

In the United States Court of Federal Claims
OFFICE OF SPECIAL MASTERS
No. 19-140V
(to be published)

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| ***** | | Chief Special Master Corcoran |
| DANA CHAMBERS, | * | |
| | * | Filed: July 22, 2022 |
| Petitioner, | * | |
| | * | |
| v. | * | |
| | * | |
| SECRETARY OF HEALTH | * | |
| AND HUMAN SERVICES, | * | |
| | * | |
| Respondent. | * | |
| | * | |
| ***** | | |

Andrew Donald Downing, Downing, Allison & Jorgenson, Phoenix, AZ, for
Petitioner.

Terrence Kevin Mangan, Jr., DOJ-Civ, Washington, DC, for Respondent.

ENTITLEMENT DECISION¹

On January 28, 2019, Dana Chambers filed a petition for compensation under the National Vaccine and Injury Compensation Program (the “Vaccine Program”).² (ECF No. 1) (“Pet.”). Petitioner alleged that she developed Undifferentiated Connective Tissue Disease (“UCTD”) as a result of the seasonal influenza (“flu”) vaccine and the Tetanus, Diphtheria, and Pertussis (“Tdap”) booster she received on October 7, 2016. Pet. at 1. Both parties now agree that Ms. Chambers meets the criteria for systemic lupus erythematosus (“SLE”), and that this is the primary injury alleged to have been vaccine-caused.

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

² The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3758, codified as amended at 42 U.S.C. §§ 300aa-10 through 34 (2012) [hereinafter “Vaccine Act” or “the Act”]. Individual section references hereafter will be to Section 300aa of the Act (but will omit the statutory prefix).

An entitlement hearing was held in this matter on October 22, 2021. Having reviewed the record, all expert reports and associated literature, and listened to the experts who testified at the hearing, I hereby deny an entitlement award. As discussed in greater detail below, Petitioner has not preponderantly established that the relevant vaccines can cause SLE, or did so here.

I. Medical History

Prior Medical History

Petitioner (a family practice physician) was born on October 21, 1969. Ex. 1 at 1. Prior to vaccination she had experienced symptoms from Raynaud syndrome³ since she was a teenager. Ex. 2 at 3–6; Ex. 4 at 33. Her family history also included a history of autoimmune rheumatic conditions: rheumatoid arthritis (“RA”) in her mother, along with Raynaud syndrome and chronic fatigue syndrome in her sister. Ex. 2 at 5–6.

In 2016 (the year of the relevant vaccination), Petitioner experienced some symptoms that could be viewed as related to the injury claimed in this case. Specifically, in January 2016 she suffered from right low back and buttock pain that radiated into her right thigh and knee. Ex. 5 at 18–20. Dr. Chambers characterized her symptoms to treaters as paresthesia and numbness in the area, adding that it had been ongoing over the prior five months, and that anti-inflammatory medications did not help improve how she felt (although she was able to work and exercise despite her discomfort). *Id.* at 18.

After an exam, treaters deemed Petitioner positive for “psychological disturbance, muscle pain, joint pain, and muscle spasm.” Ex. 5 at 18. A radiology report showed “mild to moderate spondylosis noted at the L4-L5 and L5-S1 facet joints.” *Id.* at 19. She also had “severely positive right Fortin finger [sacroiliac joint dysfunction] test,” and “mildly positive right FABER [hip pathology] test.” *Id.* Treaters opined she was experiencing “[l]umbar disc without myelopathy,” right sciatic neuropathy, right piriformis syndrome,⁴ and right sacroiliitis. *Id.* Dr. Chambers was prescribed medication, and it was recommended that she rest and discontinue exercising. *Id.*

³ Raynaud disease or Raynaud syndrome is “a primary idiopathic vascular disorder characterized by bilateral attacks of Raynaud phenomenon; it affects females more often than males.” Raynaud Disease, *Dorland’s Medical Dictionary Online*, <https://www.dorlandsonline.com/dorland/definition?id=70735> (last visited June 29, 2022). It features “intermittent bilateral ischemia of the fingers, toes, and sometimes ears and nose, with severe pallor and often paresthesias and pain, usually brought on by cold or emotional stimuli and relieved by heat; it is usually due to an underlying disease or anatomic abnormality.” Raynaud Phenomenon, *Dorland’s Medical Dictionary Online*, <https://www.dorlandsonline.com/dorland/definition?id=97633> (last visited June 29, 2022).

⁴ Piriformis syndrome (also called Levator syndrome) involves “a functional pain syndrome occurring chiefly in women under 45 years of age and consisting of chronic or recurrent episodes of vague, dull aching or pressure high in the rectum that last at least 20 minutes; the pain is often worse when sitting.” Levator Syndrome, *Dorland’s Medical Dictionary Online*, <https://www.dorlandsonline.com/dorland/definition?id=110899> (last visited June 29, 2022).

Two months later, on March 16, 2016, Dr. Chambers sought treatment at Frye Regional Medical Center (“Frye M/C”) in Hickory, North Carolina, for the same right buttocks and leg pain she had complained of in January. She informed treaters that her symptoms were mild enough to permit most exercises but persistent and otherwise unresponsive to medication. Ex. 17 at 25–26. Her exam showed tenderness in her gluteal muscles and right piriformis. *Id.* at 26. The differential diagnosis included piriformis syndrome and sacroiliitis, and a radicular cause of pain could not be ruled out. *Id.* Dr. Chambers was prescribed a muscle relaxer and referred to physical therapy (“PT”). *Id.*

Dr. Chambers returned to Frye M/C in September 2016 for evaluation of the same right buttocks pain, which had been responsive to PT until a flare-up two weeks prior. Ex. 17 at 60. Her pain was now so severe at times that it could awaken her at night. *Id.* Her differential diagnosis included radicular pain versus sacroiliitis. *Id.* An ultrasound guided piriformis injection was performed and stretching was recommended. *Id.*

Vaccinations and Initial Injury

Dr. Chambers (46 years-old at the time) received the flu vaccine and a Tdap booster on October 7, 2016, at her office. Ex. 18 at 1–2. No immediate reaction is recorded in any record.

Then, twelve days later, on October 19, 2016, Petitioner saw her partner at her practice, Dr. Ailisa Kahill, for evaluation of “body aches/pain.” Ex. 19 at 20–23. Dr. Chambers reported that she was experiencing low grade fevers, fatigue, red irritated eyes, and hip pain going into her upper legs making it difficult to walk. *Id.* at 20. She referenced her recent piriformis injection. *Id.* at 20. Petitioner also stated that she was “having spells where she is breathless and feels heart racing,” and noted a family history of supraventricular tachycardia. *Id.* She had not exercised in ten days, and had cut back on alcohol, calorie, and sugar intake without improvement of her symptoms. *Id.* She took a steroid, prednisone, for two days, “which helped some,” and also “has been on generic [birth control] for 3 months which correlates with onset of some of these symptoms.” *Id.* Overall, this record suggests that Petitioner’s symptoms had not recently sprung up unexpectedly but had existed for some time—and that treatment was being sought because of their stubbornly persistent nature.

Petitioner’s physical examination findings were all normal. Ex. 19 at 21–22. Dr. Kahill’s assessment was chronic fatigue, fever of unspecified cause, and bilateral hip pain. *Id.* at 22.

Petitioner's CRP,⁵ an inflammation biomarker, was also extremely high—135.1 mg/L, compared to a normal reference range of 0.0 to 4.9 mg/L. Ex. 4 at 14.

Approximately one week later, Petitioner took herself to the emergency room on October 26, 2016, complaining of chest pain and shortness of breath. Ex. 17 at 841–45. Her history was at this time noted to include Raynaud syndrome, the two vaccines she had received earlier that month, and the piriformis injection in September. *Id.* at 844. She recalled that after the piriformis injection, “she started to feel achy, mainly in the pelvic area.” *Id.* She had a rapid Strep test that was positive and was treated with an antibiotic. *Id.* Dr. Chambers was also experiencing a wet cough that seemed like pneumonia. *Id.* Further, she reported fever, chills, loss of energy, weakness, headache, sore throat, tachycardia, palpitations, and her vocal cords not feeling quite right. *Id.*

Petitioner was admitted to the hospital for evaluation of left lower lobe pulmonary embolus, right lower lobe pneumonia, chest pain, mild hyponatremia, elevated blood pressure, and tachycardia secondary to embolus. Ex. 17 at 841–43. Pulmonary embolus factors were deemed possibly attributable to “nonspecific illness with fatigue over the last couple of weeks, vascular procedure . . . ,⁶ use of oral contraceptive, although this has been ongoing for 30 years, and a long car ride to the beach.” *Id.* at 224. While hospitalized, Dr. Chambers had an echocardiogram on October 27, 2016, that yielded normal results. *Id.* at 299–300. After treatment improved her symptoms, she was discharged on October 28, 2016. *Id.* at 841–43.

Diagnostic Efforts and Treatment

On November 4, 2016, Petitioner had a follow-up with Dr. Kahill regarding her recent hospitalization. Ex. 9 at 18–20. She was instructed to continue on anticoagulation therapy for six months for her pulmonary embolism. *Id.* at 17. Dr. Chambers reported she had shortness of breath that was improving, body aches, mild productive cough, and that her vocal cords continued to bother her. *Id.*

Three days later Petitioner saw a rheumatologist, Dr. R. David Caldwell, to evaluate her joint pain, fatigue, and the pulmonary embolism. Ex. 19 at 26–28. Her reported history included longstanding intermittent episodes of extreme fatigue and arthralgia, occasionally associated with vocal cord dysfunction, since 2010. *Id.* at 26. This occurred every one or two years, with symptoms lasting a few weeks before resolving. *Id.* Each of these episodes seem to be related to infection: the first being Epstein-Barr Virus (“EBV”) and the most recent with pneumonia. *Id.* Dr. Chambers reported symptoms similar to this “on 10/7/16,” the day after her flu vaccine. *Id.* at 27. On exam,

⁵ CRP refers to the C-reactive protein, “a globulin that forms a precipitate with the somatic C-polysaccharide of the pneumococcus in vitro; it is the most predominant of the acute-phase proteins.” C-reactive Protein, *Dorland's Medical Dictionary Online*, <https://www.dorlandsonline.com/dorland/definition?id=100489> (last visited June 29, 2022).

