In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Originally Filed: May 9, 2022
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H.C.,	*	PUBLISHED
Petitioner,	*	No. 16-4V
v.	*	Special Master Nora Beth Dorsey
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Entitlement; Influenza ("Flu") Vaccine; Ramsay Hunt Syndrome.
Respondent.	*	

Robert J. Krakow, Law Office of Robert J. Krakow, P.C., New York, NY, for petitioner.
Colleen Hartley, U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

I. INTRODUCTION

On January 4, 2016, H.C. ("petitioner") filed a petition under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42 U.S.C. § 300aa-10 et seq. (2012)[2] alleging that as a result of an influenza ("flu") vaccination on January 4, 2013, petitioner suffered

[1] Because this Decision contains a reasoned explanation for the action in this case, the undersigned is required to post it on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). **This means the Decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material from public access.

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

from Ramsay Hunt syndrome.[3] Petition at 2-3, 7 (ECF No. 1). Respondent argued against compensation. Respondent's Report ("Resp. Rept.") at 1 (ECF No. 46).

After carefully analyzing and weighing the evidence presented in this case, in accordance with the applicable legal standards, the undersigned finds petitioner has failed to provide preponderant evidence that the flu vaccine she received caused her Ramsay Hunt syndrome. Therefore, this case must be dismissed.

II. ISSUES TO BE DECIDED

The parties agree that petitioner received the flu vaccine on January 4, 2013, that petitioner was diagnosed with Ramsay Hunt syndrome, and that the condition "results from reactivation of the varicella zoster virus" ("VZV"). Joint Submission, filed Mar. 9, 2021, at 1-2 (ECF No. 221).

The parties identify three factual issues in dispute: (1) "[t]he cause of petitioner's reactivation of Ramsay Hunt syndrome in June 2013 and recurrences thereafter;" (2) "[t]he timeline for petitioner's development of [eosinophilic granulomatosis with polyangiitis ("EGPA")], and specifically whether petitioner had eosinophilia[4] years prior to developing EGPA (also referred to as Churg-Strauss syndrome),[5] which was diagnosed in 2017; and (3) "[t]he role, if any, [. . .] petitioner's clinical picture." Joint Submission at 1 (emphasis omitted). The undersigned's findings relative to the factual issues are integrated into the causation analysis portion of this Decision.

Regarding causation, the parties dispute whether the flu vaccine caused petitioner's Ramsay Hunt syndrome pursuant to the analysis set forth in Althen v. Secretary of Health & Human Services, 418 F.3d 1274 (Fed. Cir. 2005). Joint Submission at 2.

Petitioner proffers experts Dr. Scott Zamvil and Dr. M. Eric Gershwin. Petitioner's Post-Hearing Submission ("Pet. Post-Hearing Br."), filed Sept. 9, 2021, at 2, 14 (ECF No. 250). Dr. Zamvil opines that the petitioner's flu vaccination caused reactivation of VZV, which triggered

[3] Initially, petitioner alleged that she suffered from Bell's palsy and/or Ramsay Hunt syndrome. See Petition at 7 (ECF No. 1). Once complete records and expert reports were filed, petitioner dropped her references to Bell's palsy, and thus, the relevant diagnosis is Ramsay Hunt syndrome. See Joint Submission, filed Mar. 9, 2021, at 1 (ECF No. 221). Thus, this Decision refers only to Ramsay Hunt syndrome.

[4] Eosinophilia is "the formation and accumulation of an abnormally large number of eosinophils in the blood" or "the presence of eosinophils in a location where they are not normally found." Eosinophilia, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=16719 (last visited Apr. 14, 2022).

[5] Some of the experts and treating physicians used the phrase Churg-Strauss syndrome, which is the older term for EGPA. Petitioner's Exhibit ("Pet. Ex.") 33 at 1. For clarity and consistency, the undersigned uses the newer reference, EGPA, throughout this Decision.

her Ramsay Hunt syndrome. Id. at 14. Dr. Gershwin also opines as to the significance of petitioner's EGPA and its relevance to the development of petitioner's Ramsay Hunt syndrome. Id. at 22-24. Respondent's experts, Dr. Vinay Chaudhry and Dr. Arnold I. Levinson, disagree that the flu vaccine can or did cause reactivation of petitioner's Ramsay Hunt syndrome. Resp. Post-Hearing Brief ("Br."), filed Feb. 3, 2022, at 12-13 (ECF No. 257). Instead, respondent asserts that petitioner's Ramsay Hunt syndrome was caused by VZV infection reactivation. Id.

III. PROCEDURAL HISTORY

Petitioner filed a petition on January 4, 2016, along with medical records. Petition; Pet. Exhibits ("Exs.") 1-10. Petitioner filed additional medical records from April to August 2016. Pet. Exs. 11-27. Respondent filed his Rule 4(c) Report on November 14, 2016, arguing against compensation. Resp. Rept. at 1.

Petitioner filed medical records in March and May 2017 and an expert report from Dr. Zamvil in September 2017. Pet. Exs. 28-30. On December 29, 2017, respondent filed responsive expert reports from Drs. Levinson and Chaudhry. Resp. Exs. A, C. Petitioner filed a responsive expert report from Dr. Zamvil on May 1, 2018 and an expert report from Dr. Gershwin on May 31, 2018. Pet. Exs. 32-33. Petitioner also filed updated medical records in July and August 2018. Pet. Exs. 35-36. In August 2018, respondent filed supplemental expert reports from Dr. Chaudhry and Dr. Levinson. Resp. Exs. E-F.

The undersigned held a Rule 5 conference on September 21, 2018. Rule 5 Order dated Sept. 21, 2018 (ECF No. 102). She was unable to provide her preliminary opinions, and requested additional information from the parties. Id. at 1-2. Petitioner filed medical records and declarations in October and November 2018. Pet. Exs. 37-40. The parties filed supplemental expert reports from Dr. Levinson, Dr. Chaudhry, Dr. Gershwin, and Dr. Zamvil from December 2018 to February 2019. Pet. Exs. 41, 43-44; Resp. Exs. G-H.

Petitioner filed updated medical records from June 2019 to November 2019. Pet. Exs. 45-52. During this time, the parties discussed informal resolution and began alternative dispute resolution ("ADR") proceedings in December 2019. Order Referring Case to ADR dated Dec. 30, 2019 (ECF No. 173). The case was unsuccessful in ADR and was removed on January 26, 2021. Order Removing Case from the ADR Process dated Jan. 26, 2021 (ECF No. 208). Thereafter, petitioner filed medical records, medical literature, and photographs, and respondent filed medical literature and medical literature summaries. Pet. Exs. 54-65; Resp. Exs. I-N.

An entitlement hearing was held on March 23 and 24, 2021. Transcript ("Tr.") 1, 266. Petitioner, Dr. Zamvil, Dr. Gershwin, Dr. Chaudhry, and Dr. Levinson testified. Tr. 3, 268. Post-hearing briefs were ordered. Order dated Apr. 13, 2021 (ECF No. 245). Petitioner filed her post-hearing brief on September 9, 2021, and respondent filed his responsive post-hearing brief on February 3, 2022. Pet. Post-Hearing Br.; Resp. Post-Hearing Br. On April 21, 2022, petitioner filed a reply brief. Pet. Reply to Resp. Post-Hearing Br. ("Pet. Post-Hearing Reply Br."), filed Apr. 21, 2022, at 2 (ECF No. 269).

On April 20, 2022, petitioner filed a motion for leave to file a medical article authored by Anjum et al.[6] on the basis that respondent had asserted "petitioner relie[d] 'upon a single case report' to establish causation," and "[t]hus, [] placed the issue addressed by Anjum directly into issue." Pet. Motion for Leave to File Medical Literature - Exhibit 66, filed Apr. 20, 2022, at 1 (ECF No. 266); see also Pet. Ex. 66. Respondent filed his response and objection to the motion and petitioner filed a reply on April 21, 2022. Resp. Response and Objection to Pet. Motion for Leave to File New Medical Literature, filed Apr. 21, 2022 (ECF No. 267); Pet. Reply to Resp. Response and Objection to Pet. Motion for Leave to File Medical Literature – Exhibit 66, filed Apr. 21, 2022 (ECF No. 268). The undersigned granted petitioner's motion and respondent filed his response to the article on April 26, 2022. Order dated Apr. 26, 2022 (ECF No. 270); Resp. Response to Pet. New Medical Literature, filed Apr. 26, 2022 (ECF No. 271).

This matter is now ripe for adjudication.

IV. MEDICAL TERMINOLOGY

Ramsay Hunt syndrome is a "peripheral facial nerve palsy accompanied by an erythematous vesicular rash on the ear (zoster oticus) or in the mouth." Pet. Ex. 30, Reference ("Ref.") 9 at 1.[7] It is named for the physician who described the condition, Dr. James Ramsay Hunt. Id. In addition to facial palsy and rash, other signs and symptoms may include "tinnitus, hearing loss, nausea, vomiting, vertigo, and nystagmus." Id.

Ramsay Hunt syndrome is caused by the reactivation of VZV. Pet. Ex. 30, Ref. 9 at 1. "Primary VZV infection usually produces chickenpox after which the virus becomes latent in neurons of cranial nerve ganglia (including the geniculate ganglia) and dorsal root ganglia along the entire neuraxis." Id. at 5. "VZV reactivation . . . occurs more frequently in immunocompromised persons and in the elderly." Pet. Ex. 32, Ref. 10 at 7.[8] "The molecular basis of reactivation is not known." Id.

A similar type of facial paralysis that occurs without the zoster viral rash is Bell's palsy.[9] Pet. Ex. 30, Ref. 9 at 1. In fact, "Ramsay Hunt syndrome may initially be indistinguishable from

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[6] Rani Lill Anjum et al., Medical Scientists and Philosophers Worldwide Appeal to *EMB* to Expand the Notion of 'Evidence', 25 EMJ Evidence-Based Med. 6 (2020).

[7] C. J. Sweeney & D. H. Gilden, Ramsay Hunt Syndrome, 71 J. Neurology Neurosurgery Psychiatry 149 (2001).

[8] Jeffrey I. Cohen, VZV: Molecular Basis of Persistence (Latency and Reactivation), in Human Herpesviruses: Biology, Therapy, and Immunoprophylaxis 689 (Ann Arvin et al. eds., 2007).

[9] In petitioner's medical records there are a number of references to Bell's palsy, instead of Ramsay Hunt syndrome. However, once petitioner had zoster vesicles noted in her ear, the records generally reference Ramsay Hunt syndrome. Regardless of the references in petitioner's records to Bell's palsy, her accurate diagnosis was Ramsay Hunt as agreed upon by the parties, experts, and specialists who provided care to petitioner. See Joint Submission at 1-2.

Bell's palsy," at least until zoster virus vesicles are noted. Id. Patients with Ramsay Hunt syndrome, however, usually "have more severe paralysis at onset and are less likely to recover completely." Id. Bell's palsy is not caused by VZV reactivation, but may be "associated with herpes simplex virus [] infection." Id.

EGPA "is a multisystem disorder characterized by allergic rhinitis, asthma, and prominent peripheral blood eosinophilia." Pet. Ex. 62 at 1.[10] It is "classified as a vasculitis of the small and medium sized arteries, although the vasculitis is often not apparent in the initial phases of the disease." Id. The lungs are most commonly involved, but the disease can affect the skin and other organs, including the heart, kidneys, and central nervous system ("CNS"). Id. Antineutrophil cytoplasmic antibodies ("ANCA")[11] are found in 40 to 60% of patients. Id. at 2.

"Molecular mimicry is one of the leading mechanisms by which infectious or chemical agents may induce autoimmunity. It occurs when similarities between foreign and self-peptides favor an activation of autoreactive T or B cells by a foreign-derived antigen in a susceptible individual." Pet. Ex. 55 at 1.[12] While "[f]our types of molecular mimicry have been proposed," the type most relevant here is "common or similar amino acid sequences or epitopes between the microorganisms or environmental agent and its host." Id. at 4, 4 tbl.1. An example is the shared homology between polysaccharides on the membrane of the bacteria *Campylobacter jejuni* ("*C. jejuni*") and carbohydrate structures on the myelin sheath of peripheral nerve axons. Id. at 4 tbl.1. Animal studies have shown that "[m]ice inoculated with *C. jejuni* . . . induce the development of flaccid limb weakness resembling [Guillain-Barré Syndrome ("GBS")] and confirming the role of molecular mimicry in [the] disease." Id. at 3 fig.1.

V. FACTUAL SUMMARY

A. Summary of Medical Records

1. Pre-Vaccination Records

Petitioner was 38 years old when she received the flu vaccine at issue on January 4, 2013. Pet. Ex. 1 at 20. Her past medical history was significant for childhood chickenpox, asthma,

[10] Talmadge E. King, Epidemiology, Pathogenesis, and Pathology of Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss), UpToDate, https://www.uptodate.com/contents/epidemiology-pathogenesis-and-pathology-of-eosinophilic-granulomatosis-with-polyangiitis-churg-strauss (last updated May 13, 2020).

[11] ANCA is "an autoantibody to cytoplasmic constituents of monocytes and neutrophils, found in increased amounts in some types of vasculitis. There are several different subtypes, each characterized serologically by reactivity against particular cellular antigens; some are specific to given disease states." Antineutrophil Cytoplasmic Autoantibody, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=59689 (last visited Apr. 14, 2022).

[12] Manuel Rojas et al., Molecular Mimicry and Autoimmunity, 98 J. Autoimmunity 100 (2018).

mitral valve prolapse, acute ear pain and left otitis media on July 27, 2011, ear pain and right acute otitis externa on August 6, 2012, acute pharyngitis, right anterior cruciate ligament tear in the knee with surgery, and a C-section. Pet. Ex. 2 at 59, 63, 75, 78, 82; Pet. Ex. 7 at 4; Pet. Ex. 8 at 4; Pet. Ex. 12 at 5-7; Pet. Ex. 13 at 3; Pet. Ex. 18 at 1.

Of note, petitioner's family history was significant for Bell's palsy and autoimmune illnesses. Petitioner's father had Bell's palsy (three times) and multiple myeloma. Pet. Ex. 18 at 2. She had a sister who also had Bell's palsy, and another sister with diabetes and Crohn's disease. Id.; Pet. Ex. 35 at 25. Her mother had arthritis, which began when she was young, and chronic Epstein Barr virus. Pet. Ex. 35 at 25.

Records dating back to 2010 note petitioner's history of asthma. See Pet. Ex. 13. In August 2010, petitioner had an upper respiratory infection with shortness of breath. Id. at 3, 5. She was prescribed Albuterol, in addition to the Fluticasone (Advair Diskus) and Singulair she was already prescribed. Id. at 4. In December 2010, she again had an upper respiratory infection, and reported having very bad allergies. Id. at 7-8. Her asthma medications were continued. Id. at 9. On January 18, 2011, she had fever, nasal congestion, and wheezing. Id. at 10. She was noted to be taking her asthma medication on a regular basis. Id. at 11. She tested positive for flu A. Id. at 12-13. On March 31, 2011, petitioner's medical records documented that she was taking her asthma medication regularly, and was seeing an ear nose and throat ("ENT") physician for "chronic nasal congestion." Id. at 14. Blood work drawn on March 31, 2011, revealed elevated eosinophils of 11% (range 0.0-5.0%). Id. at 20.

