In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: April 25, 2022

CAYLIN WILLIAMS,	*	No. 16-553V
Petitioner,	*	Special Master Sanders
v.	*	Ruling on Entitlement; Tetanus-Diphtheria-Acellular Pertussis ("TDaP"); Human Papillomavirus ("HPV"); Meningococcal Vaccines; Interstitial Pulmonary Fibrosis; Acute Respiratory Failure
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Michael G. McLaren, Black McLaren, et al., PC, Memphis, TN, for Petitioner.
Dhairya D. Jani, United States Department of Justice, Washington, DC, for Respondent.

RULING ON ENTITLEMENT[1]

On May 5, 2016, Donna Williams ("Mrs. Williams") filed a petition for compensation pursuant to the National Vaccine Injury Compensation Program,[2] on behalf of her then-minor daughter Caylin Williams ("Petitioner"). Pet. at 1, ECF No. 1; 42 U.S.C. §§ 300aa-1 to -34 (2012). The petition alleges that tetanus, diphtheria, and pertussis ("TDaP"), human papillomavirus ("HPV"), and meningococcal vaccines that Petitioner received on July 29, 2014, caused her to suffer from interstitial pulmonary fibrosis ("IPF")[3] and acute respiratory failure.[4] Pet. at 1.

[1] This Ruling shall be posted on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). In accordance with Vaccine Rule 18(b), a party has 14 days to identify and move to delete medical or other information that satisfies the criteria in § 300aa-12(d)(4)(B). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted Ruling. If, upon review, I agree that the identified material fits within the requirements of that provision, such material will be deleted 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 (2012).

[3] Interstitial pulmonary fibrosis ("IPF") is defined as "chronic inflammation and progressive fibrosis of the pulmonary alveolar walls, with steadily progressive dyspnea, resulting finally in death from oxygen lack or right heart failure." *Dorland's Illustrated Medical Dictionary* 1, 704 (32nd ed. 2012) [hereinafter "*Dorland's*"].

[4] Acute respiratory failure is "a [sudden] condition resulting from respiratory insufficiency, in which there is persistent abnormally low arterial oxygen tension (Pao_2) or abnormally high carbon dioxide tension ($Paco_2$)." *Dorland's* at 678.

After carefully analyzing and weighing all the evidence and testimony presented in this case in accordance with the applicable legal standards,[5] I find that Petitioner has met her burden and presented preponderant evidence that her vaccinations were the but-for cause of her IPF and acute respiratory failure.

I. Procedural History

Mrs. Williams filed a petition for compensation on behalf of Petitioner on May 5, 2016. Pet. at 1. Mrs. Williams filed a motion to amend the case caption on November 9, 2020, indicating that Petitioner had reached the age of majority. ECF No. 66. I granted Mrs. Williams' request, and the case caption was amended. ECF No. 67. Prior to the change in case caption, on May 17, 2016, Mrs. Williams filed a notice of intent to file an affidavit and medical records on a compact disc. ECF No. 7. The following day, the clerk's office received the compact disc, along with a statement of completion. Pet'r's Exs. 1–6, ECF No. 8.

Respondent filed his Rule 4(c) report on August 3, 2016, recommending that compensation be denied. Resp't's Report at 1, ECF No. 11. The presiding special master held a status conference pursuant to Vaccine Rule 5 on August 24, 2016. *See* Min. Entry, docketed Aug. 24, 2016. Following the conference, the presiding special master ordered Petitioner to file an expert report addressing three pertinent issues. Sched. Order at 1, ECF No. 12. Specifically, Petitioner's expert was to address whether the fact that Petitioner was born seven to eight weeks premature had implications for her later development, the causal relevance of Petitioner's MRSA infection[6] in July of 2014, and which, if any, of the three vaccines identified are alleged to have been causal. *Id.* Prior to filing an expert report, Petitioner submitted an additional medical record on November 7, 2016. Pet'r's Ex. 7, ECF No. 15. On December 9, 2016, Petitioner filed a status report indicating that she was consulting with experts in immunology and pulmonology and requesting an extension for filing her report. ECF No. 16. The presiding special master extended Petitioner's deadline. Non-PDF Order, docketed Dec. 12, 2016. This case was transferred to me on January 9, 2017. ECF Nos. 17–18.

On February 8, 2017, Petitioner filed an expert report from Eric Gershwin, M.D., and supporting medical literature. Pet'r's Exs. 8–48, ECF Nos. 22-1–26-6. Respondent filed his responsive expert report from Gary Rachelefsky, M.D., on June 28, 2017. Resp't's Ex. A, ECF No. 31. On June 5, 2017, Respondent filed a notice of intent to file medical literature on a compact

[5] 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 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.").

[6] A MRSA infection is an infection caused by the "methicillin-resistant Staphylococcus au'reus." *Dorland's* at 1184. Staphylococcus au'reus is defined as "a species comprising the yellow-pigmented, coagulase-positive pathogenic forms of the genus; it causes serious suppurative infections and systemic disease, including impetigo bullosa, staphylococcal pneumonia, and staphylococcal scalded skin syndrome, and has developed resistance to nearly all classes of antibiotics." *Id.* at 1765.

disc. ECF No. 32. The following day, the clerk's office received the compact disc. Resp't's Exs. C–JJ.

I held a status conference with the parties on July 25, 2017. *See* Min. Entry, docketed July 25, 2017. During the conference, I discussed Respondent's request to submit a second responsive expert report regarding the immunological aspects of Petitioner's causation theory. Sched. Order at 1, ECF No. 33. Petitioner indicated that she would not reply to Respondent's first report, but she requested the right to respond to Respondent's second report. *Id.* I ordered Respondent to submit a second expert report and for Petitioner to submit a status report regarding her intention to file a supplemental report thereafter. *Id.*

Respondent submitted a second responsive expert report from Christine McCusker, M.D., on September 8, 2017. Resp't's Exs. KK, LL, ECF Nos. 34-1, 34-2. Petitioner filed a status report on September 25, 2017, indicating that she did not wish to file a supplemental expert report and requesting this matter be set for an entitlement hearing. ECF No. 35. Respondent submitted medical literature on October 18, 2017. Resp't's Exs. MM–QQ, ECF Nos. 37-1–37-5.

I scheduled this matter for an entitlement hearing to take place on December 18–19, 2019. Hearing Order, ECF No. 39. Petitioner filed her pre-hearing brief on August 19, 2019. Pet'r's Br., ECF No. 43. Respondent filed his pre-hearing response brief on September 17, 2019. Resp't's Br., ECF No. 44. On October 11, 2019, Petitioner refiled highlighted medical literature. Pet'r's Exs. 49–59, ECF Nos. 45-1–45-12. Respondent refiled highlighted medical literature on October 16, 2019. Resp't's Exs. RR–WW, ECF Nos. 46-1–46-6. Petitioner filed a notice of intent to file exhibits on a compact disc on December 5, 2019. ECF No. 51. The next day, the clerk's office received photograph and video exhibits documenting Petitioner's condition. Pet'r's Exs. 60–69. The entitlement hearing was held as scheduled on December 18–19, 2019. *See* Min. Entry, docketed Dec. 19, 2019.

Following the entitlement hearing, I ordered Respondent to file the medical literature regarding the impact of multiple infiltrates on the immune system, which was referenced by his expert during the hearing. Sched. Order at 1, ECF No. 52. On December 26, 2019, Petitioner filed a photograph exhibit depicting the whiteboard which was displayed during the hearing. Pet'r's Ex. 70, ECF No. 53. On January 6, 2020, Respondent filed additional medical literature exhibits. Resp't's Exs. XX–AAA, ECF Nos. 54-1–54-4.