⁶ Dr. Chambers had been treated on June 3, 2016, for a follow-up from her May 2016 right posterior thigh phlebectomy of thrombosed varicose veins. Ex. 12 at 1.

her neurologic and musculoskeletal systems were deemed within normal limits. *Id.* at 28. Her previous labs showed a positive ANA,⁷ however. *Id.* at 27. Dr. Caldwell assessed arthralgia and unspecified joint issues, suggestive of an immune/autoimmune etiology, and Petitioner was started on an immunosuppressive drug. *Id.* at 19, 27.

Treatment in 2017

On January 4, 2017, Petitioner had a return visit with Dr. Caldwell to see how medication was assisting her. Ex. 15 at 11–13. Her exam was completely normal, and he proposed UCTD as a diagnosis, adding that she should undergo lab testing in four to six months. *Id.* at 12. Several months later, on May 10, 2017, Dr. Chambers had an appointment at Piedmont Rheumatology. Ex. 15 at 7; Ex. 22 at 9. She had experienced symptoms flare the prior month, beginning prednisone in response. Ex. 15 at 9. Dr. Chambers was otherwise improved at this point, and her physical exam was normal. *Id.* at 7–8. Dr. Caldwell continued Petitioner on 5 mg/day of prednisone and resumed treatment with other medications plus an antidepressant. *Id.* at 9.

Dr. Chambers saw Physician’s Assistant Mary Sears one week later, noting she started additional medication for pain the prior week. Ex. 4 at 29. Petitioner now reported “fatigue with writhing pain at [the] bilateral hips into [the] legs and weakness during flares.” *Id.* Petitioner’s problem list included restless leg syndrome (“RLS”), bilateral hip pain, and chronic fatigue since October 19, 2016. *Id.* PA Sears diagnosed petitioner with myalgia, polyarthralgia, UCTD, and gastroesophageal reflux disease without esophagitis. *Id.* at 31.

That summer, on July 18, 2017, Dr. Chambers saw neurologist Dr. Robert Yapundich for an evaluation. Ex. 14 at 4. She was deemed to possibly be suffering from “undifferentiated MCTD [mixed connective tissue disorder], migraines, RLS . . . , and intermittent bilateral leg pain.” *Id.* But Petitioner was negative for ANA and other autoantibodies, her EMG/NCS⁸ testing yielded normal results, and an exam of her lower extremities revealed no evidence of neuropathy or radiculopathy. *Id.* Petitioner also underwent MRIs on her brain, lumbar, and cervical spine later that same month, in reaction to her complaints of headache plus “pain in unspecified limb” *Id.* at 1–3. The MRI was interpreted to show potential “minimal component of hydrocephalus,” but “no appreciable brain atrophy to account for the prominence of the [supratentorial] ventricles.” *Id.* at 2.

⁷ ANA stands for antinuclear antibodies, which are “antibodies directed against nuclear antigens; ones against a variety of different antigens are almost invariably found in systemic lupus erythematosus and are frequently found in rheumatoid arthritis, scleroderma (systemic sclerosis), Sjögren syndrome, and mixed connective tissue disease.” Antinuclear Antibodies, *Dorland’s Medical Dictionary Online*, <https://www.dorlandsonline.com/dorland/definition?id=56804> (last visited July 13, 2022).

⁸ EMG stands for electromyogram, “the record obtained by electromyography.” Electromyogram, *Dorland’s Medical Dictionary Online*, <https://www.dorlandsonline.com/dorland/definition?id=15852> (last visited June 29, 2022). NCS stands for nerve conductive study. Both kinds of testing are employed to evaluate nerve function.

On August 8, 2017, Dr. Chambers returned to PA Sears for a “preventative exam, lumbar disc and connective tissue [disorder].” Ex. 4 at 17. The onset date for her UCTD was now listed as April 18, 2017. *Id.* at 18. Her medications were noted, along with the fact that she continued to have pain. *Id.* at 17. Petitioner then consulted a neurosurgeon who stated her nerve roots were fine. Ex. 1 at 23. He deemed her symptoms to be consistent with UCTD and proposed that she see a pain management physician. *Id.*

Several months later, Petitioner went back to Dr. Caldwell in November 2017. Ex. 15 at 4. Her main complaint was “several recent flares,” even as recently as the morning of the visit. *Id.* Further, she reported fatigue, increased pain, raspy voice, and persistent dry mouth. *Id.* Her assessment continued to be UCTD and arthralgia. *Id.* at 5. Thirteen days later (on November 28, 2017), Dr. Chambers went to the emergency room for back pain, nausea, and fever. Ex. 17 at 534. Then, she had a new symptom appear overnight on December 9, 2017, when she experienced severe light and noise headaches and dizziness, plus nausea and head pain. Ex. 1 at 27. Her lymphocytes were low, and her liver enzymes up (although the latter was deemed a likely artifact of medication she was taking). *Id.* Around this time, another inflammation biomarker, C-Reactive Protein, was measured as high—62.7 mg/L (normal range 0.0–4.9). Ex. 4 at 168.

Additional Treatment and SLE Diagnosis

Going forward, Petitioner continued to seek care for her ongoing, unresolved constellation of symptoms, with little proposed in the way of explanation for why they were occurring. On January 4, 2018, for example, Dr. Chambers went to Duke Health to see Dr. Kai Sun, a rheumatologist, for evaluation of her UCTD. Ex. 2 at 1–10. The history she provided included all the symptoms she had experienced prior to the vaccinations at issue. *Id.* Her neurological exam was normal, but she still had tenderness in her bilateral hips/trochanteric bursa, with no evidence of arthritis. *Id.* Dr. Sun suspected Petitioner’s back and hip pain had a mechanical explanation, and therefore recommended PT. *Id.* As for her lower leg pain, Dr. Sun deemed it to reflect possible small fiber neuropathy or RLS. *Id.* But otherwise there was a “low suspicion for an autoinflammatory syndrome,” and no typical features of family history. *Id.* at 9. The following month, Petitioner underwent a biopsy test for Sjögren’s syndrome⁹ but it was negative. Ex. 10 at 1, 6.

Because of the continued nature of her pain, Petitioner attended a 21-day program for chronic pain management at the Mayo Clinic in the spring of 2018. Ex. 15 at 36. She eventually

⁹ Sjögren syndrome is a set of complex symptoms “of unknown etiology, usually occurring in middle-aged or older women, marked by the triad of keratoconjunctivitis sicca with or without lacrimal gland enlargement, xerostomia with or without salivary gland enlargement, and the presence of a connective tissue disease, usually rheumatoid arthritis but sometimes systemic lupus erythematosus, scleroderma, or polymyositis.” Sjogren Syndrome, *Dorland’s Medical Dictionary Online*, <https://www.dorlandsonline.com/dorland/definition?id=111409> (last visited June 29, 2022).

opted to retire from medicine due to the ever-present nature of her symptoms. *Id.* at 38. She thereafter continued to seek medical assistance for different aspects of her complaints.

In October 2020, Petitioner went to Dr. Donald Jeffrey Neal, a cardiologist, and reported she had now been formally diagnosed with lupus. Ex. 75 at 2. The precise date or circumstances of this diagnosis are unclear, since I have not identified a record in which it was first proposed. Nevertheless, Dr. Chambers notes this diagnosis was based upon “an outside consultant [that] reviewed [her] studies and [her] reports and said, yes, [she] met the criteria for lupus.” Tr. at 17. And the parties do not contest its reasonableness. *See* Respondent Post-Hearing Brief at 17, filed on March 18, 2022 (ECF No. 71); Petitioner Post-Hearing Brief at 32, filed on March 18, 2022 (ECF No. 72).

Medications Petitioner was receiving at this time allowed her “marginal control” over her symptoms. Ex. 75 at 2. She also had been diagnosed with COVID-19 in August 2020, which she felt had compounded the feeling of overall malaise. *Id.* In the fall of 2020, she saw Dr. Brian Krenzel, an orthopedist, in connection with hip pain complaints. Ex. 77 at 3. Dr. Krenzel noted that Petitioner had an “autoimmune/lupus phenomenon occurring over the past couple years that has taken her out of day-to-day medical practice as a physician.” *Id.* He associated her hip pain to her systemic autoimmune issues, not an orthopedic issue. *Id.* Petitioner has continued to note to treaters that her medication course has assisted her with symptoms. Ex. 78 at 2.

II. Witness Testimony

A. Dr. Dana Chambers

Dr. Chambers testified on her own behalf at hearing. *See generally* Tr. at 4–25. She previously worked in family medicine for about 20 years, attending Presbyterian College for her undergraduate degree, and then the East Carolina University School of Medicine. *Id.* at 15. She has experience diagnosing and treating patients with rheumatological diseases, and this constituted roughly 10 to 12 percent of her practice. *Id.* at 6.

Prior to the vaccination at issue, Petitioner was healthy, and characterized herself as an “avid runner . . . went to the gym twice a week . . . enjoyed gardening . . . enjoyed travel . . . [and] enjoyed being a civic leader as well as on a lot of the hospital leadership committees.” Tr. at 6. She also had not ever been diagnosed formally with an autoimmune disease before the symptoms she alleges in this case were vaccine-caused. *Id.* at 9. And testing for autoantibodies believed associated with different autoimmune conditions have not yielded positive results. *Id.* at 9–10.

Dr. Chambers admitted, however, that she had experienced some prior illnesses. In particular, she had struggled with Raynaud syndrome since her teens, which causes “your fingers

[to] turn white and/or a light blue/purple, and they can be painful.” Tr. at 8. She also had experienced bouts of arthralgia about every two years, with 2014 constituting a particularly bad period. *Id.* at 20. Closer in time to the October 2016 vaccination, Dr. Chambers had experienced “low back pain, paresthesia, and numbness.” *Id.* at 21. She was later deemed to be experiencing piriformis syndrome, which caused her to stop running and doing yoga, and later became so painful that she sought the assistance of a pain management clinic. *Id.* at 22. She also acknowledged that a rapid strep test she received the same month as the Tdap vaccine was positive, that she had in her life experienced other flare-ups of strep, and that her October 2016 strep infection was accompanied by a wet, productive cough. *Id.* at 22–24.

