In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: October 23, 2025

NAOMI DELGADO,	*	
	*	
Petitioner,	*	No. 17-1382V
	*	
v.	*	Special Master Young
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
	*	
Respondent.	*	

Jeffrey S. Pop, Jeffrey S. Pop & Associates, Beverly Hills, CA, for Petitioner.
Mitchell Jones, United States Department of Justice, Washington, DC, for Respondent.

ENTITLEMENT DECISION[1]

On September 29, 2017, Naomi Delagado ("Petitioner") filed a petition for compensation pursuant to the National Vaccine Injury Compensation Program.[2] Pet. at 1, ECF No. 1; 42 U.S.C. §§ 300aa-1 to -34 (2018). Petitioner alleges that the Prevnar 13 vaccine she received on June 15, 2015, was the cause-in-fact of her asthma, "a condition she did not previously have." Pet. at 1. Petitioner amended her petition on November 11, 2019, to allege "[i]n the alternative, the Petitioner's pre-existing asthma which was stable and controlled was substantially aggravated by the Prevnar 13 vaccination." Am. Pet. at 10, ECF No. 36.

A careful analysis and weighing of all the evidence and testimony presented in this case in accordance with the applicable legal standards,[3] reveals that Petitioner has failed to provide

[1] Because this Decision contains a reasoned explanation for the action taken in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). This means the Decision will be available to anyone with access to the internet. In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, I agree that the identified material fits within this definition, I will redact such material from public access.

[2] National Childhood Vaccine Injury Act of 1986, Pub L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2018).

[3] While I have reviewed all of the information filed in this case, only those filings and records that are most relevant to the decision will be discussed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("[w]e generally presume that a special master considered the relevant record evidence

preponderant evidence that the Prevnar 13 vaccine she received on June 15, 2015, was the cause-in-fact of her asthma or a significant aggravation of her asthma. Accordingly, Petitioner is not entitled to an award of compensation.

I. Procedural History

Petitioner filed her petition on September 29, 2017. Pet. She filed an affidavit and medical records on October 24, 2017. Pet'r's Exs. 1–3, ECF No. 8. On March 23, 2018, Petitioner filed an expert report from Hermes J. Garban, M.D., Ph.D., and supporting medical literature. Pet'r's Exs. 4–13, ECF No. 13. Petitioner filed additional medical records on June 22 and July 12, 2018. Pet'r's Exs. 14–15, ECF Nos. 17, 19. Respondent filed his Rule 4(c) report arguing against compensation on October 11, 2018. ECF No. 23.

On December 28, 2018, Petitioner filed another expert report from Dr. Garban and medical literature. Pet'r's Exs. 16–18. On May 22, 2019, Respondent filed an expert report from Emil Bardana, Jr., M.D., and supporting medical literature. Resp't's Exs. A–B, ECF No. 27. Petitioner filed an expert report from Petitioner's treating physician, Stasha Novakovic, M.D., on November 1, 2019. Pet'r's Exs. 19–20, ECF No. 30. Medical literature supporting Dr. Novakovic's opinions was filed on November 4, 2019. Pet'r's Exs. 21–36, ECF Nos. 31–32. Petitioner filed an amended petition on November 11, 2019. Am. Pet.

Respondent filed supplemental expert reports from Dr. Bardana and medical literature on February 18, 2020. Resp't's Exs. C–D, ECF No. 44. Petitioner filed additional medical records on June 2, 2020. Pet'r's Exs. 40–41, ECF No. 48. On June 3, 2020, Petitioner filed a supplemental expert report from Dr. Novakovic and medical literature. Pet'r's Exs. 42–46, ECF No. 49. And on July 20, 2020, Petitioner filed a supplemental report from Dr. Garban. Pet'r's Exs. 47–48, ECF No. 51. On November 25, 2020, Respondent filed a supplemental report and medical literature form Dr. Bardana, and an expert report from Derek E Byers, M.D., Ph.D, and supporting medical literature. Resp't's Exs. E–G, ECF No. 54–55. On March 10, 2021, Petitioner filed supplemental expert reports and medical literature from Dr. Garban and Dr. Novakovic. Pet'r's Exs. 49–55, ECF No. 57.

On March 15, 2022, I held a Rule 5 conference where I told Petitioner that her theory pursuant to *Althen* prong one was unclear. ECF No. 59. Petitioner requested sixty days to clarify her theory. *Id.* On May 23, 2022, Petitioner filed declarations from her husband and daughter. Pet'r's Exs. 56–57, ECF No. 61. On June 1, 2022, Petitioner filed a supplemental expert report from Dr. Garban and medical literature. Pet'r's Exs. 58–65, ECF Nos. 62, 64. Respondent filed a supplemental expert report from Dr. Byers on December 19, 2022. Resp't's Ex. H, ECF No. 69.

On June 28, 2023, an entitlement hearing was scheduled for October 2024. ECF No. 70. Petitioner filed additional medical records and medical literature on June 24, September 30, October 2, October 3, and October 11, 2024. Pet'r's Ex. 66, ECF No. 72; Pet'r's Exs. 69–87, ECF

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even though he does not explicitly reference such evidence in his decision.") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.*, 527 F. App'x 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered.").

Nos. 77, 79, 85, 88. On July 5, 2024, Petitioner filed her pre-hearing brief. Pet'r's Br., ECF No. 74. Respondent filed his responsive pre-hearing brief on September 17, 2024. Resp't's Br., ECF No. 76. Petitioner filed a reply brief on October 3, 2024. Pet'r's Reply, ECF No. 84. An entitlement hearing was held on October 10 and 11, 2024. Min. Entry, docketed Oct. 11, 2024. No post-hearing briefs were filed.

II. Factual Background

A. Medical Records

Petitioner's pre-vaccination medical history is significant for a pulmonary disease. *See* Pet'r's Ex. 40 at 2. On December 23, 2003, Petitioner was seen in urgent care for diabetes complications. Pet'r's Ex. 40 at 168. During that visit, she also complained of shortness of breath ("SOB"), and cough. *Id.* She was diagnosed with bronchitis, and instructed to use "an Albuterol inhaler, two puffs four times daily to improve her breathing." *Id.* at 162. Petitioner continued to complain of this cough during a January 16, 2004 visit to the emergency department ("ED"), and noted that it had been productive for three weeks. *Id.* at 165. She was diagnosed with "recurrent bronchitis" and the albuterol medication was continued. *Id.* at 166.

One of the earliest mentions of "possible asthma" was within a medical record from a primary care physician ("PCP") visit, dated October 24, 2007. Pet'r's Ex. 14 at 534. In her medical history, it was noted that she complained of chronic cough for two months and SOB without wheezing. *Id.* at 531. The record also noted no history of asthma. *Id.* She was prescribed an albuterol inhaler and instructed to "use [two] puffs by mouth every [six] hours for [SOB]." *Id.* at 532. A medical record dated March 23, 2008, from the West Palm Beach VA Medical Center ("WPBVAMC"), noted 'asthma' under nursing discharge instructions with general information and a warning that "[r]epeat attacks are common." *Id.* at 456–57. Petitioner presented to the ED on April 4, 2008, with complaints of coughing and wheezing. Pet'r's Ex. 14 at 449. She reported that she had been to the ED multiple times for the same complaints. *Id.* "When she is given albuterol, steroids, and antibiotics she improves but relapses when weaned off steroids." *Id.* Treater impressions included chronic cough, wheezing, and seasonal allergies. *Id.* at 452. She was referred to a pulmonologist. *Id.*

On April 14, 2008, Petitioner was seen by Dr. Sateesh Veeramachaneni for a pulmonary consultation. Pet'r's Ex. 14 at 432. She had complaints of "cough with productive sputum approximately [seven] months duration and wheezing of [six] weeks duration." *Id.* Petitioner had been to the ED multiple times and been treated with steroids and antibiotics. *Id.* Petitioner reported that she was a former smoker with a history of gastroesophageal reflux disease ("GERD") and had a penicillin allergy. *Id.* Her active medications included an albuterol inhaler and prednisone for exacerbation of chronic obstructive pulmonary disease ("COPD")/asthma; flunisolide nasal spray and loratadine for allergies; mometasone furoate for breathing and guaifenesin for cough; and additional medications for infection, pain, and diabetes. *Id.* at 432–33. Physical examination revealed "hazy density throughout the upper mid and lower lung zone," which Dr. Veeramachaneni noted was "most likely secondary to a poor inspiratory effort or lack of ability to cooperate with inspiration." *Id.* at 434. Dr. Veeramachaneni also noted "subtle peripheral septal thickening in the subpleural region in the upper mid and lower lung zones [and] mild

bronchiectasis [] at the lung bases posteriorly." *Id.* She assessed Petitioner with bronchiectasis and reactive airway disease.[4] *Id.* at 435.

On May 16, 2008, Petitioner was seen at WPBVAMC for a follow-up for her bronchiectasis. Pet'r's Ex. 14 at 426. Pulmonary function testing ("PFT") revealed restrictive disease "most probably secondary to obesity," and a chest computed tomography ("CT") showed pleural changes and increased size of pulmonary arteries. *Id.* Notes from Petitioner's PCP dated July 8, 2008, indicated that she was seeing a pulmonologist for her bronchiectasis but that "[h]er cough ha[d] resolved, and she [was] no longer needing albuterol." *Id.* at 417. An ophthalmology note for an unrelated examination, dated May 19, 2009, listed Petitioner's medical history, including diabetes (on insulin) and COPD/asthma. *Id.* at 351.

The following chart summarizes Petitioner's pre-vaccination pulmonary history.[5] *See* Pet'r's Ex. 14 at 126–548.

Date/Location	**Symptoms**	**Assessment/Diagnosis**	**Treatment**
10/24/07 PCP	Chronic cough, SOB, fatigue	Cough- likely due to GERD, possible asthma	Albuterol inhaler
03/14/08 ED	Cough with yellow sputum, wheezing, SOB, low grade fever	Bronchitis	Inhaler, antibiotics, steroid
03/22/08 ED	Persistent productive cough, wheezing, SOB	Asthma exacerbation	Nebulized bronchodilators, intravenous steroids
04/05/08 ED	Coughing and wheezing	Hypersensitive pneumonitis rule out bronchial asthma	Inhaler and steroids
04/15/08 Pulmonary specialist	Cough and wheezing	Bronchiectasis, reactive airway disease	Steroid inhaler, allergy medication, cough suppressant
07/08/08 Pulmonary specialist	No complaints	Bronchiectasis without acute exacerbation	Off albuterol

On June 15, 2015, Petitioner received a pneumococcal vaccine "with no noted adverse reactions." Pet'r's Ex. 3 at 907. Four days later, on June 19, 2015, Petitioner reported to the ED with complaints of "wheezing and coughing since Tuesday[, June 16, 2015]." *Id.* at 900. Petitioner continued that she was also experiencing "productive cough, chills, SOB and vomiting since Tuesday[,] a day after receiving the [pneumococcal] shot, [she was] currently [a]febrile although having a hard time breathing." *Id.* Petitioner stated that the evening of her vaccination, "she began developing generalized malaise," and that she "ha[d] never experienced symptoms this severe in the past." *Id.* at 887. Petitioner denied a history of asthma. *Id.* Dr. Bijal Asrani diagnosed Petitioner

[4] Reactive airway disease refers to "any of several conditions characterized by wheezing and allergic reactions; the most common ones are asthma, bronchiolitis, and chronic obstructive lung disease." *Reactive Airway Disease*, DORLAND'S MED. DICTIONARY ONLINE.

[5] This is also discussed by Petitioner's expert, Dr. Novakovic, during his testimony. Tr. 58–73

with "[S]tatus asthmaticus: in the setting of recent viral [upper respiratory tract infection ("URI")]." *Id.* at 889. Other diagnoses included tachycardia, leukocytosis, and hyperglycemia in the setting of type two diabetes mellitus. *Id.* at 890. She was administered nebulizer and steroid treatments. *Id.* Petitioner was admitted to the hospital and underwent an intensive care unit ("ICU") consultation for noninvasive positive pressure ventilation. *Id.* There was "no evidence of respiratory fatigue." Pet'r's Ex. 15 at 9. Petitioner was "clinically improved/resolved, no longer tachypneic and able to ambulate without [SOB]." *Id.* She was discharged on June 23, 2015. *Id.*

Petitioner was treated again at the ED for "increasing wheezing and cough with occasional white phlegm and shortness of breath," on July 4, 2015. Pet'r's Ex. 3 at 794. She was diagnosed with bronchiectasis and treated with steroids. *Id.* On July 9, 2015, a high-resolution CT scan of the chest showed borderline bronchiectasis. *Id.* at 136–37. She returned to the ED on July 19, 2015, with worsening SOB after her steroid treatment concluded. *Id.* at 764. Petitioner was admitted and underwent a pulmonary consult with Dr. Stasha Novakovic, who recommended treatment with IV steroid, an IV antibiotic, and frequent scheduled bronchodilators. *Id.* at 757. He also advised Petitioner of the importance of avoiding triggers, optimal medications, and proper inhaler technique. *Id.* She was discharged home on July 25, 2015. Pet'r's Ex. 15 at 5–8.

On August 12, 2015, Petitioner saw Dr. Novakovic in the pulmonary clinic. Pet'r's Ex. 3 at 636. Dr. Novakovic noted that "though she carrie[d] a diagnosis of bronchiectasis, a CT of the thorax from July show[ed] barely increased dilatation of the airways with no other parenchymal abnormalities or complications of bronchiectasis." *Id.* Petitioner reported that she felt better since her discharge but had not returned to her baseline. *Id.* at 637. The assessment was "newly diagnosed, and uncontrolled asthma. She ha[d] a minimal component of bronchiectasis but this [was] not the primary issue." *Id.* Petitioner returned to the pulmonary clinic on September 22, 2015, and reported that she "had an exacerbation for the past week. Though she was better that day, she was still short of breath and had a persistent cough." *Id.* at 621. Imaging did "not show any pulmonary abnormalities." *Id.* at 622.

Two days later, on September 24, 2015, Petitioner came into the ED with an asthma attack that began the previous day and had worsened. Pet'r's Ex. 3 at 616. She had a consultation with Dr. Novakovic who noted that "after not having respiratory symptoms for [eight] years, this [was] her third exacerbation requiring hospitalization in the last three months." *Id.* at 607. Dr. Novakovic further noted that Petitioner's IgE was high and would qualify her for Xolair. *Id.* at 608. She improved with treatment and was discharged home on September 28, 2015. *Id.* at 539.