Petitioner filed an opening post-hearing brief and supporting documentation on April 30, 2020. Pet'r's Br., ECF No. 62. On June 29, 2020, Respondent filed his post-hearing response brief. Resp't's Resp., ECF No. 64. Petitioner filed her post-hearing reply brief on July 13, 2020. Pet'r's Reply, ECF No. 65. This matter is now ripe for consideration.

II. Evidence

A. Medical Records

Petitioner's medical record, diagnosis, and treatment are not in dispute in this case. Petitioner's symptom presentation and complaints to medical personnel are also not disputed by

either party. While I have reviewed the entire record, the records most relevant to Petitioner's symptomology and progression are discussed herein.[7]

1. Pre vaccination

Petitioner was born premature at thirty-two weeks on November 8, 2002. Pet'r's Ex. 6 at 426. In August of 2011, Petitioner was prescribed Desonide cream, a topical corticosteroid, to treat eczema[8] and skin hypersensitivity. Pet'r's Ex. 2 at 5–6. She continued to take steroids for dermatological concerns into 2014. *See* Pet'r's Ex. 2. She had no relevant medical conditions as a result of her prematurity and no other relevant health concerns until July of 2014. *Id.* On July 21, 2014, she presented to her pediatrician for a painful lesion on her left inner thigh that appeared two days prior. *Id.* at 37. Petitioner's pediatrician ordered testing on a cultured sample, which came back positive for MRSA. *Id.* at 94. She was started on a ten-day course of Bactrim.[9] Pet'r's Ex. 4 at 2307.

On July 28, 2014, Petitioner was evaluated for eczema and lichen simplex chronicus.[10] Pet'r's Ex. 2 at 45–46. The next day, on July 29, 2014, Petitioner presented for her twelve-year-old well-visit and noted no significant issues. *Id.* at 47. An examination of Petitioner's lungs showed that her chest was clear with "no wheezing or rales"[11] and she exhibited symmetric air entry throughout both lung fields. *Id.* at 53. She received the TDaP, HPV, and meningococcal vaccinations during this visit. *Id.* Petitioner's pediatrician encouraged her to remain in the clinic for twenty minutes following her vaccinations and to report any adverse reaction. *Id.* at 47. Her pediatrician indicated "[n]o sign[s] and symptoms of [an] allergic reaction [that were] noted or reported at the time of vaccination." *Id.*

2. Post vaccination

On July 31, 2014, Petitioner was seen by Renee Quinton, M.D., with complaints of fever, abdominal pain, vomiting, fatigue, and back pain lasting for two days. *Id.* at 57. The review of

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[7] *See supra,* note 5.

[8] Eczema is "any of various pruritic, papulovesicular types of dermatitis occurring as reactions to endogenous or exogenous agents. In acute types there may be erythema, edema, inflammatory infiltrates in the dermis, vesiculation, crusting, and scaling. In chronic types there may be lichenification, skin thickening, signs of excoriation; and areas of hyperpigmentation or hypopigmentation." *Dorland's* at 592.

[9] Bactrim is "the trademark for combination preparations of trimethoprim and sulfamethoxazole." *Dorland's* at 194. Trimethoprim is "an antibacterial closely related to the antimalarial pyrimethamine, acting by inhibiting a step in bacterial folate biosynthesis and effective against various gram-negative and gram-positive bacteria; administered orally in the prophylaxis and treatment of urinary tract infections and the treatment of pneumocystis pneumonia." *Id.* at 1968. Sulfamethoxazole is "a sulfonamide used as an antibacterial active against various gram-negative and gram-positive organisms, especially for the treatment of acute urinary tract infections[.]" *Id.* at 1801.

[10] Lichen simplex chronicus is "eczema caused by repeated itching and rubbing or scratching of the skin; it may arise spontaneously or be associated with other dermatoses. Characteristics are sharply demarcated, circumscribed, scaling patches of thickened, furrowed skin, usually on the face, neck, limbs, or anogenital region." *Dorland's* at 1034.

[11] A rale is "a discontinuous sound consisting of a series of short nonmusical noises, heard primarily during inhalation; called also crackle." *Dorland's* at 1576.

symptoms was significant for emesis,[12] lethargy, sore throat, chills, some cough, and no nasal congestion. *Id.* at 57–58. Dr. Quinton's examination of Petitioner was normal, but the visit notes indicate that Petitioner was "mild ill appearing." *Id.* at 58. Dr. Quinton determined that Petitioner likely had a viral illness, but that a reaction to her HPV vaccine could not be ruled out in light of her fever and vomiting. *Id.*

On August 2, 2014, Petitioner went to the emergency room ("ER") with complaints of a continued fever and respiratory difficulty. Pet'r's Ex. 3 at 8. Petitioner reported a cough, swollen tonsils without purulence,[13] and bilateral anterior cervical lymphadenopathy,[14] but no shortness of breath. *Id.* at 6–7; *see also* Pet'r's Ex. 2 at 58. An examination of Petitioner's lungs was normal with normal breath sounds. Pet'r's Ex. 3 at 8.

By the next day, August 3, 2014, Petitioner had developed a significant cough, chest pain, and respiratory distress and therefore presented to the Children's Hospital of Atlanta ("CHOA") – Hughes Spalding. Pet'r's Ex. 4 at 4360. She was initially placed on a high frequency nasal cannula ("HFNC"),[15] but was transitioned to bilevel positive airway pressure ("BiPAP")[16] when her oxygen levels decreased from 100% saturation to the high 80s. *Id.*; *see also* Pet'r's Ex. 2 at 62. Petitioner was prescribed a course of Rocephin,[17] but due to the severity of her condition, she was transferred the same day to Scottish Rite, a level two trauma center within the CHOA network.

[12] Emesis is another term for vomiting. *Dorland's* at 608.
[13] Purulence refers to pus or discharge. *Dorland's* at 1558.
[14] Lymphadenopathy is "a disease of the lymph nodes, usually with swelling[.]" *Dorland's* at 1083.
[15] A high frequency nasal cannula ("HFNC") is a potent "cannula that fits into the nostrils for delivery of oxygen therapy." *Dorland's* at 281.
[16] Bilateral positive airway pressure ("BiPAP") is a machine that "use[s] pressure to push air into the lungs . . . improving the level of oxygen in the blood and decreasing the carbon dioxide." *What is a BiPAP Machine and What's it Used For?,* HEALTHLINE https://www.healthline.com/health/what-is-a-bipap-machine (last visited Apr. 11, 2022).
[17] Rocephin is the "trademark for a preparation of ceftriaxone sodium." *Dorland's* at 1651. Ceftriaxone sodium is "a semisynthetic, β-lactamase–resistant, broad-spectrum, third-generation cephalosporin effective against a wide range of gram-positive and gram-negative bacteria; administered intravenously or intramuscularly." *Id.* at 312.