On the day of the October 2016 vaccination, Petitioner was feeling good, without any identified health issues. Tr. at 10. The following day, she recalled, she felt tired (which she characterized as common to post-vaccination malaise), “but as the days went on, I was developing more joint pain, more fatigue and—and just starting to not feel well.” *Id.* at 11. By that weekend, she had trouble going up her stairs, “a little bit of a shaky voice, a little bit of some unusual hoarseness, excuse me, and my eyes were starting to get a little irritated and red on top of that.” *Id.* And then a few days later, by October 11, 2016, Petitioner was finding it difficult to stand, with her joints being stiff, specifically her hips. *Id.*

Dr. Chambers continued to experience symptoms, thereafter, prompting her to seek an appointment with her practice partner, Dr. Kahill (since the two essentially served as each other’s primary care physicians out of convenience). Tr. at 12. Because the appointment had to be scheduled in a short period between their normal patient appointments, it was quite hurried, and featured only a “precursory exam of [her] lymph nodes and [her] heart and lungs.” *Id.* Petitioner was unable to give a full history at the time, just noting her hip pain, hoarseness, and red eyes. *Id.* at 12–13. Based upon this, hip x-rays were ordered that resulted in normal findings, although she did test positive for inflammatory biomarkers as well as certain autoantibodies associated generally with autoimmune conditions. *Id.* at 13. Petitioner attempted to continue working, but eventually began having to take some sick days, and finally sought emergency care on October 26, 2016. *Id.* at 14. There, she was diagnosed with a pulmonary embolus and admitted. *Id.* at 15–16.

Petitioner’s initial appointment with a rheumatologist (Dr. Caldwell) occurred on November 7, 2016, when it was decided to take an initial “wait and see” approach to treatment. Tr. at 16. She was later diagnosed with UCTD by Dr. Caldwell and started on hydroxychloroquine. *Id.* Based upon an outside consultant at a later date, her diagnosis was ultimately changed to lupus. *Id.* at 17.

Petitioner concluded her testimony by explaining how the injury has affected her life. She deals with joint pain and stiffness daily, with mornings being the toughest. Tr. at 17. She also experiences “a lot of just general exhaustion, which, well, it’s not like fatigue, like you just need a

nap; it's like you just never feel rested." *Id.* She can no longer work in medicine and is applying for long-term disability. *Id.* at 18.

B. Thomas M. Zizic, M.D.

Dr. Zizic, a rheumatologist, submitted two expert reports and testified for the Petitioner in support of her vaccine injury. *See generally* Tr. 26–132, 207–16; Report, dated Aug. 15, 2020, filed as Ex. 25 (ECF No. 29-1) ("Zizic Rep."); Report, dated May 17, 2021, filed as Ex. 80 (ECF No. 50-1) ("Supp. Zizic Rep.").

1. *Zizic Testimony*—Dr. Zizic has been a "rheumatologist and clinical immunologist on the faculty of John Hopkins University School of Medicine and in private practice as well—the last 30 [years]." Tr. at 26; Dr. Zizic Curriculum Vitae, filed as Ex. 26 (ECF No. 29-2) ("Zizic CV") at 1. He is also a Physician at John Hopkins Hospital and Good Samaritan Hospital. Zizic CV at 1. He attended the University of Wisconsin for his undergraduate for a Bachelor of Science, then going to John Hopkins Medical School. *Id.* at 26–27. He subsequently completed "an internship and residency in internal medicine, again at John Hopkins, with a stint at the Mayo Clinic as part of [his] rotations in [his] residency." *Id.* at 27. He served as a flight surgeon in the United States Air Force, returning for "a two-year fellowship in internal medicine and rheumatology, clinical immunology, and then [he] was with another two-year fellowship as [his] first two years on the faculty, and that was sponsored by the Arthritis Foundation." *Id.*

Dr. Zizic is a member of the American College of Rheumatology, of which he is a founding member. Tr. at 28–29. Dr. Zizic is board certified by the State of Maryland, Medical Examiners Physicians and Surgeons along with being grandfathered into the boards of Rheumatology, as he had worked in this area before the boards existed. Zizic CV at 2. He has served as a full-time faculty member and division lead at both John Hopkins and University of Maryland, simultaneously for seven years, then just at Johns Hopkins. *Id.* at 29. Further, he has published peer-reviewed journals on rheumatology, various connective tissue disorders, and lupus. *Id.* at 29–30. Dr. Zizic states he has treated "many hundreds" of patients with lupus and more patients than he could count dealing with connective tissue disorders. *Id.* at 35–36. Although Dr. Zizic began practicing before board certification in rheumatology was available, he was trained in rheumatology and clinical immunology. *Id.* at 28.

Dr. Zizic first discussed the nature of lupus. He deemed it a unique rheumatologic condition, since "it can involve any organ in the body, virtually, from hair to skin to eyes to mucus membranes to the vocal cords." Tr. at 43. Lungs can be impacted as well, resulting in pleurisy, sterile pneumonia, pneumonitis, hemorrhages, and cavitary nodules. *Id.* Other potential secondary problems are myocarditis, coronary arteritis, renal disease, liver disease, spleen issues, skin, joints, and the muscles. *Id.* Lupus can be difficult to diagnose, given that it can present in different organs.

Id. at 43–44. Its clinical symptoms can also appear sporadically, with flaring manifestations occurring at different times and often over years. *Id.* at 44. The diagnosis ultimately depends on clinical factors, Dr. Zizic noted, adding that the American College of Rheumatology had developed a set of classification criteria¹⁰ (although a lupus diagnosis could be proper even in the absence of satisfying all these criteria). *Id.* at 45–46.

Lupus/SLE has much in common with rheumatoid arthritis, Dr. Zizic argued. Zizic Rep. at 39. They are pathogenically similar, stemming “from a dysregulation of the immune system resulting in the formation of autoantibodies and the subsequent development of an autoimmune disease.” *Id.* Indeed, “[i]t is often said that the autoantibody immune complex disease destroying the joints in rheumatoid arthritis is very similar to what is happening in the blood and spreading throughout the body in patients with [SLE].” *Id.* He acknowledged, however, that SLE and rheumatoid arthritis would ultimately be driven by different autoantibodies. *Id.*

In Dr. Zizic’s view, lupus occurs due to a conflux of identifiable factors: heredity, hormonal factors, and then an external triggering event. Tr. at 41–43. He thus disagreed with literature filed in this case opining that the “etiopathogenesis of systemic lupus (SLE) is complex and still largely unknown.” G. D. Sebastiani & M. Galeazzi, *Infection-Genetics Relationship in Systemic Lupus Erythematosus*, 18 *Lupus* 1169, 1169 (2009) filed as Ex. 67 (ECF No. 35-1). On the contrary, Dr. Zizic maintained that significant strides had been made in the past 12 years helping illuminate the nature of lupus and its causes. Tr. at 109. He also proposed that its usual pathogenesis was understood to involve an “immune complex deposition in tissues, and that . . . causes the activation of the complement cascade and an inflammatory response that damages the condition permanently.” *Id.* at 107–08. Infection in particular could constitute the kind of environmental trigger that would incite lupus, Dr. Zizic proposed. *Id.* at 52.

Gender was a particularly important factor, since women constitute 90 percent of lupus patients. Tr. at 50. There are also some viral infections known to be associated with triggering lupus—in particular, hepatitis B, EBV, and parvovirus. *Id.* at 50–51; A. Doria et al., *Infections as Trigger and Complications of Systemic Lupus Erythematosus*, 8 *Autoimmunity Rev.* 24, 25 (2008), filed as Ex. 61 (ECF No. 34-5) (“Doria”) (noting that “SLE occurs when an environmental trigger acts on a genetically predisposed individual, leading to a loss of tolerance towards native proteins”). Dr. Zizic agreed, however, that he could not substantiate a similar association between lupus and diphtheria, tetanus, or pertussis infections. *Id.* at 111. He also could not reference science directly supporting a flu virus/SLE association, but given the wide array of flu virus strains, Dr. Zizic felt it was far more difficult to identify such a prior flu infection through blood testing. *Id.* at 109–10.

¹⁰ These diagnostic criteria were later amended in 2019 in conjunction with the European rheumatologists. Tr. at 46; see Ex. 44.

Dr. Zizic provided a brief explanation of autoimmune diseases, as context for how lupus itself might pathogenically occur. He defined them to be “chronic conditions initiated by the loss of immunological tolerance to self-antigens; they represent a heterogeneous group of disorders that afflict specific target organs or multiple organ systems.” Zizic Rep. at 37. Although different in clinical manifestation or course, they often share features like “physio-pathological mechanisms,” and can also be the product of genetic susceptibility factors that partially explain their development. *Id.*; J. Cardenas-Roldán et al., *How do Autoimmune Diseases Cluster in Families? A Systematic Review and Meta-Analysis*, 73 BMC Medicine 1, 1 (2013), filed as Ex. 40 (ECF No. 32-4). It was widely accepted by medical science, Dr. Zizic maintained, that infection could trigger an adaptive immune response that would in turn propagate an autoimmune disease. Tr. at 54; N. R. Rose, *Infection and Autoimmunity: Theme and Variations*, 24 Current Opinion Rheumatology 380 (2012), filed as Ex. 27 (ECF No. 31-1) (“Rose”).

One scientifically reliable mechanistic process for how autoimmune disease might proceed is molecular mimicry, which relies on “experimental evidence of an association of infectious agents with autoimmune disease and observed cross-reactivity of immune reagents with ‘self’ antigens and microbial determinates.” M. Oldstone, *Molecular Mimicry and Immune-Mediated Diseases*, 12 FASEB J. 1255 (1998), filed as Ex. 30 (ECF No. 31-4); Tr. at 52; Zizic Rep. at 37 (defining molecular mimicry as occurring where “similar structures shared by molecules from dissimilar genes or by their protein products” can result in a cross-reaction when autoantibodies produced in reaction to an antigenic structure attack the comparable self structure), 53. Medical literature, Dr. Zizic contended, provided examples of how molecular mimicry could mechanistically drive the process leading to lupus after infection.¹¹ Tr. at 52. For example, Doria specifically showed antigenic similarity between EBV components and the “PPGMRPP which seems to be the first epitope of SM β antibody response.” Doria at 25; Tr. at 53–54.

Another kind of immune system cell—the T cell—could also play a role in mediation of an autoimmune reaction. *See generally* Zizic Expert Rep. at 29–36. T cells are important in assisting the immune system in recognizing foreign antigens. B. Szomolay et al., *Identification of Human Viral Protein-Derived Ligands Recognized by Individual MHCI-Restricted T-Cell Receptors*, 94 Immunology & Cell Biology 573, 573 (2016), filed as Ex. 55 (ECF No. 33-9). But they could also “play a major role in the pathogenesis of common autoimmune diseases, such as type 1 diabetes, multiple sclerosis and psoriasis, where pathogen-derived peptide sequences are thought to drive the expansion of self-reactive T cells capable of mediating tissue damage.” *Id.*

In particular, Dr. Zizic maintained, “pathogenic CD8⁺ T-cell expansions may originate as an initially protective response to a viral antigen that [later] results in immune-mediated disease, caused by subsequent cross-reactivity with a self-derived pMHCI molecule.” Zizic Rep. at 47.