Petitioner had an allergy consult on October 21, 2015. Pet'r's Ex. 3 at 529. She reported a history of "recent asthma onset since she received her first Prevnar-13 shot on June 15, 2015." *Id.* "Problems started that night with her arm hurting and then she started having problems breathing." *Id.* Petitioner had "[h]igh total IgE" and a skin test positive to dust mites. *Id.* at 532. She was diagnosed with recent onset bronchial asthma. *Id.*

Since September 2015, Petitioner has continued to be seen regularly in the Pulmonary Clinic at the VA Medical Center. *See generally* Pet'r's Exs. 3, 15. She was started on Xolair on October 26, 2015. Pet'r's Ex. 3 at 526. A medical record dated April 27, 2018, detailed how Petitioner "was asymptomatic until she received a Prevnar shot in June 2015. This seems to have

triggered her asthmatic symptoms." Pet'r's Ex. 15 at 33. Petitioner reported that she had "mild intermittent exacerbations, but overall [she was] doing much better than before." *Id.* Her Xolair dosage had been decreased from biweekly to monthly since January 2015, and she used a rescue inhaler about three times per day. *Id.*

B. Lay Witnesses

1. Petitioner's Affidavit & Fact Testimony

Petitioner submitted an affidavit dated September 25, 2017. Pet'r's Ex. 1. She stated that prior to her June 15, 2015 Prevnar 13 vaccine, she "did not have any asthmatic symptoms." *Id.* at ¶ 4. Petitioner acknowledged "a respiratory issue diagnosed as bronchiectasis without exacerbation that resolved by approximately October 2007." *Id.* She noted that her diagnosis was reclassified from active to nonactive. *Id.*

The affidavit described how shortly after her vaccination, that same day, Petitioner "developed a rash and itching." Pet'r's Ex. 1 at ¶ 5. Her additional symptoms including coughing, wheezing, and breathing difficulties started the next day. *Id.* Petitioner provided a chronology of her symptoms and treatment consistent with her medical record post vaccination. *See id.* at ¶¶ 2–6. She noted that any "[c]itations to the medical records are from [her] attorneys' review of the medical records. Many of the dates referred to are based on those records." *Id.* at ¶ 3.

Petitioner testified at the hearing on October 10, 2024. Tr. 12–32. She explained that prior to 2007, her medical history included diabetes, neuropathy, bronchiectasis, and pulmonary hypertension. Tr. 14. She also noted her chronic back pain and history of GERD. Tr. 15. Despite Petitioner's history, she asserted that from December 19, 2008, through the time of her Prevnar 13 vaccine, she never had a problem that necessitated the use of her inhaler. Tr. 19–20. Petitioner stated that she kept the prescription filled, although she "never had a problem." Tr. 19. After the vaccination, Petitioner detailed how she developed what she characterized as severe asthma. Tr. 23–28. She acknowledged that she "wasn't perfectly healthy, but the asthma did a job on [her]. Tr. 28. She noted that at the time of her testimony that she was having breathing difficulties due to the weather. Tr. 28. She also described the inability to breathe when encountering lingering second-hand smoke residue, cleaning agents, and certain perfumes and deodorants. Tr. 26–27. Before her vaccination, Petitioner stated that "was a lot happier, [] and doing things before [she] got asthma." Tr. 28.

2. Andres Delgado, Sr.'s Declaration & Fact Testimony

Mr. Delgado, Sr., Petitioner's husband, submitted a declaration on May 23, 2022. Pet'r's Ex. 56. He noted that the "[c]itations to the medical records are from [his] wife's attorney's review of the medical records." *Id.* at ¶ 4. Mr. Delgado, Sr., described how for several years pre vaccination his wife "did not have any noticeable asthmatic symptoms or respiratory problems." *Id.* at ¶ 5. Less than an hour and a half post vaccination, on June 15, 2015, Petitioner complained to him of itching at the injection site that began immediately after the shot. *Id.* at ¶ 7. The location was also red and welting. *Id.* He noted that "[w]ithin approximately an hour, she started coughing. *Id.* Mr. Delgado, Sr., continued that "the following day, [Petitioner] did not improve and she was

wheezing along with coughing." *Id.* at ¶ 8. He ultimately took her to the ED after four days of her symptoms worsening, on June 19, 2015. *Id.* at ¶ 12. He described her as "wheezing heavily, had more trouble breathing[,] and even had trouble speaking." *Id.*

Petitioner's husband also testified at the entitlement hearing. Tr. 33–50. He stated that he was unaware of any occasions that Petitioner saw a health care provider for any breathing issues from 2010 up to her Prevnar 13 vaccination. Tr. 38. He added that there were no environmental changes during that time, nor did she develop any allergy symptoms, including sneezing or runny eyes. Tr. 39. Mr. Delgado, Sr., briefly described the days immediately following Petitioner's vaccination, and his account was consistent with the medical records and Petitioner's testimony. He testified that currently, Petitioner still has breathing issues, and she has difficulty around chemicals that did not affect her pre vaccination. Tr. 43–44. On cross examination, Mr. Delgado, Sr., explained that in 2015, Petitioner's daughter, Ms. Delgado lived with them, and she was a smoker. Tr. 46. He explained that she only smoked outside, but that she would come into the home wearing clothes that were exposed to her smoking. *Id.*

3. Maria Delgado's Declaration

Maria Delgado is the adult daughter of Petitioner, and she provided a declaration dated May 23, 2022. Pet'r's Ex. 57. Ms. Delgado remembered that Petitioner complained of arm pain after her vaccination, and later that evening, Petitioner "thought she was having a reaction to the vaccination." *Id.* at ¶ 5. Ms. Delgado noted that her mother's health changed after her vaccine. *Id.* at ¶ 6. She described how, "[s]ince that time, she has had some trouble breathing and asthma." *Id.* Prior to her mother's vaccination, Ms. Delgado "was not aware that [Petitioner] had asthma or had trouble breathing." *Id.* at ¶ 7.

III. Experts

A. Expert Qualifications

1. Petitioner's Expert, Hermes J. Garban, M.D., Ph.D.

Dr. Garban is a biomedical scientist. Tr. 130. He received his M.D. from the Central University of Venezuela and his Ph.D. from the Department of Microbiology, Immunology and Molecular Genetics at the University of California, Los Angeles. Pet'r's Ex. 4 at 2. His "fields of expertise are in molecular immunology, immunotherapy and vaccine development, molecular/medical pharmacology." *Id.* He currently consults and advises companies and institutions on scientific and clinical direction. Pet'r's Ex. 67 at 1; Tr. 135–36.

2. Petitioner's Expert, Stasha B. Novakovic, M.D.

Dr. Novakovic is board certified in internal medicine and pulmonary and critical care. Pet'r's Ex. 19 at 1. He received his M.D. from St. George's University School of Medicine and subsequently completed a fellowship in pulmonary critical care at Jackson Memorial University. Pet'r's Ex. 68 at 1; Tr. 52–53. He is currently a full-time pulmonary and critical care physician at the Miami VA Medical Center. Tr. 54. Dr. Novakovic was Petitioner's treating clinician. Tr. 52.

3. Respondent's Expert, Emil J. Bardana, Jr., M.D.[6]

Dr. Bardana is board certified in allergy and immunology. Resp't's Ex. B at 3. He received his M.D. from McGill University Faculty of Medicine and subsequently completed an internship at University of California Medical Center and an internal medicine residency at Oregon Health Sciences University. *Id.* at 1. He retired from active practice in 2014 and is currently a Professor Emeritus at Oregon Health Sciences University. *Id.* at 2. He has numerous publications in the field of allergy and immunology. *See id.* at 21–40.

4. Respondent's Expert, Derek E. Byers, M.D., Ph.D.

Dr. Byers is a board-certified pulmonary and critical care physician. Resp't's Ex. F at 1. He received his M.D. from University of Texas Southwestern Medical School and his Ph.D. in immunology from University of Texas Southwestern Graduate School. Resp't's Ex. G at 1. He is currently a professor of medicine at Washington University and a practicing physician. Tr. 219. He specializes in lung transplantation. *Id.* His research focuses on cellular immunology and T-cell reactions. Tr. 220.

B. Expert Reports and Testimony

1. Petitioner's Expert, Dr. Garban

Dr. Garban summarized Petitioner's medical record pre and post vaccination, along with her declaration, and opined that "[b]ased on the provided [information], there is significant evidence to support the medical theory of vaccine-triggered allergic sensitization leading to the onset of severe asthma." Pet'r's Ex. 4 at 9. He then provided background information on Prevnar 13 and characterized asthma as complex, multifactorial, and heterogeneous. *Id.* at 10. Dr. Garban explained that asthma is a common, chronic, non-communicable disease with variable respiratory symptoms and air flow limitations among patients. *Id.* The type and intensity of airway inflammation is also heterogenic in presentation. *Id.* Referring to Petitioner's status asthmaticus diagnosis, Dr. Garban quoted Papiris et al.[7] to explain that this diagnosis "relates severity to outcome and has been used to define a severe asthmatic exacerbation that does not respond to and/or perilously delays the repetitive or continuous administration of short-acting inhaled β2-adrenergic receptor agonists (SABA) in the emergency setting." *Id.* (citing Pet'r's Ex. 8 at 1). The article noted that the clinical presentation can include "episodes of increased breathlessness, cough, wheezing, chest tightness[,] or some combination of these symptoms." Pet'r's Ex. 8 at 3. Development may be abrupt or progressive, and exacerbations "are always related to decreases in expiratory (and in severe cases also in inspiratory) airflows that should be quantified objectively by lung function measurements." *Id.* Cases of severe asthma are life-threatening, and progression can occur over minutes and hours or days and weeks. *Id.* The authors cautioned that a severe exacerbation may occur during the lifetime of any asthmatic person. *Id.* Furthermore, "[o]ccasionally, acute severe asthma may present as a new problem in a patient who is unaware of his or her asthma, and diagnosis needs to be established in the [ED]." *Id.*

[6] Dr. Bardana did not testify at the hearing.

[7] Spyros A. Papiris et al., *Acute Severe Asthma*, 69 DRUGS 2363 (2009).

The Papi et al.[8] seminar paper sought to "provide a clinically focused overview of asthma, including epidemiology, pathophysiology, clinical diagnosis, asthma phenotypes, severe asthma, acute exacerbations, and clinical management of disease." Pet'r's Ex. 9 at 1. The authors noted that "[e]sinophilic high type 2 airway inflammation is present in around 50% of adults with asthma." *Id.* at 2. Where there is inflammation, Dr. Garban explained that "airway edema [consists of] cellular infiltration by eosinophils (and in some cases neutrophils), activated CD4+ T lymphocytes and mast cells, and intra-luminal mucous plugs composed of mucin glycoproteins, plasma proteins, epithelial and inflammatory cells, and cellular debris." Pet'r's Ex. 4 at 10. Dr. Garban further explained that "allergic sensitization and consequent stimulation by dendritic cells adaptive T helper 2 (Th2) cells produce interleukin[s . . .]. IL-4 drives B-cell isotype switching and IgE synthesis, which binds to mast cell high-affinity IgE receptors, leading to mast cell activation." *Id.*

The Papi et al. paper also discussed non-eosinophilic asthma and described a "neutrophil-predominant [version of the] disease with release of cytokines from [T helper cells], lymphoid cells, with activation of macrophages and release of neutrophil chemokines." Pet'r's Ex. 9 at 2. The authors noted, "with bronchiectasis as a common comorbidity of severe asthma in adults, a neutrophilic response could reflect bacterial colonisation or effects of corticosteroids on promotion of neutrophil survival and suppression of type 2 immunity, leading to the upregulation of type 1 or type 17 immunity." *Id.* at 2. Dr. Garban addressed Petitioner's bronchiectasis diagnosis, describing it as a long-term lung condition characterized by wider than normal airways. Pet'r's Ex. 4 at 11. This disease "clinically may be associated with symptoms of chronic cough and expectoration, as well as a tendency to infections." *Id.* at 11. The accompanying airway obstruction "contribute[s] to obstructive airflow limitation, and accordingly [bronchiectasis] is also a differential diagnosis to asthma." *Id.* Therefore, Dr. Garban explained, "bronchiectasis is associated in high co-morbidity with severe asthma and should be consider as part of the differential diagnosis. However, both conditions on illnesses differ significantly in their pathophysiology and etiology." *Id.*

Dr. Garban also explained that Prevnar 13 includes aluminum phosphate, an adjuvant that "enhance[es] uptake by antigen presenting cells for presentation of the protein component to CD4+ T helper cells and the tendency to induce IgE-mediated immune responses." Pet'r's Ex. 4 at 10. He reasoned that Petitioner's positive response to omalizumab, an anti-IgE monoclonal antibody, "suggested a strong IgE connection between her allergic sensitization and her asthma condition," triggered by her Prevnar 13 vaccine. *Id.*

Dr. Garban opined that Petitioner's sensitization began as a type I allergy "characterized by specific IgE, a typical Th2 skewing associated with IL-4, IL-13 cytokines, sometimes accompanied by eosinophilic inflammation." Pet'r's Ex. 4 at 11. He highlighted the presence of aluminum phosphate and the "[u]ndesired properties of aluminum adjuvants [that] comprise acute and chronic inflammation at the injection site, its Th2 immune stimulatory capacity and potential allergenic outcome." *Id.* Although he did not identify an appropriate temporal relationship, Dr. Garban asserted that Petitioner's "allergic sensitization leading to the onset of severe asthma [] appeared to be within a medically accepted time frame to infer causation." *Id.* at 12.

[8] Alberto Papi et al., *Asthma*, 391 LANCET 783 (2018).

A supplemental expert report dated December 20, 2018, clarified Dr. Garban's characterization of Petitioner's reaction as a vaccine-mediated allergic sensitization and not an IgE-mediated hypersensitivity. Pet'r's Ex. 16. The Galli et al.[9] article provided the following relevant definitions:

1. **Allergy**- An abnormal adaptive immune response directed against non-infectious environmental substances (allergens), including non-infectious components of certain infectious organisms.
2. **Allergen**- Type I: any non-infectious environmental substance that can induce IgE production (thereby 'sensitizing' the subject) so that later re-exposure to that substance induces an allergic reaction. Type II: a non-infectious environmental substance that can induce an adaptive immune response associated with local inflammation but is thought to occur independently of IgE.
3. **Allergic inflammation**- The inflammation produced in sensitized subjects after exposure to a specific allergen(s). A single allergen exposure produces an acute reaction, which is known as an early-phase reaction or a type I immediate hypersensitivity reaction. In many subjects, this is followed by a late phase reaction.
    i. **Early-phase reaction**- An IgE-mediated type I immediate hypersensitivity reaction that can occur within minutes of allergen exposure. *Reactions can be localized (for example, acute asthma attacks).
    ii. **Late-phase reaction-** A reaction that typically develops after 2–6 h[ours] and peaks 6–9 h[ours] after allergen exposure. It is usually preceded by a clinically evident early-phase reaction and fully resolves in 1–2 days.
4. **Chronic allergic inflammation**- Persistent inflammation induced by prolonged or repetitive exposure to specific allergens, typically characterized not only by the presence of large numbers of innate and adaptive immune cells (in the form of leukocytes) at the affected site but also by substantial changes in the extracellular matrix and alterations in the number, phenotype and function of structural cells in the affected tissues.

Pet'r's Ex. 62 at 2.