Pet'r's Ex. 4 at 4360. Petitioner was "started on [A]lbuterol,[18] [S]olumedrol,[19] [a] ketamine drip,[20] magnesium sulfate,[21] and [she] received a terbutaline drip[22] overnight." *See id.*

Her respiratory virus panel came back negative, and on August 5, 2014, Petitioner was prescribed a second course of Rocephin and a five-day course of Zithromax.[23] Pet'r's Ex. 2 at 64. A chest scan performed on August 6, 2014, showed "ground[-]glass opacities[24] with mild interlobular septal thickening within dependent portions of the lower lobes. There was no alveolar consolidation, or bronchiectasis[25] seen. No enlarged hilar or mediastinal lymph nodes seen either." Pet'r's Ex. 4 at 2341. The attending physician weaned Petitioner to HFNC on August 8, 2014, and then to a low-flow nasal cannula on August 11, 2014. *Id.* Petitioner then "[a]cutely" developed worsening respiratory distress and she was placed back on BiPAP. *Id*. On August 12, 2014, Petitioner was afebrile and improving on BiPAP, but her symptoms then began to worsen. *Id.* Petitioner was restarted on Bactrim. *Id.* at 2312. Cultures were taken, but none were positive for bacterial infection. *Id.* at 2311. Petitioner underwent an immunology work-up, which showed decreased T cells and NK cells, but normal B cells. *Id.* at 2319. Her treaters noted that these results were "of unclear significance in this child." *Id.* Petitioner's medical records document "an extensive infectious work[-]up given her isolated lung findings and fever, though she does not

[18] Albuterol is "a β-adrenergic agonist . . . ; administered by inhalation as a bronchodilator for the treatment and prophylaxis of bronchospasm associated with . . . chronic obstructive airway disease, the treatment of asthma-associated bronchospasm, and the prophylaxis of exercise-induced bronchospasm." *Dorland's* at 45.

[19] Solumedrol is the "trademark preparation of methylprednisolone sodium succinate." *Dorland's* at 1731. Methylprednisolone sodium succinate is "the 21-succinate sodium salt of methylprednisolone, having actions and uses similar to those of the base; it is highly soluble in water and is chiefly used for the rapid achievement of high blood levels of methylprednisolone in short-term emergency treatment; administered by intramuscular or intravenous injection." *Id.* at 1154.

[20] Ketamine hydrocholoride is "a rapid-acting general anesthetic and anesthesia adjunct, administered intramuscularly and intravenously." *Dorland's* at 983.

[21] Magnesium sulfate is "$MgSO_4 \cdot xH_2O$, a salt used as an anticonvulsant in the prophylaxis and treatment of seizures associated with toxemia of pregnancy; also used as an electrolyte replenisher; administered intramuscularly and intravenously." *Dorland's* at 1096.

[22] Terbutaline sulfate is "a β2-adrenergic receptor agonist, used as a bronchodilator for the treatment of asthma-associated bronchospasm and the treatment and prophylaxis of bronchospasm associated with chronic bronchitis, pulmonary emphysema, or other chronic obstructive airway disease; administered by oral inhalation, subcutaneously, or orally. It is also used as a tocolytic in the prevention of premature labor; administered intravenously." *Dorland's* at 1883.

[23] Zithromax is "the trademark for preparations of Azithromycin." *Dorland's* at 2092. Azithromycin is "an antibiotic, derived from erythromycin, that inhibits bacterial protein synthesis, effective against a wide range of gram-positive, gram-negative, and anaerobic bacteria; used in the treatment of mild to moderate infections caused by susceptible organisms, administered orally and intravenously." *Id.* at 187.

[24] Ground-glass generally refers to "having a filmy, hazy appearance, as in radiographs of a lung containing excess fluid." *Dorland's* at 808. Ground-glass opacities is "a radiological term indicating an area of hazy increased lung opacity through which vessels and bronchial structures may still be seen." *See* M. Infante, et al., *Differential Diagnosis and Management of Focal Ground-glass Opacities,* 33 EURO. RESPIRATORY J. 821–27 (2009).

[25] Bronchiectasis is "chronic dilatation of the bronchi marked by fetid breath and paroxysmal coughing, with the expectoration of mucopurulent matter. Types are distinguished according to the nature of the dilatations." *Dorland's* at 252.

have much evidence of systemic inflammation." *Id.* A chest CT showed Petitioner had developed interstitial pneumonia,[26] and she had to be intubated and transferred to CHOA-Egleston, a level one trauma center. *Id.* at 2315.

Petitioner was admitted to the pediatric intensive care unit ("PICU") at Egleston on August 15, 2014. *Id.* A chest X-ray showed worsening interstitial[27] opacities, pneumomediastinum,[28] and subcutaneous air. Pet'r's Ex. 2 at 73. Dr. Dawn Simon, a pediatric pulmonologist, noted that Petitioner was "admitted with respiratory failure and progressive interstitial lung disease[29] concerning for acute interstitial pneumonitis."[30] Pet'r's Ex. 4 at 2472.

On August 16, 2014, Petitioner underwent a bronchoscopy[31] and lung biopsy. *Id.* at 2341. Her bronchoscopy revealed "active bleeding with lavage,"[32] causing treaters to consider "vasculitis[33] [as] a potential etiology." *Id.* at 2340. Petitioner's pattern was "also consistent with hypersensitivity pneumonitis[,][34] however[, Petitioner's condition] ha[d] not improved in the hospital[,] which is typical when patients are removed from the offending agent found in their home environment." *Id*. Petitioner's preliminary biopsy results showed "diffuse interstitial fibrosis [with a] chronic, non-infectious process." *Id.* at 2430. The histology of Petitioner's lung biopsy revealed "severe, advanced diffuse alveolar damage[,] however[,] no trigger ha[d] been identified." *Id.* at 2472. Petitioner was placed on extracorporeal membrane oxygenation ("ECMO")[35] on August 17, 2014. *Id.* at 2351.

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[26] Interstitial pneumonia is "1. any of various types of pneumonia characterized by thickening of the interstitial tissue. 2. idiopathic pulmonary fibrosis." *Dorland's* at 1473.

[27] Interstitial means "pertaining to or situated between parts or in the interstices of a tissue." *Dorland's* at 951.

[28] Pneumomediastinum is "the presence of air or gas in the mediastinum, which may interfere with respiration and circulation and may lead to such conditions as pneumothorax or pneumopericardium. It may occur as a result of trauma or a pathologic process, or it may be induced deliberately as a diagnostic procedure. Called also *Hamman disease* [] and *mediastinal emphysema." Dorland's* at 1472.

[29] Interstitial lung disease is "a heterogeneous group of noninfectious, nonmalignant disorders of the lower respiratory tract, affecting primarily the alveolar wall structures but also often involving the small airways and blood vessels of the lung parenchyma; slowly progressive loss of alveolar-capillary units may lead to respiratory insufficiency and death." *Dorland's* at 536.

[30] Pneumonitis is "inflammation of the lungs." *Dorland's* at 1475.

[31] A bronchoscopy is an "examination of the bronchi through a bronchoscope." *Dorland's* at 253.

[32] Lavage is "1. the irrigation of an organ, such as the stomach or bowel. 2. to wash out, or irrigate." *Dorland's* at 1009.

[33] Vasculitis is "inflammation of a blood or lymph vessel[.]" *Dorland's* at 2026.

[34] Hypersensitivity pneumonitis is "a respiratory hypersensitivity reaction to repeated inhalation of organic particles, usually in an occupational setting, with onset a few hours after exposure to the allergen. Characteristics include fever, fatigue, chills, unproductive cough, tachycardia, and tachypnea; in the chronic form there is interstitial fibrosis with collagenous thickening of the alveolar septa. There are many specific types . . . . Called also *allergic* or *extrinsic allergic alveolitis.*" *Dorland's* at 1475.