¹¹ On cross-examination, however, Dr. Zizic agreed that the EB virus can be reactivated—and that Dr. Chambers previously had been found to possess that infection. Tr. at 112.

Thus, an initial T cell reaction “can diversify, often through antibody/B cell-directed processing, to focus on the wild-type, unmodified antigen, which might drive subsequent amplifying immune responses to self-antigen.” *Id.*; M. J. Mamula et al., *Breaking T Cell Tolerance with Foreign and Self Co-Immunogens: A Study of Autoimmune B and T cell Epitopes of Cytochrome C^I*, 149 J. Immunology 789 (1992), filed as Ex. 56 (ECF No. 33-10). This mechanism for autoimmunity was relevant herein because “[t]here is growing evidence that modified autoantigen structure plays a role in initiating the specific immune responses observed in human rheumatic diseases.” Zizic Rep. at 47; L. Casciola-Rosen et al., *Cleavage by Granzyme B is Strongly Predictive of Autoantigen Status: Implications for Initiation of Autoimmunity*, 190 J. Explorative Medicine 815 (1999), filed as Ex. 57 (ECF No. 34-1).

Vaccines could also trigger an autoimmune process leading to SLE, like their wild infectious counterparts. Tr. at 50–51. Vaccines as a general matter provoked an immune response comparable to infection, and thus could in theory cause the same reaction. *Id.* at 53. Indeed, in Dr. Zizic’s view an autoimmune reaction had a heightened possibility in the context of vaccination. Although “an infection with the virus may not produce an ‘overwhelming apoptotic event’ leading to autoimmunity, . . . that same viral antigen in the presence of adjuvants would be capable of generating such an event.” Zizic Rep. at 51. A vaccine would also impact the immune response generally, which includes the “cytokines and chemokines and eventually a broad disturbance in the normal immunologic balance.” Tr. at 54. One cytokine in particular, IL-6, “stimulates the liver to produce C-reactive protein,” which in turn is an inflammation biomarker. *Id.* at 55.

A number of different studies showed not only that the flu vaccine could produce autoimmune injury via molecular mimicry, but more generally linked the vaccine to lupus or comparable rheumatologic conditions. Tr. at 43. One study had revealed a direct link between the influenza virus vaccine and the secretion of antibodies relevant to lupus. M. Abu-Shakra et al., *Influenza Virus Vaccination of Patients with SLE: Effects on Generation of Autoantibodies*, 21 Clinical Rheumatology 369, 371 (2002), filed as Ex. 69 (ECF No. 35-3) (“Abu-Shakra”).

Abu-Shakra tested the blood of 24 women who had already been diagnosed with SLE to evaluate how receipt of the flu vaccine would impact the generation of a autoantibodies at three points in time: vaccination, six weeks later, then 12 weeks. Abu-Shakra at 370. The researchers tested for seven autoantibodies, including anti-SM, which Dr. Zizic characterized as “99 percent specific” to lupus. Tr. at 57. Abu-Shakra observed a general increase in amounts of certain autoantibodies associated with lupus within six weeks of vaccination. *Id.* at 57–59; Abu-Shakra at 371. Abu-Shakra did not, however, identify any associated “specific clinical response” in connection with these increases, and concluded that “[p]atients with SLE should be encouraged to receive the influenza vaccine.” *Id.* at 372. Dr. Zizic nevertheless argued that because Dr. Chambers was not being treated for SLE at the time of her vaccination, her risk from vaccination was distinguishable from a person already being treated (thus implying that the benefits of treatment

canceled out the otherwise likely deleterious impact of vaccination—despite Abu-Shakra’s finding to the contrary). Tr. at 61–62.

Turning to the facts of this case, Dr. Zizic concurred that Dr. Chambers had been properly diagnosed with lupus, noting that the diagnostic criteria he had discussed were largely met. Petitioner had “ANA positivity,” which is considered a threshold for an SLE diagnosis, along “with low complements [which is] almost pathognomonic of lupus.” Tr. at 31, 46. She also displayed a number of the other relevant clinical criteria, with none of the excluding circumstances. *Id.* at 47–48. In addition, she was likely susceptible for an autoimmune disease based upon “a family history of rheumatoid arthritis, thyroid disease, and Raynaud’s.” *Id.* at 40. She had experienced Raynaud-like myalgias, arthralgias, and fever, and “within a week of getting her immunization, she got pleurisy.” *Id.* In fact, the pleurisy itself led Dr. Zizic to propose it likely that Dr. Chambers experienced lupus pneumonitis, since the record suggested she later experienced comparable symptoms including respiratory/lung-oriented problems. *Id.*

The vaccines Petitioner received at the beginning of October 2016¹² were likely the environmental trigger for her lupus, Dr. Zizic opined. He particularly considered the flu vaccine as more likely causal than the Tdap, which he admitted he could not identify the same level of support for in medical literature. Tr. at 127. First, he observed a distinction between Petitioner’s pre- and post-vaccination status. She had no clear symptoms before vaccination,¹³ and prior tests were negative for the most common likely lupus autoantibodies. *Id.* at 79. Thus, something changed in Petitioner’s condition after vaccination (although to some extent this aspect of his opinion required disregarding the evidence of Petitioner’s pre-vaccination symptoms as potentially related).

Dr. Zizic contested Dr. Miner’s opinion that Dr. Chamber’s lupus was more likely caused by an infectious pneumonia. Tr. at 86. He instead read the medical record to establish only the existence of pneumonia-like inflammation, or pneumonitis, which can be a sign of lupus rather than the result of a wild infection. *Id.* at 86–87. Moreover, Petitioner reported no benefit from the antibiotic therapy she received, further undermining the likelihood that she had experienced a bacterial infection. Supp. Zizic Rep. at 2. Otherwise, her chest x-ray around the time of hospitalization was normal, the blood cultures twice were negative, and her white blood count was not high enough to be consistent with some kind of “smoldering” pneumonia. Tr. at 87–88.¹⁴ The

¹² Dr. Zizic deemed the flu vaccine more likely causal in this case than the Tdap. Tr. at 127.

¹³ Dr. Zizic, however, admitted on cross-examination that the record showed that Dr. Chambers had a history of lupus-like symptoms prior to vaccination, as well as arthralgia-like flare-ups every few years, although he declined to comment on whether this was significant given the overall record. Tr. at 114.

¹⁴ However, on cross-examination Dr. Zizic agreed that “viral infections frequently *do not cause* an elevated white blood cell count.” Tr. at 120–21 (emphasis added).

lung pain Dr. Chambers experienced was also more likely part of her lupus symptoms than characteristic of pneumonia. *Id.* at 89–90.

The timeframe in which Dr. Chambers’ symptoms arose was also consistent with vaccine causation, in Dr. Zizic’s opinion. Petitioner showed first symptoms days after vaccination. Tr. at 81. Her October 2016 bloodwork (obtained 12 days post-vaccination) also revealed the existence of an ongoing and active inflammatory process. *Id.* at 83–84. In particular, it revealed the presence of the CRP inflammatory biomarker, which Dr. Zizic proposed could be attributed to an upregulation of IL-6 caused in turn by the flu vaccine. *Id.* at 54–55. By October 19, 2016, Petitioner’s symptoms became more acute—“chills, fatigue, fever, malaise, those constitutional symptoms,” which in Dr. Zizic’s view, “could be part of an acute inflammatory reaction, including the early symptoms of lupus.” *Id.* at 85–86; Ex. 19 at 20. All of the above was more consistent with causation due to the flu vaccine received shortly before than “an Epstein-Barr infection two years ago or a flare of that infection from two years earlier.” Tr. at 212–13.

2. *Reliance on Wang Meta-Analysis*—Dr. Zizic made a point of highlighting one particular item of literature as strongly supporting a vaccine-SLE association. B. Wang et al., *Vaccinations and Risk of Systemic Lupus Erythematosus and Rheumatoid Arthritis: A Systematic Review and Meta-Analysis*, 16 *Autoimmunity Reviews* 756 (2017), filed as Ex. 73 (ECF No. 35-7) (“Wang”). Indeed, he emphasized that Wang was integral to his opinion. Tr. at 63 (deeming Wang “a magnificent study”), 65–66. For this reason, I address it (and some of the sub-articles upon which it relies) separately from my summary of Dr. Zizic’s opinion, and with a little more specificity than I might in other cases.

Wang is a “meta-analysis”—an article that purports to synthesize the data from a number of individual studies into one larger study, which can then (presumably) reach conclusions based on agglomeration of data that in a smaller study was too limited in sample or otherwise to render statistically-reliable results. Federal Judicial Center & National Research Council of the National Academies, *Reference Manual on Scientific Evidence* 607 (3d ed. 2011). Wang specifically incorporated, and attempted to merge, data from 16 individual studies, 12 of which considered the associated risk between different vaccines and SLE (as opposed to RA). Wang at 759 (Table 1). Importantly, even among the 12 studies specific to SLE, not all are facially relevant herein. Thus, *nine* of the 12 on-point studies evaluated the relationship between SLE and other vaccines not at all implicated in this case, such as the varicella zoster, hepatitis B, human papillomavirus (“HPV”), or anthrax vaccines. *Id.* Others only reference “vaccinations,” without specifying which were considered. *Id.* And Petitioner (despite my specific request during the hearing) ultimately only filed the sub-studies relied upon in Wang specifically involving the flu vaccine (or at least some version of it). Tr. at 127–29.¹⁵

¹⁵ Wang also included in its meta-analysis two articles authored by Drs. David and Mark Geier considering the association between SLE and the HBV or HPV vaccines. *See* Wang at 759 n.38, n.48 (Table 1). Neither study was

Wang determined that (in Dr. Zizic’s reading) “vaccinations increased the risk of lupus to one and a half relative risk, in other words, 50 percent more likely to get lupus with vaccination.” Tr. at 72. He noted that overall, its determination of an SLE-vaccine association possessed a 95 percent confidence range¹⁶ of 1.05 up to 2.12, with a reliable P value of 0.024.¹⁷ Wang at 758; Tr. at 72. Dr. Zizic vouched effusively for Wang’s methodologic rigor. Tr. at 65–69. Wang was also judicious in considering more narrow outcomes when excluding articles deemed potentially infected by bias, such as studies funded by pharmaceutical companies. Tr. at 75; Wang at 760 (Table 3).