Dr. Garban asserted that unlike a hypersensitivity, which manifests after re-exposure to an initial sensitizing agent, the mechanism at play here "involved an initial adjuvant-mediated immunoreactivity–triggered by the aluminum phosphate contained in the [Prevnar 13]–for primary immunization and priming (sensitizing) the immune system to further responses." Pet'r's Ex. 16 at 2. Petitioner's reaction hours following her vaccination, instead of immediately thereafter, "suggests an inflammatory-allergic-reaction following [Prevnar 13] vaccination." *Id.* "IgE-mediated sensitization, which is the propensity to develop IgE antibodies against common

[9] Stephen J. Galli et al., *The Development of Allergic Inflammation*, 454 NATURE 445 (2008).

environmental allergens, is associated with a lymphocyte [Th2] skewed immune response and a high risk of allergic respiratory disease." *Id.* Dr. Garban asserted that "IgE sensitization was associated with a higher risk of asthma." *Id.*

The Galli et al. article identified many factors that "affect the likelihood of developing clinically significant sensitization: host genotype, type of allergen, allergen concentration in the environment and [presences of enhancing agents], [and] the pattern of contact of the immune system with allergens." Pet'r's Ex. 62 at 4. In addition to defining key terms, the authors further explained the differences between the types of allergic inflammation. *Id.* at 5. Early phase or type I immediate hypersensitivity reactions "mainly reflect the secretion of mediators by mast cells at the affected site." *Id.* The mast cells in susceptible individuals "already have allergen-specific IgE bound to their surface high-affinity IgE receptors." *Id.* Galli et al. continued that this preformed mediator release "contributes to the acute signs and symptoms," and can include "contraction of bronchial smooth muscle (producing airflow obstruction and wheezing), and increased secretion of mucus (exacerbating airflow obstruction in the lower airways and producing a runny nose)." *Id.*

The authors next explained that late-phase reactions occur when "mast cells responding to IgE and allergen also release a broad range of newly synthesized cytokines, chemokines and growth factors," that "are released more slowly than the preformed mediators." Pet'r's Ex. 62 at 5. They acknowledged that "[i]t is not understood why [this does] not develop in all sensitized subjects," and noted that when it does occur, "there may be no clear clinical demarcation between the end of the early phase and the onset of the late phase." *Id.* at 7. In asthma patients, the late phase reaction is found in the lower airways and involve Th cells, eosinophils and monocytes. *Id.* Lastly, the authors explained how continuous or repetitive allergen exposure leads to persistent inflammation, and "changes in the structural cells at the affected sites" to cause chronic allergic inflammation. *Id.* There is no clear understanding of this process, but the authors noted this process occurs in chronic asthma patients. *Id.*

> The complex interactions between affected airway epithelial cells and the underlying mesenchymal cells, which together are known as the 'epithelial–mesenchymal trophic unit' and are thought to regulate the tissue remodeling characteristic of chronic allergic inflammation of the airways, have been likened to those at a persistent wound. In patients with asthma, mast cells can appear in increased numbers in the smooth muscle of the airway, placing this potent source of mediators that can influence smooth muscle function in intimate proximity to this crucial target-cell population. This may contribute to the development of 'non-specific airway hyperreactivity' to agonists such as histamine, cys-LTs and methacholine, which is a hallmark of asthma.

Id. at 8. The authors identified respiratory viruses including, rhinoviruses, influenza virus, and respiratory syncytial virus as common infections which "can produce a marked exacerbation of the signs and symptoms of asthma." *Id.* Furthermore, "[t]he increased levels of IgE observed in many allergic subjects can drive another amplification mechanism in allergic disorders." *Id.* at 8.

Dr. Garban also cited the Johansson et al.[10] article that explained revisions to the nomenclature re: allergic and allergy-like reaction proposed by the World Allergy Organization ("WAO") in 2003. Pet'r's Ex. 16 at 2 (citing Pet'r's Ex. 17). The article provided definitions for: (1) hypersensitivity- "objectively reproducible symptoms or signs initiated by exposure to a defined stimulus at a dose tolerated by normal persons," (2) allergy- "a hypersensitivity reaction initiated by specific immunologic mechanisms," and (3) atopy- "a personal and/or familial tendency, usually in childhood or adolescence, to become sensitized and produce IgE antibodies in response to ordinary exposures to allergens." *Id.*

According to the WAO, generally an allergy is not defined by increased IgE levels; although, a symptomatic inflammatory reaction that is IgE initiated may be dominated by allergen-specific monocytes. Pet'r's Ex. 17 at 2. "Asthma resulting from immunological reactions should be called allergic asthma." *Id.* A second article filed by Dr. Garban noted that a "higher risk of asthma associated with IgE sensitization is well known," but the authors also suggested that "reverse causation, i.e. infection/airway disease having an influence on IgE sensitization status," could be occurring. Pet'r's Ex. 18 at 9.[11] "[I]t is possible that, in persons with lower chronic airway disease, IgE sensitization does confer an increased risk of hospital admission due to exacerbation of disease." *Id.*

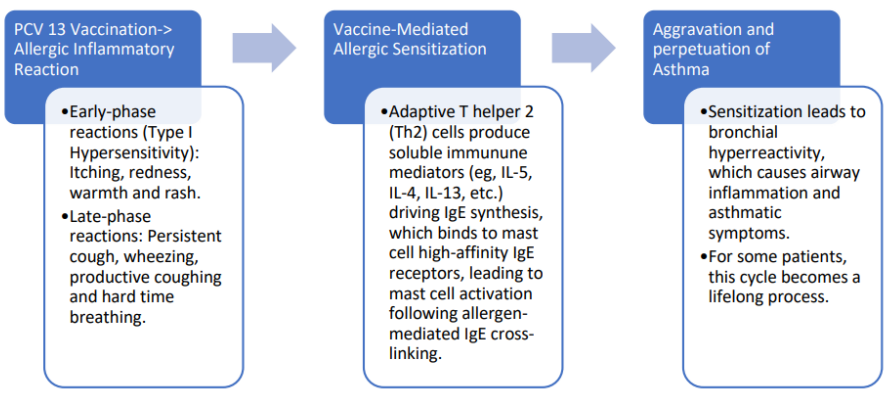
Dr. Garban's second supplemental report clarified that his theory is applicable to Petitioner to explain causation-in-fact, but he added that even "assuming [Petitioner] had controlled asthma, the evidence that the vaccine substantially aggravated her asthma turning it into a chronic condition of severe asthma is compelling." Pet'r's Ex. 37 at 2. A third supplemental report re-presented several arguments previously made and reiterated the significance of Petitioner's extreme exacerbation of symptoms following her vaccination. *See* Pet'r's Ex. 47. Dr. Garban also noted that Petitioner "did not have hypereosinophilia at any point in her life and she did not have elevated IgE until after hospitalized for severe asthma in 2015." *Id.* at 4. In a short follow-up report, Dr. Garban narrowed his biological mechanism to a vaccine-caused aggravation of Petitioner's (pre-existing and stable) asthmatic condition. Pet'r's Ex. 55 at 3. He noted that his theory is illustrated by Petitioner's vaccination to symptom temporality and "[c]linical evidence including positive therapeutic response." *Id.* Lastly, Dr. Garban advocated for "examin[ing Petitioner's] case in its singularity and not dilute it on a series of arguments and discussions pertaining to a generalization of the potential severe effects of a vaccine." *Id.*

A final supplement report filed by Dr. Garban was focused on "providing a single, cohesive theory to explain and address solely *Althen* prong one regarding how the Prevnar-13 can cause an allergic inflammatory reaction and aggravation of Petitioner's asthmatic stable condition." Pet'r's Ex. 58 at 1. He summarized his hypothesis with Figurine 1, reproduced below:

[10] S.G.O. Johansson et al., *Revised Nomenclature for Allery for Global Use: Report of the Nomenclature Review Committee of the world Allergy Organization, October 2003*, 113 J. Allergy Clinical Immunology 832 (2004).

[11] Tea Skaaby et al., *IgE Sensitization to Inhalant Allergens and the Risk of Airway Infection and Disease: A Population-Based Study*, 12 PLOS ONE (2017).

Figure 1.- Proposed scientific/medical rationale related to the matter of Mrs. Naomi Delgado.



Abbreviations: Th2= Adaptive T helper 2; IL-5= interleukin-5; IL-4=interleukin-4; IL-13= interleukin-13; IgE= Immunoglobulin E.

Id. at 4.

Dr. Garban continued to explain the specifics of Petitioner's injury during his testimony. *See* Tr. 130–210. He asserted that Petitioner suffered a Type 1 hypersensitive reaction "in the mild spectrum." Tr. 158. When asked if Petitioner's reaction would qualify as anaphylaxis, Dr. Garban stated that he "wouldn't call anaphylaxis what she had," but later added, "when she increased in the events that took her to a respiratory component, it could be an anaphylactic reaction that is not taken to the extreme side of very severe. It could be a mild anaphylaxis." Tr. 158–59. According to Dr. Garban, Petitioner "initially had a Type 1 hypersensitivity[, a]nd she manifest[ed], and it was documented that she started having itching, redness, the warm rash," and some inflammation. Tr. 159. Her symptoms "extended to the loss of function not only in the local area," known as an atopic reaction, but also to other areas, including asthma. Tr. 141. Dr. Garban explained that "acute or early phase of hypersensitivity, of hypersensitivity reaction happens from seconds, minutes and can be extended to hours." Tr. 141. Following this initial allergic inflammatory response, "in the later hours of development or days of development immediate to the vaccination, you have the late-phase development, which is the persistent cough that she started manifesting, . . . and also that hard time breathing." Tr. 159–60.

Vaccine-associated hypersensitivity reactions "are not uncommon," according to Dr. Garban, but he added that "severe hypersensitivity as anaphylaxis, for instance, they are really, really rare." Tr. 147. Indeed, "serious acute onset, presumably IgE-mediated or IgG and complement-mediated anaphylactic or serious delayed onset T-cell-mediated systemic reactions are considered extremely rare." Tr. 148. Dr. Garban asserted that any vaccine component "[f]rom the antigen that has been used to generate a specific target, also to the adjuvant and also to the stabilizing agent, the hard part of that," can cause a hypersensitivity reaction. Tr. 149. He specifically noted "the material that is the CRM 197, the aluminum phosphate or aluminum compounds in general and also the polysorbate [80]." Tr. 150.

The aluminum phosphate was of particular concern for Dr. Garban, because of its role "to not only enhance the immune response in terms of the vaccine, but also it serves as a depot to maintain a localized content of the vaccine in the site of injection in order to favor the immune response." Tr. 153. He asserted that there is new research on "the use of aluminum compounds in order to redirect the immune response toward a Th2-type of response that will elicit the production of cytokines," including IgE. *Id.* Dr. Garban continued, asserting that "aluminum phosphate will somehow bring the immune cells." Tr. 154. Some of those cells are there to generate cytokines that will switch IgG to IgE and lead to "induction of B-cells that are the ones that produce the immunoglobulins to the production of IgE." *Id.* This process is articulated in the HogenEsch[12] paper. *See* Pet'r's Ex. 7. HogenEsch asserted that "[a]luminum compounds can further enhance the immune response by direct or indirect stimulation of dendritic cells, activation of complement and by inducing the release of chemokines." Pet'r's Ex. 7 at 1. The depot effect, initially "suggested that the slow release of alum-precipitated antigens from the injection site resulted in prolonged exposure of the immune system to vaccine antigens" and it was thought that in the case of alum-precipitated diphtheria toxoid, "some antigen is retain[ed] at the injection site for at least [seven] weeks." *Id.* at 2. HogenEsch noted that later challenges to this theory "suggest that sustained release of antigen from a depot site over days or weeks is unlikely to contribute to the adjuvant effect of aluminum compounds." *Id.* Although Dr. Garban noted that CRM 197, polysorbate 80, and aluminum phosphate can work together to cause an immune-mediated response, in Petitioner's case, a hypersensitivity reaction "can turn into a[n] entirely different process that is modulating the immune system in order to acquire a different reactivity to a different component that w[as] not present even in the vaccine but to other environmental triggers and substance." Tr. 156.

The Verstraelen et al.[13] paper described "the mechanism and cell types involved in allergic asthma." Pet'r's Ex. 25 at 1. The authors described the disease as clinical and "characterized by airway obstruction, airway inflammation and airway hyperresponsiveness to a variety of stimuli." *Id.* The process begins with "[a]irway hyperresponsiveness and bronchial inflammation [following] the inhalation of an antigen." *Id.* at 3. The article explained how the allergen is intercepted by antigen presenting cells that activate helper T cells and lead to lymphocyte activation, including B cells. *Id.* "Allergic asthma is characterized by increased IgE production by B cells." *Id.* The authors asserted that the link between IgE and airway hyperresponsiveness is mast cells. *Id.* They explained that "[i]n the lungs, mast cells are found in bronchial airway connective tissues and in peripheral intra-alveolar spaces . . . and their numbers increase after allergen exposure." *Id.* Asthma patients have an increased number of localized mast cells "within the bronchial smooth muscle bundles and the bronchial epithelium, and infiltrate in the airway mucous glands." *Id.* Once re-exposed to the allergen, "cross-linking of antigen by mast cell IgE antibodies" on the receptor cell occurs. *Id.* "This cross-linking has been well documented to trigger activation of signaling cascades and causes mast cell degranulation and synthesis of proinflammatory molecules." *Id.* at 3–4. "Mediators produced by mast cells are categorized into preformed mediators, . . . [and t]hey cause the symptoms of immediate-type hypersensitivity." *Id.* at 4.

[12] Harm HogenEsch, *Mechanisms of Stimulation of the Immune Response by Aluminum Adjuvants*, 20 VACCINE 534 (2002).

[13] S. Verstraelen et al., *Cell Types Involved in Allergic Asthma and Their Use in* In Vitro *Models to Assess Respiratory Sensitization*, 22 TOXICOLOGY IN VITRO 1419 (2008).

Once an early-phase asthmatic reaction occurs, "a more severe and prolonged late-phase asthmatic reaction" may follow. Pet'r's Ex. 25 at 4. The article then explained how a hypersensitivity reaction can evolve into a chronic condition.

> In general, mast cell-derived mediators induce airway constriction, increase vascular permeability, enhance [airway hyperresponsiveness], induce mucus secretion, and promote the recruitment of inflammatory cells into the airways after several hours of allergen challenge, especially eosinophils, but also T cells, macrophages, basophils, neutrophils, and structural cells like epithelial cells, fibroblasts, endothelial cells, and [airway smooth muscle] cells. These inflammatory cells can produce a vast array of inflammatory mediators, namely chemokines, cytokines and [leukotrienes], that act either directly on the airway or indirectly through neural mechanisms, promoting the chronic characteristic of the airway inflammation after repeated allergen exposure. As a result of this chronic inflammation, airway tissue is continuously being injured and healed, leading to structural changes of the airways that may account for the decline in airway function seen in patients over the years. These structural changes are collectively referred to as airway remodeling.

Id. (internal citations omitted).

Dr. Garban described this secondary process as the adaptive Th2 response "that will produce immune mediators that will redirect the cells of the immune system to produce now immunoglobulin E. And this [] IgE, starts acting whenever they recognize the triggering substance that, again, [he] must emphasize, not necessarily are the same component of the vaccine." Tr. 161. Because the immune system is now sensitized according to Dr. Garban, "once it gets engaged, then it starts binding to these cells called mast cells through the high affinity receptor for IgE and so in that case trigger an allergic response." *Id.* This activity initiates "that bronchoreactivity, the bronchial reactivity that is a hallmark of the asthmatic response." *Id.* Dr. Garban was asked whether this Th2 cell activation occurred in the immediate or late phase of Petitioner's immune system response. Tr. 165. He stated, "what you have is probably on the late/early phase start," and continued, that "definitely in the first hours you have that window of engaging or engagement of a Th2 type of response. And this can last for days." *Id.* Without the vaccine, this IgE sensitivity would not have occurred. *Id.* Dr. Garban asserted that this hyperreactivity can cause an acquired sensitivity to new environmental triggers and "an allergic response, and in this case, an asthmatic atopic response." Tr. 162. He further argued that Petitioner's clinical management provided evidence of IgE mediation, "because then when she was treated with Xolair, that even a specific antibody that blocks that IgE, the binding of IgE to the mast cell, then the disease was a fairly controlled." Tr. 163.