2. Post-Vaccination Records[13]

On January 10, 2013, about six days after her vaccination, petitioner developed left-sided facial numbness. Pet. Ex. 2 at 39. She sought treatment at Urgent Care, where she was noted to have subjective left-sided facial paresthesia and mild left-sided facial drooping. Id. at 41. A head computerized tomography ("CT") scan showed moderately severe opacification of the right sphenoid sinus, with possible sinusitis. Id. at 87. Petitioner was diagnosed with Bell's palsy, and treatment was initiated with steroids, eye drops, and Valtrex. Id. at 42.

Petitioner returned to Urgent Care on January 13, 2013 with complaints of facial pain, and was prescribed Percocet. Pet. Ex. 2 at 31, 35. Her diagnosis remained Bell's palsy. Id. at 35. The next day, January 14, 2013, petitioner saw neurologist, Dr. Naomi T. Feuer. Pet. Ex. 6 at 11.[14] Physical examination revealed complete left-sided facial weakness and two vesicles were present in the left ear. Id. Due to the presence of zoster vesicles in her ear, petitioner's

[13] From 2013 forward, petitioner was seen by numerous physicians, and had repeated and frequent laboratory and diagnostic testing and treatment, including numerous surgical procedures. This summary includes relevant portions of her diagnostic studies and medical care but is not exhaustive.

[14] This record is from a visit with Dr. Feuer on August 28, 2013, but it contains notes from petitioner's prior visits with Dr. Feuer. See Pet. Ex. 6 at 11-13. It does not appear that full records from visits prior to August 28, 2013 were filed.

diagnosis was changed to Ramsay Hunt syndrome. Id. Magnetic resonance imaging ("MRI") showed abnormal enhancement of the left facial nerve, consistent with her diagnosis. Id.

Subsequently, on January 16, 2013, petitioner was seen by neuro-ophthalmologist, Dr. Cristiano Oliveira. Pet. Ex. 8 at 2. Examination revealed that petitioner was unable to close her left eye with mild keratopathy in the left eye, but she had normal visual function. Id. at 7. Eye drops and gabapentin were prescribed, and follow up with a corneal specialist was recommended. Id. Petitioner was seen by Dr. Kevin Brown on January 17, 2013. Pet. Ex. 24 at 5. He confirmed the diagnosis of Ramsay Hunt syndrome, noted sensorineural hearing loss, prescribed continuing steroid treatment, and recommended a repeat MRI. Id. at 6-7. The MRI was performed on January 28, 2013, and it again showed abnormal enhancement of the facial nerve. Pet. Ex. 6 at 38. Petitioner returned to Urgent Care on January 30, 2013 for sore throat, headache, and earache. Pet. Ex. 2 at 16. She was given an antibiotic, Zithromax, and Percocet for pain. Id. at 20. An audiogram performed on January 31, 2013 showed sensorineural hearing loss in the left ear. Pet. Ex. 24 at 16.

On February 7, 2013, Dr. David M. Simpson diagnosed "severe facial paralysis associated with Ramsay Hunt syndrome." Pet. Ex. 18 at 2. He found "[v]ertigo and hearing [symptoms] indicate[d] associated vestibular and auditory [nerve] involvement. MRI show[ed] facial [nerve] enhancement, [consistent with] inflammation." Id. Dr. Simpson observed that petitioner had "received appropriate antiviral and corticosteroid [treatment]" and recommended vestibular rehabilitation. Id. If she did not improve, facial nerve decompression could be considered. Id. at 2-3.

On February 11, 2013, petitioner followed up with Dr. Feuer, who observed slight improvement in petitioner's facial strength. Pet. Ex. 6 at 11. Electromyography ("EMG") performed on February 14, 2013 was consistent with "[s]evere facial neuropathy with marked axonal loss and denervation change." Pet. Ex. 18 at 4-5. On February 22, 2013, petitioner was seen by ophthalmologist Dr. Hilary J. Ronner. Pet. Ex. 3 at 1-2. Petitioner's visual acuity had decreased due to keratitis,[15] paralytic lagophthalmos,[16] and paralytic ectropion.[17] Id. at 2-3; Pet. Ex. 4 at 576. Dr. Ronner recommended procedures to address these problems, and on March 12,

[15] Keratitis is "inflammation of the cornea." Keratitis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=26834 (last visited Apr. 14, 2022).

[16] Lagophthalmos is "a condition in which the eye cannot be completely closed." Lagophthalmos, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=27482 (last visited Apr. 14, 2022).

[17] Paralytic ectropion is "eversion of the margin of the lower eyelid as a result of paralysis of the facial nerve, and loss of contractile power of the orbicularis oculi muscle." Paralytic Ectropion, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=72379 (last visited Apr. 14, 2022).

2013, petitioner had a bilateral brow lift, left lid load, and canthoplasty.[18] Pet. Ex. 4 at 572, 576-77.

Petitioner underwent acupuncture treatment in March and April 2013 with limited improvement. Pet. Ex. 21 at 3-6, 8, 10-11. On March 24, 2013, she had approximately 5% of movement in her left cheek and mouth, with prognosis for recovery fair to poor. Id. at 5-6. On March 29, 2013, Dr. Adam R. Stracher documented that "probably avoiding flu vaccine in future is reasonable." Pet. Ex. 13 at 23.

On April 8, 2013, petitioner saw Dr. Feuer for follow up. Pet. Ex. 6 at 12. Petitioner reported that she continued to have dizziness and anxiety, and that she also had agoraphobia and photophobia. Id. Her medications included Valtrex, Cymbalta, and clonazepam. Id. Blood work drawn on May 17, 2013 showed elevated eosinophils at 19.3% (range 0-7%) and elevated absolute eosinophils at 1.2 (range < 0.7). Pet. Ex. 2 at 85.

Petitioner saw Dr. Feuer for follow up on June 20, 2013 with complaints of chronic bilateral jaw pain and a blister in her right nostril for the past few weeks. Pet. Ex. 6 at 12. MRI done on June 22, 2013 showed resolution of the left facial nerve enhancement.[19] Id. at 42. On June 27, 2013, petitioner was seen by otolaryngologist Dr. David I. Kutler, who documented that she had a recurrence of her Ramsay Hunt syndrome, and that her facial nerve paralysis had worsened. Pet. Ex. 11 at 29-30. Petitioner also had erosion of her nasal vestibule that was attributed to Afrin and steroid nasal sprays. Id.

In July 2013, petitioner was diagnosed with post-herpetic neuralgia. Pet. Ex. 17 at 6. She was treated with Norco and gabapentin. Id. She was seen several times in August 2013 with complaints of facial pain. See Pet. Ex. 22 at 882, 889. She had another recurrence of Ramsay Hunt documented by Dr. Feuer on August 28, 2013. Pet. Ex. 6 at 13, 16.

Petitioner was seen by her ENT physician, Dr. Joel M. Shugar, on September 19, 2013. Pet. Ex. 16 at 12. He documented that her right nostril lesion had progressed to involve her right upper lip. Id. He questioned whether petitioner had an immune deficiency disorder. Id. at 12-14. Throughout September 2013, petitioner saw many different health care providers for treatment of her nasal lesion. See, e.g., Pet. Ex. 13 at 27-29; Pet. Ex. 14 at 2. CT performed on October 8, 2013 revealed a 1.3 cm nasal septal perforation. Pet. Ex. 16 at 31-32. Blood work reported on October 24, 2013 documented that petitioner had elevated absolute eosinophils,

[18] Canthoplasty is "plastic surgery of the medial and/or lateral canthus, especially section of the lateral canthus to lengthen the palpebral fissure; also the surgical restoration of a defective canthus." Canthoplasty, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=7744 (last visited Apr. 14, 2022).

[19] This MRI also showed an abnormality of the parotid gland, which was not related to petitioner's Ramsay Hunt syndrome. Pet. Ex. 6 at 42. As that finding is not relevant to this Decision, it will not be discussed further.

Proteinase-3 antibodies, and C-reactive protein ("CRP").[20] Pet. Ex. 7 at 12, 15-16. Nasal biopsy was performed on October 25, 2013 to "[r]ule out" Wegener's granulomatosis[21] [. . .].[22] Pet. Ex. 16 at 39. Pathological diagnosis was "[n]ecrotic material and mucus with [] acute and chronic inflammation" and "[u]lcerated granulation tissue." Id.

On October 28, 2013, petitioner was admitted to the Emergency Department of Mount Sinai Hospital with chief complaint of nasal cellulitis. Pet. Ex. 4 at 455-57. History of present illness included petitioner's history of Ramsay Hunt syndrome, a "pseudomonal facial abscess for 1 mo[nth], [and] possible Weg[e]ner's [g]ranulomatosis [presenting with] chronic facial ulceration/abscess to [right] nares." Id. at 459. Physical examination revealed a large cavitary lesion with redness and purulent drainage of the right nostril. Id. at 460. She also had left eye droop. Id. Admitting history was performed by Dr. Geena Varghese, who questioned whether petitioner had Wegener's granulomatosis, and noted that ANCA labs would be checked. Id. at 475. Blood work showed elevated eosinophils. Pet. Ex. 16 at 4.

Petitioner was admitted for IV antibiotics and seen by infectious disease specialist, Dr. Jeffrey Gumprecht. Pet. Ex. 4 at 475. Dr. Gumprecht also questioned whether petitioner had Wegener's granulomatosis due to her nasal ulcer. Id. at 476. Petitioner was seen by rheumatologist, Dr. Mark D. Horowitz on October 29, 2013, and he noted that petitioner's CT scan showed a "granulomatous process in [the] nasal septum and pansinusitis." Id. at 481-82, 502-04. Petitioner was discharged on October 30, 2013, with the plan to have an outpatient evaluation for Wegener's granulomatosis. Id. at 483-89.

On November 2, 2013, laboratory results revealed that petitioner had a positive ANCA screen, with elevated P-ANCA Titer of 1:160 (normal < 1:20) and C-ANCA Titer of 1:40 (normal < 1:20). Pet. Ex. 4 at 499. Comments explaining the results noted that "[t]he P-ANCA pattern and autoantibodies to myeloperoxidase (MPO) are commonly associated with microscopic polyangiitis, [and] [EGPA]." Id. Comments for C-ANCA explained that "[t]he C-ANCA pattern and autoantibodies to Proteinase-3 (PR3) may be seen in most patients with

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[20] Absolute eosinophils were 1545 (range 15-500 cells/mcL). Pet. Ex. 7 at 12. Proteinase-3 AB were > 8.0 (range < 1.0 AI). Id. at 15. The lab report states, "Autoantibodies to Proteinase-3 [] are accepted as characteristic for Wegener's granulomatosis. They are detectable in 95 [percent] of the histologically proven Wegener's granulomatosis cases." Id.

[21] Wegener's granulomatosis, or granulomatosis with polyangiitis, is "a multisystem disease . . . characterized by necrotizing granulomatous vasculitis involving the upper and lower respiratory tracts, glomerulonephritis, and variable degrees of the ANCA-associated type of small vessel vasculitis." Granulomatosis with Polyangiitis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=79488 (last visited Apr. 14, 2022). It can cause "necrotic lesions of the nose and ulcerations in the mouth due to vasculitis of larger vessels." Id.

[22] [. . .] Potential complications associated with use of [. . .] include neutropenia, agranulocytosis, arthralgias, . . . and skin necrosis." Kachui C. Lee et al., Complications Associated with Use of Levamisole-[. . .].

Wegener's granulomatosis, but also in 30% of patients with microscopic polyangiitis and [EGPA]." Id.

Blood work drawn on October 28 and November 22, 2013 revealed elevated Proteinase-3 autoantibodies. Pet. Ex. 16 at 1, 8. Comments explained that "[a]utoantibodies to Proteinase-3 (PR3) are accepted as characteristic for Wegener's granulomatosis. They are detectable in 95 [percent] of the histologically proven Wegener's granulomatosis cases." Id. Petitioner's absolute eosinophils on November 22, 2013 were high at 718 (range 15-500 cells/mcL). Id. at 5.

On November 5, 2013, petitioner returned to Dr. Gumprecht, who concluded that petitioner's nasal breakdown and septal perforation were "[. . .] than Wegener's [granulomatosis]." Pet. Ex. 7 at 10. On November 22, 2013, Dr. Horowitz noted petitioner's abnormally elevated Proteinase-3 and eosinophils. Pet. Ex. 20 at 13. He documented that [. . .]. Id. Dr. Horowitz opined that the "entire presentation [was] consistent with [. . .] ("CIMDL") with secondary elevated antiProteinase-3 antibodies."[23] Id.

Biopsies of the upper lip and nose were done to rule out Wegener's granulomatosis. Pet. Ex. 20 at 6. December 3, 2013 pathology report showed "[u]lcerated mucosa with underlying granulation tissue, skeletal muscle, acute and chronic inflammation with fibrosis, and marked eosinophilic and histiocytic [] infiltration." Id. No granulomas[24] or vasculitis were seen. Id. A right nasal cavity biopsy conducted on December 11, 2013 found "[u]lcerated, necrotic respiratory tissue with granulation tissue and mixed acute and chronic inflammation composed of predominantly plasma cells and eosinophils." Pet. Ex. 16 at 77.

In January and June 2014, petitioner had facial reanimation and reconstructive surgical procedures. Pet. Ex. 4 at 280-86, 410-13. The second of these procedures was followed by an infection at the site where a tendon was harvested for use in the facial procedure. Pet. Ex. 7 at 4-5. Petitioner began post-operative occupational therapy in July 2014. Pet. Ex. 27 at 6-7.

In April 2015, petitioner had additional facial reconstructive surgery, followed by Botox injections for pain and facial spasms from June 2015 through January 2016. Pet. Ex. 4 at 45-47; Pet. Ex. 26 at 6-9, 22, 31-32, 44-45. On February 22, 2016, petitioner sought treatment for left ear pain. Pet. Ex. 15 at 36. No vesicles were seen in her left ear canal at that time. Id. at 38.

B. Dr. Arye Rubinstein's Diagnosis of EGPA

Arye Rubinstein, M.D., Ph.D., is a Professor of Pediatrics, Microbiology, and Immunology at the Albert Einstein College of Medicine at Montefiore Hospital. Pet. Ex. 28 at 2-3. Dr. Rubinstein saw petitioner on December 15, 2016. Pet. Ex. 35 at 83. At that time, he

[23] The undersigned notes that this record is handwritten and difficult to read.

[24] Granuloma is "a small, nodular, delimited aggregation of mononuclear inflammatory cells or a similar collection of epithelioid cells." Granuloma, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=20934 (last visited Apr. 14, 2022). "Some granulomas contain eosinophils and plasma cells . . . ." Id.

noted that petitioner's eosinophilia was resolving. Id. He noted that petitioner's sister had eosinophilic esophagitis ("EoE").[25] Id. Dr. Rubinstein questioned whether petitioner had an autoimmune disorder, noting her family history (sister with diabetes and Crohn's disease, mother with arthritis and chronic Epstein Barr virus, and father with multiple myeloma). Id. Based on petitioner's positive ANA[26] and P-ANCA results, Dr. Rubinstein considered Wegener's granulomatosis and EGPA, noting that 50% of EGPA cases have elevated P-ANCA. Id. He concluded that "[t]aken together[,] the most likely diagnosis is a variant of eosinophilic granulomatosis." Id.

After additional testing, Dr. Rubinstein summarized his findings and conclusions in a "Letter of Medical Necessity" dated February 15, 2017. Pet. Ex. 28. The letter summarizes petitioner's past medical history, her evaluation for eosinophilia, and her diagnosis of EGPA. See id. at 1-2. Dr. Rubinstein's diagnoses included absence of antibody responses to polysaccharide antigens,[27] EGPA, recurrent shingles, recurrent *Staphylococcus* and *Pseudomonas* infections, urticaria, histaminemia, and history of Ramsay Hunt syndrome. Id. at 1.