Cross-examination, however, revealed some limitations to Wang. For example, only two of the 12 SLE-specific studies specifically considered the impact of the flu vaccine,¹⁸ and (contrary to the aggregated results achieved when disparate vaccines were considered together) the p value obtained in those studies was not statistically significant (.105), while the relative confidence interval (.97 to 1.39) was far worse than other findings. Tr. at 97–98; Wang at 760 (Table 3). In fact, one of two specific flu vaccine-SLE studies showed a relative risk of .95—meaning that the effect of vaccination was arguably *ameliorative*. Tr. at 100; I. Persson et al., *Risks of Neurological and Immune-Related Diseases, Including Narcolepsy, after Vaccination with Pandemrix: A Population- and Registry-Based Cohort Study with Over 2 Years of Follow-Up*, 275 J. Internal Medicine 172 (2014) filed as Ex. 85 (ECF No. 62-3) (“Persson”). Dr. Zizic nevertheless maintained that if risk was looked at on the basis of shorter time frames (which would be most relevant to this case), the risk was higher, reaching 1.52. Tr. at 99–101.

The deficiencies in the sub-articles relied upon in Wang go deeper than merely whether their observations have statistical significance, however. Persson, for example, involved an adjuvanted version of the flu vaccine (Pandemrix) aimed at the H1N1 wild virus strain—and *never*

filed or specifically relied upon by Petitioner in this case. I nevertheless note that the Geiers have repeatedly, and over a lengthy period of time, been deemed to be questionably-competent and scientifically-unreliable experts in the Vaccine Program—casting significant doubt on *any* studies they have authored. *See, e.g., America v. Sec’y of Health & Hum. Servs.*, No. 17-542V, 2022 WL 278151, at *8 n.16 (Fed. Cl. Spec. Mstr. Jan. 4, 2022) (detailing numerous prior Vaccine Program cases in which the Geiers were noted to have been fully discredited as competent experts); *see also Combs v. Sec’y of Health & Hum. Servs.*, No. 14-878V, 2018 WL 1581672, at *8 (Fed. Cl. Spec. Mstr. Feb. 15, 2018).

¹⁶ In the context of evaluation of medical treatments, a result of more than 1.0 suggests a negative impact of the studied treatment, whereas less than one suggests a protective effect. *Dwyer v. Sec’y of Health & Hum. Servs.*, No. 03-1202V, 2010 WL 892250, at *65, 70 (Fed. Cl. Spec. Mstr. Mar. 12, 2010).

¹⁷ “P value” (shorthand for probability value) is a statistical concept that describes how likely it is that a particular data-established outcome would have occurred by random chance. P Value, *Dorland’s Medical Dictionary Online*, <https://www.dorlandsonline.com/dorland/definition?id=116692> (last visited July 14, 2022). Generally, the smaller the p-value, the stronger the evidence that the outcome at issue is not due to chance. A p value of less than .05 is typically considered statistically significant. *Id.*

¹⁸ None of the studies included in the Wang meta-analysis considered the SLE-Tdap vaccine association. Tr at 102.

administered in the United States.¹⁹ Persson was also primarily focused on a putative association with a completely distinguishable condition, narcolepsy. *See, e.g.,* Persson at 187. Thus, its relevance to a case involving a wholly-different formulation of the flu vaccine is facially questionable. And Persson’s authors expressly *discounted* that any of their findings showed any connection with *any* other autoimmune disorders. Persson at 185 (“[w]e also found no positive associations could be established between Pandemrix and any of the immune-related disorders (except vaccination reactions) . . . [t]he absence of an increase in risk events related to typical autoimmune diseases, *for example systemic lupus erythematosus* . . .”) (emphasis added).

The same distinctions are relevant to the second article considered in Wang specific to the SLE-flu vaccine connection—a case-control study.²⁰ L. Grimaldi-Bensouda et al., *The Risk of Systemic Lupus Erythmatosus Associated with Vaccines*, 66 *Arthritis & Rheumatology* 1559 (2014), filed as Ex. 83 (ECF No. 62-1) (“Grimaldi-Bensouda”). Based on an admittedly small sample (105 SLE patients, compared to 712 controls) who had been vaccinated at two different points in time (12 or 24 months before clinical symptoms onset of SLE), Grimaldi-Bensouda’s authors determined that “exposure to vaccines is not associated with an increased risk of developing SLE.” Grimaldi-Bensouda at 1566. Comparable percentages of the SLE sample received the flu or Tdap-like vaccines (e.g., containing one or more of that vaccine’s components), without evidence of a heightened risk for SLE. *Id.* at 1563 (Table 2).

A third article that was included in the Wang meta-analysis did demonstrate a possible association between RA (which has some, if limited, commonality with SLE) and the flu vaccine, and was for that reason offered by Dr. Zizic in this case. P. Ray et al., *Risk of Rheumatoid Arthritis Following Vaccination with Tetanus, Influenza and Hepatitis B Vaccines Among Persons 15–59 Years of Age*, 29 *Vaccine* 6592, 6594–95 (2011), filed as Ex. 71 (ECF No. 35-5) (“Ray”). Ray’s authors conducted a retrospective study of approximately one million members of a large health maintenance organization. Ray at 6593. Although the paper’s focus was on whether a putative link between the hepatitis B vaccine and RA could be substantiated, its authors also considered RA rates after receipt of flu or tetanus vaccines, since they were “[t]he two most common vaccines given” to the studied population. *Id.*

¹⁹ *D’Tiole v. Sec’y of Health & Hum. Servs.*, No. 15-085V, 2016 WL 7664475, at *20–21 (Fed. Cl. Spec. Mstr. Nov. 28, 2016) (explaining that the crucial aspect of the Pandemrix vaccine’s ability to cause narcolepsy is in how it is manufactured, which is different than the vaccines made in the United States), *mot. for review den’d*, 132 Fed. Cl. 421 (2017), *aff’d*, 726 F. App’x 809 (Fed. Cir. 2018).

²⁰ A case-control study is a retrospective “longitudinal epidemiologic study in which participating individuals are classified as either having (cases) or lacking (controls) some outcome and their histories are examined for the presence of specific factors possibly associated with that outcome.” Retrospective Study, *Dorland’s Medical Dictionary Online*, <https://www.dorlandonline.com/dorland/definition?id=109047> (last visited July 14, 2022). Further, “[c]ases and controls are often matched with respect to certain demographic or other variables but need not be.” *Id.*

Ray's authors performed two analyses within their overall study. The first was a cohort study,²¹ in which the authors identified 378 instances of RA, observing a higher risk of disease within 180- or 365-days following immunization. *Id.* at 6593, 6595. These determinations were deemed statistically significant. *Id.* at 6694 (Table 3). Ray also included a second analysis—a case-control study—because the number of cases evaluated in the cohort study was deemed too limited (given temporal onset definitions that excluded samples from the cohort study). *Id.* at 6594. In the case-control analysis, 415 RA patients were considered and matched against 1,245 controls, but “[c]ases were not significantly more likely than controls to have received any of the three vaccines in any of the intervals examined.” *Id.* at 6595. Ray concluded that the association observed between the flu vaccine and RA in the cohort study was only “possible,” but was not then confirmed by the case-control study (which relied on a greater quantum of data). *Id.* at 6596. Ultimately, Ray's authors returned in their conclusion to their primary concern—whether the *hepatitis B vaccine* was associated with RA—and proposed it was not, although they noted limitations in the study overall that made its determinations not fully reliable. *Id.*

Even though Ray did not address lupus specifically, Dr. Zizic maintained it involved “the same kind of autoimmune autoantibody immune complex kinds of damage,” making its findings relevant. Tr. at 107. He also acknowledged that Ray's two analyses were inconsistent in their embrace of a flu vaccine-RA relationship, but maintained that the study was biased, due to its “big pharma” sponsorship, and asserted (without substantiation) that its authors added the case-control analysis solely to undermine their initial findings, which cast vaccination in a negative light. Tr. at 102–03, 104 (analysis was “jerry-rigg[ing] it”).

B. Respondent's Expert: Jonathan D. Miner, M.D., Ph.D.

Dr. Miner is board-certified in internal medicine and rheumatology, and he testified on behalf of Respondent, while also submitting two written expert reports. *See generally* Tr. at 134–205; Report, dated Nov. 25, 2020, filed as Ex. A (ECF No. 39-1) (“Miner Rep.”); Report, dated Feb. 22, 2022, filed as Ex. C (ECF No. 70-1) (“Supp. Miner Rep.”).

Dr. Miner attended Brigham Young University for his undergraduate degree, with a double major in Russian and Zoology. Tr. at 134; Dr. Miner Curriculum Vitae, filed as Ex. B (ECF No. 39-8) (“Miner CV”) at 1. He then did a combined M.D./Ph.D. program at the University of Oklahoma College of Medicine. Tr. at 134–35, Miner CV at 1. His Ph.D. was in biochemistry and molecular biology, although he also did thesis “work on mechanisms of inflammation and

²¹ A cohort study is a prospective “longitudinal epidemiologic study in which the groups of individuals (cohorts) are selected on the basis of factors that are to be examined for their effects on outcomes, e.g., the effect of exposure to a specific risk factor on the eventual development of a particular disease, and are then followed over a period of time to determine the incidence rates of the outcomes in question in relation to the original factors.” Prospective Study, *Dorland's Medical Dictionary Online*, <https://www.dorlandsonline.com/dorland/definition?id=109045> (last visited July 14, 2022).

migration of white blood cells to sites of infection or injury.” Tr. at 135. Dr. Miner did residencies in internal medicine and rheumatology at Washington University in St. Louis School of Medicine and Barnes-Jewish Hospital. *Id.*; Miner CV at 1. In continuing his education, Dr. Miner performed post-doctoral research at the Washington University of St. Louis with a virologist looking at immune responses. Tr. at 135.

Dr. Miner began his own laboratory at Washington University in St. Louis in 2017, later moving to the University of Pennsylvania. Tr. at 135; Miner CV at 1, 6. The NIH-funded laboratory that Dr. Miner runs studies “animal models of lupus-like disease in mice that have human mutations.” Tr. at 135–36. This specifically includes the gamma herpesviruses-mediated progression of disease caused by infections like EBV. *Id.* at 136. Dr. Miner also sees rheumatology patients in clinic, and has treated “many dozens” at Washington University; at the lupus clinic, “there were 500 to 600 patients total cared for by a group of physicians” in all. *Id.* at 136–37. Dr. Miner has published over 70 articles and book chapters that relate to “rheumatic diseases, and many of the—much of the original research relates to these human disease-causing mutations associated with lupus-like diseases and how viruses and microbes interact with the host to potentiate disease.” *Id.* at 137. On cross-examination, however, Dr. Miner admitted that he has written only a single article addressing lupus directly, instead usually focusing on “lupus-like disease.” *See id.* at 161–62.