Outside the context of vaccines, Dr. Garban testified about "examples in the scientific literature of aluminum salts inducing sensitization to substances that might not normally be considered as antigens." Tr. 163. This "possible indirect adjuvanticity" is also related to food allergies. *Id.* Dr. Garban suggested that a sensitivity reaction may have also been influenced by exposure to previous adjuvants or vaccine components. Tr. 166–67. Specifically, "in the case of

[Petitioner] somehow the presence of these adjuvants or components of vaccines of previous vaccine, might result or more likely than not resulted into that sensitization." Tr. 167. The period of four days between Petitioner's vaccination and her relevant symptoms "leading to the drastic aggravation of asthma symptoms suggested the engagement of a reactive Type 2 Th2 IgE-mediated inflammatory response responsible for the worsening of the respiratory symptoms and therefore setting the stage for a deteriorating chronic asthmatic condition." Tr. 169.

Dr. Garban summarized his causation theory as applied to Petitioner's case. He stated that Prevnar 13 vaccine components triggered an "allergic Type 1 hypersensitivity immune response." Tr. 170. During that response, Petitioner experienced "inflammatory signs, redness, swelling, heat, et cetera." *Id.* Dr. Garban asserted that Petitioner's reaction to her vaccination developed into "a more severe or a more elaborated allergic response" or atopy. Tr. 170–71. This included "another set of immune reactions that were happening there surrounding this event that promote an allergic sensitization . . . in the sight of the injection, but also it starts being more systemic." Tr. 171. Dr. Garban also described this process as a "chronic type of reactivity where then the deterioration of function or loss of function will -- of the immune system start having this reactivity to other kind of antigen." *Id.* There were no viral or bacterial infections identified in Petitioner's medical history that may have played a role in her symptoms. Tr. 172. Dr. Garban did note that Petitioner's pre-existing conditions and a "contributing comorbidity [] might [have] took that route that was triggered by the vaccine." *Id.* However, for Dr. Garban, Petitioner's "period of seven years without any respiratory event and after the vaccination, you start having cardinal signs and symptoms that start happening that's suggestions of an allergic reaction to the vaccination." Tr. 172–73. He described that reaction time as immediate, stating, "it's seconds to minutes that happen that kind of reactivity." Tr. 173.

Dr. Garban described the two stages of Type 1 hypersensitivity: immediate reactions and late-phase reaction. Tr. 174. The former, initial phase is "a sudden response within minutes of exposure to the allergen, while the late phase may develop [four] to 12 hours post early phase reaction and can last for up to 24 to 73 hours." Tr. 174. In Petitioner's case, "you have a clear Type 1 hypersensitivity exhibiting very beautiful distinction between the early and late phases of both and also the evolution into a possible or more likely than not circle where chronicity will establish then further sensitization." Tr. 174–75. Petitioner's cough and asthma exacerbation also provide clear evidence of vaccine causation, according to the Haber et al.,[14] article filed by Dr. Garban. *See* Pet'r's Ex 50 at 4. This article documented "adverse events reports following [Prevnar 13] in adults aged ≥19 years reported to the [VAERS] from June 2012 to December 2015." *Id.* at 1. There was one account each of cough, asthma exacerbations, and bronchospasm out of 138 medical conditions in non-death serious reports in persons aged ≥ 65 years following Prevnar 13 in VAERS. *Id.* at 4. The authors noted "the limitations of VAERS, which may include underreporting, varying quality of reports, and the lack of an unvaccinated comparison group." *Id.* at 5.

In response to my questioning, Dr. Garban asserted that Petitioner's status asthmaticus diagnosis from June 19, 2015, was the result of her increased sensitivity following her vaccination

[14] Penina Haber et al., *Post-Licensure Surveillance of 13-Valent Pneumococcal Conjugate Vaccine (PCV13) in Adults Aged ≥19 Years Old in the United States, Vaccine Adverse Event Reporting System (VAERS), June 1, 2012–December 31, 2015,* 34 VACCINE 6330 (2016).

and any subsequent asthmatic event would also relate back to her vaccination. Tr. 192. He clarified that any post-vaccination allergic reaction that Petitioner suffers affects the "reactivity of her airway" and is consistent with her June 19, 2015 presentation and could be rightly attributed to her vaccine. Tr. 208.

2. Petitioner's Expert, Dr. Novakovic

Petitioner's treater, Dr. Novakovic provided multiple expert reports and testimony in support of her claim. In his first report, Dr. Novakovic opined that "[t]he temporal relationship between the administration of the vaccine and the drastic worsening of [Petitioner's] asthma supports the conclusion that these two events are related." Pet'r's Ex. 19 at 3. He described how she first experienced symptoms of an adverse reaction to the vaccine "within an hour," and as her breathing worsened, "she had no choice but to seek help in the [ED]." *Id.* Dr. Novakovic noted that "there were no significant events affecting [Petitioner's] medical history or her respiratory system in the weeks and months prior to June 2015." *Id.* He specified that pre vaccination, there were no new respiratory symptoms; no "new environmental triggers, allergens, noxious fumes or inhalational toxins;" and no travel or address change. *Id.* "Following the vaccination, she became [Dr. Novakovic's] sickest asthma patient for a period of time and continues to struggle with her disease more than four years later." *Id.* Dr. Novakovic noted Petitioner's improvement but stated that she still requires injections and intermittent steroids. *Id.* He opined that "there is no medical basis to attribute her sudden decompensation in respiratory status to anything other than the vaccination." *Id.* Dr. Novakovic acknowledged "[e]ven though the facts of [Petitioner's] case strongly suggest a causative relationship, there have not been very many reported cases of asthma as a direct result of a pneumonia vaccine." *Id.* at 4.

Dr. Novakovic categorized Petitioner's urticaria, cough, wheezing and SOB as indicative of a type I hypersensitivity reaction to the vaccine. Pet'r's Ex. 14 at 4. He asserted that Petitioner's respiratory symptoms and ensuing "hypersensitivity reactions with manifestations centered in the lung" have been reported following exposure to injected allergens. *Id.* These reactions are generally short lived; however, Petitioner's asthma symptoms continue years later. *Id.* That is because "[t]he specific mediators generated by the [P]revnar vaccine, in contrast to traditional pneumococcal vaccines, turn out to be vital in the allergic response typical of asthma." *Id.* The conjugated nature of Prevnar 13 "elicit[s] a stronger immune response and activate[s] a cascade that is dependent on T-cells, in contrast to the T-independent responses of unconjugated vaccines." *Id.* at 5. T cells in turn drive production of antibodies, eventually IgE. *Id.* at 4. Dr. Novakovic stated that "[i]t is widely believed that Th2 cells play a pivotal role in the pathogenesis of asthma. These cells influence antibody production towards the generation of IgE." *Id.* at 4–5. Dr. Novakovic asserted that because of asthma's association with an IgE-reaction in almost all cases, "the sensitization to environmental triggers which is fundamental in asthma is [likewise] an IgE-driven process." *Id.* at 5. Conversely, exposure to allergens such as pet dander or dust mites is not a risk factor for individuals without IgE antibodies. *Id.* In lifelong asthmatics, "[t]he consistent allergic response caused by IgE over time is due to both the long life of IgE-secreting B cells as well as the stability of mast cells in the soft tissues." *Id.*

Dr. Novakovic argued that Petitioner's elevated IgE levels three months post vaccination "lends support to the argument that her immune system by that time was altered on a permanent

basis, since levels of IgE are generally not abnormally elevated in patients without pathology." Pet'r's Ex. 19 at 5. Her high levels are evidence of over sensitization "to common environmental triggers, leading to allergic and asthmatic symptoms." *Id.* This cycle of 1) sensitization, 2) trigger or infection, and 3) symptom manifestation that reinforces the sensitization, is "a lifelong process" in patients like Petitioner. *Id.*

The Cockcroft[15] book chapter on allergens was filed with Dr. Novakovic's report and cited to support his assertion that injected allergens can trigger respiratory reactions. *See* Pet'r's Ex. 23. Cockcroft asserted that ingested and injected allergens can trigger an isolated bronchial asthma that manifests as a type I-mediated hypersensitivity. *Id.* at 14. He offered that these reactions are occasionally "centered primarily within the lung." *Id.* However, he added that "[it] is likely that these most often represent systemic allergic reactions in asthmatic individuals who have a preexisting high level of airway hyperresponsiveness and therefore develop disproportionately severe bronchospasm." *Id.* Cockcroft listed nut/shellfish allergies and insect bites as examples of ingested and injected allergens, respectively, "as the cause of severe unexplained status asthmaticus." *Id.*

A supplemental report filed by Dr. Novakovic made it clear that he is "willing once again to accept the assumption that [Petitioner] had asthma back to 2008." Pet'r's Ex. 42 at 2. "Rather than try to disprove that the patient had any evidence of asthmatic respiratory disease prior to that event, [he] tried to convey the abruptness and the severity of its worsening." *Id.* Dr. Novakovic discounted the opinion of the medical resident that attributed Petitioner's June 15, 2015 asthmatic attack to a viral infection. *Id.* He opined that "infections are generally overdiagnosed as a cause of exacerbations of asthma" and added that non-infectious triggers are often overlooked. *Id.* at 3. In Petitioner's case, Dr. Novakovic did not identify "typical findings of a respiratory infection that generally include sick contacts, fever, characteristic bandemia in her bloodwork (excess of white cells released by the bone marrow usually signifying infection) or radiographic changes." *Id.* He noted the difficulty in proving or disproving a viral infection in the ED but asserted that "if this was in fact the case, we would have to accept the unlikely happenstance that the infection triggered her symptoms at the exact same time that the vaccine was administered, in the absence of the typical clinical manifestations of a virus." *Id.*

Dr. Novakovic also included a table listing Petitioner's eosinophil levels as detailed in her medical records from September 2, 2003, through February 19, 2020. Pet'r's Ex. 42 at 7–8. He noted that Petitioner's recorded levels were between 140 and 220 from 2003 until March 14, 2008, and April 5, 2008, when her levels jumped to 960 and 830 respectively. *Id.* at 7. Petitioner's levels went back down to 250 on July 8, 2008, and again remained below 220 (April 14, 2009 reading) until June 19, 2015, when she reached 400. *Id.* On July 4 and 19, 2015, Petitioner's eosinophil count jumped back up to 900 and 800 respectively. *Id.* She dropped to 300 on September 22, 2015, before having one more spike to 900 on September 24, 2015. *Id.* Petitioner's levels then fell, and she consistently tested at 400 in February and May of 2016, 300 through August 1, 2017, and back down to 200 beginning November 21, 2017, through February 19, 2020. *Id.* at 7–8. Although her levels were higher than her baseline in 2008 and again in 2015, during these peak counts,

[15] D.W. Cockcroft, *Allergens, in* ASTHMA: BASIC MECHANISMS AND CLINICAL MANAGEMENT, 507 (3rd ed. 1998).

Petitioner's test results did not reveal levels that would indicate hypereosinophilia (over 1500) or even a medically significant elevated eosinophil count. *Id.* at 4.

In his second supplemental report, Dr. Novakovic reiterated that Petitioner had pre-existing asthma but stressed that the nature of her condition pre vaccination differed dramatically from her flare in 2015. *See* Pet'r's Ex 49. He noted that from 2008 until 2015, Petitioner's treatment consisted of intermittent mometasone use, and she "avoided any exacerbations severe enough to result in medical visits and trips to the [ED] for about seven years." *Id.* at 1. In comparison, from 2015 to 2017, "her asthma was not controlled despite maximal doses of Symbicort, frequent steroid courses, rescue inhaler use several times daily and monoclonal antibody injections." *Id.* He asserted that "both her condition as well as the medication requirements were so much worse after June of 2015 that they cannot objectively be compared in any way to anything she experienced prior." *Id.* at 2. Dr. Novakovic conceded that Petitioner's "medical comorbidities as well as certain environmental and social triggers [can be] complicating factors in the patient's asthma." *Id.* However, he argued that Petitioner had these factors prior to her 2015 vaccination and remained stable. *Id.* Therefore, they "cannot be blamed for [Petitioner's] sudden deterioration." *Id.*

During his testimony, Dr. Novakovic distinguished Petitioner's history of bronchiectasis and pulmonary dysfunction with her post-vaccination asthma. He defined bronchiectasis as dilated airways, explained pulmonary hypertension, and characterized asthma largely by noting respiratory symptoms that indicate a "limitation in expiratory air flow." Tr. 57. Dr. Novakovic explained that all three conditions "can coexist in the same patient, but they are caused by different pathophysiological properties." Tr. 58. Going through Petitioner's medical records pre vaccination, Dr. Novakovic stated that Petitioner was diagnosed with a URI and acute bronchitis in 2007, bronchitis and asthma exacerbation in March of 2008. Tr. 58–60. On April 5, 2008, Petitioner was diagnosed with hypersensitivity pneumonitis, which Dr. Novakovic defined as "an allergic disease that is directed towards a very specific allergen and results in a very abnormal chest imaging." Tr. 61. He noted the significance of this diagnosis based in part on Petitioner's elevated eosinophil count "suggesti[ng] that the patient's disease process may be related to an allergy." *Id.* Petitioner's treatment for her conditions included care from a pulmonologist, and her IgE levels were measured in April of 2009 with normal results. Tr. 63. Based on this test, Dr. Novakovic determined that Petitioner "may have had Type 2 asthma, but her IgE levels were normal at the time." Tr. 64. He explained that her asthma may still be IgE-mediated, "but it sill means that IgE was not a prominent component of her disease at the time." *Id.* Relying on literature from the Global Initiative for Asthma, Dr. Novakovic asserted that Petitioner's treatment, "includ[ing] as-needed inhaled steroids or daily low-dose inhaled steroids," was successful in controlling her asthma. Tr. 65. Dr. Novakovic contrasted this treatment regimen with Petitioner's course in 2015 of long-acting beta antagonists, which is used to treat severe asthma that is otherwise uncontrolled. *Id.*

Dr. Novakovic noted that Petitioner's IgE levels were elevated in 2015, but he asserted that "her total serum IgE was also elevated throughout her life because of her continued allergic response to tree pollen and house dust mites." Tr. 66. He referred to Petitioner's history of allergic rhinitis dating back into childhood and hypereosinophilia in 2008, but Dr. Novakovic acknowledged testing of IgE levels in 2008, was also within normal limits. Tr. 68. He opined that Petitioner's pre-existing respiratory condition was episodic asthmatic symptoms and disagreed

with her hypersensitivity pneumonitis diagnosis. Tr. 71. Furthermore, notwithstanding Petitioner's episodes, Dr. Novakovic did not believe that Petitioner suffered from asthma from 2007 through 2009. Tr. 72. Regarding Petitioner's symptoms in 2007, 2008, and 2009, Dr. Novakovic testified that she "exhibited wheezing, cough and [SOB] prior to 2015, but there was a drastic difference in the severity of symptoms." Tr. 75. He described the severity, noting "her requirement for medication, steroids, [ED] visits, just the escalation of therapy needed just to keep her out of the hospital as well as the fact that there is a change in the IgE levels prior and after that." Tr. 85.

Although not an immunologist, Dr. Novakovic highlighted in his education "pulmonary boards [] represented by asthma, and that component includes the biology, the immunology and the allergic Type 2 eosinophilic asthma as well." Tr. 87–88. He presented the theory that a Prevnar 13 component, "most likely, aluminum, but also possible the protein pneumococcal polysaccharide primed her immune system which then resulted in this severe hypersensitivity reaction which occurred in June 2015." Tr. 88. Dr. Novakovic named the reaction an IgE-mediated response and described it as "a very brisk allergic, rapid type of response to a perceived allergen or a danger signal by the body." *Id.* He relied on the HogenEsch paper to assert that when the body processes aluminum adjuvant in the Prevnar 13 vaccine, NLRP3, a receptor protein linked to chronic disease, activates. Tr. 89. Dr. Novakovic testified about "studies suggest[ing] that aluminum adjuvants induced a differentiation of Th2 cells that drive an eosinophilic inflammatory response and TSH cells that stimulate antibody production," and referenced HogenEsch, Batista-Duharte et al.,[16] and Guimaraes et al.[17] Tr. 89–92.