Dr. Rubinstein noted that in January 2014, petitioner developed Ramsay Hunt syndrome on the left side. Pet. Ex. 28 at 1. Subsequently, she had corrective surgeries complicated by infections and a nasal abscess. Id. She was "found to have [an] elevated [Immunoglobulin E ("IgE")][28] to > 18,000 and eosinophilia." Id. Petitioner's extensive rheumatology workups from 2013 to 2015 were negative except for P-ANCA and C-ANCA. Id. She also had elevated eosinophils at 17% (1,300), IgE was elevated at IU/mL > 5000.0 (range < 100.0), Proteinase-3 (PR3) Antibody Qualitative was positive with results of > 8.0 (range 0.0-0.9), histamine was 8.84 (high), and IL-6 was high at 27 (normal < 1.0). Id. at 1-2.

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[25] Eosinophilic esophagitis, or EoE, is "inflammation caused by eosinophilic infiltration of the esophageal mucosa." Eosinophilic Esophagitis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=73847 (last visited Apr. 14, 2022). Other records, including records from Dr. Rubinstein, state that petitioner's daughter, not her sister, has EoE. See Pet. Ex. 28 at 2; Pet. Ex. 35 at 25; Pet. Ex. 37 at 4.

[26] The undersigned believes Dr. Rubinstein meant to write "ANCA," and not "ANA."

[27] Specific or selective antibody deficiency ("SAD") is a disorder that results in "an inability to produce specific [Immunoglobulin G ("IgG")] antibodies to polysaccharide antigens." Tr. 374.

[28] Immunoglobulins are "structurally related glycoproteins that function as antibodies." Immunoglobulin, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=24894 (last visited Apr. 14, 2022). Immunoglobulin E, or IgE, "has the unique function of mediating immediate hypersensitivity [] reactions; it binds to specific receptors on basophils and mast cells and triggers the release of mediators on contact with antigen." Id.; see also Peter. J. Delves, Acquired Immunity, Merck Manual, https://www.msdmanuals.com/home/immune-disorders/biology-of-the-immune-system/acquired-immunity# (last reviewed Sept. 2021) (explaining how IgE antibodies trigger "immediate allergic reactions" when "[bound] to basophils . . . in the bloodstream and to mast cells in tissues").

Dr. Rubinstein's assessment was that petitioner's "clinical picture [was] consistent with . . . EGPA." Pet. Ex. 28 at 2. He noted "[t]he disease usually appears in the 40s-50s." Id. He explained that

> [EGPA] presents in [three] stages:
>
> The allergic stage is reported by most patients presenting with allergic rhinitis and asthma. It is followed by the hyper eosinophilia that is often associated, as reported by [petitioner], with malaise, [fever of unknown origin], cough, [and] abdominal pain. Many patients also develop high IgE levels by this time. The vasculitic stage follows later. It is accompanied by severe pulmonary granulomas, vascular complications with ulcerations, intestinal granulomas[,] and often peritonitis.
>
> Cytokines participate in this autoimmune process. Patients with [EGPA] have markedly increased serum levels of interferon alpha and interleukin 2 (IL-2) TNF-alpha and interleukin 1 beta (IL-1beta) and IL-6. IL-6, which is elevated in [petitioner], is reported to be an important triggering factor of the autoimmune process. At the same time IL-6 was shown to trigger mast cell replication, which may explain the histaminemia in [petitioner].
>
> The Ramsey Hunt syndrome and recurrent shingles may also be due to the immune activation in [EGPA] leading to persistence of VZV infection and suggest[ing] caution with immunosuppressive therapy as often used for [EGPA].
>
> The family history of [petitioner], including EoE, Crohn's disease, arthritis, multiple myeloma, persisting EBV infection is intriguing.

Id. (emphasis omitted).

Petitioner continued to see Dr. Rubinstein for follow up and treatment of her EGPA with Cinqair (reslizumab)[29] intravenous infusions. See Pet. Exs. 35, 45, 54. On April 10, 2018, she was noted to be taking levocetirizine for her allergies. Pet. Ex. 35 at 12. The only allergy noted was to penicillin, which caused hives. Id. Dr. Rubinstein's assessment was EGPA with lung involvement (chronic). Id. at 13. At that visit, she received her routine infusion of reslizumab and she also received the recombinant VZV vaccine. Id. Petitioner had no local reaction to the vaccine, although she complained of feeling foggy several hours after vaccination. Id. This problem resolved the next day. Id. At a previous visit, on March 28, 2017, she received the pneumococcal polysaccharide PPSV23 vaccination. Id. at 59. There is no documentation to suggest that she had any reaction to that vaccination. See id.

[29] Cinqair is given to patients "whose asthma is not controlled with current asthma medicines and who have high levels of eosinophils" to "reduce[] poorly controlled, severe eosinophilic asthma symptoms and attacks." About CINQAIR, Cinqair, https://www.cinqair.com/about-cinqair/ (last visited Apr. 14, 2022).

C. Petitioner's Hearing Testimony and Declaration

Prior to January 4, 2013, petitioner was recovering from a knee surgery but was otherwise in excellent health. Tr. 7. Petitioner explained that in her twenties, she suffered from exercise-induced asthma when exercising outside, but she stated she never used her inhaler and was never prescribed any medication for asthma. Tr. 7-8.

On cross-examination, petitioner was questioned about prescriptions for Singulair in 2011 and 2012, Nasonex in 2012, Advair in 2010 and 2011, and Albuterol in 2010. Tr. 63 (citing Pet. Ex. 1 at 30-31, 33-35; Pet. Ex. 13 at 4, 7-8). Petitioner did not dispute receiving those prescriptions, but explained that "Nasonex [was not] something that [she] would have taken for asthma," and "Singulair is not necessarily an asthma medication" and "not something that [she] would necessarily take for asthma." Tr. 63-64. Regarding her Albuterol prescription, she stated she always kept that prescription because that was her rescue inhaler. Tr. 64. And for Advair, she agreed that it may have been prescribed, but "[t]hat doesn't mean that [she] necessarily used it." Tr. 71.

Petitioner also testified that prior to the vaccination at issue, she had been treated for allergies, including seasonal allergies, mold, and cats and dogs with fur, with Benadryl, Allegra, or Claritin. Tr. 8-9. On cross-examination, she clarified that "[she] always had allergies," but "[did not] have asthma." Tr. 65. She speculated that she "could have taken [Singulair] for allergies, but [she] didn't have asthma." Tr. 69.

On August 6, 2012, petitioner stated that she was spending a lot of time in the pool and developed right ear pain that she thought was swimmer's ear. Tr. 11. She did not have an infection and "[did not] believe that [she] was given medication or anything for it." Id. Sometime after August 2012, petitioner re-tore her anterior cruciate ligament in her right knee for which she received surgery for in October 2012 and had physical therapy thereafter. Tr. 12.

After receiving the flu vaccine at issue here on January 4, 2013, petitioner stated that "[her] legs started shaking" and "[she] felt extremely sick" that night.[30] Tr. 14; see also Pet. Ex. 39 at ¶ 6. For the remainder of the weekend, petitioner remained in bed with flu-like symptoms. Tr. 15. At that time, she had no facial pain or ear pain. Id. On Thursday morning, January 10, petitioner had difficulty drinking her coffee and noticed "[her] face freeze." Tr. 17; see also Pet. Ex. 39 at ¶ 7 (noting the incorrect date of this occurrence). She thought she was having a stroke and went to the local Urgent Care, where she was told she had Bell's palsy. Tr. 17-18. She continued to have difficulty closing her eye, keeping her eye shut, and blinking. Tr. 19-20. A few days later, on January 13, she woke up with excruciating pain behind her left ear. Tr. 20-21; see also Pet. Ex. 39 at ¶ 9. She returned to Urgent Care, where vesicles were seen in her ear. Tr. 20. It was recommended that she see a neurologist. Tr. 20-21.

Petitioner saw Dr. Feuer the following day, on January 14, 2013. Tr. 22. At the time of that visit, petitioner's "pain was overwhelming" and her "face was completely disfigured." Id.

[30] January 4, 2013 was a Friday.

Dr. Feuer saw vesicles in her ear and diagnosed her with Ramsay Hunt syndrome. Id. Petitioner stated that Dr. Feuer told her it is "probable and likely that [] [petitioner] had a response to the flu shot." Id. Thereafter, petitioner saw other specialists, including an ophthalmologist and audiologist, due to her difficulty closing her eye and ear pain. Tr. 22-23. Her pain with sound and light continued to worsen, and she developed vertigo. Tr. 24-25. In February 2013, petitioner continued to see specialists. Tr. 26-29. During this time, "[her] face looked disfigured, and [she] had difficulty eating, speaking[,] and making normal facial expressions." Pet. Ex. 39 at ¶ 11.

In March 2013, she had platinum bars inserted in her eyelids to help with blinking and eye closure and she had a brow lift to even out her face and help with her vertigo. Tr. 29-30, 34. Petitioner continued to be in pain and her health was deteriorating. Tr. 35; Pet. Ex. 39 at ¶ 13. She was on multiple pain medications and nerve blockers, she felt foggy, and she would not eat or drink. Tr. 35-36; Pet. Ex. 29 at ¶ 14. She was depressed, suicidal, and paranoid. Tr. 36; Pet. Ex. 39 at ¶¶ 14, 16. She "was not in a very good mental state" and "was [at] the lowest point in [her] life." Tr. 40; see also Pet. Ex. 39 at ¶ 14.

In March 2013, either in the weeks before or after her March 2013 facial surgery, [. . .]. Tr. 36-37, 97-101; Pet. Ex. 39 at ¶ 17. She believed she started using Afrin in 2013 to help with the side effects of [. . .] Ramsay Hunt syndrome. See Tr. 107. From March to June 2013, she "was still in a tremendous amount [of pain]" and she and her treating physicians could not manage her pain. Tr. 39. During the summer of 2013, petitioner [. . .] to try prescribed medications. Tr. 105-06; Pet. Ex. 39 at ¶ 20. By November 2013, before a surgery she had scheduled, she permanently [. . .]. Tr. 39, 44; Pet. Ex. 39 at ¶¶ 23-24, 27. Prior to the January 2013 flu vaccination, petitioner did not use Afrin [. . .]. Tr. 13; Pet. Ex. 39 at ¶ 18.

Petitioner testified that by 2015, her allergies and asthma became unmanageable. Tr. 49-50. She began seeing Dr. Rubinstein in 2016 for her allergies, asthma, fatigue, and urticaria. Tr. 48, 51. Dr. Rubinstein diagnosed her with EGPA, and she was given a new inhaler, which she started using, and a EpiPen. Tr. 52. Since the EGPA diagnosis, her treatment includes Cinqair, an intravenous medicine administered every three weeks at the hospital, and Hyqvia, a subcutaneous IVIG plasma therapy she self-administers every two weeks for three hours a day. Tr. 53.

The January 4, 2013 flu vaccination was not her first flu vaccination. Tr. 78-82. Petitioner stated that she received a flu vaccine every year, and would normally get flu-like symptoms for 24 hours after the vaccine. Tr. 57. She testified, however, that the January 2013 flu vaccination was different. Id. She never developed Ramsay Hunt syndrome or Bell's palsy after her prior flu vaccinations, but she has been diagnosed with the flu virus. Tr. 82. Petitioner stated she has not received a flu vaccine since January 2013. Tr. 83. She testified that to her knowledge, and based on what her treating physicians have told her, "there's nothing else that . . . should or could have caused this" other than her flu vaccination on January 4, 2013. Tr. 58. Since January 2013, she has received shingles and pneumococcal vaccinations. Tr. 85-86. Additionally, she received Covid-19 vaccines without incidence of Ramsay Hunt syndrome. Tr. 76.

At the time of the hearing in March 2021, petitioner was appreciative that she could "get up and move [her] body, and that [she was] not in the pain that [she] ha[d] been [in]." Tr. 43. She still "[could not] drink without a straw[] [or] without things flying out of [her] mouth," and "still ha[d] extensive amount[s] of doctors' visits," but "[she was] grateful that [she was] able to get up every day and move [her] body without pain." Id. She suffers from synkinesis,[31] which she described as her facial nerves "learning to work again[] [but are] rewired the wrong way" so her "brain tells the nerves to do the wrong thing." Tr. 46. In addition to the Cinqair and Hyqvia she received, petitioner takes two Benadryl pills every night and two Allegra pills every morning. Tr. 53-54.

D. Declaration of Debra Kessler

Debra Kessler is petitioner's friend. Pet. Ex. 40 at ¶ 1. She has known petitioner for more than ten years and they used "see[] each other almost every day." Id. at ¶¶ 2, 7. She has "witnessed [petitioner's] deteriorating physical condition" since January 2013. Id. at ¶ 3. Ms. Kessler found "it difficult to understand [petitioner] when she spoke." Id. She would often help petitioner by feeding her and helping with her medications. Id. "[Petitioner] seemed to have lost all senses and . . . her pain was severe." Id. at ¶ 4. In July 2013, petitioner told Ms. Kessler [. . .], but by December 2013, when their families spent the holidays together, petitioner was [. . .]. Id. at ¶¶ 7-8.

VI. EXPERT OPINIONS

A. Petitioner's Expert, Scott S. Zamvil, M.D., Ph.D.[32]

1. Background and Qualifications

Dr. Zamvil is a board-certified neurologist with 19 years of experience and is currently working as a Professor of Neurology at the University of California, San Francisco while participating in active patient care as a Neurology Attending at University of California, San Francisco, Moffett-Long Hospitals. Pet. Ex. 30 at 1-2; Pet. Ex. 31 at 1. After receiving his Ph.D. and M.D. from Stanford Medical School, he completed an internship and residency before beginning his teaching career at Harvard Medical School. Pet. Ex. 31 at 1. Since then, he has "cared for hundreds of patients with neuroinflammatory conditions, including . . . acute and recurrent [CNS] viral infections" such as shingles and Ramsay Hunt syndrome. Pet. Ex. 30 at 1. Dr. Zamvil has "expertise in molecular mimicry" and focuses his research "on understanding how antigen-presenting cells (APC) present CNS autoantigens for T cell recognition." Id. at 2. Throughout his career, Dr. Zamvil has served on various professional societies and committees and had authored or co-authored over 150 publications. Pet. Ex. 31 at 2-3, 14-16.

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[31] Synkinesis is "an unintentional movement accompanying a volitional movement, such as the facial contortions accompanying severe exertion." Synkinesis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=48544 (last visited Apr. 14, 2022).

[32] Petitioner filed three expert reports authored by Dr. Zamvil. See Pet. Exs. 30, 32, 44.

2. Opinion

a. Althen Prong One

Dr. Zamvil opined that Ramsay Hunt syndrome is most commonly due to VZV reactivation. Pet. Ex. 44 at 2. More specifically, he explained that Ramsay Hunt syndrome is caused by "activation of herpes zoster, which is latent in the geniculate ganglion." Pet. Ex. 30 at 7. The geniculate ganglion is the sensory ganglion (a group of nerve cell bodies) of the facial nerve. Ganglion Geniculi Nervi Facialis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=78055 (last visited Apr. 14, 2022). Citing Sweeney and Gilden's review article, Dr. Zamvil stated that VZV, the virus that causes chickenpox, can remain dormant in the nerve ganglion after active infection. Pet. Ex. 30 at 9 (citing Pet. Ex. 30, Ref. 9 at 5). The virus remains dormant in the nerve until it is reactivated, which can cause "paralysis of the facial nerve," known as Ramsay Hunt syndrome. Id. Vesicles seen in the outer portion of the ear canal can confirm the condition. Pet. Ex. 30, Ref. 9 at 1.