[35] Extracorporeal membrane oxygenation ("ECMO") is also called extracorporeal life support. *Dorland's* at 590. It is defined as "the provision of respiratory support by circulating the blood through an artificial lung consisting of two compartments separated by a gas-permeable membrane, with the blood on one side and the ventilating gas on the other[.]" *Id.* at 1805.

By August 18, 2014, Petitioner's treaters were considering several etiologies for her condition, including an "idiosyncratic Bactrim reaction, [an] infectious etiology ([but] all evaluations so far [were] negative), rheumatologic [causes] (however[,] inflammatory markers [were] only mildly elevated), [and] inhalational/toxin exposure." *Id*. at 2472. Dr. Simon noted that the family questioned Petitioner's vaccinations as being responsible for her condition, "in particular the HPV [vaccine.]" *Id.* Dr. Simon wrote that "in reviewing the VAERS [database, she found] no description of lung injury." *Id.* She did "not believe a second bronchoscopy w[ould] shed any further light on the etiology[]" for Petitioner's condition. *Id.* at 2473. Petitioner's treaters at Egleston described her condition as "an end[-]stage irreversible injury," and informed her parents that "her only chance for survival [wa]s lung transplantation." *Id.* at 2472. They also noted that Petitioner was "[status post] pulse steroid without significant improvement." *Id.* Progress notes dated August 18, 2014, list Petitioner's diagnoses as status asthmatics, pneumonia, acute respiratory failure, hypoxemia,[36] hyponatremia,[37] pneumomediastinum, pneumothorax[38] on right, and idiopathic pulmonary fibrosis.[39] *Id.* at 2407.

On August 24, 2014, Petitioner was transferred to the University of Kentucky for possible lung transplantation. Pet'r's Ex. 2 at 75. The admission note for this procedure listed her diagnosis as acute respiratory failure with an unclear etiology. *See* Pet'r's Ex. 5 at 245. Approximately one month later, on September 25, 2014, Petitioner underwent a successful bilateral lung transplantation. *Id.* at 1115, 1462. She was discharged from the hospital on October 16, 2014. *Id.* at 1462. During post-surgical follow up on October 21, 2014, Petitioner's treaters noted that she was tolerating her immunosuppressive therapies well and was able to play and walk without dyspnea.[40] Pet'r's Ex. 6 at 2. Petitioner underwent a repeat bronchoscopy and lung biopsy on November 3, 2014, and the results showed no evidence of rejection. *Id.* at 139. Petitioner's filed medical records to-date detail Petitioner's extensive follow up care, therapies, and recovery.[41] Petitioner has not filed additional medical records.

B. Witness Statements

Mr. and Mrs. Williams both testified about their daughter's health prior to her July 29, 2014 vaccinations, and her rapid deterioration immediately thereafter. Their testimony was consistent with the medical record and each other. They provided additional information about Petitioner's symptoms at home and their encounters with medical personnel while they were attempting to obtain a diagnosis for her condition. Mrs. Williams testified that Petitioner did not have any residual effects from prematurity with respect to her lungs or pulmonary function. Tr. 16:22–25. She stated that Petitioner had received vaccinations from birth up until her last scheduled round of immunizations on July 29, 2014. Tr. 17:19–20.

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[36] Hypoxemia means "deficient oxygenation of the blood[.]" *Dorland's* at 908.
[37] Hyponatremia is the "deficiency of sodium in the blood." *Dorland's* at 903.
[38] Pneumothorax is "an accumulation of air or gas in the pleural space . . . ." *Dorland's* at 1476.
[39] Pulmonary fibrosis is the "chronic inflammation and progressive fibrosis of the pulmonary alveolar walls, with steadily progressive dyspnea, resulting finally in death from oxygen lack or right heart failure." *Dorland's* at 702. Also called Hamman-Rich syndrome and interstitial pulmonary fibrosis. *Id.*
[40] Dyspnea is "breathlessness or shortness of breath; difficult or labored respiration." *Dorland's* at 582.
[41] *See supra,* note 5.

Mrs. Williams explained that the entire family went on a trip to Busch Gardens in the days before Petitioner's vaccinations. Tr. 19:23–25. During the vacation, Petitioner did not express any concerns or exhibit any signs that she was in respiratory distress. Tr. 20:10–12. Upon the family's return from the trip, Petitioner received the vaccinations at issue in this case. Tr. 21:2. Mrs. Williams testified that Petitioner did not have any breathing issues on the day of her vaccinations. Tr. 21:6–7. She noted that Petitioner received the TDaP and meningococcal vaccines in her left arm and the HPV vaccine in her right arm. Tr. 23:3–8. The next day, she noted that Petitioner ran a fever of 105 degrees Fahrenheit. Tr. 21:17. Mrs. Williams also noted that Petitioner had swelling in her left arm. Tr. 22:11. Mrs. Williams testified that she tried unsuccessfully to break Petitioner's fever by following her sister's advice to alternate between Tylenol and Motrin. Tr. 23:15–17.

From there, Mrs. Williams described how medical professionals initially reacted to her daughter's symptoms. The first time Mrs. Williams and her husband took Petitioner to the ER, "[t]hey put us in a room and we waited." Tr. 27:25. Eventually, "they swabbed [her] for strep," and then "they sent us home." Tr. 23:20–21. Petitioner was given "a prescription for antibiotics," but "[t]hey didn't [identify] a diagnosis or anything." Tr. 28:1–2. Meanwhile, Petitioner had developed breathing problems and she wasn't getting better. Tr. 28:9–12. Mrs. Williams noted that Petitioner's symptoms had started the day after vaccination with arm swelling and a fever. Tr. 24:11–13. She stated that soon thereafter, Petitioner "would just lay around and she wouldn't eat." Tr. 27:4. Petitioner "would just stay in bed." Tr. 27:5. Once Petitioner started having breathing problems, "[s]he just would do this rapid breathing and she really became confined to [her] bed." Tr. 28:15–16.

Mrs. Williams explained that the first ER they went to was WellStar, a local facility in Austell, Georgia. Tr. 29:22–23. After Petitioner's symptoms worsened, Mrs. Williams and her husband took Petitioner to Hughes Spalding Children's Hospital in Atlanta. Tr. 29:23–24. Mrs. Williams stated that Petitioner was airlifted from Hughes Spalding to CHOA – Scottish Rite and was then placed in the intensive care unit ("ICU"). Tr. 30:16–17, 31:9. After she was placed in the ICU for a couple of days, Petitioner's condition started to improve, and Scottish Rite was preparing to release her. Tr. 31:24–25. However, when Petitioner "tried to get up and she fell," they reconsidered. Tr. 32:3–5. Shortly thereafter, medical personnel told Petitioner's parents that "they had done all they could do at Scottish Rite and [they] needed to take her to Egleston for more testing and stuff." Tr. 32:6–8. Mrs. Williams stated that after Petitioner was transferred to Egleston, she was placed in a coma. Tr. 32:11.

Mr. Williams recounted much of Mrs. Williams' account. He noted that ER personnel did "pretty much nothing as far as [he was] concerned." Tr. 55:22–23. He described how they "wouldn't give [Petitioner] an X-ray." Tr. 55:23. They "gave [Petitioner] medicine," and "watched her for a couple of hours and then they released her." Tr. 55:23–25. Mr. Williams remembered that on the following Sunday, they were on the way to church and "she was really panting a lot." Tr. 56:6–8.