Dr. Novakovic asserted that "[a]luminum compounds persist for up to [eight] to 11 years post vaccination the human body. This fact, combined with repeated exposure, may account for a hyperactivation of the immune system and subsequent chronic inflammation." Tr. 92. In Petitioner's case, Dr. Novakovic noted four total previous vaccinations "which contained aluminum in the 11 years preceding her [Prevnar 13] vaccine in June of 2015." Tr. 93. He explained that "any one of these vaccines could have primed her immune system to develop IgE against this compound." *Id.*

I asked Dr. Novakovic to clarify his position as it relates to the nature of Petitioner's hypersensitivity. He agreed that Petitioner was not anaphylactic; however, asserted that hers was "not a typical manifestation of anaphylaxis, but . . . that it worked along the same mechanisms." Tr. 123. The mechanism, overproduction of IgE due to the introduction of an aluminum adjuvant, "activates the chronic inflammasome system." Tr. 125. He noted that he did not "have a definitive answer because [he has not] seen it explained in the medical literature either." *Id.* Dr. Novakovic also clarified that it was likely Petitioner "had some degree of asthma prior to 2015." Tr. 127. In the several years preceding her vaccination, the condition was controlled, and she was asymptomatic. Tr. 127. He reiterated that the re-emergence of her symptoms, and to that degree of severity, would not have occurred without her June 15, 2015. *Id.*

[16] Alexander Batista-Duharte et al., *Systemic Immunotoxicity Reactions Induced by Adjuvanted Vaccines*, 20 INT'L IMMUNOPHARMACOLOGY 170 (2014).
[17] Luisa Eca Guimaraes et al., *Vaccines, Adjuvants and Autoimmunity*, 100 PHARMACOLOGICAL RSCH. 190 (2015).

3. Respondent's Expert, Dr. Bardana

Dr. Bardana began his first submitted expert report with a detailed recount of Petitioner's medical record and witness statement. *See* Resp't's Ex. A at 1–26. He then indicated his disagreement with Petitioner's theory of the case and progression of her illness, asserting that "Dr. Garban essentially undervalue[d] from consideration the medical history prior to vaccination on June 15, 2015." *Id.* at 26. Most importantly for Dr. Bardana is the "significant recorded evidence that [Petitioner] developed adult-onset asthma on the heels of an acute viral bronchitis in September of 2007." *Id.* He added that pre vaccination, Petitioner had "established adult-onset, intermittent asthma and allergic rhinitis controlled" by an inhaled corticosteroid and a steroid nasal spray. *Id.* at 28.

On the day of Petitioner's vaccine, she experienced a localized reaction, which Dr. Bardana characterized as a common event that occurs in approximately 10% of recipients. Resp't's Ex. A at 28. He noted that when Petitioner was seen at the ED four days after her vaccination, her diagnosis was status asthmaticus in the setting of a recent viral URI. *Id.* He acknowledged that Petitioner was eventually treated with antibiotics, suggesting that her bronchitis may not have been viral, as originally believed by her treaters. *Id.* at 29. Dr. Bardana opined that Petitioner's symptoms were more likely due to "a deep seated, possibly resistant, pathogen which had precipitated severe asthma." *Id.* He criticized the use of the phrase of "reactive airways disease" in Petitioner's medical records, explaining that this phrase is synonymous with asthma and is otherwise unhelpful. *Id.* at 30. "The term is nonspecific and has no clinical meaning. It does not have a specific ICD code and is not a diagnosis." *Id.* Furthermore, Dr. Bardana took issue with the identification of Petitioner's obesity as the causal factor. *Id.* He listed a "variety of other co-morbid factors which have played a potentially negative role in her asthmatic illness, i.e., prior tobacco abuse, vitamin D deficiency, allergic rhinitis and allergies to housedust mite and tree pollen, possible obstructive sleep apnea, GERD, etc." *Id.* Alternatively, Dr. Bardana was unable to find any reports of IgE-mediated reactions, including asthma, that were "ascribed to Prevnar 13 and/or aluminum hydroxide." *Id.* at 33. He countered Dr. Garban's assertion that Petitioner's response to Omalizumab is indicative of an IgE sensitization by noting that Petitioner meets the clinical requirement for Omalizumab use, namely a (pre-existing) allergy to a perennial allergen. *Id.*

In a supplemental report, Dr. Bardana reiterated many of his initial opinions. *See* Resp't's Ex. C. He opined that Petitioner's medical records revealed that "she was diagnosed with [asthma], responded to treatment[,] and had confirmatory physical findings." *Id.* at 4. Dr. Bardana further stated that "[t]he apparent lack of continuity of care and perhaps unavailability of records made it appear her providers were unmindful about her primary condition." *Id.* The plethora of diagnoses, including GERD, asthma, and hypersensitivity pneumonitis, suggested to Dr. Bardana that Petitioner's treaters were unable to ascertain the true nature of her condition. *Id.* He was therefore unsure why "between 2007 and 2017 there were only two attempts to conduct pulmonary function studies, neither of which is available." *Id.* at 5.

Dr. Bardana agreed with the admitting ED physician's 2015 diagnosis of status-asthmaticus in the setting of recent viral URI, despite Petitioner's assertion at the time that her

illness was related to her Prevnar 13 vaccine. Resp't's Ex. C at 5. Noting that Dr. Novakovic's June 2015 asthma diagnosis based on Petitioner's "symptoms ([SOB], wheezing, coughing, chest tightness and difficulty with exertion, her physical exam findings (wheezing, limited air movement and prolonged expiratory phase) and her appropriate though generally short-lasting response to aggressive asthma management," Dr. Bardana identified these same symptoms in medical records from 2007 through 2009. *Id.* He then questioned why Dr. Novakovic was hesitant to accept asthma as a diagnosis during those previous flare ups. *Id.*

According to Dr. Bardana, Petitioner's condition is more specifically defined as "Type 2-like-eosinophilic asthma." Resp't's Ex. C at 7. He explained that this phenotype is more common in adult-onset asthma patients and usually "require[s] glucocorticosteroids to maintain control." *Id.* He also disputed any evidence of hyperreactivity. *Id.* Dr. Bardana suggested that because Petitioner "never had the demonstration of variable expiratory airflow obstruction which is a sine qua non in verifying the diagnosis of asthma," her diagnosis is best characterized as presumptive based on her clinical presentation. *Id.*

In a brief supplemental follow-up, Dr. Bardana asserted that Petitioner's treatment regimen between 2009 and 2015 included "Mometasone (Asmanex) by inhaler on a daily basis with stand-by Albuterol." Pet'r's Ex. D at 2. Dr. Bardana also asserted that Petitioner had not been exposed to Prevnar 13 prior to her 2015 vaccination; therefore, she could not have been pre-sensitized, leading to an immediate allergic reaction. *Id.* Dr. Bardana did not discount Petitioner's localized itchy rash with swelling immediately following vaccination at the injection site. *Id.* He characterized this as a nonspecific irritant reaction and argued that "[i]t does not signify the presence of IgE-sensitization." *Id.* Further, Petitioner's cough, wheezing, and SOB that same day "reflected the later onset of an acute viral infection" which precipitated her asthmatic symptoms four days later. *Id.* Dr. Bardana asserted "that [Petitioner's] total serum IgE was also elevated throughout her life because of her continued allergic response to tree pollen and housedust mite." *Id.* at 3. Accordingly, there is no medical or scientific evidence that she suffered from sensitization. *Id.* at 4.

A third supplemental report continued to explain the nuance of Petitioner's diagnosis. *See* Resp't's Ex. E. Dr. Bardana asserted that most often, asthma manifests in childhood, but "[a]fter 40 years of age, most new-onset asthma cases are non-allergic." *Id.* at 1. He continued that "[i]n the older age group, asthma usually begins during or after a[URI]." *Id.* at 2. "In 2007 [Petitioner] suffered an acute onset of asthma attributed to a viral infection which precipitated three [ED] visits and commitment to chronic controller/reliever medication until the acute symptoms of 2015 which were also attributed to an acute viral infection." *Id.* Dr. Bardana maintained that the association of symptom onset with Petitioner's vaccine is "based on a subjective belief" that relies wholly on chronology. *Id.* He clarified that Petitioner's comorbidities compromised her ability to cope with her viral infection and exacerbated her asthma flare. *Id.*

To support his contention that Petitioner's condition was precipitated by an infection, Dr. Bardana argued that her condition was refined from an initial characterization as a viral URI to viral bronchitis followed by secondary infection to bacterial bronchitis. Resp't's Ex. E at 4. Knowing that URIs are the most common asthma trigger, Petitioner's "providers unanimously felt

she had an infectious process (viral followed by bacterial) and treated her with aggressive antibiotic management." *Id.*

Dr. Bardana agreed with Dr. Novakovic in that Dr. Bardana improperly used the term hypereosinophilia. Resp't's Ex. E at 5. He clarified that he "should have used the phrase elevated peripheral blood eosinophils." *Id.* He further noted that "eosinophilia is associated with [Petitioner's] atopic condition," and the presence of eosinophils can be suppressed by exogenous corticosteroids, stress and some types of infections. *Id.* Dr. Bardana conceded that "neither [he] nor Dr. Novakovic can make definitive statements regarding [Petitioner's] total serum IgE," due to sparse testing. *Id.* at 6.

4. Respondent's Expert, Dr. Byers

In his first written expert report, Dr. Byers asserted that "the central tenet" of Dr. Garban's biological mechanism for causation "is that an 'immediate early reaction' would require pre-formed, allergen-specific IgE to be present in [Petitioner's] skin and airways on June 15, 2015 that was directed to some putative component in the [Prevnar 13] vaccine." Resp't's Ex. F at 7. Relying on literature (Nials & Uddin)[18] filed by Petitioner, Dr. Byers asserted that acute sensitization "usually require[s] multiple systemic administrations of the allergen in the presence of adjuvant" and takes 14 to 21 days. *Id.* at 7. The Nials and Uddin article defined human asthma as "a chronic inflammatory disorder of the airways [that] is characterised by airway inflammation, persistent airways hyperresponsiveness (AHR) and intermittent, reversible airways obstruction." Pet'r's Ex. 13 at 1. Noting that the underlying cellular and biochemical processes underlying chronic asthma are poorly understood, the authors looked to mouse models in lieu of human models with substantial ethical considerations. *Id.* Ultimately, they found that "[c]hronic allergen exposure [reproduced] allergen dependent sensitisation, a Th2-dependent allergic inflammation characterised by eosinophilic influx into the airway mucosa, and AHR." *Id.* at 3.

Dr. Byers argued that "[i]f Petitioner had pre-formed IgE of the scale to induce an immediate allergic reaction and allergic sensitization as Dr. Garban suggested, then her skin reaction at the time of vaccination would have been much more profound" than the common, nonspecific symptoms that Petitioner experienced post vaccination. Resp't's Ex. F at 7. Dr. Byers expressed certainty that Dr. Garban "would agree that the development of de novo IgE within a few days sufficient to lead to severe and persistent allergic asthma like [Petitioner] experienced would require a much longer time frame than a few hours to days of exposure." *Id.* He noted that Petitioner had never received the Prevnar 13 vaccine. *Id.* However, Petitioner had received several vaccines with aluminum adjuvant from 2003 through 2016, "including two that also contained pneumococcus antigens, with no side effects and no evidence of a sensitization process that would be required for an 'immediate early or acute' hypersensitivity response." *Id.* at 7.

Dr. Byers conceded in his report that "elevations in IgE, eosinophilia, and type 2 cytokines are all biomarkers of allergic disease," but he cautioned that they "do not necessarily impart causation for asthma." Resp't's Ex. F at 8. He surmised that one plausible explanation would be that some undetermined environmental factor that Petitioner was continually exposed to and at the

[18] Anthony T. Nials & Sorif Uddin, *Mouse Models of Allergic Asthma: Acute and Chronic Allergen Challenge*, 1 DISEASE MODELS & MECHANISMS 213 (2008).

time of vaccination acted as a trigger. *Id.* at 8. "Through the process of vaccination, she then became immunologically primed to the undetermined environmental trigger that persisted in her local environment and resulted in . . . the pathological manifestations of severe asthma." *Id.* Dr. Byers described this theory as "superficially compelling but an unlikely hypothesis with no medical evidence." *Id.* at 9. These opinions are also held in Dr. Byers's supplemental report filed December 19, 2022. *See* Resp't's Ex. H. He noted that "Dr. Garban's opinion has remained consistent in that the temporal relationship of vaccination and development of severe persistent asthma within days following vaccination provides enough evidence for cause-and-effect." *Id.* at 1. Likewise, he "restate[d his] original conclusion that it is not biologically plausible to ascribe the severe acute asthma exacerbation to the vaccination that was received just days before." *Id.* at 4.

At hearing, Dr. Byers testified that there is no dispute that Petitioner suffered from severe asthma and asserted that "the crux of the case really rests upon what the likelihood is of a Prevnar vaccination to have led to severe asthma." Tr. 230. He explained that asthma is "a heterogeneous disease that's characterized by variable episodes of obstructed airflow characterized clinically by cough, [SOB,] and wheezing." Tr. 230. Dr. Byers testified that the condition "ebbs and flows due to whatever [inhaled] trigger contributes to the asthma." Tr. 235. Under the umbrella of asthma, Dr. Byers described endotypes that occur in different populations or are distinguished by the presence or absence of Type 2 inflammation. Tr. 232–33. He identified Type 2 as the same as "so-called Th2" and noted that it indicates "a type of cytokine pathway that's produced by CD4 T-cells." Tr. 233. However, Dr. Byers continued, it "is not just about cytokine, and there's overlap with other inflammatory pathways." *Id.* The Type 2 inflammation occurs and "it's really IL-4, IL-5 and IL-13 are sort of the center of activity that then induces a number of other Type 2 inflammatory-type cells like eosinophils, basophils, mast cells that are involved in the allergic response or the Type 2 response." Tr. 234. This production of IgE production "leads to things like airway hyperreactivity, smooth muscle hyperplasia and mucus production [that] are the characteristics of asthma." *Id.* And "typically Type 2 inflammation [is] characterized by this sort of IgE eosinophil, if you want to look at biomarkers of inflammation." *Id.* Dr. Byers noted that "Type 2 inflammation can happen anywhere. This isn't a unique lung issue." *Id.*

In Petitioner's case, Dr. Byers stated "[i]t's hard to say if this specifically was an IgE-mediated process or not." Tr. 236. He noted that although this was Petitioner's first Prevnar 13 vaccine, she had been exposed to components of the vaccine through prior vaccinations with "no reported history of escalating hyperreactivity to any of these components." *Id.* Assuming that there was a Type 1 hypersensitivity, he stated that they "resolve fairly quickly. So the likelihood of having long-term persistent symptoms as a result of that [would] invoke two different pathways that a single vaccine could induce." Tr. 237. He asserted that hypothesis would require him to "ignore the effect of the respiratory inhaled stimulus and triggers that really promoted her disease process." *Id.* Dr. Byers acknowledged that the cause of asthma remains unknown, despite advancements in treatment through the use of biologics. *Id.* He stressed the difference between identifying the cause of asthma generally and a trigger. Tr. 238. The cause is "a combination of environmental exposure and genetic predisposition" that is seen in "all severe, complex, chronic diseases." *Id.* Triggers, conversely, are identifiable. *Id.* They include perfumes, animal dander, smoke, or maybe be exercise- or cold-induced; "[b]ut all of these triggers or stimuli are things that are inhaled into the airways." *Id.*