At the outset of his testimony, Dr. Miner discussed some of the injuries or conditions Petitioner may have experienced. For example, Dr. Chambers had previously complained of symptoms associated with Raynaud syndrome, which Dr. Miner defined to be “characterized by vasospasm, where blood vessels become narrowed in the fingers, and this can cause skin color changes and even pain or skin ulcers on the fingertips.” Tr. at 138. Raynaud syndrome can in some cases progress into a full rheumatic or other systemic autoimmune condition. *Id.* at 138–39. Dr. Chambers’ demonstrated history of struggling with Raynaud syndrome symptoms was, in Dr. Miner’s opinion, “a strong suggestion of predisposition to systemic autoimmunity.” *Id.* at 139.

Dr. Miner next discussed SLE, characterizing it as a syndrome in which “patients are very frequently unique” in comparison to each other from a clinical/symptomatic perspective. Tr. at 139. Patients with SLE typically display a positive ANA, although possession of this autoantibody alone is an insufficient basis for an SLE diagnosis. *Id.* (“there are 32 million Americans with a positive ANA, and only about 1.5 million that have lupus”). Individuals with lupus can also experience “skin disease, photosensitivity, arthritis, kidney disease; and another patient might have blood clots, skin rash, and Raynaud’s.” *Id.* at 139–40. Thus, although there exist specific diagnostic criteria used in the context of studies (in order to ensure conformity among scientific research), actually diagnosing lupus can be very difficult given its multivariable presentation, with Dr. Miner comparing the effort to “putting together a thousand-piece puzzle.” *Id.* at 140.

Regarding causes, Dr. Miner agreed both genetic and environmental factors could be significant. Tr. at 142. In particular, symptoms flares, or worsening of existing symptoms, can be triggered by some environmental factors. *Id.* Nevertheless, Dr. Miner emphasized the commonly chronic, smoldering nature of rheumatic conditions like SLE (which can exist over a long period of time in a mild form), observing that “patients before they’re diagnosed [] have symptoms that wax and wane or are misattributed.” *Id.* at 144.

SLE was therefore not, in Dr. Miner’s estimation, likely a condition that would suddenly manifest simply due to an external trigger. Indeed, he denied a trigger was necessary at all, noting that animal studies had revealed that lupus could arise simply due to a genetic predisposition, “in an enclosed environment that has no microbes.” Tr. at 143, 158 (“patients develop rheumatic diseases inexplicably and suddenly all the time”). He agreed that associations with certain infections, like EBV, had been reliably established. *Id.* at 148. And while different kinds of biologic mechanisms (including molecular mimicry) had been posited as potentially driving the autoimmune process leading to SLE, in his view there remained considerable uncertainty as to the disease’s pathologic features. *Id.* at 147.

Dr. Miner did not fully embrace the proposed SLE diagnosis for Petitioner. He acknowledged that the UCTD diagnosis had record support, and that he understood why lupus might have been thought to potentially characterize Petitioner’s presentation overall. Tr. at 140–41. However, Petitioner had never tested positive for other lupus autoantibodies. *Id.* at 141. And she had experienced lupus-like flares prior to vaccination, which would have better supported a UCTD diagnosis—especially if she had ever been tested for ANA (although she was not prior to vaccination). *Id.* at 142–43. Regardless, Dr. Miner allowed that the SLE diagnosis was reasonable, and otherwise deferred to Petitioner’s treating physicians in embracing it. *Id.* at 141–42.

Nevertheless, Dr. Miner opined that it was “extremely unlikely” that the flu or Tdap vaccines could cause SLE. Tr. at 145–46, 150. At best, it was possible (but still “extremely unlikely”) that a vaccine could cause a transient symptoms flare. *Id.* at 145. Dr. Miner added that he did not know of any generally accepted medical literature that supported connecting either vaccine to SLE. *Id.* at 147.

In challenging the “can cause” aspect of Dr. Zizic’s theory, Dr. Miner attempted to rebut a number of the articles offered to support a vaccine-SLE association. Ray, for example, was inapposite for the simple reason that Dr. Chambers had not been diagnosed with RA—the illness that was Ray’s focus. Tr. at 146–47. And Dr. Miner rejected the idea that RA was interchangeable with SLE for present causation purposes. *Id.* at 147. In reaction to Abu-Shakra, Dr. Miner allowed that it was “not entirely unreasonable that a vaccine could . . . temporarily induce autoantibodies or a higher level of autoantibodies that were preexisting,” much like other medications could. *Id.*

at 151, 176; *see* Abu-Shakra at 370–72. But Dr. Chambers had tested *negative* for the autoantibodies discussed in Abu-Shakra, reducing the value of its findings in this case. *Id.* at 151.

Dr. Miner found Wang wanting for two reasons. First, he criticized the overall value of a meta-analysis paper. Tr. at 147; *See* Wang. In Dr. Miner’s view, this kind of study can be infected by publication bias, to the extent it includes some studies over others, and may also erroneously summarize or aggregate data from among the chosen sub-studies. Tr. at 147. In addition, the studies Wang discussed (which involved RA and SLE, plus a number of irrelevant vaccines) were too disparate for this kind of big-picture comparison. *Id.* at 179 (“[d]ifferent proteins are all very different from each other; different adjuvants are different from each other; and different diseases are different from each other”); Supp. Miner Rep. at 1 (Persson study involved narcolepsy, while Grimaldi-Bensouda included a number of vaccines other than the flu or tetanus vaccines). Otherwise, Dr. Miner argued, the data discussed in Wang actually showed no clear relationship between vaccination and SLE. Supp. Miner Rep. at 1. And the “influenza studies in this paper showed a relative risk of .95 and .9. . . if there’s any trend, it was a trend toward a *protective* effect.” Tr. at 180–81 (emphasis added).

Dr. Miner also provided an overview of Petitioner’s medical history, noting throughout how it was consistent with the conclusion that she had related symptoms that spanned the timeframe before and after vaccination (suggesting an onset that predated vaccination, or at least that vaccination had nothing to do with her illness). For example, even before vaccination she had experienced pre-vaccination inflammation and pain overnight, interfering with her sleep and leading to morning stiffness that did not improve despite several weeks of rest. Tr. at 152. It thus looked to Dr. Miner as if “the wheels of autoimmune arthritis or joint pain were in motion” even before vaccination. *Id.* In addition, Petitioner’s CRP levels (based on post-vaccination testing performed in October 2016) were, in Dr. Miner’s view (and also treaters like Dr. Sun), “extraordinarily high,” and therefore “a clear sign of severe systemic inflammation.” *Id.* at 153; Miner Rep. at 3. In his experience, this kind of reading in the context of SLE would be considered attributable to “infection until proven otherwise.” Tr. at 153–54.

Dr. Miner thus concluded that medical record evidence better supported a different causal factor than vaccination. Petitioner’s initial hospitalization toward the end of October 2016 was most likely attributable to a “severe infection, like a viral infection, causing a viral pneumonia that then transitioned to almost like—almost like an organizing pneumonia, which can be an autoimmune pneumonia, almost, or immunopathology related to a viral infection that has cleared.” Tr. at 154. Organizing pneumonia,²² he asserted, can occur “in patients who are prone to autoimmune disease, but they can also happen in the wake of viral infections, and in many cases,

²² Dr. Miner did allow for the possibility, as Dr. Zizic asserted, that Dr. Chambers suffered from lupus pneumonitis, but deemed that no more likely than a cause of “immunopathology triggered in the context of infection.” Tr. at 156–57.

we don't know for sure why they were triggered, but lupus pneumonitis is not very common." *Id.* at 154–55. Petitioner's fever, cough, and hoarseness were also more suggestive of an infectious process than some other cause.²³ *Id.* at 155. Another possibility was that Petitioner had experienced an EBV reactivation, perhaps associated with the strep infection she was likely experiencing (as corroborated by the positive rapid strep test result that Petitioner admitted she had obtained). *Id.* Although Dr. Miner conceded that such a reactivation could not be proven on the basis of this record, he deemed it far more likely causal than the flu vaccine. *Id.* at 189.

Dr. Miner did not deem it significant that the infectious cause at issue had not been identified. In his experience, infections can be missed, and "[t]hey can happen with fewer minimal symptoms, and then later on, you can have immunopathology where there's a response and the virus is eliminated, but that prolonged sustained immune response induces damages." Tr. at 186. Dr. Miner also disagreed with the supposition that a chronic condition like SLE could not have a viral cause, since viruses can reactivate in a chronic manner. *Id.* At bottom, however, and although Dr. Miner did not dispute that no specific triggering cause for Petitioner's SLE could be identified, infection remained far more likely causal in this case of Petitioner's SLE than the Tdap or flu vaccines. *Id.* at 158.

On cross-examination, Dr. Miner noted a distinction between Dr. Zizic's two proposed mechanisms, loss of tolerance driven by T cells and molecular mimicry. Tr. at 167. He observed that "[y]ou can lose tolerance for a variety of reasons," and thus the autoimmune mechanism of molecular mimicry was not integral to instigating such loss. *Id.* He also denied that an autoimmune cross-reaction instigated by molecular mimicry was required to cause SLE in all cases, stating that "you don't have to invoke mimicry to develop lupus. It's not necessary." *Id.* He did, however, admit that it was at least plausible that the wild flu virus could lead to some other forms of systemic autoimmune disease. *Id.* at 202.

III. Procedural History

After the claim's initiation in January 2019, Petitioner filed many medical records in this case, completing the process by February 2019. ECF No. 9. Respondent filed a Rule 4(c) report on November 30, 2020, stating Petitioner did not meet her burden of preponderant evidence. ECF No. 38. Petitioner filed an expert report and supplement by Dr. Zizic. Zizic Rep.; Supp. Zizic Rep. Respondent submitted their own expert report in response along with a supplement. Miner Rep.; Supp. Miner Rep. This case was then reassigned to me. Order, dated Jan. 29, 2021 (ECF No. 43). After discussions the case was set for an entitlement hearing on October 22, 2021, in Washington, D.C. ECF No. 46. Both parties submitted pre-hearing briefs on the matter, with the hearing

²³ Dr. Miner also noted (consistent with Dr. Zizic) that this would not necessarily be expected for infection or pneumonia. *Id.*

occurring as scheduled. Both parties filed post-hearing briefs on the matter, and it is now ripe for resolution. ECF No. 71; ECF No. 72.