Both of Petitioner's parents noted that she is no longer recommended for vaccination. *See* Tr. 37:17–18. Mrs. Williams did not offer a reason, but Mr. Williams stated that, Petitioner's "immune system is weakened due to the medication[]" she is on. Tr. 37:17–18, 82:20–21.

Petitioner's testimony was brief and consistent with her parents' accounts. She identified the first symptom she remembers as "not having any energy to do anything." Tr. 69:20–21. She stated that she felt like she "had a cold maybe but ten times worse." Tr. 69:22–23.

Lastly, Petitioner's aunt Mrs. Nina Lagarde, testified. She noted that when Petitioner was in the ICU, her treaters "tried to say she had asthma." Tr. 85:14. Petitioner's aunt noted that she is an ER nurse practitioner, and she was the one who told medical personnel about the vaccines as a possible cause. Tr. 85:20–21. She noted that "nothing else made sense" and asked the attending to "just scan [Petitioner's] arm" and to "do an echo." Tr. 85:21–24. Mrs. Lagarde emphasized that she is a nurse practitioner, not a medical doctor and she is not testifying as an expert. Tr. 86:4–8. Although she was upfront with hospital staff about her belief that Petitioner's condition was vaccine caused, they never identified a cause, "[t]hey just said something attacked . . . ." Tr. 85:20–21, 93:7–8.

C. Medical Literature

i. ChILD

Interstitial lung disease in children ("chILD") is an umbrella term for a group of respiration disorders that are "characterized by inflammatory and fibrotic changes that affect alveolar walls." Pet'r's Ex. 17 at 1, ECF No. 23-1.[42] A chILD syndrome diagnosis requires:

> the presence of at least [three] of the following [four] criteria in the absence of other known disorders: (a) respiratory symptoms (cough, rapid breathing, or exercise intolerance), (b) signs (resting tachypnea,[43] crackles, retractions, digital clubbing, failure to thrive, or respiratory failure), (c) hypoxemia, and (d) diffuse chest infiltrates on chest X-ray or computed tomography (CT) scan.

Pet'r's Ex. 10 at 3, ECF No. 22-3.[44] There have been several different systems that have been developed for the classification of lung diseases in children. In the late 1990s, researchers developed "four histopathologically distinct subgroups of idiopathic interstitial pneumonias: usual interstitial pneumonia ("UIP"), desquamative interstitial pneumonia ("DIP") and a closely related pattern termed respiratory bronchiolitis-associated ILD, acute interstitial pneumonia (formerly Hamman-Rich syndrome), and non[-]specific interstitial pneumonia ("NSIP")." Pet'r's Ex. 17 at 1. ChILD cases have also been categorized more recently by diagnosticians into the following groupings: "1) exposure-related ILD; 2) systemic disease-associated ILD; 3) alveolar structure disorder-associated ILD; and 4) ILD specific to infancy." *Id.*

[42] A. Clement, et al., *Interstitial Lung Diseases in Children,* 5 ORPHANET J. RARE DISEASES 1–24 (2010).
[43] Resting tachypnea is the "excessive rapidity of breathing[]" while at rest. *Dorland's* at 1868.
[44] J. Soares, et al., *Childhood Interstitial Lung Diseases: An 18-year Retrospective Analysis,* 132 PEDIATRICS 684–91 (2013).

Another classification system first groups such conditions into "'Disorders More Prevalent in Infancy' and 'Disorders not Specific to Infancy.'" Pet'r's Ex. 15 at 3, ECF No. 22-8.[45] This type of "classification strategy recognizes that some disorders present largely in infancy, but may also develop later in childhood or even adulthood, whereas the second category acknowledges that infants can develop conditions that are more common in older children and adults." *Id*. The diseases seen more often in older children include, "systemic diseases, idiopathic disorders [DIP, UIP, NSIP and lymphoid interstitial pneumonia [("LIP")], unclassifiable ILD[,] and also infectious disorders." Pet'r's Ex. 17 at 2. Although these conditions are iterations of lung disease, the classifications are important for treatment. *Id.* In some cases where there is clear evidence of inflammation, corticosteroids can be quite effective. *Id.* In other cases, steroids can exacerbate the injury. *Id.* In the most severe chILD cases, such as in Petitioner's case, a lung transplant is the only viable treatment option. Early identification of the nature of a patient's condition can expedite treatment, particularly in cases where organ donation and transplantation are needed. *See id.*

The rarity of chILD cases has limited the ability of researchers to conduct clinical trials or epidemiological studies. Pet'r's Ex. 14 at 5, ECF No. 22-7.[46] Due to the wide spectrum of the syndrome, the outcome for cases "is highly variable with a mortality rate around 15%." Resp't's Ex. H at 1;[47] *see also* Pet'r's Ex. 17 at 1. In general, "[a]n overall favorable response to corticosteroid therapy is observed in around 50% of cases, often associated with sequelae such as limited exercise tolerance or the need for long-term oxygen therapy." *See id.* There is much more information on the etiology, progression, and treatment of ILD in adults, which is sometimes used to help understand and characterize chILD cases. ILD in adults is classified by histology; however, these schemes "are not satisfactory for [all] pediatric cases which seem to comprise a broader spectrum of disorders." Pet'r's Ex. 17 at 1.

ii. Pulmonary Fibrosis

Fibrosis occurs when tissue repair is dysregulated and "the excess accumulation of extracellular matrix components ("ECM")" leads to scarring. Pet'r's Ex. 47 at 1, ECF No. 26-4.[48] Pulmonary fibrosis ("PF") is a condition that includes acute, treatment-resistant disease and involves "the progressive and irreversible destruction of lung architecture caused by scar formation that ultimately leads to organ malfunction[] and death from respiratory failure." *Id*. While idiopathic pulmonary fibrosis ("IPF") is a type of ILD seen in adults, there are some studies that suggest that IPF is "not believed to occur in children." Pet'r's Ex. 13 at 5, ECF No. 22-6.[49] A study by Nathan et al. states that pulmonary fibrosis has not been identified as a distinct child entity with diagnostic criteria. N. Nathan, et al., *Review: Pulmonary Fibrosis in Children,* 8(9) J. CLIN. MED. 1–15 (2019). The authors found "that adult radiologic and histologic lung fibrosis patterns partially

[45] G. Kurland, et al., *An Official American Thoracic Society Clinical Practice Guideline: Classification, Evaluation, and Management of Childhood Interstitial Lung Disease in Infancy,* 188 AM. J. RESPIRATORY CRIT. CARE MED. 376–94 (2013).
[46] T. Vece, et al., *Diagnosis and Management of Diffuse Lung Disease in Children,* 12 PED. RESPIRATORY REV. 238–42 (2011).
[47] *See* Clement, et al., *supra* note 42.
[48] T.A. Wynn, *Integrating Mechanisms of Pulmonary Fibrosis,* 208 J. EXP. MED. 1339–50 (2011).
[49] J. Popler, et al., *New Coding in the International Classification of Diseases, Ninth Revision, for Children's Interstitial Lung Disease,* 142 CHEST 774–80 (2012).

fail to precisely describe pediatric PF lesions and that [in usual interstitial pneumonia], the most common aspect of IPF, is exceptionally or never observed in childhood." *Id.* at 2. The few identified cases of PF in children exhibit "a different pattern than in adults, with more inflammatory cell recruitment and less fibroblast recruitment and ECM deposition." *Id.* at 7. The authors contended that "pediatric PF . . . may have a different meaning in children, than in adults, with more cellular recruitment, less collagen deposition, and less parenchymal[50] destruction." *Id.* at 10.