Dr. Byers expressed hesitation about linking asthma to vaccines without any supporting studies "because asthma is so common and vaccines are so common, ascribing a specific cause and effect from a single vaccination to lead to asthma is more likely to happen by chance than to have true cause and effect." Tr. 239. He did not see the link between the vaccine and the production of IgE. Tr. 239–40. Dr. Byers argued that it is not biologically plausible in the period asserted for highly specific IgE production "through the process of B-cell development and affinity maturation," that then "binds to the surface of these cells that then release all the inflammatory mediators that cause asthma." Tr. 240. He referenced one epidemiological study "that talked about the development of asthma within 60 days after vaccination," but then stated that it "warrants further study." Tr. 241. Even in mouse models where they have been sensitized using aluminum, Dr. Byers explained that "[i]t's only after [the mice] are subjected to the ovalbumin through the airways that you get an asthma effect." *Id.*

Another point that Dr. Byers contested was how this acute IgE response is intertwined with chronic asthma, because this presentation involves an "acute phase where she came to the emergency room in an acute flare within four days following the vaccination versus the long-term, severe, persistent asthma." Tr. 242. Dr. Byers agreed with Dr. Garban that Type 1 hypersensitivity is applicable here. Tr. 243. "Type 1 hypersensitivity defines how we can develop pre-existing IgE in our body." *Id.* He noted that "[i]t doesn't have to be in our lungs," and "upon re-exposure, there is a response that occurs within minutes to hours to that re-exposure to that allergen." *Id.*

Dr. Byers also took issue with the contention that Petitioner's alleged asthma trigger was not inhaled. Tr. 277. He asserted that "asthma attacks occur from something you inhale." *Id.* Anaphylaxis and bronchospasm can occur "from having exposure to something that's not necessarily in the airways," but Dr. Byers did not think that is what occurred here or in any instance where the diagnosis is asthma. *Id.* In the case of an inhaled trigger, Dr. Byers conceded that "an acute respiratory tract infection can alter forever the airways." Tr. 284. Consequently, it is possible that some sort of inhaled allergen could cause a permanent change and make Petitioner's asthma worse again. *Id.* Dr. Byers did not see any evidence that a vaccine, specifically Prevnar 13, could do that. *Id.*

C. Petitioner's Rebuttal Testimony

1. Dr. Novakovic

On rebuttal, Dr. Novakovic discussed the differences and similarities between aluminum hydroxide and aluminum phosphate in the context of adjuvants. He submitted the Zhang et al.[19] paper and asserted that although "the authors stated that there's a much more robust neutrophilic response with aluminum hydroxide," he did not think which adjuvant was used "plays much role in the mechanism" that Petitioner's experts presented. Tr. 294. Both adjuvants "function through the same mechanism . . . activating NLRP3, which then shifts the immune response toward the Th2 pathway and then generates the class switch that Dr. Garban talked about to IgE." Tr. 295. He continued, "[f]rom an immunological perspective, aluminum-containing adjuvants induce IgE-mediated hypersensitivity reactions." Tr. 296. Dr. Garban noted that Petitioner received two

[19] Ting Zhang et al., *Research Progress of Aluminum Phosphate Adjuvants and Their Action Mechanisms*, 15 PHARAMACEUTICS 1756 (2023).

vaccines containing an aluminum adjuvant in February and June of 2015, diphtheria and pneumococcal respectively. Tr. 297, 299. He agreed that when Petitioner received the first adjuvanted vaccine in February, there was no evidence of an allergic reaction. Tr. 304.

2. Dr. Garban

Dr. Garban used the Galli et al. paper to better explain "the late phase in the inflammatory allergic inflammation and the allergic response after that early phase that happened and the release of cytokines and activation of the immune response." Tr. 306. He asserted that the figure within the article shows how the "Th2 cells are orchestrating the whole molecular and cellular phenomenon here and resulting in the activation of cellular factors and also humeral factors such as immunoglobulin E or IgE, affecting, at the end, the airway." Tr. 307 (citing Pet'r's Ex. 62). Furthermore, the figure shows lung damage that "will then sensitize that area to another kind of triggering." *Id.* These injured lung cells, according to Dr. Garban, "are more sensitive to other kind of stimuli such as smoke, viral infection or other type of things that will then trigger the asthmatic event, and this contributes to the severity." Tr. 308. He continued, the increased IgE levels with increased levels of the receptor or the surface of B-cells "will cause that in the absence of the antigen, this reaction, this cross-linking happened and the activation of cells, and again, further damage [] in the system." *Id.* Dr. Garban described it as "a vicious cycle." Tr. 309.

Next, Dr. Garban described the depot effect of the aluminum phosphate in Prevnar 13. He testified it will bring together antigens in the vaccine, including different strains of streptococcus and CRM 197 to stimulate the immune system. Tr. 309. Dr. Garban explained "that depot effect, at least they last for weeks and months and it has been even reported, years, where it's still remaining – complexes have been found in the site of injection." Tr. 309–10.

I asked how the pathogenic nature of IgE sensitization following the introduction of an inhaled antigen relates back specifically to the Prevnar 13 vaccine, an injectable. Dr. Garban stated that "the allergic inflammatory response that we have described upon vaccination is going to generate a more systemic effect than we described and respiratory effect in this case and causing these asthma related symptoms." Tr. 311. He continued that this process continues in perpetuity and "some of these generation of these factors that are not what we desire, as we call an allergic reaction is a nondesire or a very extreme, unusual phenomenon that happen upon the challenge with a targeted antigen." *Id.* Ultimately, the perpetuation is caused by the depot effect. *Id.*

IV. Applicable Legal Standards

A. Standard of Adjudication—Burden of Proof

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

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991).

B. Standard of Adjudication—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).

In Program cases, contemporaneous medical records and the opinions of treating physicians are favored. *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1325, 1326 (Fed. Cir. 2006) (citing *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274, 1280 (Fed. Cir. 2005)). Indeed, when reviewing the record, a special master must consider the opinions of treating physicians. *Capizzano*, 440 F.3d at 1326. This is because "treating physicians are likely to be in the best position to determine whether 'a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" *Id.* In addition, "[m]edical records, in general, warrant consideration as trustworthy evidence. The records contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium. These records are also generally contemporaneous to the medical events." *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

While a special master must consider these opinions and records, they are not "binding on the special master or court." § 13(b)(1). Rather, when "evaluating the weight to be afforded to any such . . . [evidence], the special master . . . shall consider the entire record . . . ." *Id.* There is no presumption that medical records are accurate and complete as to all the patient's physical conditions. *Kirby v. Sec'y of Health & Hum. Servs.,* 997 F.3d 1378, 1383 (Fed. Cir. 2021) (finding that "[b]ecause a reasonable fact finder could conclude that [Petitioner's] testimony [wa]s not inconsistent with her medical records . . . it was not arbitrary and capricious for the special master to credit [Petitioner's] testimony" over her medical records).

Where there are inconsistencies, special masters are within their discretion to award contemporaneous medical records greater weight than later conflicting testimony. *See Cucuras,* 993 F.2d at 1528 (holding that the special master's reliance on contemporaneous medical records over conflicting oral testimony given after the fact was not arbitrary or capricious); *see also Burns,* 3 F.3d at 417 (holding that the decision of whether to accord greater weight to contemporaneous medical records or later given testimony is "uniquely within the purview of the special master"). Indeed, the Court of Federal Claims has outlined four potential explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2)

the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *LaLonde v. Sec'y of Health & Hum. Servs.,* 110 Fed. Cl. 184, 203–04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014).

Despite the weight afforded to 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." (emphasis omitted)).

C. Standards for Adjudication—Causation

To receive compensation through 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 actually caused by a vaccination. See §§ 11(c)(1), 13(a)(1)(A); *Capizzano*, 440 F.3d at 1319-20. Because Petitioner does not allege she suffered a Table Injury, she must prove a vaccine she received caused her injury. To do so, Petitioner must establish, by preponderant evidence: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Althen*, 418 F.3d at 1278.

A petitioner must offer a scientific or medical theory that answers in the affirmative the question: "can the vaccine[] at issue cause the type of injury alleged?" *See Pafford v. Sec'y of Health & Hum. Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004), *mot. for rev. denied*, 64 Fed. Cl. 19 (2005), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2006). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 548–49. A petitioner is not required to identify "specific biological mechanisms" to establish causation, nor are they required to present "epidemiologic studies, rechallenge[] the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities." *Capizzano*, 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280). Scientific and "objective confirmation" of the medical theory with additional medical documentation is unnecessary. *Althen*, 418 F.3d at 1278–81; *see also Moberly*, 592 F.3d at 1322. 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. However, 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). Furthermore, as the Federal Circuit has made clear, "simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof." *LaLonde v. Sec'y*

of Health & Hum. Servs., 746 F.3d 1334, 1339 (Fed. Cir. 2014) (citing *Moberly*, 592 F.3d at 1322). Testimony that merely expresses the possibility—not the probability—is insufficient, by itself, to substantiate a claim that such an injury occurred. *See 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). 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). Rather, "[a] petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case." *Moberly*, 592 F.3d at 1322.

Next, a petitioner must prove that the vaccine actually did cause the alleged injury in a particular case. *See Pafford*, 2004 WL 1717359, at *4; *Althen*, 418 F.3d at 1279. A petitioner does not meet this obligation by showing only a temporal association between the vaccination and the injury; instead, the petitioner "must explain *how* and *why* the injury occurred." *Pafford*, 2004 WL 1717359, at *4 (emphasis in original). In particular, Petitioner must prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)); *see also Pafford v. Sec'y of Health & Hum. Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006). The received vaccine, however, need not be the predominant cause of the injury. *Shyface*, 165 F.3d at 1351. The special master in *Pafford* noted petitioners "must prove [] both that her vaccinations were a substantial factor in causing the illness . . . and that the harm would not have occurred in the absence of the vaccination." 2004 WL 1717359, at *4 (citing *Shyface*, 165 F.3d at 1352). A reputable medical or scientific explanation must support this logical sequence of cause and effect. *Hodges v. Sec'y of Health & Hum. Servs.*, 9 F.3d 958, 961 (Fed Cir. 1993) (citation omitted).

Lastly, a petitioner must show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d at 1278. For example, if a petitioner's theory involves a process that takes several days to develop after vaccination, an injury that occurred within a day of vaccination would not be temporally consistent with that theory. Conversely, if the theory is one that anticipates a rapid development of a reaction post-vaccination, the development of the alleged injury weeks or months post-vaccination would not be consistent with that theory. *See de Bazan*, 539 F.3d at 1352. Causation-in-fact cannot be inferred from temporal proximity alone. *See Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992); *Thibaudeau v. Sec'y of Health & Hum. Servs.*, 24 Cl. Ct. 400, 403–04 (1991); *see also Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1983) ("[w]ithout more, [a] proximate temporal relationship will not support a finding of causation").

D. Standards for Adjudication—Significant Aggravation

Additional analysis is required to determine whether Petitioner's vaccination significantly aggravated her pre-existing injury. The elements of an off-Table significant aggravation case are set forth in *Loving*. *See Loving*, 86 Fed. Cl. at 142-44; *see also W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1357 (Fed. Cir. 2013) (holding that "the *Loving* case provides the correct framework for evaluating off-table significant aggravation claims"). The *Loving* court combined the *Althen* test, which defines off-Table causation cases, with a test from *Whitecotton*. *Whitecotton*

v. Sec'y of Health & Hum. Servs., 17 F.3d 374 (Fed. Cir. 1994), *rev'd sub nom.*, *Shalala v. Whitecotton*, 514 U.S. 268 (1995) (concerning on-Table significant aggravation cases). The resultant test has six components, which are:

> (1) the person's condition prior to administration of the vaccine, (2) the person's current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person's current condition constitutes a 'significant aggravation' of the person's condition prior to vaccination, (4) a medical theory causally connecting such a significant worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) a showing of a proximate temporal relationship between the vaccination and the significant aggravation.

Loving, 86 Fed. Cl. at 144.

The statute defines "significant aggravation" as "any change for the worse in a pre-existing condition which results in markedly greater disability, pain, or illness accompanied by substantial deterioration in health." § 33(4).

In determining whether Petitioner is entitled to compensation, the special master shall consider all materials 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 her 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). A petitioner who satisfies her 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). However, if a petitioner fails to establish a prima facie case, the burden does not shift. *Bradley v. Sec'y of Health & Hum. Servs.*, 991 F.2d 1570, 1575 (Fed. Cir. 1993).

In considering the reliability of a petitioner's evidence of a prima facie case, the special master may consider alternative causes for a petitioner's condition that are reasonably raised in the record, even if the respondent does not pursue a formal alternative cause argument. *Doe v. Sec'y of Health & Hum. Servs.*, 601 F.3d 1349, 1358 (Fed. Cir. 2010). Thus, in weighing a petitioner's case-in-chief, a special master may consider evidence that the petitioner's alleged injury could have been caused by alternative causes. *Id.*

E. Standards for Adjudication—Alternative Causation

A petitioner who satisfies all three prongs of the *Althen* test (or all six prongs of the *Loving* test) has established a prima facie showing of causation. *Hammitt v. Sec'y of Health & Hum. Servs.*, 98 Fed. Cl. 719, 726 (2011). Where a petitioner demonstrates by a preponderance of the evidence that she suffered an injury caused by vaccination, the government must not

merely prove the existence of an alternative cause, but that such an alternative actually caused the injury. *Knudsen*, 35 F.3d at 549. Additionally, a factor unrelated "may not include 'any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness or condition.'" § 13(a)(2); *see also Doe*, 601 F.3d 1349 (opining that an idiopathic diagnosis cannot be a "factor unrelated," as it is idiopathic).

"Regardless of whether the burden ever shifts to the [R]espondent, the special master may consider the evidence presented by the [R]espondent in determining whether the [P]etitioner has established a prima facie case." *Flores v. Sec'y of Health & Hum. Servs.*, 115 Fed. Cl. 157, 162-63 (2014); *see also Stone v. Sec'y of Health & Hum. Servs.*, 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."); *de Bazan*, 539 F.3d at 1353 ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the [P]etitioner's evidence on a requisite element of the [P]etitioner's case-in-chief."); *Pafford*, 451 F.3d at 1358-59 ("[T]he presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the vaccination. . . . [T]he Special Master properly introduced the presence of the other unrelated contemporaneous events as just as likely to have been the triggering event as the vaccinations.").

V. Discussion

A. *Loving* Factor One: What was Petitioner's Condition Prior to Administration of the Vaccine?

Petitioner's medical record provides the best evidence of the nature of her condition prior to vaccination. As early as October 30, 2007, Petitioner's symptoms gave one treater the impression of "possible asthma." Pet'r's Ex. 14 at 534. Nursing discharge instructions from a March 23, 2008 trip to the ED, included a substantial section on asthma with general information on the condition, a list of several potential triggers: "pollen, dust, animal dander, molds, some foods, respiratory infections, exposure to smoke, exercise, or emotional stress[; and a note that r]epeat attacks are common." *Id.* at 456–58. Also included were symptoms to be concerned about in the case of a recurrence and circumstances that would warrant a return to the ED. *Id.* One month later in April, Petitioner's active medications included an inhaler and steroids for the exacerbation of COPD/asthma. *Id.* at 433.