IV. Applicable Legal Standards

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

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a “Table Injury”—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a “Non-Table Injury”). See Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); see also *Moberly v. Sec’y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec’y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).²⁴ In this case, Petitioner does not assert a Table claim.

For both Table and Non-Table claims, Vaccine Program petitioners bear a “preponderance of the evidence” burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the “trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact’s existence.” *Moberly*, 592 F.3d at 1322 n.2; see also *Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec’y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was “not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury.” *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec’y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)); *Pafford v. Sec’y of Health & Hum. Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen*, 418 F.3d at 1278: “(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

²⁴ Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec’y of Health & Hum. Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec’y of Health & Hum. Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff’d* 104 F. Appx. 712 (Fed. Cir. 2004); see also *Spooner v. Sec’y of Health & Hum. Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury.”

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

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec’y of Health & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed “not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act’s preponderant evidence standard.” *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras*, 121 Fed. Cl. at 245.

In discussing the evidentiary standard applicable to the first *Althen* prong, the Federal Circuit has consistently rejected the contention that it can be satisfied merely by establishing the proposed causal theory’s scientific or medical *plausibility*. See *Boatmon v. Sec’y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019); see also *LaLonde v. Sec’y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) (“[h]owever, in the past we have made clear that simply identifying a ‘plausible’ theory of causation is insufficient for a petitioner to meet her burden of proof” (citing *Moberly*, 592 F.3d at 1322)). And petitioners always have the ultimate burden of establishing their *overall* Vaccine Act claim with preponderant evidence. *W.C. v. Sec’y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted); *Tarsell v. United States*, 133 Fed. Cl. 782, 793 (2017) (noting that *Moberly* “addresses the petitioner’s overall burden of proving causation-in-fact under the Vaccine Act” by a preponderance standard).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner’s medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec’y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine “did cause” injury, the opinions and views of the injured party’s treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 (“medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a

‘logical sequence of cause and effect show[s] that the vaccination was the reason for the injury’”) (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec’y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

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

The third *Althen* prong requires establishing a “proximate temporal relationship” between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase “medically-acceptable temporal relationship.” *Id.* A petitioner must offer “preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder’s etiology, it is medically acceptable to infer causation.” *de Bazan v. Sec’y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must align with the theory of how the relevant vaccine can cause an injury (*Althen* prong one’s requirement). *Id.* at 1352; *Shapiro v. Sec’y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand*, 105 Fed. Cl. 353 (2012), *aff’d mem.*, 503 F. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec’y of Health & Hum. Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for rev. denied* (Fed. Cl. Dec. 3, 2013), *aff’d*, 773 F.3d 1239 (Fed. Cir. 2014).

B. Legal Standards Governing Factual Determinations

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required

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

As noted by the Federal Circuit, “[m]edical records, in general, warrant consideration as trustworthy evidence.” *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Hum. Servs.*, 95 Fed. Cl. 598, 608 (2010) (“[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law”), *aff'd*, *Rickett v. Sec'y of Health & Hum. Servs.*, 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). It is reasonably expected that claimants will report to their medical treaters the “facts” relevant to what they are experiencing as truthfully as possible (although claimants may also contemporaneously report causal suppositions that reflect their own non-professional views as well). *Cucuras v. Sec'y of Health & Hum. Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) (“[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms”).

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Hum. Servs.*, No. 03–1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are often found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Hum. Servs.*, 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) (“[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.”)).

However, the Federal Circuit has also noted that there is no formal “presumption” that records are accurate or superior on their face to other forms of evidence. *Kirby v. Sec'y of Health & Hum. Servs.*, 997 F.3d 1378, 1383 (Fed. Cir. 2021). There are certainly situations in which compelling oral or written testimony (provided in the form of an affidavit or declaration) may be

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

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

C. *Analysis of Expert Testimony*

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

- (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community.

Terran, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

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

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

D. Consideration of Medical Literature

Both parties filed numerous items of medical and scientific literature in this case, but not all such items factor into the outcome of this decision. While I have reviewed all the medical literature submitted in this case, I discuss only those articles that are most relevant to my

determination and/or are central to Petitioner’s case—just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec’y of Health & Hum. Servs.*, No. 2015–5072, 2016 WL 1358616, at *5 (Fed. Cir. Apr. 6, 2016) (“[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision”) (citation omitted); *see also Paterek v. Sec’y of Health & Hum. Servs.*, 527 F. App’x 875, 884 (Fed. Cir. 2013) (“[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered”).

ANALYSIS

I. Overview of SLE

Although Petitioner’s UCTD diagnosis is more clearly discernible from the filed records, the experts largely agreed that SLE was also a reasonable diagnosis under the circumstances, and ultimately Petitioner seemed to embrace it as her vaccine injury. *See* Tr. at 140–41; Zizic Rep. at 60 (maintaining that Petitioner’s UCTD “evolved into SLE” due to vaccination). I will therefore treat SLE as the injury in question.

SLE is characterized by

a chronic, inflammatory, often febrile multisystemic disorder of connective tissue that proceeds through remissions and relapses; it may be either acute or insidious in onset and is characterized principally by involvement of the skin (*cutaneous l. erythematosus*), joints, kidneys, and serosal membranes. The etiology is unknown, but it may be a failure of regulatory mechanisms of the autoimmune system, since there are high levels of numerous autoantibodies against nuclear and cytoplasmic cellular components. The condition is marked by a wide variety of abnormalities, including arthritis, arthralgias, nephritis, central nervous system manifestations, pleurisy, pericarditis, leukopenia or thrombocytopenia, hemolytic anemia, an elevated erythrocyte sedimentation rate, and the presence in the blood of distinctive cells called LE cells.

Systemic Lupus Erythematosus, *Dorland’s Medical Dictionary Online*, <https://www.dorlandsonline.com/dorland/definition?id=87476> (last visited July 7, 2022).

In the Program, SLE and other forms of lupus have not been addressed frequently as possible vaccine injuries.²⁵ None of the reasoned decisions involving SLE, however, that I have

²⁵ Prior Program reasoned decisions constitute persuasive (if non-binding) authority. Hanlon, 40 Fed. Cl. at 630. It is therefore reasonable to review similar determinations involving comparable facts and theories. Indeed, given the “inquisitorial” nature of the special master function, it would be remiss for a special master not to look at how the same fact pattern and/or argument has been treated in prior decisions.

been able to identify have resulted in the determination that the petitioner established causation. *See, e.g., Andrews v. Sec’y of Health & Hum. Servs.*, No. 16-196V, 2021 WL 5755328, at *1 (Fed. Cl. Spec. Mstr. Oct. 21, 2021) (flu vaccine not shown to cause SLE); *Johnson v. Sec’y of Health & Hum. Servs.*, No. 10-578V, 2016 WL 4917548, at *1, 8 (Fed. Cl. Spec. Mstr. Aug. 18, 2016) (HPV vaccine alleged to have caused SLE); *Harris v. Sec’y of Health & Hum. Servs.*, No. 10-322V, 2014 WL 3159377, at *1, 14–19 (Fed. Cl. Spec. Mstr. June 10, 2014) (minor child alleged to have suffered from SLE as a result of the HPV vaccine).

Andrews is particularly on point (even though, unlike here, the SLE diagnosis in *Andrews* was disputed, and ultimately not found to have been established). There, as here, the petitioner relied on Dr. Zizic as her expert. *Andrews*, 2021 WL 5755328, at *5–6, 9–10. The arguments Dr. Zizic made to support causation were also comparable to those advanced in this case. Thus, he maintained SLE was an autoimmune disease known to be associated with vaccines, and that it could proceed post-vaccination via the mechanism of molecular mimicry. *Id.* at 6. But the causation theory was rejected, with the special master noting that Dr. Zizic’s arguments closely tracked contentions he had made in a comparable case decided, and dismissed, by the same special master. *Id.* at 18–19.

Two other cases involved many of the same theories as asserted herein, bulwarked by the same experts or items of literature, although the injury asserted was RA. But these cases also were unsuccessful. *Monzon v. Sec’y of Health & Hum. Servs.*, No. 17-1055V, 2021 WL 2711289 (Fed. Cl. Spec. Mstr. June 2, 2021); *Moran v. Sec’y of Health & Hum. Servs.*, No. 16-538V, 2021 WL 4853544 (Fed. Cl. Spec. Mstr. Oct. 4, 2021).

In *Moran*, the claim that the flu vaccine can cause RA was rejected. *Moran*, 2021 WL 4853544, at *1. (*Moran* is the prior case referred to in *Andrews*, where Dr. Zizic offered a theory comparable to that already rejected by the same special master. *Andrews*, 2020 WL 5755328, at *18). Dr. Zizic provided in *Moran* an opinion very similar to what was proposed in this matter, invoking an autoantibody-driven cross-reaction as the pathogenic disease process, caused by molecular mimicry between flu vaccine antigenic components and self structures, along with a possible additional T cell response. *Moran*, 2021 4853544, at *7–8. He also cited articles like Ray (which had more direct relevance in that context than herein) and Wang. *Id.* at *11–12. But the special master was unpersuaded, noting that (a) Ray was not in fact supportive of the causation theory when its two related sub-studies were looked at holistically, and (b) Wang had greater deficiencies despite Dr. Zizic’s embrace of it. *Id.* at *27–29.

I denied entitlement in *Monzon*, where a claimant alleged that the Tdap vaccine could cause RA. *Monzon*, 2021 WL 2711289, at *1. Although the decision to dismiss turned on some points a bit different than what are most at issue herein (in *Monzon*, the innate immune response was proposed as the mechanism of autoimmunity), the *Monzon* petitioner also invoked Wang as strong

evidence of a vaccine association (discussing Ray in the course of such argument). *Id.* at *6–7. But I specifically noted the extent to which Wang included sub-studies that were inconsistent with its greater findings, and that it otherwise included too few studies specifically relevant to Tdap vaccine. *Id.* at *22.

II. Petitioner Has Not Carried Her Burden of Proof²⁶

Petitioner has not demonstrated an entitlement to compensation—both because she has not shown that the flu vaccine (her expert’s admitted focus during the hearing) likely can cause SLE, and (more importantly) because the record does not permit me to conclude that the vaccine “did cause” her disease, even if it could in theory.