Most studies indicate that patients with IPF "ha[ve] an [sic] life expectancy of 2–6 [years] after diagnosis." Pet'r's Ex. 47 at 1;[51] *see also* Resp't's Ex. TT at 1, ECF No. 46-3.[52] "The majority of patients demonstrate a slow, gradual progression over many years." Resp't's Ex. I at 11.[53] The mortality rate is high, because "the only effective treatment available for progressive lung fibrosis is lung transplantation." Pet'r's Ex. 47 at 1. This is compounded by the fact that "pathological mechanisms that account for disease progression are poorly understood but likely involve alterations in innate inflammatory cells, epithelial cells, and fibroblasts." Pet'r's Ex. 56 at 1, ECF No. 45-8.[54] It can occur following viral infections, exposure to toxins, following chemotherapy, or accompanying autoimmune disease. Pet'r's Ex. 47 at 1.

There is debate surrounding the role of inflammation in the development of pulmonary fibrosis. *Id.* at 2. Dr. Thomas Wynn contended that "inflammatory mediators clearly play a role in both the initiation and progression of some forms of pulmonary fibrosis." *Id.* at 3. Dr. Wynn noted that "many forms of the disease are believed to be induced, at least initially, by a strong inflammatory response." *Id.* at 2. This is based on elevated levels of TNF in some patients with an idiopathic etiology and mice models that show an over-expression of cytokines in the lungs. *Id.* While animal studies provided some support for the role of inflammation, "it remains unclear whether any of the experimental models truly duplicate the idiopathic form of the disease that is commonly seen in humans." *Id.*

Immediately following tissue damage in humans, epithelial cells "release inflammatory mediators . . . that trigger[] clotting and [the] development of provisional ECM." *Id.* This process results in "[p]latelet aggregation and subsequent degranulation" to "promote[] blood vessel dilation and increased permeability" and allows the "efficient recruitment of inflammatory cells." *Id.* These cells, including neutrophils and macrophages, "eliminate any invading organisms." *Id.* Cytokines are also produced, and they "amplify the inflammatory response and trigger fibroblast proliferation." *Id.* Fibroblasts are "highly responsive to growth factors/cytokines," such as TGF-

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[50] Parenchyma refers to "the essential or functional elements of an organ[.]" *Dorland's* at 1382.
[51] *See* Wynn, *supra* note 48.
[52] D. Galati, et al., *Peripheral Depletion of NK Cells and Imbalance of the Treg/Th17 Axis in Idiopathic Pulmonary Fibrosis Patients,* 66 CYTOKINE 119–26 (2014).
[53] G. Raghu, et al., *An Official ATS/ERS/JRS/ALAT Statement: Idiopathic Pulmonary Fibrosis: Evidence-based Guidelines for Diagnosis and Management,* 183 AM. J. RESPIRATORY CRIT. CARE MED. 788–824 (2011).
[54] D.N. O'Dwyer, et al., *Influences of Innate Immunity, Autophagy, and Fibroblast Activation in the Pathogenesis of Lung Fibrosis,* 311 AM. J. PHYSIOL. LUNG CELL MOL. PHYSIOL. 590–601 (2016).

beta, IL-1beta, IL-6, IL-13 and IL-33." Resp't's Ex. UU at 2, ECF No. 46-4.[55] Studies on the role of cytokines in the development of pulmonary fibrosis have suggested that TGF-beta is the "prototypical 'profibrotic' mediator." *Id.* at 5.

TGF-beta1 "promotes ECM accumulation, . . . drives phenotypic changes of fibroblasts," and "promotes fibroblast proliferation in patients with IPF." *Id.* These cytokines "are recruited from a variety of sources," and once activated, they initiate regeneration of the damaged tissue by a process where "epithelial/endothelial cells divide and migrate over the temporary matrix to regenerate the damaged tissue." Pet'r's Ex. 47 at 2. Scars can result at any stage of this process, "likely explaining the complex nature of pulmonary fibrosis." *Id.*

In clinical trials, TNF inhibitors were effective "but, because TNF can inhibit collagen synthesis in myofibroblasts, TNF antagonists might have the undesired effect of worsening the disease." *Id.* at 3. Evidence of increased TNF levels alongside IL-1beta induced fibrosis suggests a connection. *See id*. Chemokines and profibrotic cytokines are increased by IL-1beta "illustrating how [an] acute lung injury initiated by proinflammatory cytokines and neutrophils can quickly evolve[] to a progressive fibrotic response." *Id.*

Alternatively, IPF is "often characterized as exhibiting highly progressive fibrotic disease in the absence of detectable inflammation." *Id.* at 2. Unlike other forms of ILD, evidence that "an active inflammatory response is not a strict prerequisite[,] likely explains why standard autoinflammatory therapies, including corticosteroids and cytotoxic agents[,] have shown little efficacy." *Id.*; *see also* Resp't's Ex. TT at 8.[56] Additionally, "[d]epletion of NK and Th17 cells along with a[n un]compromised [regulatory T lymphocyte] compartment delineate the existence of an 'immune profile' in IPF that may be more closely assimilated to that observed in the cancer model." Resp't's Ex. TT at 8. The Galati et al. study sought to "investigate the distribution of peripheral immune subsets in patients affected by clinically stable idiopathic pulmonary fibrosis." *Id.* at 5. The author's "exclusion criteria were acute disease exacerbation, and systemic administration of corticosteroids, and/or immune-suppressive drugs at enrollment or in the previous [sixty] days." *Id.* at 2. They found a significant decrease in the number of NK cells in IPF patients, which is contrary to a previous, smaller study. *Id.* at 5. Potential reasons for this difference include different diagnostics for IPF, different exclusionary criteria, and "the inclusion [of a] control group of patients affected by other interstitial lung diseases instead of healthy subjects." *Id*. Although there was a difference in NK cell levels in IPF patients, "there are [sic] no information addressing dynamics of NK and NKT cells in IPF pathogenesis for any comparison with our data." *Id.* There is so much we don't know about "the nature of how or which inflammatory immune cells may be contributing to pathogenesis," that "it is likely that the immunosuppressive agents we have used to date may not have effective[ly] targeted the profibrotic actions of innate immune cells." Pet'r's Ex. 56 at 4.[57]

There have been several potential "triggers [identified] that initiate and maintain fibrotic pulmonary remodeling" but they are controversial. *See* Resp't's Ex. UU at 1. These include

[55] S. Kolahian, et al., *Immune Mechanisms in Pulmonary Fibrosis,* 55:3 AM. J. RESPIRATORY CELL MOL. BIOL. 309–22 (2016).
[56] *See* Galati, et al., *supra* note 52.
[57] *See* O'Dwyer, et al., *supra* note 54.

infections, environmental and occupational pollutants, obesity, diabetes mellitus, pulmonary hypertension, gastroesophageal reflux, and connective tissue diseases/autoimmune disorders. *Id.* There is evidence that "immune cells have more opportunity to cross talk with structural cells of the lung than was previously appreciated." Pet'r's Ex. 56 at 8. Researchers have discovered the "release of IL-17 from neutrophils promotes fibroblast proliferation." *Id.* Other literature suggests that "neutrophils can activate TGF-beta," and "further promote fibrogenesis by blocking autophagy and increasing ECM deposition." *Id.* Fibroblasts, if activated by dysregulation, can be "highly responsive to growth factors/cytokines, such as connective tissue growth factor, ("CTGF"), platelet-derived growth factor ("PDGF"), [TGF-beta, various interleukins,] as well as aberrantly activated profibrotic pathways, . . . that maintain fibrotic tissue transformation." Resp't's Ex. UU at 2.