Although there was initial disagreement among the experts about the onset of Petitioner's condition, they all eventually agreed that Petitioner likely suffered from asthma prior to her vaccination. Petitioner's experts, Drs. Garban and Novakovic, both assumed that Petitioner had pre-existing asthma in their second supplemental expert reports, submitted on November 12, 2019, and March 10, 2021, respectively. *See* Pet'r's Exs. 37, 49. Respondent's expert Dr. Bardana noted that Petitioner had intermittent asthma that developed in 2007. *See* Resp't's Ex. A. Dr. Byers likewise asserted that Petitioner suffered from asthma prior to her vaccination with a flare that occurred in 2015. *See* Resp't's Ex. F.

Despite preponderant evidence that Petitioner suffered from asthma for several years prior to her vaccination, Petitioner asserted that she did not suffer from pre-existing asthma. Petitioner

was definitive in her written declaration, stating that she did not have asthmatic symptoms before she received the vaccine. Petitioner maintained in her amended petition that following her June 15, 2015 vaccination, Petitioner "developed asthma, a condition she did not previously have." Am. Pet. at 1. She continued that her asthma was "caused-in-fact" by her vaccination. *Id.* In her prehearing brief, filed on July 5, 2024, Petitioner continued to assert that she "ha[d] provided persuasive evidence establishing that onset of her asthma following administration of the Prevnar 13 vaccine was within a medically appropriate timeframe to infer causation." Pet'r's Br. at 7. Petitioner also testified that she was diagnosed with asthma following her July 15, 2015 vaccination, and prior to that she suffered from pulmonary hypertension. Tr. 16.

Because Petitioner's condition was described as asthma as early as 2007 by her treaters, it could not have been caused by a subsequent vaccine seven years later. Furthermore, both of Petitioner's experts ultimately abandoned any assertation that Petitioner did not suffer from asthma pre vaccination. Therefore, Petitioner has not presented preponderant evidence of a causation claim. A petitioner cannot succeed on a claim of causation-in-fact where the alleged condition preexisted the vaccination. *See W.C.,* 704 F.3d at 1354–55 (affirming the special master's denial of compensation of a claim of causation-in-fact because "[i]f a petitioner has a disorder before being vaccinated, the vaccine logically cannot have caused the disorder"). Alternatively, Petitioner submitted that she "may have had controlled asthma prior to the Prevnar 13 vaccination of June 15, 2015. If so, the vaccination substantially aggravated the controlled asthma into a severe and uncontrolled asthma." Am. Pet. at 1. Petitioner described the possibility of pre-existing asthma, in the alternative to her causation claim, as "mild and controlled." Pet'rs Br. at 7.

Despite agreement about the diagnosis, there is much dispute about the severity of Petitioner's condition. The last medical record that mentions pulmonology concerns pre vaccination, is a July 8, 2008 record, that noted at that time, Petitioner was no longer in need of her inhaler. Pet'r's Ex. 17 at 417. Prior to that, beginning as early as 2003 and certainly by October of 2007, Petitioner presented to the ED and to other medical providers on multiple occasions with pulmonary symptoms consistent with asthma. She complained of productive cough and SOB, and Petitioner necessitated treatment including steroids and antibiotics. During a series of medical visits beginning in 2007, asthma repeatedly appeared as a potential diagnosis, alongside bronchiectasis. Petitioner's own expert, Dr. Garban, acknowledged that "bronchiectasis is associated in high co-morbidity with severe asthma and should be considered as part of the differential diagnosis." Pet'r's Ex. 4 at 11. Notably on April 4, 2008, Petitioner reported that her condition was uncontrolled, and the medical record states that "when she [was] given albuterol, steroids, and antibiotics she improve[d] but relapse[d] when weaned off steroids." Pet'r's Ex. 14 at 449. Petitioner reported that these symptoms had been over the course of the preceding year. *Id.* There is preponderant evidence that during this timeframe, Petitioner was suffering from asthma symptoms that were more severe than in other times pre vaccination.

Following this series of episodes, Petitioner insisted that she did not require treatment for any asthmatic symptoms for the next seven years from 2008 through 2015. Furthermore, Petitioner testified at hearing that she continued to fill her prescription during that time (although she did not take her prescribed dose) to keep unexpired treatment on hand in the case of need. While there is preponderant evidence in Petitioner's medical record to support Respondent's claim that Petitioner suffered from asthma before 2015, including at least one significant flare in 2007-2008,

Petitioner's asthma was stable and possibly asymptomatic for several years before her Prevnar 13 vaccination.

B. *Loving* Factor Two: What is Petitioner's Current Condition (or Her Condition Following the Vaccination, if Also Pertinent)?

Petitioner presented to the ED four days post vaccination with complaints of coughing and wheezing since the day after her vaccine. Pet'r's Ex. 3 at 900. Similar to her 2008 complaints, Petitioner reported productive cough, wheezing, and SOB, with the additional symptoms of vomiting and chills. Petitioner's medical record again provides the best evidence of the nature of her condition during this time. In the ED, Petitioner stated that she had never had such severe symptoms before. She was admitted to the hospital on June 19, 2015, and remained for four days. Pet'r's Ex. 15 at 9. During her hospitalization, Petitioner was diagnosed with status asthmaticus in the setting of recent viral URI. In the ensuing days and weeks, Petitioner was seen several times in the ED and diagnosed with bronchiectasis. Similar to March and April of 2008, Petitioner was treated with steroids and bronchodilators. By September 24, 2015, Petitioner was treated for a severe asthma attack and her doctor noted it was her third incident in as many months. Pet'r's Ex. 3 at 607. She was placed on Xolair and sent home upon improvement. Petitioner remained on Xolair to manage her bronchial asthma. Petitioner's medical records illustrate a clear exacerbation of her asthma, following an asymptomatic period, around the time of her vaccination.

Furthermore, Petitioner's filed literature provides additional context to the severity of status asthmaticus. Noting that the phrase could be problematic due to "a number of limitations [] concerning the quantification of unresponsiveness," the Papiris et al. article suggested the nomenclature, *acute severe asthma.* Pet'r's Ex. 8 at 1. This phrase "relat[es] severity mostly to a combination of the presenting signs and symptoms and the severity of cardiorespiratory abnormalities observed." *Id.* 1–2. These patients require "close observation plus aggressive administration of bronchodilators (SABAs plus ipratropium bromide via a nebulizer driven by oxygen)[,] and oral or intravenous corticosteroids are necessary to arrest the progression to severe hypercapnic respiratory failure . . . that requires [ICU] admission." *Id.* at 2. This definition is consistent with the treatment and concerns documented in Petitioner's medical record of her treatment in June of 2015. Furthermore, this aggressive treatment is more severe than Petitioner's presentation during her care in 2008.

C. *Loving* Factor Three: Does Petitioner's Current Condition (or Condition After Vaccination) Constitute a "Significant Aggravation" of Her Condition Prior to Vaccination?

To determine whether there is a "significant aggravation" of Petitioner's condition, it is necessary to compare her condition before vaccination to her condition after vaccination. The statute defines "significant aggravation" as "any change for the worse in a pre-existing condition which results in markedly greater disability, pain, or illness accompanied by substantial deterioration in health." § 33(4). There is no dispute between the parties that Petitioner's condition worsened, beginning in June of 2015, although there is disagreement about the role of vaccination, and the extent to which it may have permanently altered the nature of her asthma. Petitioner had steadily decreased her treatments and testified that she had not used her inhaler in the years prior

to the 2015 exacerbation. Furthermore, she had not complained of the symptoms commonly associated with asthma to a medical provider for the same period of years prior to her vaccination. The reemergence of symptoms, the series of ED visits and hospitalization, and the introduction of Xolair and other treatments used for severe forms of asthma, provide preponderant evidence of significant aggravation of Petitioner's asthma in the days following her June 15, 2015 vaccination.

D. *Loving* Factor Four/*Althen* Prong One: Medical Theory of Causation

The theory of causation that Petitioner presented has evolved somewhat over the course of several rounds of written expert reports and testimony. In his first report, Dr. Garban opined that Petitioner suffered a vaccine-triggered allergic sensitization that began as type I allergy resulting in IgE upregulation. He filed literature that defined a type I allergy as a reaction to the initial exposure to an allergen "that can induce IgE production so that later re-exposure to that substance induces an allergic reaction." Pet'r's Ex. 62 at 3. Dr. Garban reasoned that the aluminum adjuvant in the vaccine is an allergen that can cause acute and chronic inflammation, T helper cell response, and production of IgE leading to asthma exacerbation.

Despite Dr. Bardana's conflation of Dr. Garban's use of the "type I" modifier, the literature that Dr. Garban filed distinguished a type I allergen (a substance that can induce IgE production) and a type I allergic inflammation (a process that is IgE mediated, also referred to as a type I immediate hypersensitivity reaction). Dr. Garban's attempt to address this confusion is where things become unclear. Dr. Garban wrote that "his potential causal mechanism on the matter of [Petitioner] involved an initial adjuvant mediated immunoreactivity." Pet'r's Ex. 16 at 2. He suggested, without explicitly stating, that this is unlike a hypersensitivity that "involve[s] an initial sensitizing exposure to an antigen followed by a subsequent re-exposure." *Id.* However, Dr. Garban does not define immunoreactivity. Dorland's defines immunoreaction as "the reaction that takes place between an antigen and its antibody or between an antigen and an immunocyte sensitized to it." *Immunoreaction*, DORLAND'S MED. DICTIONARY ONLINE. This definition is broad enough to cover any and all immune responses that the experts have discussed and is therefore unhelpful. It lends credibility to Dr. Bardana's argument that Dr. Garban is asserting a hypersensitivity reaction, while simultaneously arguing a primary exposure to the allergen. At this point, it seems Dr. Garban was characterizing Petitioner's reaction as an initial response to aluminum phosphate and not the result of a re-exposure. He asserted that the primary exposure of aluminum adjuvant in the Prevnar 13 vaccine sensitized Petitioner's immune system to overreact to later exposure to antigens. Dr. Garban does not identify the kinds of later antigens to which he refers but noted that "common environmental allergens" are at play. Pet'r's Ex. 16 at 2. This initial adjuvant mediated immunoreactivity theory is vague and does not find support, even in theory, in the medical literature that Petitioner filed.

In his final written report, Dr. Garban submitted a figure to illustrate his asserted causation theory. The chart breaks down the pathogenesis of Petitioner's asthma exacerbation into three steps: 1. Allergic Inflammatory Reaction- type I hypersensitivity (localized itching/swelling) followed by type II late phase reaction (coughing/wheezing); 2. Allergic Sensitization- IgE synthesis leading to mast cell activation; and 3. Aggravation and Perpetuation- bronchial hyperreactivity. Pet'r's Ex. 58 at 1. This explanation is in direct contrast to his prior assertion that Petitioner did **not** suffer from a type I hypersensitivity. Dr. Garban confirmed this development

when he testified that Petitioner suffered from an allergic response—a (non-anaphylactic) type 1 hypersensitivity, with a systemic, respiratory manifestation. Tr. at 199–200. He then used a snowball metaphor to explain an "increasing in terms of catching up on the sensitivity to other antigens that then will result in the increasing frequency of asthmatic events and chronicity and severity of these asthmatic events." Tr. at 200. Ultimately, Dr. Garban asserted that Petitioner's reaction was a sort of type 1 hypersensitivity reaction that developed into a self-perpetuating chronic condition.

Although Dr. Garban was initially equivocal when characterizing the acute allergic inflammatory reaction in Petitioner's case, Dr. Novakovic always categorized Petitioner's reaction as a type 1 hypersensitivity. As noted, a hypersensitivity is an expedited response to a re-exposure. This definition and the first iteration of Dr. Garban's theory are mutually exclusive, and it appears that Dr. Garban eventually abandoned any argument that Petitioner's Prevnar 13 vaccine was her primary/initial exposure to aluminum adjuvant. Therefore, I do not find that Petitioner has presented preponderant evidence of a biological mechanism that includes an allergic, acute reaction, absent a re-exposure.

Dr. Garban highlighted the role of aluminum adjuvants in enhancing an immune response of Th2 production of IgE cytokines, which are central to an allergic asthmatic response. Petitioner's and Respondent's experts agree that IgE has been linked to the development of allergic asthma. *See* Tr. 243. Furthermore, Dr. Byers described "the roles of aluminum salt in terms of caus[ing] allergic reactions," as "enticing." Tr. 244. He conceded that adjuvants ignite antibody responses in Type 2 inflammation and acknowledged Th2 cells in the role of asthma. Notably Dr. Byers acknowledged "some cases that where asthma flares might have occurred after the vaccine, but [he asserted], there is not conclusive evidence that it was causative." Tr. 245. Petitioner is not required to submit conclusive evidence of causation. She submitted a theory supported by medical literature, that identifies several components of the Prevnar 13 vaccine that potentially contribute to the upregulation of IgE cytokines.

Dr. Garban was also equivocal about whether the aluminum adjuvant was the cause of Petitioner's reaction, noting the potential role of polysorbate 80 and CRM 197. When asked directly if he believed the aluminum adjuvant is the responsible antigen, he testified, "I don't know in this case." Tr. 198. Dr. Garban suggested that it could be one or a combination of any of the components of Prevnar 13. He acknowledged, he "[did not] know and [could not] guarantee . . . which component of the vaccine start[s] the whole process in terms of triggering or was the allergen that triggered the disease." Tr. 200. Dr. Novakovic identified CRM 197 at the potential initiator of Petitioner's allergic response. He noted that the Prevnar 13 vaccines's conjugated nature and use of the carrier protein "elicit[ed] a stronger immune response and activate[d] a cascade that is dependent on T cells." Pet'r's Ex. 19 at 4. Dr. Novakovic's theory then dovetails with Dr. Garban with his assertion that T cells "drive[] B cell differentiation into Ig-secreting plasma cells," producing, among other antibodies, IgE. *Id.* Both experts rely on the ability of specific antigens to "cause some rare events of anaphylaxis or allergic response," and "[d]efinitely type I hypersensitivity." Tr. 200. Petitioner has presented preponderant evidence that the Prevnar 13 vaccine, via one or more components including aluminum phosphate and CRM 197, could trigger an allergic inflammation, IgE-mediated type I immediate hypersensitivity reaction.

However, Petitioner's theory does not end there. Petitioner further asserted that the Prevnar 13 vaccine can cause the "onset and persistence of status asthmaticus." Pet'r's Ex. 16 at 2.

Dr. Novakovic testified that a hypersensitivity reaction can permanently alter the immune system due to the sustained high IgE levels over an extended period of time. Pet'r's Ex. 19 at 5. This sensitization is reinforced over the lifetime of the patient, resulting in asthmatic symptoms following exposure to common environmental triggers. *Id.* The Galli et al. article described how chronic allergic inflammation can occur "[w]hen allergen exposure is continuous or repetitive, inflammation persists, and many innate and adaptive immune cells derived from the blood can be found in the tissues at sites of allergen challenge." Pet'r's Ex. 62 at 5. This leads to structural changes "with marked altered function of the affected organs." *Id.* Furthermore, Petitioner's filings that explained the nature of allergic inflammation all noted that hypersensitivity reactions are temporary: hours to days in case of an early phase reaction and days in late phase reactions. Petitioner's theory does not persuasively explain how a hypersensitivity reaction that is precipitated by a contained, single vaccination constitutes a repetitive or continuous exposure to an antigen extensive enough to cause chronic inflammation.