Dr. Zamvil agreed with respondent's experts that "VZV is a well-documented cause of Ramsay Hunt syndrome." Pet. Ex. 32 at 2. He conceded that flu vaccination and wild flu infection are not commonly known causes of Ramsay Hunt syndrome. Id. Although he agreed that the flu vaccine is not a commonly known cause, Dr. Zamvil stated that it has been associated with Ramsay Hunt syndrome. Pet. Ex. 44 at 1. He proffered "[s]everal possible mechanisms" that could account for the development of petitioner's initial episode of Ramsay Hunt syndrome following her flu vaccination. Pet. Ex. 30 at 8. He explained that "[t]hese possibilities are not mutually exclusive; each one could lead to reactivation of VZV." Id.

The first "possible" mechanistic theory proposed by Dr. Zamvil is based on molecular mimicry, specifically that the flu vaccine "could contain protein sequences (epitopes) that are common with VZV." Pet. Ex. 30 at 8. "Through molecular mimicry, vaccination with Fluvirin could lead to a secondary (amplification) T cell or B cell (antibody) immune response in a person that has had chicken pox." Id. "T cells and antibodies that enter the geniculate ganglion [could] cause paradoxical VZV reactivation, leading to facial weakness, pain[,] and vesicle formation." Id. Using a BLAST search,[33] Dr. Zamvil identified a similar 13 amino acid sequence between the flu A hemagglutinin in the vaccine and a protein in VZV (envelope glycoprotein H). Id. He proposed this example of sequence homology as "one possibility" of how molecular mimicry could occur. Tr. 139, 143.

Dr. Zamvil acknowledged that the finding of similar protein sequences did not "guarantee T cell or antibody cross reactivity." Pet. Ex. 30 at 8. After conceding this point, he suggested an alternate theory, stating "that exposure to one virus can amplify CNS recruitment of CD8+ T

[33] A BLAST (Basic Local Alignment Search Tool) search is an unbiased homology search offered by the National Institute of Health, National Center for Biotechnology Information. Pet. Ex. 30 at 8; Tr. 144. For a description of Dr. Zamvil's process for conducting the BLAST search, see Tr. 144.

cells[34] that recognize an unrelated virus, even when the unrelated virus is not detected in the CNS." Id. (citing Pet. Ex. 30, Ref. 14 at 1-2).[35] Based on this observation, he opined that "cross-reactivity may not be required" for reactivation to occur. Id. Instead, he testified that a "virus may activate another virus." Tr. 141. In support of this alternative idea, Dr. Zamvil referenced the Matullo et al. paper. See Pet. Ex. 30, Ref. 14.

In Matullo et al., the authors studied "concurrent immune challenges." Pet. Ex. 30, Ref. 14 at 1. Their "hypothesis [was] that viruses need not replicate in the tissue in which they cause disease; specifically, [] a peripheral infection might trigger CNS pathology." Id. In the study, the CNS of mice were infected with the measles virus and their peripheral systems were infected with the lymphocytic choriomeningitis virus. Id. They found infection with only one of the viruses did not cause illness, however, "[c]o-infection resulted in a 12-fold increase in the number of CD8+ T cells in the brain as compared to measles virus infection alone." Id. Based on the study, the authors suggested that the "recruitment of peripherally activated CD8+ T cells to the CNS can potentiate neuroinflammation." Id. at 2. The findings "raise[d] the possibility that concomitant immune challenges may be an important cause of the neuroinflammation of some human CNS diseases, perhaps accounting for the inability to identify a discrete pathogenic trigger within affected brain tissues." Id. They concluded that "a condition that compromises and activates the blood-brain barrier and adjacent brain [tissue] can render the CNS susceptible to [a] pathogen-independent immune attack." Id. at 1. Dr. Zamvil used the study to illustrate the point that even though the CD8+ T cells did not recognize the virus; they were able to activate another virus in the CNS. Tr. 166-67.

Dr. Zamvil's "second possibility" for how the flu vaccine could trigger reactivation of VZV to cause Ramsay Hunt syndrome was based on "molecular mimicry between Fluvirin and myelin or neuronal autoantigens." Pet. Ex. 30 at 10; see also Tr. 139-40. He asserted that "[h]omologies exist between [flu] A hemagglutinin and contactin-associated protein-1 and neurofascin, two proteins associated with neuropathy." Pet. Ex. 30 at 10. He also seemed to suggest a variation on this theory, hypothesizing that the "[flu] vaccination cause[d] a T cell and antibody response that elicit[ed] CNS inflammation (i.e. within or near the geniculate ganglion) that promote[d] reactivation of latent VZV."[36] Id.

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[34] CD8+ T cells are "T lymphocytes that carry the CD8 antigen." CD8 Cells, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=64001 (last visited Apr. 14, 2022). T lymphocytes are "cells primarily responsible for cell-mediated immunity." T Lymphocytes, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=87562 (last visited Apr. 14, 2022). "When activated by antigen, T lymphocytes proliferate and differentiate into T memory cells and the various types of regulatory and effector T cells." Id.

[35] Christine M. Matullo et al., NCS Recruitment of CD8+ T Lymphocytes Specific for a Peripheral Virus Infection Triggers Neuropathogenesis During Polymicrobial Challenge, 7 PLoS e1002462 (2011).

[36] It was not clear whether this variation was part of Dr. Zamvil's theory based on the Matullo et al. article, or a different theory.

The third proposed mechanism posited by Dr. Zamvil is based on activation of the innate immune response, in contrast to his first two theories that implicated the adaptive immune response. Pet. Ex. 30 at 10. Dr. Zamvil opined that the flu vaccine "may trigger [the] innate immune master regulator of inflammation, NF-κB." Id. He explained that "[m]any infectious organisms activate the immune system through Toll-like receptors (TLRs), a family of proteins that are expressed on all nucleated cells." Id. The NF-κB dependent pathway is activated by TLRs, and is considered to be the "master regulator of inflammation." Id. This pathway "leads to production of type I interferon (IFN)-ß, which can have proinflammatory or anti-inflammatory activities." Id.; see also Tr. 184. Additionally, Dr. Zamvil stated that innate immune cells also serve as "antigen presenting cells" that can "direct proinflammatory T cell differentiation." Pet. Ex. 30 at 11; see also Tr. 185. Dr. Zamvil explained that in this theory, he does not propose that the innate immune system exclusively targeted the geniculate ganglion of the facial nerve. Tr. 186-88.

Although Dr. Zamvil stated that he offered three theories, in his reports and at the hearing he discussed variations of his theories, two of which are described above. An additional variation on a theory, described by Dr. Zamvil, was how the vaccine can activate an immune response due to local damage created by the needle tract during vaccination. Tr. 164. This causes innate cells to be activated, and they make T cells become proinflammatory. Id. The innate cells make T cells "traffic" into the CNS where they cause myelin destruction.[37] Id. The response is called "epitope spreading." Tr. 165. Dr. Zamvil also discussed the concept of "bystander activation." Tr. 167. He testified that "bystander activation is what leads to the epitope spreading that can occur." Id. His testimony on this point was somewhat confusing because although he discussed the concept of epitope spreading, he also testified that he was not suggesting that "epitope spreading occurred." Id.

In support of his opinions that the flu vaccine can trigger reactivation of VZV and thereafter cause Ramsay Hunt syndrome, Dr. Zamvil cited a 2010 case report by Gurbuz et al.[38] See Pet. Ex. 30, Ref. 10. The Gurbuz et al. authors described the clinical course of a 66-year-old female who presented to a health care provider "with complaints of weakness, running nose, [and] headache." Id. at 1. She had received a flu vaccination ten days earlier. Id. Antibiotics were prescribed. Id. One week later, she had continued to have "dizziness, nausea[,] and vomiting," and was admitted to the hospital. Id. On day three of her hospitalization, she had new symptoms of "hearing loss, earache[,] and itchy and painful vesicles on the right ear [and] the right side . . . of [her] tongue. Id. Two days later, she had paralysis of the right side of her face. Id. She was subsequently diagnosed with Ramsay Hunt syndrome. Id.

Gurbuz et al. provided background information about Ramsay Hunt syndrome, explaining that VZV causes chickenpox, and afterward the "virus resides silent and inactive

[37] Again, this aspect of his theory may have been related to Dr. Zamvil's reliance on the Matullo et al. article, but it was not entirely clear.

[38] Melek Kezban Gurbuz et al., A Case of Ramsay Hunt Syndrome After Inactive Influenza Vaccine, 6 J. Int'l Advanced Otology 419 (2010).

within the [CNS] for long years." Pet. Ex. 30, Ref. 10 at 3. They noted that "[a]dvanced age, chronic-systemic diseases, [and] immune deficiency conditions may cause reactivation." Id. Importantly, they did not reach any conclusion about whether the flu vaccine played a role in the cause of the patient's Ramsay Hunt syndrome. See id. They stated, "[i]n our case, pathophysiology of [Ramsay Hunt syndrome] after seasonal [flu] vaccine is not clear. There is a possibility that transient immune-deficient condition just after vaccination might have [] triggered reactivation of the inactive VZV." Id. They also acknowledged there was no other similar case of Ramsay Hunt syndrome reported after flu vaccination reported in the literature. Id. While they questioned whether there was a "transient immune suppression" caused by vaccination, they concluded that any causal mechanism associating vaccination and Ramsay Hunt syndrome was "not explainable yet." Id. The authors did not comment on the significance of the patient's symptoms of weakness, runny nose, or headache, for which she was prescribed antibiotics. See id. at 1-3.

Dr. Zamvil cited a report by Rothova et al.,[39] describing a case of reactivated VZV that caused panuveitis[40] following H1N1 flu vaccination. Pet. Ex. 32, Ref. 5 at 1. The authors reported "a recurrence of bilateral VZV-associated panuveitis following vaccination against flu H1N1 in a 60-year-old male patient with previous VZV-induced [acute retinal necrosis] after an interval of 20 years of disease inactivity." Id. The patient was diagnosed with bilateral panuveitis seven days after vaccination. Id. Intraocular fluid tested positive for VZV. Id. However, tests for CD4 and CD8 cells and immunoglobulins revealed normal levels. Id. The authors suggested a hypothesis of causation which "might have been associated with a (temporary) decrease in cellular immunity." Id.

In addition, Dr. Zamvil cited an article by Walter et al.,[41] who reported three cases of reactivation of herpes virus infections after vaccinations. Pet. Ex. 32, Ref. 6 at 1. The first case involved herpes zoster reactivation of the left T-10 dermatome following hepatitis A vaccine, with a repeat episode of herpes zoster following the second dose of the hepatitis A vaccine. Id. The second patient had reactivation of left thoracic herpes zoster after a flu vaccination in 1996. Id. Of note, the patient had received flu vaccines in the two prior and two subsequent years without incident. Id. The third patient had herpes zoster reactivation in the trigeminal nerve after rabies and Japanese encephalitis vaccinations. Id. The authors questioned whether an immunomodulation or immunosuppressive effect explained a "possible link between vaccination and reactivation of herpesvirus infections." Id.

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[39] Aniki Rothova et al., Reactivation of Acute Retinal Necrosis After Flu H1N1 Vaccination, 95 Brit. J. Ophthalmology 291 (2011).

[40] Panuveitis is "inflammation of the entire uveal tract." Panuveitis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=36655 (last visited Apr. 14, 2022). Uvea is the "vascular layer of [the] eyeball," made of the iris, ciliary body, and choroid. Tunica Vasculosa Bulbi, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=115933 (last visited Apr. 14, 2022).

[41] Roland Walter et al., Reactivation of Herpesvirus Infections After Vaccinations?, 353 Lancet 810 (1999).

On cross-examination, Dr. Zamvil agreed that Ramsay Hunt syndrome is not an autoimmune disease. Tr. 194-95. He also agreed that there was no case report that established a causal association between the flu vaccine and Ramsay Hunt syndrome. Tr. 198-99. Additionally, Dr. Zamvil agreed that "VZV reactivation [] is the cause of Ramsay Hunt syndrome." Tr. at 171; see also Pet. Ex. 30 at 7.

b. Althen Prong Two

Regarding Althen Prong Two, a logical sequence of cause and effect, Dr. Zamvil stated that petitioner "had latent herpes zoster in her geniculate ganglion." Pet. Ex. 30 at 12. He opined that the flu vaccine "trigger[ed] an adaptive immune response to [flu] determinants that [led] to reactivation of VZV, likely by cross-reactivity to shared determinants with VZV, myelin proteins[,] or axonal proteins." Id. Alternatively, he opined that the flu vaccine "activate[d] an innate immune response driven by NF-κB that [led] to damage in the geniculate ganglion. Cytokines activate[d] the type 1 interferon pathway, which can also lead to transcription of genes that activate herpes zoster." Id. He found "[t]his sequence of events culminate[d] in an outbreak of shingles in the facial nerve with paralysis and pain." Id.

Petitioner had a number of recurrences of Ramsay Hunt syndrome that were not temporally associated with her flu vaccination. Regarding her subsequent recurrences, Dr. Zamvil made it clear that he "did not claim that there was a direct association between [petitioner's] January 4, 2013[] vaccination" and her recurrences of Ramsay Hunt syndrome. Pet. Ex. 32 at 1. However, he believed "it [was] likely that once triggered by her [] 2013[] [flu] vaccination, [petitioner] experienced increased susceptibility to VZV reactivation due to other stressors." Id.

Dr. Zamvil disagreed with respondent's expert, Dr. Chaudhry, who opined that petitioner's VZV reactivation was caused by an altered immune competence related to pre-existing EGPA. Pet. Ex. 32 at 3. Dr. Zamvil opined that there was "no significant evidence" that petitioner's eosinophilic illness pre-dated her January 4, 2013 vaccination. Id. While "[s]he had eosinophilia, [and] high proteinase-3 Ab and CRP, [] her biopsy did not show granulomatosis or polyangiitis to support diagnoses of Wegener's [granulomatosis] or [EGPA]." Pet. Ex. 30 at 12. Therefore, Dr. Zamvil did not consider an eosinophilic illness or EGPA to be potential causes of petitioner's Ramsay Hunt syndrome. See id. Moreover, Dr. Zamvil did not believe that petitioner had any pre-exiting condition that contributed to her Ramsay Hunt syndrome. Tr. 177-78.

Additionally, Dr. Zamvil did not believe that petitioner's initial episode of Ramsay Hunt syndrome was caused by [. . .] until after the vaccination at issue here. Pet. Ex. 32 at 3-4; Pet. Ex. 44 at 1.

Dr. Zamvil agreed that none of petitioner's treating physicians attributed her Ramsay Hunt syndrome to her flu vaccination. Tr. 200-01.

On cross-examination, Dr. Zamvil admitted that he did not know why the flu vaccine at issue triggered petitioner's Ramsay Hunt syndrome in January 2013, even though she had received flu vaccinations in the past, and had previously been ill with the flu virus, and those events did not trigger her Ramsay Hunt syndrome. Tr. 213. He suggested that there may have been some unique reason related to the January 2013 vaccine, but when asked what that was, he responded, "I don't know." Tr. 213-14.

c. Althen Prong Three

As for Althen Prong Three, Dr. Zamvil provided somewhat inconsistent opinions as to the date of onset of petitioner's Ramsay Hunt syndrome. In his first expert report, he opined that petitioner's onset was two weeks after vaccination and consistent with the case report by Gurbuz et al. Pet. Ex. 30 at 12. The patient described by Gurbuz et al. developed painful vesicles in her right ear approximately 20 days after vaccination and developed facial palsy two days later. Pet. Ex. 30, Ref. 10 at 1.