iii. Immune Response

While there are conflicting perspectives on the role of the immune system in the development of IPF, there is also disagreement on the effect of multiple immune triggers occurring simultaneously within the body. In the Boyce et al.[58] study, researchers tested whether there is "an association between recent vaccination with a pertussis-containing vaccine and increased severity of respiratory syncytial virus ("RSV")[59] infection." Resp't's Ex. VV at 1, ECF No. 46-5. This study focused on the pertussis vaccination because the acellular pertussis vaccine contains a toxoid. *Id.* Even in this inactivated form, the authors found that the pertussis toxin "enhances the magnitude of the antibody response to the simultaneously delivered antigens." *Id.* at 2. Researchers hypothesized that evidence "to support the role of the host immune response as a determinant of RSV disease severity," would have included a more severe RSV disease course in "[i]nfants immunized with an experimental formalin-inactivated RSV vaccine [when compared to an unvaccinated group]," following exposure to the wild virus. *Id.* The authors found that in mice, "exposure to [the] pertussis toxoid (which is a component of all pertussis vaccines) was associated with an altered cellular and humoral immune response to RSV infection and with increased mobility and mortality." *Id.* at 4. This "suggest[s] that enhanced illness was the result of selection activation of type 2 CD4+ [Th] lymphocytes, leading to altered cytokine and immunoglobulin production." *Id.* Ultimately, the authors noted that the results from the murine model were not duplicated in children. *Id.* Researchers found that receipt of a recent pertussis vaccination did not increase illness severity or likelihood of hospitalization. *Id.* The authors cautioned that "[t]he reason for the disparity between the animal data and [human subjects] is unknown." *Id.*

The McDonald et al.[60] study sought to answer the question, "[h]ow do cells of the innate immune system find their way to sites of sterile inflammation?" Pet'r's Ex. 48 at 3, ECF No. 26-5. The authors defined sterile inflammation as an immune system process that occurs where there

[58] T. Boyce, et al., *Pertussis Vaccination and the Risk of Respiratory Syncytial Virus-Association Hospitalization,* 23 J. PEDIATRIC INFECT. DIS. 897–901 (2004).

[59] Respiratory syncytial virus ("RSV") refers to "any of a group of viruses belonging to the genus *Pneumovirus,* isolated originally from chimpanzees . . . . In humans, they cause respiratory disease that is particularly severe in infants, in whom it causes bronchiolitis [] and sometimes pneumonia." *Dorland's* at 2064.

[60] B. McDonald, et al., *Innate Immune Cell Trafficking and Function During Sterile Inflammation of the Liver,* 151 GASTROENTEROLOGY 1087–95 (2016).

is cell death in the absence of infection. *Id.* at 1. This process "is required for processes that include organ development, tissue repair[,] and host defense." *Id.* The researchers focused on liver disease and noted that "there are few treatments beyond liver transplantation for patients with end-stage disease." *Id.* They cautioned that "molecular mechanisms that control immune cell trafficking during sterile inflammation may be organ and tissue specific." *Id.* at 7. In other words, "lessons learned from the skin or kidney are not necessarily applicable to the liver microvasculature." *Id.* They used information from prior recent studies that described "cellular and molecular mechanisms of immune cell recruitment to damaged tissues, as well as the cell types that mediate tissue repair and homeostasis." *Id.*; *see also* Pet'r's Ex. 58 at 3, ECF No. 45-10.[61] The McDonald et al. study revealed "the molecular mechanisms that enable immune cells to traffic to sites of sterile inflammation in the liver[,] as well as the contributions of innate immune cells during tissue repair." Pet'r's Ex. 48 at 1. It also showed that neutrophils respond to the liver injury by "infiltrating the site of injury within minutes." *Id.* at 3. The release of damage associated molecular patterns ("DAMPs") "from dead cells[,] stimulates [the] endothelium to present adhesion molecules and chemokines on their surface to draw neutrophils out of the mainstream of blood and initiate a well-described recruitment cascade." *Id.* Still within the context of sterile inflammation, "neutrophils migrate via intravascular channels rather than into the parenchyma[,] and through the interstitium." *Id.* at 4. This "neutrophil influx is focused precisely into areas of tissue injury where they are observed to exhibit swarming behavior." *Id.* The authors noted that this swarming "has been observed in multiple models of sterile inflammation[,] as well as infections." *Id.*

The authors of the McDonald et al.[62] article further noted that macrophage infiltration at the site of sterile inflammation also occurred one- to- two- days after the neutrophils arrive. *Id.* at 5. They continued that "[m]onocytes have many functions, . . . including production of inflammatory mediators, clearance of dead neutrophils, stimulation of extracellular matrix production, regeneration of parenchymal cells, and angiogenesis." *Id.* In addition to inflammatory monocytes, anti-inflammatory monocytes are produced that "promote resolution (IL-10, transforming growth factor beta, and VEGF) to shift the [] response from active inflammation toward resolution and restitution." *Id.* The "in situ reprogramming [of inflammatory monocytes to an anti-inflammatory phenotype] was induced by local production of anti-inflammatory cytokines (IL-10 and IL-4) and was required for clearance of necrotic debris and deposition of new extracellular matrix scaffolding in the healing wound." *Id.* Lastly, they noted that "monocytes have been found to patrol the microvasculature monitoring for danger[, and]monocytes have been observed to continuously crawl throughout tissue micro-vessels." *Id.* at 6. The authors found that "[u]pon encountering infection or tissue injury, these monocytes rapidly exit the blood vessels and begin producing cytokines and chemokines to summon other immune cells." *Id.*

III. Experts

A. Expert Backgrounds

1. Petitioner's Expert, Eric Gershwin, M.D.

[61] V. Colmenares, et al., *Human Papillomavirus Immunization is Associated with Increased Expression of Different Innate Immune Regulatory Receptors,* 19:7 CLIN. & VACCINE IMMUNOLOGY 1005–11 (2012).
[62] *See* McDonald, et al., *supra* note 60.

Dr. Gershwin received his medical degree from Stanford University in 1971. Pet'r's Ex. 9 at 1, ECF No. 22-2. He is licensed to practice in several states, including California, and holds board certifications in internal medicine, internal medicine with a subspecialty in rheumatology, and allergy and clinical immunology. *Id.* at 2. Dr. Gershwin has an honorary doctorate, or "Honoris Causa," from the University of Athens, Greece, in recognition of his lifetime contributions in immunology and medicine. *Id.* at 1. Dr. Gershwin has also been awarded the AESKU Prize in Autoimmunity for his lifetime contribution in immunology and the Vasco Da Gama Prize for "a lifetime of deep explorations in immunology to benefit mankind." *Id.*

Dr. Gershwin's post-doctoral training includes a two-year residency at the Tufts-New England Medical Center in Boston, Massachusetts, two years as a clinical associate in immunology at the National Institutes of Health in Bethesda, Maryland, and two years as an Assistant Professor of Medicine in Rheumatology and Allergy at the University of California School of Medicine in Davis, California ("UC Davis"). *Id.* at 2. Dr. Gershwin then went on to become the Director of the Special Immunology Diagnostic Laboratory at UC Davis. *Id.* He has been a Professor of Medicine, specializing in Rheumatology and Allergy, at UC Davis since 1981 and a Chief of the Division of Rheumatology/Allergy and Clinical Immunology since 1982. *Id.* at 1.

