmed Dr. Tabechian's "suspicion of an overlap inflammatory muscle disease, dermatomyositis, based on his skin findings at onset, and interstitial lung disease." (*Id.* at 1385.) Petitioner's vaccine is not mentioned again until his July 20, 2022 encounter with Dr. Edgerton, roughly five-and-a-half years post-vaccination. (Ex. 204, p. 12.) However, Dr. Edgerton does not suggest any causal role for petitioner's vaccination. (*Id*.) Thus, no treater ever confirmed causal relationship between petitioner's flu vaccination and dermatomyositis beyond merely noting temporal proximity.[28]

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[27] There is a notation in the medical record by Dr. Tabechian indicating that petitioner should "stop" receiving the influenza vaccine. (Ex. 2, p. 914.) A treating physician's decision to withhold vaccination can be probative. *Tarsell v. United States*, 133 Fed. Cl. 782, 797 (2017) (citing *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1376 (Fed. Cir. 2009)). However, it is not necessarily indicative of the treating physician's view as to causation. *Matthews v. Sec'y of Health & Human Servs*., 157 Fed. Cl. 777, 788 (2021) (finding no error where "[r]egarding the allergy notation, the Special Master's decision noted the data suggesting that those who suffer from GBS 'are generally cautioned against receipt of the flu vaccine without specific respect to the underlying trigger of their prior GBS.'") Here, Dr. Tabechian did not explain his reasoning in noting that petitioner should not receive the flu vaccine (specifically Afluria) (Ex. 2, p. 914) and this notation was entered on the same date that Dr. Tabachian otherwise noted he was considering starting petitioner on methotrexate, an immune suppressive therapy. The package insert for Afluria warns that the effectiveness of the vaccine is impacted by immunosuppressive therapy. (Ex. 28, p. 4.)

[28] *See Caves v. Sec'y of Health & Human Servs.*, No. 07-443V, 2010 WL 5557542, at *20 (Fed. Cl. Spec. Mstr. Nov. 29, 2010) ("[T]here is a difference between a statement 'associating' a vaccine with a disease and a statement that a vaccine caused a disease."), *mot. for rev. denied*, 100 Fed. Cl. 119 (2011), ***aff'd***, 463 F. App'x 932 (Fed. Cir. 2012); *Cedillo v. Sec'y of Health & Human Servs.*, 617 F.3d 1328, 1348 (Fed. Cir. 2010) (holding that the special master did not err in refusing to afford significant weight to the opinions of treating physicians "simply indicating an awareness of a temporal, not causal, relationship" between the vaccination and the condition); *see also Veryzer v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 344, 355 (2011) (finding that the special master properly determined that the statements provided by petitioner's treaters fail to establish causation as "petitioner's physicians doubted that his condition was vaccine-related," and "[w]hen physicians entertained the idea of vaccine-relatedness, the 'driving factor' was the fact that petitioner's condition developed post-vaccination"); *Ruiz v. Sec'y of Health & Human Servs.*, No. 02-156V, 2007 WL 5161754, at *13-14 (Fed. Cl. Oct. 15, 2007) (reasoning that medical records confirming the temporal proximity between the vaccination and onset without concluding that the vaccine caused onset were insufficient to support vaccine-causation); *Tosches v. Sec'y of Health & Human Servs.*, No. 06-192V, 2008 WL 440285, at *13-15 (Fed. Cl. Spec. Mstr. Jan 31, 2008) (finding that petitioner's reliance on statements of treating physicians who recognized that the vaccination preceded onset but did not conclude that there was a causal relationship could not support petitioner's burden under the second *Althen* prong); *Egan ex rel. Gum v. Sec'y of Health & Human Servs.*, No. 05-1032V, 2009 WL 1440240, at *15 (Fed. Cl. Spec. Mstr. May 1, 2009) ("The essence of the

VI. Conclusion

Although petitioner has my sympathy for the pain and discomfort he has endured, for all the reasons discussed above, I find that he has not met his burden of proof. Therefore, pursuant to § 300aa-12(d)(3)(A) and Vaccine Rule 10, this decision concludes that petitioner is not entitled to an award of compensation. Absent a timely motion for review, the Clerk is directed to enter judgment dismissing this case for insufficient proof in accordance with Vaccine Rule 11(a).

IT IS SO ORDERED.

s/Daniel T. Horner
Daniel T. Horner
Special Master

undersigned's ruling against a logical sequence of cause and effect and thus finding against petitioner is [in part] that the treating doctors did not consider the vaccine causative of [petitioner's] TM.")