At the hearing, however, Dr. Zamvil testified that petitioner's onset was six days after vaccination. Tr. 176. Specifically, the vaccine was administered on January 4, and onset of symptoms was January 10. Id. He opined that petitioner likely had a "secondary immune response here, meaning an amplification," so the time frame from vaccination to onset was "very short, within a matter of four to ten days," with a "peak" around days five to six. Tr. 175. He further testified that the onset of petitioner's illness was appropriate based on his mechanistic theories. Tr. 176.

B. Petitioner's Expert, M. Eric Gershwin, M.D.[42]

1. Background and Qualifications

Dr. Gershwin is board certified in internal medicine, rheumatology, and allergy and clinical immunology. Pet. Ex. 34 at 2. He completed his M.D. at Stanford University, after which he completed an internship and residency at Tufts-New England Medical Center in Boston, Massachusetts and worked as a clinical associate in immunology at the National Institutes of Health in Bethesda, Maryland. Id. at 1-2. He currently works in the Division of Rheumatology, Allergy, and Clinical Immunology at the University of California at Davis as a professor and chief of the division. Id. Dr. Gershwin has been bestowed with numerous honors and awards throughout his career, and he has held various editor and reviewer positions on medical journals. Id. at 3, 5-7. He has authored or co-authored over 1,000 publications during his career. Id. at 8-130.

2. Opinion

Dr. Gershwin did not opine on the cause of petitioner's Ramsay Hunt syndrome or address the issue of vaccine causation. Pet. Ex. 33 at 1. His opinions were limited to petitioner's

[42] Petitioner filed three expert reports authored by Dr. Gershwin. See Pet. Exs. 33, 41, 43.

diagnosis of EGPA, and specifically the question of whether she had EGPA prior to her vaccination and the onset of her Ramsay Hunt syndrome. Id.

Dr. Gershwin first provided background information about the illness, and then opined as to the onset of petitioner's EGPA. He explained that EGPA is a rare condition with an incidence rate "rang[ing] from approximately 0.5 to 7 per million people." Pet. Ex. 33 at 1. It is a "small vessel, necrotizing vasculitis," with clinical characteristics including "allergic rhinitis, polyposis of the sinuses[,] and asthma. Id. "It also includes systemic features, including fever and weight loss," but the primary "focus of immunopathology" is asthma. Id. at 1-2. The majority of patients have lung infiltrates that are described as "transient and patchy." Id. at 2. Criteria for the diagnosis of EGPA include a history of asthma, eosinophilia, another organ involvement, increased IgE, and positive ANCA results. Tr. 257.

From a biological point of view, the illness is characterized by elevated eosinophilia and "nonspecific elevated [IgE] levels in the sera" of most patients. Pet. Ex. 33 at 2. Other abnormal labs include ANCA. Id. Histologically, "small vessel angiitis and extravascular necrotizing granulomas, usually containing eosinophilic infiltrates" may be seen. Id. at 3. Vasculitis "typically involves both arteries and veins in pulmonary and systemic vessels." Id. Lung tissue may have "necrotizing vasculitis and areas resembling eosinophilic pneumonia." Id. Other body systems may be involved, including the skin and subcutaneous tissue. Id.

Regarding the onset of petitioner's EGPA, Dr. Gershwin opined that she had "no significant history of allergic rhinitis," "no change in her asthma symptoms," and "no evidence of pulmonary infiltrates prior to [] vaccination." Pet. Ex. 33 at 3. In his expert report, Dr. Gershwin opined that petitioner did not have "clinically significant evidence of [EGPA] before the acute clinical markers described by Dr. Rubenstein in 2017." Id. He disagreed with respondent's expert, Dr. Levinson, who opined that petitioner had eosinophilia and EGPA prior to her diagnosis of Ramsay Hunt syndrome. Id. Dr. Gershwin stated that Dr. Levinson used outdated criteria from the American College of Rheumatology, and therefore, "misinterpreted the laboratory report of March 31, 2011." Id.

Dr. Gershwin explained that on March 31, 2011, petitioner's "total eosinophil count was only 700 and the 11.1% [was] [] the percentage of eosinophils in her total white cell count." Pet. Ex. 33 at 3 (citing Pet. Ex. 13 at 20). According to Dr. Gershwin, "[t]rue eosinophilia is defined on the basis of the absolute number of cells, not the percentage." Id. He opined that petitioner did not have true eosinophilia until later in her clinical course. Id. For example, on July 16, 2014, petitioner's "absolute eosinophil count was only 400," which Dr. Gershwin characterized as "well below the normal level." Id. (citing Pet. Ex. 4 at 193). Dr. Gershwin opined petitioner developed EGPA in 2017, four years after her vaccination, when she had a "dramatic elevation of IgE to a level greater than 18,000 on February 16, 2017," as well as a positive P-ANCA and C-ANCA. Id. at 3-4.

However, at the hearing, Dr. Gershwin testified that "in retrospect," petitioner had "clinical manifestations" of EGPA when she had a positive ANCA result in 2013.[43] Tr. 253. But he did not agree that onset of petitioner's EGPA occurred prior to her vaccination on January 4, 2013, or that petitioner's EGPA reactivated her latent VZV (Ramsay Hunt syndrome). Tr. 243-45.

Instead of attributing the cause of petitioner's Ramsay Hunt syndrome to EGPA, Dr. Gershwin opined that petitioner "had an autoimmune predisposition." Pet. Ex. 33 at 4. He noted that petitioner's family members had autoimmune illnesses, including "[EoE], Crohn's disease, arthritis, and multiple myeloma," and "[t]hese would in fact indicate an individual with a striking genetic predisposition to immunopathology." Id.

Dr. Gershwin emphasized that EGPA is an autoimmune illness, not an immune deficiency. Pet. Ex. 43 at 1. He agreed that "immune suppression can result when immune suppressive drugs are used to treat [EGPA] autoimmunity," but there was "no evidence in the medical records to suggest that [petitioner] had clinical immune suppression" that played a role in the cause of her initial Ramsay Hunt episode. Id.

Dr. Gershwin also testified that the flu vaccine played no role in the development of petitioner's EGPA. Tr. 238-39. He believed that petitioner probably developed EGPA [. . .]. Tr. 239. He explained that [. . .], which is an irritant that causes inflammation and hypersensitivity pneumonitis. Tr. 244.

In summary, Dr. Gershwin opined that petitioner's EGPA was not relevant to the cause of her Ramsay Hunt syndrome. Tr. 236. He stated that there are no reports of EGPA causing Ramsay Hunt syndrome. Tr. 236-37. He opined that petitioner was not older, she did not have recurrent infections, she had no weight loss, and she was not immunodeficient.[44] Tr. 237-38. In summary, Dr. Gershwin opined that petitioner's EGPA did not present prior to her flu vaccine or the onset of her Ramsay Hunt syndrome. Tr. 243-44.

C. Respondent's Expert, Vinay Chaudhry, M.D.[45]

1. Background and Qualifications

Dr. Chaudhry is a neurology professor at Johns Hopkins University School of Medicine. Resp. Ex. C at 1; Resp. Ex. D at 1. He is board certified in neurology, neuromuscular diseases, electrodiagnostic medicine, and clinical neurophysiology. Resp. Ex. C at 1; Resp. Ex. D at 29.

[43] Petitioner's positive ANCA screen and elevated P-ANCA and C-ANCA were reported on November 2, 2013. Pet. Ex. 4 at 499.

[44] Petitioner was diagnosed with SAD by Dr. Rubenstein in 2017. Tr. 374; Pet. Ex. 28 at 1. However, according to respondent's expert Dr. Levinson, it did not play a role in the development of her Ramsay Hunt syndrome. Tr. 374-76.

[45] Respondent filed three expert reports authored by Dr. Chaudhry. See Resp. Exs. C, E, H.

After completing medical training in India, including a B.Sc., M.B., B.S., internship, and junior residency, Dr. Chaudhry completed a neurology residency and fellowship in the United States. Resp. Ex. D at 2. He "ha[s] an active clinical practice and evaluate[s] over 2000 patients a year mostly related to peripheral nerve disease." Resp. Ex. C at 1. Dr. Chaudhry has authored or co-authored over 200 publications. Resp. Ex. D at 3-17. Given his experience over his career, "[he is] considered an expert in evaluation and treatment of patients with peripheral neuropathies including facial neuropathies." Resp. Ex. C at 1.

2. Opinion

Dr. Chaudhry opined that petitioner "suffered from Ramsay Hunt [s]yndrome caused by reactivation of VZV infection due to her underlying eosinophilic granulomatosis, a condition known to reduce immune competence and [cause] VZV activation. [The] [f]lu vaccine didn't play a causative role." Resp. Ex. C at 10. In his expert reports, Dr. Chaudhry discussed Ramsay Hunt syndrome, recurrent zoster infections, EGPA, and the manifestation of these conditions in petitioner's case.

As described by Dr. Chaudhry, "Ramsay-Hunt syndrome is a peripheral facial nerve palsy accompanied by an erythematous vesicular rash on the ear." Resp. Ex. C at 8. Petitioner developed "left sided facial nerve [] palsy with incomplete left eye closure, tearing in the left eye, impaired chewing, [] dribbling, biting of the lips and inside of the cheeks[,] as well as slurred speech." Id. She had two vesicles in the left external ear. Id. Dr. Chaudhry opined that "[t]he presence of facial palsy with vesicles in the ear is [a] rather typical presentation of Ramsay-Hunt syndrome." Id. He found petitioner was treated appropriately for the illness with valacyclovir and prednisone. Id. Dr. Chaudhry noted that "[petitioner] had rather severe facial palsy," confirmed by her EMG that "showed severe left facial neuropathy." Id. She had a number of corrective surgical procedures and Botox injections, and her course was complicated by infections. Id.

The etiology of Ramsay Hunt syndrome is reactivation of VZV infection "in the geniculate ganglion of the facial nerve." Resp. Ex. C at 8. Dr. Chaudhry explained the mechanism of the illness as follows: once a person has chicken pox, the virus does not go away. Tr. 284. After the initial infection, the virus resides in the ganglion in a latent form. Id. Ramsay Hunt syndrome occurs when there is reactivation of the virus in the facial nerve ganglion. Tr. 284-85. It is not known why the virus becomes reactivated, but there are some risk factors or triggers. Tr. 285. Often there is not a cause. Id. Triggers include age, seasonal variations, and Wegener's granulomatosis. Id. (citing, e.g., Resp. Ex. C, Tab 3).[46] Dr. Chaudhry testified that vaccination has not been identified as a trigger. Id.

Dr. Chaudhry further explained that the DNA of VZV "can be detected by polymerase chain reaction in the trigeminal and geniculate ganglion confirming that VZV becomes latent in these ganglion and that reactivation of the virus causes Ramsay Hunt syndrome." Resp. Ex. C at

[46] Peter K. Wung, Herpes Zoster in Immunocompromised Patients: Incidence, Timing, and Risk Factors, 118 Am. J. Med. 1416.e9 (2005).

8 (citing Resp. Ex. O at 1-2).[47] Dr. Chaudhry opined that "[t]here is no reason to additionally invoke [f]lu vaccination . . . playing a causative role in [petitioner's] Ramsay Hunt syndrome." Id.

Additionally, Dr. Chaudhry noted in his first expert report that petitioner's treating physicians agreed that VZV infection caused her condition. Resp. Ex. C at 8. He testified at the hearing that there was no evidence in petitioner's medical record to suggest that any of her doctors attributed her Ramsay Hunt syndrome to her flu vaccination. Tr. 313, 332. There are references in the records which state that petitioner has an allergy to the flu vaccine. Tr. 313, 332-34. However, Dr. Chaudhry testified that often an allergy noted in a patient's records is usually based on a subjective history provided by the patient. Tr. 335. Thus, he opined that a record stating that petitioner had an allergy to the flu vaccine cannot be interpreted to suggest that any of her treating physicians held an opinion that the flu vaccine played a causal role in her Ramsay Hunt syndrome. Tr. 313, 335.

After her initial episode of Ramsay Hunt syndrome, petitioner had approximately four recurrences, none of which were associated with vaccination. Tr. 293-94; Resp. Ex. C at 9. Dr. Chaudhry explained that petitioner's first recurrence was in June 2013. Tr. 293; Resp. Ex. C at 9. It was not related to vaccination. Tr. 293; Resp. Ex. C at 9. She may have had another recurrence in August 2013, when lesions were seen in her left ear. Tr. 293; Resp. Ex. C at 9. Dr. Chaudhry stated that this recurrence was also not associated with any vaccination. Tr. 293; Resp. Ex. C at 9. He found her third recurrence was February 22, 2016, when one possible vesicle was noted. Tr. 294. Petitioner's fourth recurrence, according to Dr. Chaudhry, was February 12, 2018, when petitioner again had left ear pain with vesicles in her left ear. Id. Dr. Chaudhry observed that none of these episodes were associated with vaccination. Tr. 293; Resp. Ex. C at 9.

Dr. Chaudhry disagreed with Dr. Zamvil's opinion that "once triggered," petitioner had an "increased susceptibility to future reactivations." Resp. Ex. E at 2. Instead of the vaccine triggering petitioner's Ramsay Hunt syndrome, Dr. Chaudhry agreed with petitioner's treating physician, Dr. Rubinstein, who stated in 2017 that petitioner's "Ramsay Hunt syndrome and recurrent shingles may [] be due to the immune activation in [EGPA] leading to persistence of VZV infection." Id. (quoting Pet. Ex. 28 at 2); see also Tr. 298-300.

Moreover, in October 2013, petitioner's treating physicians questioned whether she had Wegener's granulomatosis with facial ulceration and an abscess to her right nose. Pet. Ex. 4 at 455-59. Dr. Chaudhry explained that subsequent diagnostic testing revealed abnormal lab values[48] and CT scan showed erosion of the nasal septum consistent with a granulomatous

[47] Yasushi Furuta et al., Detection of Varicella-Zoster Virus DNA in Human Geniculate Ganglia by Polymerase Chain Reaction, 166 J. Infectious Diseases 1157 (1992).

[48] Dr. Chaudhry referenced the following abnormal diagnostic laboratory results: P-ANCA 1:160, C-ANCA 1:40, eosinophils 13%, Proteinase-3 antibodies >8.0, IgE 1:1800; CRP 5.03. Resp. Ex. C at 9.

process, along with painful gums, jaw, and face, and fatigue, all consistent with EGPA. Resp. Ex. C at 9.

Dr. Chaudhry opined that EGPA may have played a role in triggering petitioner's Ramsay Hunt syndrome. Tr. 340-41. He based his opinion on the fact that patients with Wegener's granulomatosis, a similar disease, have a twenty times higher incidence rate of Ramsay Hunt syndrome. Tr. 341. "Wegener's granulomatosis is a form of systemic vasculitis characterized by necrotizing granulomatous inflammation." Resp. Ex. C, Tab 3 at 2. Like Ramsay Hunt syndrome, herpes zoster (shingles) is caused by reactivation of VZV, and also occurs after a primary infection with the virus in childhood. Id. To illustrate the risk for developing zoster reactivation in Wegener's granulomatosis, Dr. Chaudhry cited Wung et al. See id. Of a total of 180 patients with Wegener's granulomatosis, eighteen "suffered a total of 19 herpes zoster episodes over a [] follow-up period of 27 months." Id. at 1. Although the majority of the patients had herpes zoster outbreaks while on immunosuppressive medication for their Wegener's granulomatosis, many patients had discontinued these medications when their herpes zoster outbreaks occurred. Id. at 7. The two risk factors identified in the study were renal dysfunction and female sex. Id. at 8.