A. Althen Prong Two

The medical record is unsupportive of the conclusion that Dr. Chambers’ SLE occurred as a result of the flu or Tdap vaccines. This is grounds for a denial of entitlement even if Petitioner *had* been able to demonstrate that the flu or Tdap vaccines can cause SLE.

First, the record preponderantly establishes that Petitioner displayed symptoms that could be deemed consistent with progressing SLE *long before* vaccination. In 2016 alone, she experienced repeated pain in her lower back and lower limbs that cannot simply be ascribed to over-exertion. She also has acknowledged that she experienced Raynaud syndrome-associated symptoms many times prior to vaccination. Petitioner herself seemed to think, when she obtained treatment from her medical partner, Dr. Kahill, that her symptoms related to her pre-vaccination state, based on the nature of how she reported her complaints (and even suggested the supposition that her birth control, which she had been taking for several months by that time, was correlated to symptoms onset). Ex. 19 at 20.

Such a record is not merely consistent with the conclusion that Petitioner had a *propensity* to experience autoimmune conditions. Rather, it also suggests that the incremental process leading to Petitioner’s SLE may have been well underway at the time of vaccination. Certainly, the experts in this case agreed that SLE is a complex disease that does not present in a specific or consistent way, from one patient to another. Tr. at 43–44, 139–40.

Second, it appears most likely Petitioner experienced some infectious process in the timeframe between vaccination and her seeking of emergency treatment—and that this explains her severe symptoms that October 2016, after the vaccinations. Although I accept Petitioner’s argument that an EBV reactivation is not proven on the basis of this record, the positive rapid strep

²⁶ This Decision only reviews the *Althen* prongs most relevant to the determination and analyzes those prongs in order of their significance to the outcome.

test result cannot be as easily ignored, along with the respiratory symptoms she displayed at the time of her hospitalization. The abnormally high CRP inflammatory biomarker was also, as Dr. Miner persuasively established, more likely evidence of an underlying infectious process than attributable to cytokine increases attributable to a vaccine that was received nearly two weeks before. Although no specific infection was ever identified as causal of the embolism Petitioner experienced, treaters certainly did not specify the vaccines she received earlier that month as causal (and I otherwise do not find Petitioner's symptoms were a pneumonitis attributable directly to SLE).

Overall, Petitioner's medical history for the entirety of 2016 is unsupportive of the determination that her early October 2016 vaccinations caused her to develop SLE. Plainly she experienced a variety of symptoms pre-vaccination that either establish a propensity for autoimmunity or reflect SLE-like manifestations—but in either event they are plainly related to her subsequent diagnosis and allow for a strong possibility that her illness predated vaccination. Moreover (and even if I simply treat her difficulties before October 2016 as merely establishing her susceptibility), the record after vaccination only establishes a temporal, coincidental association with her disease process, which unfolded over a long period of time thereafter. The record does not reveal any vaccine reaction reported to treaters at any time, few if any testing results that could be connected to some vaccine-caused occurrence. After October 2016, the record established an unfolding progression of symptoms consistent with the slow manifestation of SLE, but not a process that likely was a vaccine response, especially in light of her symptom's chronicity. And no treaters ever proposed vaccine causation at any later date.

B. Althen Prong One

The evidence offered to prove an association between SLE, and the flu vaccine was unpersuasive and incomplete. As a general matter, Dr. Zizic over-relied on analogies involving distinguishable vaccines or autoimmune illnesses that would not be fully comparable to the vaccines at issue in this case, or SLE itself. The fact that vaccines have in *other* contexts been associated with *distinguishable* autoimmune injuries does not lead to the inexorable conclusion that the same is true with respect to SLE, simply because it too is an autoimmune disease. Similarly, while other wild infections, like EBV, might be associated with SLE, the same has not been demonstrated to be true for the flu or Tdap wild virus. Tr. at 109, 110–11.

The proposed mechanisms by which SLE would pathogenically manifest post-vaccination were also inadequately established.²⁷ Dr. Zizic relied on a combination of innate and immune

²⁷ Even though claimants are never *compelled* to establish a biologic mechanism in proving a vaccine “can cause” a given injury, where they attempt to do so it is wholly reasonable for a special master to evaluate whether the evidence offered is reliable, persuasive, and/or preponderantly established. *D’Tiolev. Sec’y of Health & Hum. Servs.*, 726 Fed. Appx. 809, 811 (Fed. Cl. 2018) (“[n]othing in *Althen* or *Capizzono* requires the Special Master to ignore probative epidemiological evidence that undermines petitioner’s theory.”).

response, without clearly or preponderantly showing how all “parts” of the mechanism fit together into a pathologic process. Thus, the fact that the flu vaccine can increase cytokines transiently does not mean that it can do so for long enough trigger the onset of SLE. The T cells Dr. Zizic identifies as later driving disease course reflect a cellular or adaptive immune response, but their role was not persuasively connected to vaccination. Dr. Zizic’s opinion focused much more on the argument that the vaccines would directly stimulate an autoimmune aberrant response either through cytokines or antibodies that cross-react than a demonstration that T cell attacks causing a break in tolerance could be shown to be vaccine-associated. But he did not even attempt to make the kind of homology showing between vaccine antigens and self structures that other cases routinely propose. See e.g., *Yalacki v. Sec’y of Health & Hum. Servs.*, 146 Fed. Cl. 80, 91–93 (2019) (affirming a decision denying entitlement for petitioner not supporting her theory).²⁸

Dr. Zizic also did not reliably establish that either vaccine causes the appearance of pathogenic antibodies critical to SLE’s progression. At best, literature like Abu-Shakra showed that some autoantibodies associated with SLE have been observed to be increased after receipt of the flu vaccine—but does this also mean that the vaccine is capable of *driving* them from the time of vaccination to sufficient levels to trigger disease? Not only does Abu-Shakra not say this, but in fact the article underscores the need for SLE patients to *receive* vaccines. Abu-Shakra at 372. Dr. Zizic’s responsive contention that the treatments SLE patients receive would themselves somehow “block” the putatively harmful impact of the flu vaccine—meaning the lowered risk is only applicable when existing SLE patients are vaccinated—was underwhelming and speculative. And although Dr. Zizic possessed sufficient credentials to opine generally in this case, he does not have the kind of demonstrated specific immunologic-oriented knowledge to overcome these evidentiary deficiencies through his own testimony or personal vouching for the causal theory.

The Wang meta-analysis proved to be far less compelling than Dr. Zizic maintained. Admittedly, Wang facially supports Petitioner’s claim about an association between at least the flu vaccine and SLE. And while I do not accept at face value Dr. Zizic’s “vouching” for Wang’s persuasiveness, his contentions about its methodological reliability were not rebutted. Wang was not simply a review article discussing what prior studies had found, but instead purports to take specific data findings from those prior studies and, in effect, “combine” them into a larger study, allowing for more refined results that the sub-studies could obtain. It is certainly conceivable that a carefully constructed meta-analysis *could* identify statistically significant and epidemiologically reliable association that smaller studies could not.

But is Wang *itself* reliable to that degree, such that it stands in this case as firm evidence supporting vaccine causality? As already noted, Wang has been offered in many prior cases

²⁸ At most, Dr. Zizic cited Doria’s showing of some antigenic similarity between EBV and SLE. Doria at 25. This cannot simply be applied to a vaccine with a distinguishable underlying wild viral or bacterial basis.

involving RA (a rheumatic condition that is somewhat comparable to SLE) on behalf of petitioners—but the article has consistently been found wanting, for many of the same reasons it proved to be deficient herein. *Monzon*, 2021 WL 2711289, at *22; *Moran*, 2021 WL 485354, at *29. This has generally been because it has been determined that Wang’s overall value as a methodologically reliable meta-analysis²⁹ is inherently undermined by the fact that it builds its findings on the basis of studies focusing on distinguishable vaccines or illnesses. Wang at 759 (Table 1). Persson’s focus, for example, was on narcolepsy and a totally different version of the flu vaccine. Persson at 175–76. And some items included in Wang that facially support Petitioner’s contentions, like Ray, are not wholly supportive (and Dr. Zizic did not persuasively establish that I should only take into account *half* of Ray’s findings, rejecting those that were inconsistent due to purported authorial bias). In short, not enough of Wang’s “inputs” were sufficiently consistent with Petitioner’s causation theory to deem the article as supportive of causation as Dr. Zizic urged.

Overall, both experts were reasonably qualified to offer the opinions they did in this case (although Dr. Zizic’s background in clinical immunology was not equivalent to him being deeply steeped in the study of how vaccines may adversely impact the immune system). But Dr. Miner more persuasively set forth reasons why the flu or Tdap vaccines cannot likely cause SLE. And prior compelling decisions in the Program, as discussed above, cast considerable doubt not merely on the contention that SLE can be vaccine-associated, but more broadly that *any* chronic rheumatologic condition could be triggered by vaccination. *See generally Andrews*, 2021 WL 5755328; *Moran*, 2021 WL 4853544; *Monzon*, 2021 WL 2711289; *Johnson*, 2016 WL 4917548. These cases do not compel the outcome in this case but given that many of them involved not only the same causal theory but Dr. Zizic himself as the expert, they cannot be readily distinguished. It has not been preponderantly established that the flu or Tdap vaccines can likely cause SLE.

²⁹ Ironically, in cases where the Respondent has offered a meta-analysis to cast doubt on a vaccine’s association with a disease or injury, *petitioners* have directly attacked the value of this kind of study, making arguments comparable to why such a study may not be wholly persuasive or reliable in this case either (i.e., that it exhibits selection bias in the studies included, or incorporates data that is not truly comparable). *See e.g., Dinh v. Sec’y of Health & Hum. Servs.*, No. 16-171V, 2022 WL 730258, at *11–12 (Fed. Cl. Spec. Mstr. Feb. 14, 2022).

CONCLUSION

A Program entitlement award is only appropriate for claims supported by preponderant evidence. Here, Petitioner has not made such a showing. Thus, and although I have great sympathy for Petitioner's struggle in dealing with her health problems, Petitioner has not demonstrated entitlement to compensation.

In the absence of a motion for review filed pursuant to RCFC Appendix B, the Clerk of the Court **SHALL ENTER JUDGMENT** in accordance with the terms of this Decision.³⁰

IT IS SO ORDERED.

/s/ Brian H. Corcoran

Brian H. Corcoran

Chief Special Master

³⁰ Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment if (jointly or separately) they file notices renouncing their right to seek review.