Petitioner's experts both rely on the IgE mediated nature of allergic asthma to assert that the Prevnar 13 vaccine caused Petitioner's antibody upregulation and continued sensitization to common, environmental substances. The theory follows that these allergens then trigger asthma attacks that are more severe and occur more often. This argument suggests that elevated IgE levels are necessary for ongoing airway hyperactivity. While the medical literature does provide evidence for this process occurring upon continuous exposure to triggering allergens, there is not preponderant evidence presented that the vaccine causes increased IgE levels for an extended period of time to cause hyperreactivity. The flow chart that Dr. Garban created to illustrate his proposed biological mechanism described the vaccine-mediated allergic sensitization leading to the perpetuation of asthma. *See* Pet'r's Ex. 58 at 1. "Adaptive [Th2] cells produce soluble immune mediators driving IgE synthesis, which binds to mast cell high-affinity IgE receptors, leading to mast cell activation." *Id.* Dr. Garban does not discuss mast cell activation syndrome ("MCAS") specifically, and his testimony is limited to the conclusion that this process generates an allergic reaction. He does not explain how mast cell activation, a process that produces mediators that "cause the symptoms of immediate-type hypersensitivity" lead to ongoing airway hyperactivity. *See* Pet'r's Ex. 25 at 4. However, the Verstraelen et al. article explained the process: 1) mast cells that are circulating in bronchial airway connective tissue; 2) re-exposure to a triggering allergen "causes mast cell degranulation and synthesis of proinflammatory molecules;" and 3) this mediator release manifests as a hypersensitivity." *Id.* at 3–4. The hypersensitivity is followed by a late phase reaction, and the newly recruited "inflammatory cells can produce a vast array of inflammatory mediators," that promote chronic airway inflammation "after repeated allergen exposure." *Id.* at 4–5. Again, the key link is repeated exposure to the allergen. During his testimony, Dr. Garban referred to the depot effect to assert the prolonged exposure to aluminum following a Prevnar 13 vaccination, but he did not address HogenEsch's caution "that sustained release of antigen from a depot site over days or weeks is unlikely to contribute to the adjuvant effect of aluminum compounds." Pet'r's Ex. 7 at 2.

Dr. Byers contested Petitioner's assertion that Petitioner could develop an asthma exacerbation from an injected antigen but acknowledged that bronchospasms "can occur from

having exposure to something that's not necessarily in the airways." Tr. 277. The Verstraelen et al. paper, filed by Petitioner, described chronic asthma following repeated re-exposure to an inhaled allergen. The authors did not contemplate an injected allergen as a trigger for airway hyperreactivity. Dr. Garban relied on the Cockcroft chapter to assert that an injected allergen can cause a respiratory reaction, despite its rare occurrence. Indeed, Cockcroft wrote that "[i]solated bronchial asthma induced by allergens introduced into the body via routes other than inhalation is uncommon but has been reported." Pet'r's Ex. 23 at 14. He also noted that "these most often represent systemic allergic reactions in asthmatic individuals who have a preexisting high level of airway hyperresponsiveness and therefore develop disproportionately severe bronchospasm." *Id.* This would suggest that an injected allergen would only have this type of effect on someone who is already hyperresponsive, as opposed to the argument presented in this case that the allergen could cause such a condition. Cockcroft also discussed chronic airway hyperreactivity, but in the context of continued exposure to inhaled allergens. He named occupational hazards and environmental triggers, such as dust mites, and asserted that an "IgE--antigen reaction occurring continuously in the airways will lead to exacerbation of clinical asthma." *Id.* at 12. Cockcroft also acknowledged that other immunological reactions may be responsible for bronchial and parenchymal destruction, with the development of (proximal) bronchiectasis." *Id.* at 13. Unlike Petitioner's experts, Cockcroft also highlighted the importance of repeated exposure to an inhaled allergen for a chronic condition to develop. Dr. Byers ultimately conceded that "a single exposure to some sort of respiratory viral illness can cause lifelong change in the airways . . . and so it is possible that she could come back into contact with some sort of inhaled allergen or inhaled trigger that can make her asthma worse again." Tr. 284. However, repeated exposure would be needed following the initial hypersensitivity. Dr. Byers argued that he could "find no evidence in [his] review of the literature that support[s] a Prevnar 13 vaccination causing asthma." Tr. 280.

Dr. Byers also highlighted the absence of large-scale studies to support Petitioner's theory in this case. However, such evidence is not required for a claim to be successful and are rarely done, if even possible. Petitioner has identified several avenues for a potential biological mechanism; however, each one fails to connect the injected vaccine to a hyperreactive airway susceptible to chronic, severe asthma attacks.

1. Petitioner's experts have abandoned any mechanism that does not rely on a type 1 hypersensitivity reaction, which by definition, involves re-exposure.
2. Petitioner's experts have not explained how a type 1 hypersensitivity extends beyond a late phase reaction, without repeated exposure to the offending allergen or a pre-existing hyperreactivity.
3. Petitioner's experts have not explained how a single Prevnar 13 vaccination, four months after a prior aluminum adjuvanted vaccine, constitutes repeated exposure substantial enough to trigger sustained elevated IgE levels.
4. Petitioner's experts have not explained how an injected allergen can cause a severe asthma flare necessary for structural change, absent pre-existing levels of hyperreactivity.

While Petitioner's theory has pieces that make sense under certain circumstances, such as the ability of an inhaled allergen to cause a respiratory reaction, and the ability for an acute hypersensitivity reaction to develop into chronic allergic asthma, they do not all fit together to

create a cohesive theory. Furthermore, the hyperreactivity necessary for an injected allergen to trigger a severe bronchospasm would also need to predate the vaccine, precluding but-for causation of the significant aggravation. While Petitioner has presented preponderant evidence that the Prevnar 13 vaccine can cause a type 1 hypersensitivity reaction, she has not presented preponderant evidence that the vaccination is the catalyst for the type of allergen re-exposure necessary for chronic, severe asthma.

E. *Loving* Factor Five/*Althen* Prong Two: Logical Sequence of Cause and Effect

Petitioner described the nature of her symptoms in 2015 as more severe than ever before, and the medical records support that assertion. However, Petitioner's medical records first mentioned Petitioner's pulmonary symptoms in 2003. While she was diagnosed with bronchitis and not asthma at that time, the medication prescribed included a daily inhaler in response to sustained symptoms that did not immediately improve. She was on this medication for several weeks and eventually stabilized for several years until she had another acute respiratory event in 2008 that was significantly worse than 2003. Her cough and SOB returned, more severe, and this time, those symptoms were associated with asthma. In addition to steroids and an inhaler, Petitioner was prescribed antibiotics as a part of her treatment, indicating a possible infectious trigger. Petitioner's 2015 presentation arc is then parallel to her exacerbation in 2008. Petitioner had an acute pulmonary symptoms, specifically productive cough, wheezing, and SOB, and all symptoms were again more severe than the previous flares. She went to the ED several times, and her treaters considered several differential diagnoses before ultimately developing a treatment plan consistent with asthma. Specifically, Petitioner was diagnosed in the ED with asthma pursuant to a URI. Petitioner's symptoms returned when she initially attempted to wean off daily medication (similar to 2008), but eventually she stabilized, and her symptoms eased. These acute respiratory events are similar in their presentation, treatment, symptom course, and suspected infectious trigger, with a progressively more severe iteration each time. Petitioner has provided preponderant evidence that her symptoms worsened in June of 2015, but Petitioner further bears the burden of providing preponderant evidence of the vaccine's role in this progression of her pre-existing condition.

Petitioner's causation theory must be applicable to the facts and circumstances in her case. The theory relies on the premise that exposure to components of the Prevnar 13 vaccine, including aluminum phosphate, can cause a hypersensitivity reaction. Again, the evolution of Dr. Garban's opinion must be noted. In his report, he was initially adamant that Petitioner did not suffer a hypersensitivity reaction, because this 2015 Prevnar 13 vaccine was the primary exposure to whatever antigen triggered her asthmatic exacerbation. Specifically, he suggested that the Prevnar 13 sensitization or priming resulted in the onset and persistence of IgE-mediated allergic asthma, unrelated to any previous exposure to an aluminum adjuvant and without the need for re-exposure. Pet'r's Ex. 16 at 3. During his testimony however, Dr. Garban stated "the presence of these adjuvants or components of vaccines of previous vaccine, might result or more likely than not resulted into [her] sensitization." Tr. 167. Dr. Garban stated that immediately post vaccination, Petitioner demonstrated a "systemic manifestation, like respiratory manifestation" that "demonstrates that whatever was in that vaccine triggered an allergic response." Tr. at 199. He described it as a mild, type 1 hypersensitivity without anaphylaxis. Tr. 138. Dr. Novakovic also testified that Petitioner's reaction "was a type I hypersensitivity [that] just happened not to

manifest with severe vasodilation," and while not "a typical manifestation of anaphylaxis, [] worked along the same mechanisms." Tr. 122–23.

Drs. Garban and Novakovic both opined that in Petitioner's case, the aluminum adjuvant in her June 15, 2015 vaccine was most likely the culprit allergen. Pet'r's Ex. 4 at 11–12; Tr. 88. However, they both acknowledged that a hypersensitivity reaction necessitates a prior exposure for sensitization. Furthermore, hypersensitivity reactions are replicable. Respondent's expert, Dr. Byers noted that Petitioner had received at least four previous vaccines that contained aluminum: Pneumovax in 2004 and 2013, and TdaP in 2005 and February of 2015. Resp't's Ex. F at 11. None of these vaccinations occurred close in time to Petitioner's 2003 or 2007 manifestations of respiratory symptoms. Dr. Byers took issue with attributing Petitioner's acute, localized reaction, immediately post vaccination, as a type I hypersensitivity and countered that Petitioner "tolerated" four previous instances of aluminum adjuvanted vaccinations, "including two that also contained pneumococcus antigens, with no side effects and no evidence of a sensitization process." *Id.* at 7. Dr. Novakovic asserted that Petitioner's previous vaccinations, containing aluminum and pneumococcal polysaccharide, "primed her immune system which then resulted in this severe hypersensitivity" in June of 2015. Tr. 88. Dr. Garban pointed to Petitioner's "itching, redness, the warm rash and some inflammatory site [] swelling," as evidence of an early-phase, allergic reaction followed by a chronic asthma exacerbation that left her susceptible to more frequent and severe asthma attacks in the future. Tr. at 159–60.

However, both of Petitioner's experts acknowledged that Petitioner's initial reaction on June 15, 2015, was mild with no evidence of respiratory symptoms until the late phase reaction that occurred hours later. Petitioner's IgE levels then jumped to 900 and 800 in July of 2015, and the only other time in Petitioner's medical history when her levels had been that high was in March and April of 2008. It is during this time period that Petitioner had first been diagnosed with status asthmaticus. This exacerbation was not associated with any of Petitioner's previously received adjuvanted vaccines. Similar to what occurred in 2008, following ED visits and inpatient treatment in 2015, Petitioner's IgE levels returned to counts of 400 and lower. Although Petitioner remained on medication to control her symptoms beyond 2015, she was likewise prescribed a daily inhaler to control her asthma in 2008. The medical literature filed by Petitioner suggests that it is possible for an injected allergen to cause a severe, systemic respiratory hypersensitivity reaction, such as an asthma attack, in cases where a person already suffers from hyperreactivity. Petitioner's 2008 reaction, with a similar clinical presentation, clear worsening respiratory symptoms from a previous acute, respiratory condition, and elevated IgE levels is persuasive evidence that Petitioner's 2015 reaction is a continuation of the progression of her asthma following allergen exposure. It is evidence of a pre-existing airway hyperreactivity that was triggered in or around the time of her vaccination. There is also evidence in the medical record to suggest that Petitioner's treaters in 2008 (antibiotics prescription) and 2015 (status asthmaticus in the setting of URI diagnosis) believed her triggers to be infections. This is consistent with the medical literature's explanation of progressively worsening reactions following re-exposure to an allergen.

There is clear evidence, conceded by both sides, that Petitioner suffered from an allergic reaction immediately following her vaccination on June 15, 2015. However, there is not preponderant evidence that Petitioner suffered from chronic allergic inflammation due to the Prevnar 13 vaccine. There is preponderant evidence that she was already sensitized and susceptible

to an isolated bronchial asthma attack as described by Cockcroft. The filed medical literature further explained how Petitioner's localized reaction evolved into systemic injury was in the context of acute bronchial asthma. The clear differences between Petitioner's symptoms immediately following her vaccination (localized, redness, itching, swelling) and four days later (systemic, wheezing, coughing, SOB) do not, without explanation, support one extended process. Dr. Garban did not persuasively address the effect of the previous vaccine(s) on the sensitization process or how Petitioner's medical history of a prior asthma exacerbation in 2008 would fit into his theory. His simple dismissal of her 2008 incident as too remote in time to contribute to her 2015 exacerbation, eight years later, is unpersuasive and undercuts his assertion that Petitioner's future allergic reactions that involve the reactivity of her airways can be traced back to a vaccine administered over eight years prior. Petitioner presented preponderant evidence that she suffered from an acute vaccine-caused reaction; however she did not present preponderant evidence that any one or combination of the Prevnar 13 components discussed at the hearing caused her to develop a more systemic chronic asthma.

Dr. Novakovic's reliance on timing is insufficient to establish causation when balanced against the filed literature that repeatedly discussed the random nature of asthma attacks in people with severe and chronic allergic asthma. Notably, Petitioner did not file literature that links the Prevnar 13 vaccine to chronic allergic asthma, although other environmental triggers that Petitioner was exposed to on a daily basis were identified.

F. *Loving* Factor Six/*Althen* Prong Three: Proximate Temporal Relationship

There is no dispute between the parties that Petitioner's initial reaction shared an appropriate temporal relationship with her Prevnar 13 vaccine. However, Respondent contested any assertion that this immediate, localized reaction was an early phase, hypersensitization. Petitioner's contention that the immediate reaction developed into a late phase, inflammatory reaction is also contested by Respondent. The Galli et al. article explained that "[l]ate-phase reactions typically develop [two to six hours] after allergen exposure and often peak after [six to nine hours]." Pet'r's Ex. 62 at 1. Furthermore, a late-phase reaction "is usually preceded by a clinically evident early-phase reaction and fully resolves in [one to two] days." *Id.* That is inconsistent with Petitioner's assertion that her late-stage reaction continued to cause new reactions years later. Petitioner has not presented preponderant evidence that her asthmatic symptoms that began on or around June 19, 2015, have an appropriate temporal relationship with her vaccination to be consistent with a late-phase reaction or chronic allergic inflammation. Additionally, Petitioner has not presented preponderant evidence that her subsequent asthma flares in response to new environmental factors have an appropriate temporal relationship to her June 15, 2015 vaccination to support causation. Petitioner's vaccine-caused initial, localized reaction is insufficient, without a late phase reaction or chronic allergic inflammation link, to meet the temporality burden.

V. Conclusion

After a careful review of the record, Petitioner has failed to provide preponderant evidence that her June 15, 2015 Prevnar 13 vaccine caused or significantly aggravated her status asthmaticus, resulting in more severe and more frequent asthma flares that can be related back to

her vaccination. Accordingly, Petitioner's claim is **DENIED**. Absent a timely motion for review, the Clerk is directed to enter judgment dismissing this case for insufficient proof in accordance with Vaccine Rule 11(a). [20]

IT IS SO ORDERED.

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

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