Dr. Chaudhry explained EGPA is vasculitis of small and medium blood vessels. Tr. 301. EGPA is an illness characterized by phases, and Dr. Chaudhry opined that petitioner's records showed that she experienced the phases known to occur with this condition. Resp. Ex. C at 9. The first phase is the "[p]rodromal phase with asthma," which generally occurs "in the second and third decades of life." Id.; Resp. Ex. E at 3; see also Resp. Ex. C, Tab 4 at 1.[49] He explained that petitioner had a history of asthma requiring treatment with Albuterol, Advair, and Singulair. Resp. Ex. C at 9. She had seen a pulmonologist for at least three years prior to her initial episode of Ramsay Hunt syndrome. Id. Dr. Chaudhry cited references to petitioner's medical records showing that in August and December 2010, she had upper respiratory infections. Resp. Ex. E at 6-7. On both occasions, petitioner was noted to have a history of asthma, and was taking Albuterol, Fluticasone, and Montelukast (Singulair) for her asthma. Id. In January 2011, petitioner had a sore throat, ear pain, nasal congestion, and wheezing. Id. at 7. Again, her history of asthma was documented, and she was on the medications described above. Id. In March 2011, she had nasal congestion, and again her history of asthma was noted. Id.

The second phase of EGPA is the "[e]osinophilic phase." Resp. Ex. C at 9; Resp. Ex. C, Tab 4 at 1. Dr. Chaudhry stated that this phase is characterized by malaise, fever of unknown origin, cough, and abdominal pain. Resp. Ex. C at 9. Dr. Chaudhry stated that petitioner had eosinophilia in 2011. Id. (citing Pet. Ex. 13 at 20). In March 2011, her eosinophils were elevated at 11.1%, with an elevated absolute count of 700. Resp. Ex. E at 3 (citing Pet. Ex. 13 at 20).

[49] Talmadge E. King, Clinical Features and Diagnosis of Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss), UpToDate, https://www.uptodate.com/contents/clinical-features-and-diagnosis-of-eosinophilic-granulomatosis-with-polyangiitis-churg-strauss (last updated Sept. 12, 2017).

Based on the characteristic phases of EGPA, petitioner's clinical course evidencing a history of asthma and sinus issues back to 2010, and petitioner's elevated eosinophils in March 2011, Dr. Chaudhry placed onset of petitioner's EGPA in March 2011. Tr. 304-06.

Dr. Zamvil and Dr. Chaudhry disagreed about the significance of petitioner's abnormal eosinophilia levels in 2011, and specifically about whether an "absolute eosinophil count is more reliable" than a percentage value. Resp. Ex. E at 3. Dr. Chaudhry cited to King, who noted "peripheral blood eosinophilia absolute levels greater than 10 percent of the total leukocyte count should prompt suspicion for EGPA." Id. (citing Resp. Ex. C, Tab 4 at 4). Regardless of which method is more reliable, percentage versus absolute count, Dr. Chaudhry concluded that petitioner had elevated eosinophils in March 2011. Id.

Dr. Chaudhry prepared a chart demonstrating petitioner's eosinophil levels from 2008 until 2017, as seen below:

Date	% Eosinophils (Abn- bolded)	Absolute # (abnl bolded)	Ref (%ULN/ Absolute ULN)	Exhibit
12/31/08	2.7%	200	5/300	25-15
3/31/11	**11/1%%**	**700**	*5/4.5 (should be 0.45)*	13-20
1/28/13	3.5%	300	*5/450 (New York Hospital laboratories)*	9-370
3/7/13	**13%**	**1250**	7/600	9-354
5/17/13	**19.3%**	**1200**	7/700	Exhibit 2 p 84- significant eosinophilia probably allergies
10/24/13	**15.3%**	**1545**	8/500	7-12
10/28/13	**13.1%**	**1200**	6/600	4- 501
10/28/13	**14.9%**	**1500**	8/500	7-29
10/29/13	**13.8%**	**1100**	6/600	4-482
11/7/13	7.7%	**547**	8/500	20-016
11/19/13	**12%**	**860**	7/600	9-303
11/22/13	**13.8%**	**718**	8/500	7-23
12/8/13	**9.6%**	413	8/500	7-21
1/15/14	**13/12%**	**1330/1330**	7/600	9-307, 329
6/3/14	**14%**	**860**	7/600	19-11
7/11/14	3.4%	400	6/600	4 -201
7/12/14	3.6%	400	6/600	4-198
7/14/14	**14.5%**	**700**	6/600	4-197
7/15/14	1.5%	100	6/600	4-193
7/16/14	**6.1%**	400	5/600	4-193
7/17/14	**8%**	500	6/600	4-192
7/18/14	4.9%	400	6/600	4-192

3/26/15	**7%**	470	6/600	9-92
4/27/16	**13%**	**1200**	8/500	15-40
2/15/17	**17%**	**1300**		28-01
3/28/17	**9%**	**600**	/300	29-6
3/28/17	**11%**		5%	29-10
5/4/17	6%	**400**	/300	29-4

Resp. Ex. E at 3-4.

The fact that petitioner's eosinophils fluctuated, and were not always abnormal, is not unusual according to Dr. Chaudhry. Resp. Ex. E at 4 (citing Resp. Ex. C at 4 ("Eosinophilia, however, is occasionally missed because of rapid spontaneous, or glucocorticoid-induced reductions or fluctuations in eosinophil counts.")).

The next phase of EGPA is the vasculitis phase, characterized by "pulmonary granulomas, vascular complications with ulcerations, intestinal granulomas[,] and peritonitis." Resp. Ex. C at 9; see also Resp. Ex. C, Tab 4 at 1. Dr. Chaudhry noted that petitioner had facial ulcerations. Resp. Ex. C at 9. Ultimately blood tests were done that revealed eosinophilia and ANCA antibodies, and Dr. Rubenstein made the diagnosis of EGPA. Id. Dr. Chaudhry concluded that petitioner's EGPA "played a critical role in reactivation of the VZV infection leading to Ramsay Hunt syndrome." Id. at 10. Dr. Chaudhry further opined that petitioner's EGPA was not caused by the flu vaccine. Id.

Next, Dr. Chaudhry discussed Gurbuz et al., a case report of a patient who developed Ramsay Hunt syndrome following flu vaccine, referenced by Dr. Zamvil. Resp. Ex. C at 10 (citing Pet. Ex. 30, Ref. 10). Dr. Chaudhry noted that prior to the onset of Ramsay Hunt syndrome, the patient complained of an illness (weakness, runny nose, and headache) and was prescribed Amoxicillin, an antibiotic, presumably for a bacterial infection. Resp. Ex. C at 10; Pet. Ex. 30, Ref. 10 at 1. Further, Dr. Chaudhry observed that the authors suggested that the flu vaccine could cause "transient immunosuppression" but failed to provide any evidence to support that proposition. Resp. Ex. C at 10.

Dr. Chaudhry also took issue with Dr. Gershwin's opinion that the manifestation of petitioner's EGPA diagnosis did not become clear until "February 16, 2017, four years after . . . vaccination." Resp. Ex. E at 5. Dr. Chaudhry believed Dr. Gershwin failed to account for (1) petitioner's right nasal lesion in March 2013; (2) the reference to Wegener's granulomatosis, facial ulceration, and abscess of the right nose in October 2013; (3) elevated P-ANCA, C-ANCA, and eosinophils in October 2013; (4) CT scan abnormalities in 2013; (5) autoantibodies to Proteinase-3 in November 2013; and (6) abnormal eosinophils in July 2014. Id. at 5-6. Dr. Chaudhry believed these abnormal findings suggested the diagnosis of EGPA between 2013 and 2017. Id. at 5. Moreover, when taking into account petitioner's history of asthma, Dr. Chaudhry believed petitioner may have had the illness as early as 2010. Id. at 5-7. And at the hearing, he concluded that petitioner's onset of EGPA was in 2011, when she had elevated eosinophils. Tr. 305-06.

Regardless of when petitioner developed EGPA, Dr. Chaudhry opined that a trigger is not needed for reactivation of VZV to occur. Tr. 340. "There is no reason to additionally invoke [the] [f]lu vaccination . . . playing a causative role in [petitioner's] Ramsay Hunt syndrome, a syndrome well known to occur following reactivation of VZV infection." Resp. Ex. C at 8. Although he believed EGPA was a "possib[le] [] cause" for petitioner's initial episode of VZV reactivation, he did not hold this opinion to a probable or more likely than not standard. Tr. 340-42.

In summary, Dr. Chaudhry disagreed that the flu vaccine can cause or did cause petitioner's VZV reactivation. Resp. Ex. C at 10. He opined that "latent VZV infection is common with virtually all patients who have had chicken pox," and "known risk factors for reactivation are age, sex, race, seasonal variation, and altered immune competence such as with hematological malignancies, stem cell transplants, HIV, inflammatory diseases (Wegener's [granulomatosis] and Crohn's disease), use of immunosuppression[,] and diabetes." Id. But he emphasized that no infection or preceding vaccination is needed for VZV reactivation. Id.

D. Respondent's Expert, Arnold I. Levinson, M.D.[50]

1. Background and Qualifications

Dr. Levinson is board certified in internal medicine and allergy and clinical immunology and is an Emeritus Professor of Medicine and Neurology at the Perelman School of Medicine at the University of Pennsylvania School of Medicine. Resp. Ex. A at 1; Resp. Ex. B at 2. He received his M.D. from University of Maryland. Resp. Ex. B at 1. After completing an internship and one year of residency, he was a fellow at Johns Hopkins Hospital, a postdoctoral fellow in immunobiology at the University of Pennsylvania School of Medicine, a postdoctoral fellow in immunology at the University of California San Francisco Medical Center, and an allergy and clinical immunology fellow at the University of Pennsylvania School of Medicine. Id. Over his career of more than 30 years, Dr. Levinson has "evaluated and treated patients with a broad range of immune-mediated diseases including autoimmune, hypersensitivity and immunodeficiency disorders." Resp. Ex. A at 1. Dr. Levinson has held various editorial positions and memberships in honorary, professional, and scientific societies, and has authored or co-authored over 150 publications. Resp. Ex. B at 2-4, 10-21.

2. Opinion

Dr. Levinson's opinions focused on Dr. Zamvil's three causal mechanisms proffered to explain how the flu vaccine could cause Ramsay Hunt syndrome. Resp. Ex. A at 5. He also addressed the evolution of petitioner's "nasal and sinus disease," or EGPA, and its role in the development of petitioner's Ramsay Hunt syndrome. Id. at 6-8.

Before addressing Dr. Zamvil's opinions, Dr. Levinson explained the cause of Ramsay Hunt syndrome and described the mechanism of VZV reactivation. He explained that Ramsay Hunt syndrome

[50] Respondent filed three expert reports authored by Dr. Levinson. See Resp. Exs. A, F, G.

> is caused by reactivation of [VZV] in the geniculate ganglion. VZV is a ubiquitous, human alpha herpesvirus that produces varicella on primary infection. The virus then becomes latent in ganglionic neurons along the entire neuraxis. With a decline in VZV-specific cell-mediated immunity in elderly and immunocompromised individuals, defects in innate immunity or the presence of anti-cytokine antibodies, the virus reactivates from one or more ganglia and travels peripherally via the sensory nerve root, to the innervated target tissue (skin, cornea, auditory canal, etc.). Typically, a single dermatome[51] is involved, although two or three adjacent dermatomes may be affected. The lesions usually do not cross the midline. Reactivation of VZV is often complicated by severe pain, which may last indefinitely (post-herpetic neuralgia) as was the case [with petitioner].

Resp. Ex. A at 6.

Dr. Levinson then analyzed each of Dr. Zamvil's proposed causal mechanisms. He noted that the first theory, that the "[flu] vaccination could trigger an adaptive immune response to VZV . . . relies on three foundational principles." Resp. Ex. A at 8. These principles are (1) "that the [flu] viral antigens in the [flu] vaccine and VZV antigens share molecular motifs," (2) "that the [flu] vaccine induced a cross-reactive immune response to the shared antigens," and (3) "that said cross-reactive immune response led to VZV reactivation in the geniculate ganglion which ultimately resulted in . . . clinical symptoms of Ramsay Hunt syndrome." Id. at 8-9.

Dr. Levinson noted several problems with this theory.[52] First, as conceded by Dr. Zamvil, there is "no evidence that this putative example of molecular mimicry actually induces any type of cross-reactive adaptive immune response to the VZV nucleocapsid molecule . . . or . . . any other putative epitopes shared by [the flu vaccine] viral antigens and VZV antigens." Resp. Ex. A at 9.

The second problem Dr. Levinson identified was that there is no evidence that "cross-reactive shared epitope specific T cells . . . enter the geniculate ganglion and . . . become activated by resident latent VZV virus." Resp. Ex. A at 9. "[I]n the latently infected geniculate ganglion, . . . [one] can't detect a peptide." Tr. 387. Dr. Levinson explained that there is no evidence to suggest that latent VZV produces nucleocapsid proteins. Resp. Ex. A at 9. "[T]he

[51] Dermatome is "the area of skin supplied with [] nerve fibers by a single spinal nerve." Dermatome, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=13359 (last visited Apr. 14, 2022).

[52] Although Dr. Levinson disagreed with Dr. Zamvil's opinions, he prefaced his opinions at the hearing by recognizing and acknowledging Dr. Zamvil's "cutting-edge research," which is deserving of significant credit. Tr. 378.

putative shared epitope would likely not be expressed by cells in the geniculate ganglion due to the . . . limited transcription[53] of DNA by latent VZV." Id.

In support of this aspect of Dr. Levinson's opinion, and the fact that molecular mimicry is unlikely to play a role in VZV reactivation, respondent filed an article by Depledge et al.[54] Resp. Ex. M. The authors explained that after a primary infection (chickenpox), VZV infection reactivates in approximately one-third of those infected, causing herpes zoster, which frequently leads to neurological complications. Id. at 1. VZV is difficult to study because it is a human pathogen that does not cause disease in animals, so experimental animal models have not been helpful in researching the disease. Id. Because animal studies are not possible, researchers use cadaver human ganglia naturally infected with VZV. Id. at 6. Research limitations have posed significant difficulties in attempts to identify viral transcripts and their corresponding proteins. Id. Based on available research, "VZV protein expression in human ganglia appears to be absent or extremely rare."[55] Id. Two viral proteins (VLT and ORF63) have been identified, and while they may have "the potential to be translated during latency, these viral proteins could not be detected in latently infected human ganglia by immunohistochemistry." Id. Based on existing research, the reasons or causes of "VZV reactivation are poorly understood." Id. at 10.

Thus, Dr. Levinson opined that there is no data to support Dr. Zamvil's suggestion that T cells would migrate to the geniculate ganglion and recognize presenting peptides, and then that interaction would lead to reactivation. Tr. 388-89. Moreover, if such a theory were correct, Dr. Levinson opined that he would expect patients who get zoster vaccines to develop VZV reactivation, not protection, due to the potential for homology and molecular mimics between the zoster vaccine and VZV, but that has not been seen or reported. Tr. 389.

Dr. Levinson noted that Dr. Zamvil conceded that his first theory could be improbable. Resp. Ex. A at 9. Thus, Dr. Zamvil suggested an alternative theory, referencing an article he suggested supported the idea that "concomitant infection with [] two viruses" could cause neuropathology. Id. (citing Pet. Ex. 30, Ref. 14). However, Dr. Levinson observed that "this outcome was only observed in animals," where an active brain infection was induced. Id. (citing Pet. Ex. 30, Ref. 14 at 11). Dr. Levinson distinguished the facts in Matullo et al. from those here. Id. at 9-10. He explained that in the research reported by Matullo et al., there was "concurrent active viral infection in the geniculate ganglion, which [c]ould promote the immigration of . . . T cells and elicitation of tissue injury," inconsistent with the facts of petitioner's case. Id.

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[53] Transcription is "RNA synthesis using a DNA template." Illustrated Dictionary of Immunology 713 (3d ed. 2009).

[54] Daniel P. Depledge et al., Molecular Aspects of Varicella-Zoster Virus Latency, 10 Viruses 1 (2018).

[55] For a more complete explanation, see Resp. Ex. M at 5, fig.2 (schematic illustration of the reactivation of VZV).

The second theory posited by Dr. Zamvil was "that molecular mimicry between [the flu vaccine] and myelin or neuronal autoantigens could cause a T cell and antibody response that elicit[ed] CNS inflammation [] within or near the geniculate ganglion[] that promote[d] reactivation of latent VZV." Resp. Ex. A at 10 (internal citations omitted). Dr. Zamvil gave an example based on shared similar sequences between flu A hemagglutinin and contactin associated protein 1 and neurofascin, proteins associated with neuropathy. Id. Because Dr. Zamvil did not cite to any medical literature or studies in support of this example, Dr. Levinson stated that he was unable to evaluate it. Id. Moreover, citing the National Academy of Medicine, formerly called the Institute of Medicine, Dr. Levinson noted that many examples of homology exist, but "the vast majority of these are not associated with biologically relevant autoimmune phenomena or actual human disease." Id. at 10 (citing Resp. Ex. A, Tab 12 at 3-4).[56]

Dr. Zamvil's third theory is "that by stimulating the activation of NFκ-B," the flu vaccine may trigger an immune reaction that causes VZV reactivation. Resp. Ex. A at 11. Dr. Zamvil cited an article by Haralambieva et al.,[57] that described a study on 159 adults, ages 50-74 years old, who received a flu vaccine. Pet. Ex. 30, Ref. 18 at 1. The frame of reference for the study was the lack of knowledge about "how age affects adaptive immunity and immune memory due to vaccination, particularly in regard to [flu] response." Id. Their goal was to "identify baseline, early[,] and late transcriptional signatures []in peripheral blood mononuclear cells[]" following vaccination. Id. at 2. One of their findings was the "involvement of known immune function-related genes in the development of memory B cell response," including "a member of the NF-kappa-B inhibitor family[], which is involved in inflammatory response and apoptosis." Id. at 3. Dr. Zamvil opined that the study "found gene sets and genes . . . demonstrating significant associations . . . with memory B cell response[s] [which] suggest[ed] the importance of . . . NF-κB cell signaling . . . and transcriptional regulation gene signatures in the development of memory B cell response after [flu] vaccination." Pet. Ex. 30 at 11. Dr. Zamvil used this finding to assert that "activation of innate immunity becomes a third mechanism that could contribute to reactivation of VZ[V] following Fluvirin." Id.

Dr. Levinson explained that the Haralambieva et al. study was not relevant because it "did not investigate how innate immune activation following immunization with the trivalent [flu] vaccine might lead to reactivation of VZV." Resp. Ex. A at 11. While Dr. Levinson acknowledged that "an early innate immune response [can] facilitate[] development of an antigen-specific adaptive immune response," he opined that "these observations in no way provide a basis for claiming that vaccination with Fluvirin or any killed [flu] virus vaccine would cause an innate immune reaction that causes reactivation of latent VZV." Id. Moreover, Dr. Levinson found it "difficult to understand how and why such a putative innate immune reaction would exclusively target the geniculate ganglion." Id.

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[56] Inst. of Med., Evaluating Biological Mechanisms of Adverse Events, in Adverse Effects of Vaccines: Evidence and Causality 57, 70-71 (Kathleen Stratton et al. eds., 2012). Respondent filed only two pages of this chapter; however, this text is well known to the undersigned.

[57] Iana H. Haralambieva et al., Transcriptional Signatures of Influenza A/H1N1-Specific IgG Memory-Like B Cell Response in Older Individuals, 34 Vaccine 3993 (2016).

In addition to addressing Dr. Zamvil's proposed causal mechanisms, Dr. Levinson also discussed petitioner's EGPA, and its relevance to her initial episode of Ramsay Hunt syndrome. Resp. Ex. A at 6-8. Generally, Dr. Levinson agreed with the opinions of Dr. Rubenstein, petitioner's immunologist. Id. at 7. Dr. Levinson explained that EGPA is a "systemic vasculitis [] characterized by granulomatous inflammation of small and medium arteries. It is typically preceded by a history of asthma . . . . Other early clinical features include allergic rhinitis, nasal polyps, and sinusitis." Id. There are three phases of the disease, as previously explained above. Id. These phases may "overlap and may not be clearly distinguishable." Id. Petitioner had "asthma, seasonal allergies, recurrent sinusitis, [] eosinophilia, and eosinophilic infiltrates on lip biopsy, which "qualif[ied] her for the diagnosis of EGPA." Id. at 7-8.

Dr. Levinson explained that the diagnosis of EGPA can be difficult to make, especially in petitioner's case, where she had symptoms that were thought to be [. . .]. Resp. Ex. A at 8. Regardless, Dr. Levinson opined that her correct diagnosis was EGPA. Id. He believed that "petitioner's systemic inflammatory process" may have been "ongoing" when petitioner had her initial Ramsay Hunt syndrome in January 2013, but that the "full clinical declaration of EGPA may have been delayed by the corticosteroids she received as treatment" for Ramsay Hunt syndrome. Id. Dr. Levinson noted that corticosteroids are also used to treat EGPA; and he explained that "EGPA occurs in some patients with asthma after their treatment with [] corticosteroids is discontinued." Id. He also opined that petitioner's EGPA may have played a role in the second episode of Ramsay Hunt syndrome, which petitioner had in June 2013. Id. at 12. However, Dr. Levinson clarified in a supplemental report that he did not hold these opinions to a reasonable degree of medical probability. Resp. Ex. F at 3.

In summary, Dr. Levinson opined that petitioner's flu vaccination did not cause petitioner's reactivation of VZV or the development of her Ramsay Hunt syndrome. Resp. Ex. A at 12. He questioned whether petitioner may have had EGPA when she developed her initial episode of Ramsay Hunt syndrome in January 2013, as well as the second episode in June 2013. Id. at 8, 12.

VII. LEGAL AUTHORITY AND ANALYSIS

A. Standards for Adjudication

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

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). In particular, petitioner must prove that that the vaccine was "not only

[the] but-for cause of the injury but also a substantial factor in bringing about the injury." Id. at 1321 (quoting Shyface v. Sec'y of Health & Hum. Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner who satisfies this burden is entitled to compensation unless respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B).

B. Factual Issues

A petitioner must prove, by a preponderance of the evidence, the factual circumstances surrounding her claim. § 13(a)(1)(A). To resolve factual issues, the special master must weigh the evidence presented, which may include contemporaneous medical records and testimony. See Burns v. Sec'y of Health & Hum. Servs., 3 F.3d 415, 417 (Fed. Cir. 1993) (explaining that a special master must decide what weight to give evidence including oral testimony and contemporaneous medical records).

Medical records generally "warrant consideration as trustworthy evidence." Cucuras v. Sec'y of Health & Hum. Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). However, greater weight is typically given to contemporaneous records. Vergara v. Sec'y of Health & Hum. Servs., No. 08-882V, 2014 WL 2795491, at *4 (Fed. Cl. Spec. Mstr. May 15, 2014) ("Special Masters frequently accord more weight to contemporaneously-recorded medical symptoms than those recorded in later medical histories, affidavits, or trial testimony."). Contemporaneous medical records are presumed to be accurate. See Cucuras, 993 F.2d at 1528. The weight afforded to contemporaneous records is due to the fact that they "contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium." Id. To overcome the presumptive accuracy of medical records, a petitioner may present testimony which is "consistent, clear, cogent, and compelling." Sanchez v. Sec'y of Health & Hum. Servs., No. 11-685V, 2013 WL 1880825, at *3 (Fed. Cl. Spec. Mstr. Apr. 10, 2013) (citing Blutstein v. Sec'y of Health & Hum. Servs., No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)), mot. for rev. denied, 142 Fed. Cl. 247 (2019), vacated on other grounds & remanded, 809 F. App'x 843 (Fed. Cir. 2020).

There are situations in which compelling testimony 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) ("[L]ike any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking."); Lowrie v. Sec'y of Health & Hum. Servs., No. 03-1585V, 2005 WL 6117475, at *19 (Fed. Cl. Spec. Mstr. Dec. 12, 2005) ("[W]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent." (quoting 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))). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1379 (Fed. Cir. 2009); Bradley v. Sec'y of Health & Hum. Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

Despite the weight afforded medical records, special masters are not bound rigidly by those records in determining onset of a petitioner's symptoms. Valenzuela v. Sec'y of Health & Hum. Servs., No. 90-1002V, 1991 WL 182241, at *3 (Fed. Cl. Spec. Mstr. Aug. 30, 1991); see also Eng v. Sec'y of Health & Hum. Servs., No. 90-1754V, 1994 WL 67704, at *3 (Fed. Cl. Spec. Mstr. Feb. 18, 1994) (Section 13(b)(2) "must be construed so as to give effect also to § 13(b)(1) which directs the special master or court to consider the medical records (reports, diagnosis, conclusions, medical judgment, test reports, etc.), but does not require the special master or court to be bound by them").

C. Causation

To receive compensation under the Program, petitioner must prove either: (1) that she suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that she received, or (2) that she suffered an injury that was caused by a vaccination. See §§ 11(c)(1), 13(a)(1)(A); Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1319-20 (Fed. Cir. 2006). Petitioner must show that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface, 165 F.3d at 1352-53).

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

The causation theory must relate to the injury alleged. The petitioner must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen, 35 F.3d at 548-49. Petitioner cannot establish entitlement to compensation based solely on his assertions; rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether petitioner is entitled to compensation, the special master shall consider all material in the record, including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in petitioner's favor when the evidence weighs in his favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in petitioner's favor).

"Expert medical testimony which merely expresses the possibility—not the probability—of the occurrence of a compensable injury is insufficient, by itself, to substantiate the claim that such an injury occurred." LaCour v. Sec'y of Health & Hum. Servs., No. 90-316V, 1991 WL 66579, at *5 (Fed. Cl. Spec. Mstr. Apr. 15, 1991); accord Burns v. Sec'y of Health & Hum.

Servs., No. 90-953V, 1992 WL 365410, at *6 (Fed. Cl. Spec. Mstr. Nov. 6, 1992), aff'd, 3 F.3d 415. The Federal Circuit has likewise made clear that the mere possibility of a link between a vaccination and a petitioner's injury is not sufficient to satisfy the preponderance standard. Moberly, 592 F.3d at 1322 (emphasizing that "proof of a 'plausible' or 'possible' causal link between the vaccine and the injury" does not equate to proof of causation by a preponderance of the evidence); Waterman v. Sec'y of Health & Hum. Servs., 123 Fed. Cl. 564, 573-74 (2015) (denying petitioner's motion for review and noting that a possible causal link was not sufficient to meet the preponderance standard); Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019). While certainty is by no means required, a possible mechanism does not rise to the level of preponderance. Moberly, 592 F.3d at 1322; see also de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1351 (Fed. Cir. 2008).

D. Analysis

1. Althen Prong One: Petitioner's Medical Theory

Under Althen Prong One, petitioner must set forth a medical theory explaining how her vaccine could have caused her alleged injuries. Andreu, 569 F.3d at 1375; Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation must be informed by a "sound and reliable medical or scientific explanation." Knudsen, 35 F.3d at 548; see also Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioner relies upon a medical opinion to support her theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen v. Sec'y of Health & Hum. Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better than the soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

The undersigned finds petitioner failed to prove by preponderant evidence that the flu vaccination she received caused her Ramsay Hunt syndrome. There are several reasons for this finding.

Petitioner proposed what appears to be a unique claim, that a flu vaccination can cause reactivation of VZV so as to cause Ramsay Hunt syndrome. However, none of the articles filed by petitioner offer support for any of the theories proffered by Dr. Zamvil. Generally, the takeaway from the relevant medical literature is that while there are some triggers for VZV reactivation, such as female sex, age, and immunosuppression, reactivation can occur in the absence of any identifiable trigger.

Additionally, the mechanism of VZV reactivation is not known. It has not been linked to vaccinations. While petitioner did file a case report[58] of Ramsay Hunt syndrome following flu vaccination, that patient had been ill and an antibiotic had been prescribed for her illness. The significance of the patient's antecedent infection or its role in triggering reactivation was not addressed. Further, the patient was older, and thus, her age may have been another risk factor for VZV reactivation. And while the authors noted the temporal association of vaccination, they did not conclude that the flu vaccine caused VZV reactivation.

Ramsay Hunt syndrome is not an autoimmune disease, a fact that Dr. Zamvil readily acknowledged. However, two of his proposed causal mechanisms are based on molecular mimicry, a mechanism associated with autoimmune illnesses. Molecular mimicry has been accepted in the Vaccine Program as a sound and reliable mechanism for how the flu vaccine can initiate an autoimmune process resulting in GBS. See, e.g., R.S. v Sec'y of Health & Hum. Servs., No. 15-1207V, 2019 WL 7631017, at *32 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), mot. for rev. denied, 2020 WL 4049758 (Fed. Cl. 2020); Reichert v. Sec'y of Health & Hum. Servs., No. 16-697V, 2018 WL 4496561, at *15 (Fed. Cl. Spec. Mstr. Aug. 2, 2018). GBS is not thought to be caused by reactivation of a prior virus that remains dormant in nerve ganglion. In contrast, Ramsay Hunt syndrome is caused by reactivation of a prior VZV infection. Because Ramsay Hunt syndrome is not an autoimmune disease, molecular mimicry is not a good theoretical fit.

Even if it were a good fit, there is no evidence to support the notion that VZV reactivation is caused by molecular mimicry. The first molecular mimic suggested by Dr. Zamvil is homology between flu A hemagglutinin in the vaccine and a protein in VZV. His second proposed homology is between flu A hemagglutinin and contactin-associated protein and/or neurofascin. The problems with these suggested homologies were identified by Dr. Levinson, who showed that there is no evidence that either of the examples proposed by Dr. Zamvil actually induce a cross-reactive adaptive immune response. Dr. Zamvil cited no foundational evidence, medical literature, research, studies, or other evidence of any such cross-reaction. Dr. Zamvil conceded that point.

Further, there is limited knowledge about the degree to which latent VZV is capable of producing proteins that could be mimics of any similar amino acid sequence in the vaccine. As explained in Depledge et al., "VZV protein expression in human ganglia appears to be absent or extremely rare." Resp. Ex. M at 6. Although Dr. Zamvil and Dr. Levinson disagree on this point, the Depledge et al. study describes what is known about human ganglia infected with latent VZV, and based on the research done in the study, there appears to be insufficient evidence to support the theory of molecular mimicry. It also does not appear that any of the literature filed suggests that molecular mimicry plays a role in VZV reactivation.

[58] The undersigned acknowledges the Anjum et al. article filed by petitioner, in which the authors recommend that "'[c]ausal evidence' should . . . include different types of evidence, including case studies and cases reports, which can in some cases provide valuable information for understanding causation and causal mechanisms. This is particularly important when dealing with rare disorders." Pet. Ex. 66 at 1. The undersigned agrees and has taken into account the case report cited by petitioner. However, there are factual issues presented in the case report that raise questions, including whether the patient may have had an antecedent infection.

Dr. Zamvil's theory based on concomitant viruses is also problematic. The Matullo et al. study induced a "co-infection model," but that model presents facts and circumstances that are not present here. In Matullo et al., the CNS of mice were infected with measles virus and the peripheral systems were infected with a different virus. A key finding was that peripherally activated T cells potentiated neuroinflammation of the CNS. The study "raise[d] the possibility that concomitant immune challenges may be an important cause of the neuroinflammation of some human CNS diseases." Pet. Ex. 30, Ref. 14 at 2. But this possibility is not applicable here where there is no evidence that petitioner had an active infection in her brain. Dr. Zamvil did not show that latent VZV in the geniculate ganglion is equivalent to an active measles infection of the brain.

Dr. Zamvil's theory based on the innate immune system and the Haralambieva et al. study of older adults who received the flu vaccine also misses the mark. The findings of the study broadly support the idea that early innate immune responses can facilitate the development of adaptive immune responses. But, as explained by Dr. Levinson, the study does not explain how the flu vaccine could cause reactivation of VZV. In a variation on the theory, Dr. Zamvil suggested that T cells "traffic" into the CNS where they cause myelin destruction. Tr. 164. He discussed the concepts of "epitope spreading" and "bystander activation." Tr. 164-68. But then Dr. Zamvil explained that he wasn't proposing these concepts occurred in this case.[59] Overall, his theories based on the innate immune system were disjointed and confusing.

Another problem with Dr. Zamvil's opinions arise from his use of the words "possible" and "possibility" in his expert reports and at the hearing when describing his different mechanistic theories. For example, in his first expert report, he opined that "[s]everal possible mechanisms could account for the development of [petitioner's] Ramsay Hunt [s]yndrome." Pet. Ex. 30 at 8. He stated that "[t]hese possibilities are not mutually exclusive." Id. And when referring to his second mechanism, he referred to it as "[a] second possibility." Id. at 10. In his second expert report, Dr. Zamvil stated, "I suggested possible mechanisms for the association of Ramsay Hunt syndrome with [flu] vaccination." Pet. Ex. 32 at 5. At the hearing, Dr. Zamvil testified about "one possibility" and a "second possibility." Tr. 139, 148. He also referred to his proposed mechanisms at the hearing as "one possibility, the first possibility" and "the other possibilities." Tr. 159.

Opinions expressed as possibilities, however, are not sufficient to establish causation. See, e.g., Garner v. Sec'y of Health & Hum. Servs., No. 15-063V, 2017 WL 1713184, at *16 (Fed. Cl. Spec. Mstr. Mar. 24, 2017) (providing the petitioner's expert provided conclusory reasoning for "possible" vaccine causation is "not sufficient"), mot. for rev. denied, 133 Fed. Cl. 140 (2017); LaCour, 1991 WL 66579, at *5 ("Expert medical testimony which merely expresses the possibility—not the probability—of the occurrence of a compensable injury is insufficient, by itself, to substantiate the claim that such an injury occurred."); Moberly, 592 F.3d at 1322 (emphasizing that "proof of a 'plausible' or 'possible' causal link between the vaccine and the injury" does not equate to proof of causation by a preponderance of the evidence); Waterman,

[59] Specifically, Dr. Zamvil testified that "bystander activation . . . leads to the epitope spreading," but then clarified that "[he was] not saying that epitope spreading occurred." Tr. 167.

123 Fed. Cl. at 573-74 (denying petitioner's motion for review and noting that a possible causal link was not sufficient to meet the preponderance standard). While certainty is by no means required, a possible mechanism does not rise to the level of preponderance. Moberly, 592 F.3d at 1322.

In addition, in his second expert report, Dr. Zamvil declared, "I have made no 'causality claim' in this case, as asserted by Dr. Levinson." Pet. Ex. 32 at 8. This declaration is confusing and seemingly inconsistent with the purpose of his expert reports and testimony, which was to present casual theories about how vaccination could cause illness. This inconsistency is also present when Dr. Zamvil uses the words "possible" and "possibilities," alongside phrases like "medical certainty" and "more likely than not." He ultimately professed that he held his opinions to the standard of, "more likely than not." See id. Regardless, the undersigned found Dr. Zamvil's opinions to be less persuasive due to his inconsistent and confusing use of different standards, two of which are not applicable here (possibility and medical certainty).

Overall, the hypotheses suggested by Dr. Zamvil were underdeveloped and unsupported by evidence as they pertain to the cause of VZV reactivation. When evaluating whether petitioners have carried their burden of proof, special masters consistently reject "conclusory expert statements that are not themselves backed up with reliable scientific support." Kreizenbeck v. Sec'y of Health & Hum. Servs., No. 08-209V, 2018 WL 3679843, at *32 n.44 (Fed. Cl. Spec. Mstr. June 22, 2018), mot. for rev. denied, 141 Fed. Cl. 138 (2018), aff'd, 945 F.3d 1362 (Fed. Cir. 2020). "The undersigned will not rely on opinion evidence that is connected to existing data only by the ipse dixit of the expert. Instead, special masters are expected to carefully scrutinize the reliability of each expert report submitted." Prokopeas v. Sec'y of Health & Hum. Servs., No. 04-1717V, 2019 WL 2509626, at *19 (Fed. Cl. Spec. Mstr. May 24, 2019) (internal quotations omitted).

In summary, petitioner has not offered a sound and reliable medical theory in support of her claim. Thus, the undersigned finds petitioner has not met the preponderant evidentiary standard with respect to the first Althen prong.

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

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

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting Althen, 418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528. The

petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, petitioner may satisfy his burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

The central issue here is whether the flu vaccine caused petitioner's Ramsay Hunt syndrome. The undersigned finds petitioner has failed to prove by preponderant evidence that it did for the following reasons.

Petitioner had chickenpox as a child. Thus, she had the requisite infection with varicella zoster which must occur as a sort of condition precedent to reactivation of the virus. Petitioner's clinical course was consistent with Ramsay Hunt syndrome caused by VZV reactivation. Petitioner had the characteristic vesicles, which confirmed the diagnosis of Ramsay Hunt syndrome. Moreover, the medical literature shows VZV reactivation is the cause of Ramsay Hunt syndrome. All of the experts agreed on this point.

The undersigned generally finds opinions of a treating physician to be persuasive evidence of causation. While some of petitioner's treating physicians noted the temporal association between petitioner's flu vaccine and the onset of her Ramsay Hunt syndrome, none of them opined that her Ramsay Hunt syndrome was caused by her vaccination. This is particularly important because she was seen by so many physicians and specialists.

One of petitioner's treating physicians, Dr. Stracher, stated, "probably avoiding flu vaccine in future is reasonable." Pet. Ex. 13 at 23. This statement is minimally supportive, but not persuasive evidence of causation in the context of all of the facts and circumstances here. The statement suggests that Dr. Stracher supported petitioner's request to avoid the flu vaccine in the future. Similarly, a record identifying an allergy to the flu vaccine does not constitute evidence of causation. Allergies are often reported by patients, and without additional supportive evidence, notations of allergies may not provide persuasive evidence of causation.

The statement by Dr. Stracher is similar to that discussed in Austin. Austin v. Sec'y of Health & Hum. Servs., No. 05-579V, 2018 WL 3238608 (Fed. Cl. Spec. Mstr. May 15, 2018), mot. for rev. denied, 141 Fed. Cl. 268 (2018), aff'd, 818 Fed. App'x 1005 (Fed. Cir. 2020). In Austin, a treating physician adjusted the child's vaccination schedule due to concerns by the parents about possible adverse side effects. Id. at *27. Chief Special Master Corcoran found that the physician's actions of changing the vaccination schedule, without more, was "not sufficiently strong" evidence of causation. Id. While a "treating physician's recommendation to withhold a particular vaccination can be probative evidence of a causal link between the vaccination and an injury sustained, special masters are less likely to find a causal link where the treater does not seem to have a sound scientific rationale—or, as here, offers no explanation at all." Id.

While her treating physicians did not attribute her Ramsay Hunt syndrome to the flu vaccine, Dr. Rubinstein did question whether petitioner's Ramsay Hunt syndrome and recurrences were due to EGPA. He stated, "[t]he Ramsay Hunt syndrome and recurrent shingles

may also be due to the immune activation in [EGPA] leading to persistence of VZV infection." Pet. Ex. 28 at 2. Because he did not evaluate petitioner until later in time, his opinions were necessarily based on his review of medical records and/or a history provided by petitioner. Moreover, he used the word "may," which suggests that while he questioned the relationship between petitioner's EGPA and Ramsay Hunt syndrome, his opinion was not held to the standard of "more likely than not."

The experts devoted substantial time to the issue of whether petitioner's eosinophilia or undiagnosed EGPA played a role in the development of her Ramsay Hunt syndrome. Petitioner received the flu vaccine at issue on January 4, 2013. Prior to her vaccination, she had a history of asthma that was significant enough to require treatment with Albuterol, Advair, and Singulair. In 2010, she had two episodes of upper respiratory infections. In January and March 2011, she again had complaints of nasal congestion, sore throat, and symptoms consistent with upper respiratory infections. She continued to take medications for her asthma. Notably, petitioner had elevated eosinophils in March 2011.

Petitioner's experts opined that there was no significant evidence that petitioner's eosinophilic illness pre-dated her vaccination on January 4, 2013. Dr. Zamvil did not consider EGPA or an eosinophilic illness to be a potential cause of petitioner's Ramsay Hunt syndrome. He did not believe that petitioner had any pre-exiting condition that contributed to her Ramsay Hunt syndrome. Dr. Gershwin concurred, although he agreed that in hindsight, the onset of petitioner's EGPA was when she had positive ANCA results, which occurred in November 2013.

Respondent's expert, Dr. Chaudhry, opined that petitioner had EGPA prior to her flu vaccine and Ramsay Hunt syndrome. Based on petitioner's history of asthma, episodes of nasal congestion in 2010 and early 2011, and elevated eosinophils in March 2011, he placed onset of petitioner's EGPA in March 2011. However, as he explained at the hearing, he did not hold this opinion to the standard of more likely than not. Dr. Levinson, like Dr. Chaudhry, also questioned whether petitioner's underlying systemic vasculitis played a role in the development of her Ramsay Hunt syndrome. But, like Dr. Chaudhry, Dr. Levinson also did not hold these opinions to a reasonable degree of probability. In conclusion, they agreed with Dr. Rubinstein.

The undersigned acknowledges that petitioner is not required to eliminate other potential causes in order to be entitled to compensation. See Walther v. Sec'y of Health & Hum. Servs., 485 F.3d 1146, 1149-52 (Fed. Cir. 2007) (finding petitioner does not bear the burden of eliminating alternative independent potential causes). However, she finds it reasonable to consider "evidence of other possible sources of injury"—here, petitioner's EGPA illness—in determining "whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."[60] Stone v. Sec'y of Health & Hum. Servs., 676 F.3d 1373, 1379 (Fed. Cir. 2012). "[T]he presence of multiple potential causative agents makes it

[60] In the parties' joint submission, the parties identify a fact in dispute regarding the role, [. . .]. However, there was no evidence to suggest that [. . .] use caused or contributed to her development of Ramsay Hunt syndrome. Thus, the undersigned finds that [. . .] is not relevant to the issue of her alleged vaccine-related injury.

difficult to attribute 'but for' causation to the vaccination." Pafford, 451 F.3d at 1358-59; see also Walther, 485 F.3d at 1151 n.4.

As to the recurrent episodes of Ramsay Hunt syndrome, Dr. Zamvil testified that he never intended to argue that they were caused by the flu vaccine. His point was that once Ramsay Hunt syndrome was triggered, it was more likely that petitioner would have recurrences. However, the undersigned has found that petitioner has failed to prove that the flu vaccine can cause Ramsay Hunt syndrome. Therefore, and for the reasons described above, the undersigned finds that the petitioner has failed to prove that the flu vaccine caused her initial episode of Ramsay Hunt syndrome.

Because the petitioner has not proven that the vaccination caused her initial episode of Ramsay Hunt, it follows that petitioner has failed to prove that the vaccination caused any of petitioner's recurrences. This finding is consistent with petitioner's clinical course described in the medical records, and as described by Dr. Chaudhry.

Moreover, as testified to by Dr. Chaudhry, and supported by the medical literature, there is no need to implicate any trigger in the development of petitioner's Ramsay Hunt syndrome. While there are some risk factors associated with VZV reactivation, it occurs in the absence of any such risk factors. As Dr. Chaudhry opined, it is not necessary to invoke the flu vaccine as a cause, when no trigger is necessary for VZV reactivation to occur.

For all of the reasons described above, the undersigned finds that petitioner has failed to provide preponderant evidence of a logical sequence of cause and effect required under Althen Prong Two.

3. Althen Prong Three: Proximate Temporal Relationship

Under Althen Prong Three, petitioner must provide "preponderant proof that the onset of symptoms occurred within a time frame for which, given the understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352. The acceptable temporal association will vary according to the medical theory advanced in the case. See Pafford, 451 F.3d at 1358. A temporal relationship between a vaccine and an injury, standing alone, does not constitute preponderant evidence of vaccine causation. See, e.g., Veryzer, 100 Fed. Cl. at 356 (explaining that "a temporal relationship alone will not demonstrate the requisite causal link and that petitioner must posit a medical theory causally connecting the vaccine and injury"), aff'd, 475 F. App'x 765 (Fed. Cir. 2012).

Dr. Zamvil's opinions as to onset were a bit inconsistent. In an expert report, he opined that the onset of petitioner's Ramsay Hunt syndrome two weeks after vaccination. He opined that this time frame was consistent with the patient described by Gurbuz et al., who developed painful vesicles in her right ear approximately 20 days after vaccination, and facial palsy two days later. However, the Gurbuz et al. authors did not implicate the theory of molecular mimicry as the causal mechanism of the patient's Ramsay Hunt syndrome.

At the hearing, Dr. Zamvil testified that petitioner's onset was six days. He opined that she likely had a secondary immune response or amplification, and that the time frame from vaccination to onset was "very short, within a matter of four to ten days," although he also stated that onset could occur up to a month after vaccination. Tr. 175. Dr. Zamvil opined that the onset of petitioner's illness was appropriate based on his mechanistic theories.

Respondent's experts did not refute the fact that there was a temporal association between petitioner's flu vaccination and the onset of her Ramsay Hunt syndrome.

Regardless of the minor inconsistencies in Dr. Zamvil's opinions as to Althen Prong Three, the undersigned finds there was a temporal association between vaccination and the onset of petitioner's Ramsay Hunt syndrome. However, a temporal association alone is insufficient for petitioner to show vaccine causation for her alleged injury, and thus, petitioner is not entitled to compensation.

VIII. CONCLUSION

It is clear from the medical records and hearing testimony that petitioner has experienced significant pain and suffering, and she has undergone extensive surgical procedures and treatment for her Ramsay Hunt syndrome, as well as her other illnesses. The undersigned extends her sympathy to petitioner for the tremendous hardships she has experienced. However, the undersigned's Decision cannot be based upon sympathy for the petitioner but rather an analysis of the evidence and application of the law.

For the reasons discussed above, the undersigned finds that petitioner has not established by preponderant evidence that she is entitled to compensation and her petition must be dismissed. In the absence of a timely filed motion for review pursuant to Vaccine Rule 23, the Clerk of Court **SHALL ENTER JUDGMENT** in accordance with this Decision.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master