Dr. Gershwin is also a fellow with the American Academy of Allergy and Immunology, the American College of Physicians, and the American College of Rheumatology. *Id.* at 3–4. He currently serves as the editor-in-chief for the Journal of Autoimmunity and Clinical Reviews in Allergy, as co-editor-in-chief for Autoimmunity Reviews, and as co-editor for Reviews in Autoimmunity. *Id.* at 5. Dr. Gershwin's curriculum vitae lists numerous books, book chapters, and research papers of which he is a listed author. *See id.* at 8–125.

During the hearing, he noted that he has testified in the Program before. Tr. 97:19–21. He also stated that he has "seen and treated patients with immunological issues for nearly [fifty] years." Tr. 100:8–9. Dr. Gershwin highlighted that he has published "nearly 1,000 papers, books[,] and reviews" during that time. Tr. 100:10–11. He noted that he has "been funded by the [National Institute of Health] for basic and clinical research in immunology without interruption continuously since 1975[.]" Tr. 100:14–16. Dr. Gershwin testified that he has consulted on approximately five to seven chILD cases throughout the course of his career, as they are "exceedingly rare" cases. Tr. 102:13–23.

Dr. Gershwin submitted one expert report and testified during the entitlement hearing. *See* Pet'r's Ex. 8, ECF No. 22-1; Tr. 97–169, 285–318. Petitioner offered Dr. Gershwin as an expert in immunology without objection, and I recognized him as such. Tr. 103:11–15.

2. Respondent's Expert, Dr. Gary S. Rachelefsky, M.D.

Dr. Rachelefsky received his medical degree from Washington University in St. Louis, Missouri in 1967. Resp't's Ex. B at 1, ECF No. 28-2. Dr. Rachelefsky completed a residency in pediatrics at Johns Hopkins University in Baltimore, Maryland in 1970. *Id.* He completed fellowships in epidemiology and allergy and immunology at the Center for Disease Control and the UCLA School of Medicine in 1972 and 1974, respectively. *Id.* He holds board certifications in pediatrics and allergy and immunology. *Id.* Dr. Rachelefsky currently serves as a Professor of Allergy and Immunology at the David Geffen School of Medicine at UCLA. *Id.* He is also the

Associate Director of the Allergy-Immunology Training Program at the UCLA's medical school. *Id.* Dr. Rachelefsky serves as the Director of the Executive Care Center for Asthma, Allergy & Respiratory Diseases at UCLA. *Id.* Dr. Rachelefsky holds memberships in numerous professional societies, committees, and advisory boards dedicated to pediatrics, allergy and immunology, and asthma. *Id.* at 5–10. Dr. Rachelefsky's curriculum vitae lists numerous books, book chapters, and research papers of which he is a listed author. *See id.* at 13–35. He submitted one expert report and did not testify at the entitlement hearing. *See* Resp't's Ex. A.

3. Respondent's Expert, Christine McCusker, M.D.

Dr. McCusker received her medical degree from McMaster University Medical School in Ontario, Canada in 1993. Resp't's Ex. LL at 1, ECF No. 34-2. Dr. McCusker completed a residency in pediatrics at Montreal Children's Hospital in Quebec, Canada in 1996. *Id.* at 2. She also completed a fellowship in allergy and immunology at McGill University in Quebec, Canada in 1999. *Id.* Dr. McCusker completed a post-doctoral research fellowship in immunology at the same institution in 2000. *Id.* Dr. McCusker has been a physician in the emergency department of Montreal Children's Hospital and McGill University since 1999. *Id.* at 5. She has been the Director of the Clinical Immunology Laboratory at the same institution since 2004. *Id.* Since 2009, Dr. McCusker has also served as an Associate Professor of Allergy and Immunology in the Pediatrics Department of McGill University. *Id.* at 3. She currently serves as the Research Director of Meakins-Christie Laboratories. *Id.* Dr. McCusker is board-certified in pediatrics and holds several professional credentials in allergy and immunology. *Id.* at 2–3. She has received numerous honors and has delivered a plethora of national and international lectures. *Id.* at 4–7. She is a member of several academic committees and societies. *Id.* at 13–15. Her curriculum vitae lists extensive publications, including articles, abstracts, book chapters, and editorials of which she is a listed author. *See id.* at 20–26. Some of the articles address cytokine activity. Tr. 174:22–24.

During the hearing, Dr. McCusker explained that as part of her clinical practice, she spends half of her time seeing patients and the other half "either in research or in administration or in teaching[.]" Tr. 172:10–17. She testified that the patients she treats in her immunology clinic are referred to her by specialists. Tr. 173:1–12. Dr. McCusker stated that she sees pediatric patients with pulmonary fibrosis and has treated approximately four patients with chILD. Tr. 173:22–25, 174:11.

Dr. McCusker submitted one expert report and testified at the entitlement hearing. *See* Resp't's Ex. KK; Tr. 170–238, 243–284. Respondent offered Dr. McCusker as an expert in pediatric immunology, pediatric clinical allergy/immunology, and pediatrics without objection, and I recognized her as such. Tr. 176:6–14.

B. Expert Review

1. Petitioner's Expert, Eric Gershwin, M.D.

In general, Dr. Gershwin's practice was approximately 10% focused in pediatrics. Tr. 130:11–12. Over the course of his practice, he has "seen hundreds of patients in a given year, particularly with immune deficiencies." Tr. 130:14–15. He noted that he "actually wrote or edited

the first textbook of pediatric rheumatology." Tr. 130:12–13. He explained that "[t]he prevalence [of chILD cases] is about one in a million per children under the age of [sixteen]." Tr. 130:19–20. In the past ten years, Dr. Gershwin has seen pediatric patients with connective tissue disease and lupus, in addition to two with "a disease like this [case]." Tr. 131:7–11.

Dr. Gershwin was qualified as an expert in immunology, and he provided a brief overview of the immune system and "two major types of immunity." Tr. 103:25, 104:1–2. The innate system, Dr. Gershwin explained, is analogous to a first responder. Tr. 104:5. When a person is vaccinated, innate system cells "produce cytokines that facilitate the immune system." Tr. 104:6–7. Indeed, Dr. Gershwin noted that "[t]he FDA requires that you show that vaccines produce cytokines." Tr. 121:16–17. He continued that there are different types of cytokines that are produced in different bodily systems. Dr. Gershwin described them as signal transmitters and said they are "responsible for cell health" and "cell pathology in some cases." Tr. 104:18–21. Proinflammatory cytokines "will facilitate or promote scarring or connective tissue repair." Tr. 105:8–9. Dr. Gershwin testified that the process of inflammation, "might be local or it might be systemic." Tr. 105:24–25. He added that an inflammatory response does not have to occur in a vacuum. Dr. Gershwin stated that inflammation can coincide with "something else happening in a different part of the body," to produce a result different or more severe than if the body was only confronted with one type of stress. Tr. 106:4–25, 107:1. For example, Dr. Gershwin explained that someone that suffers from food allergies may try to "avoid those foods [because] they might produce itching [or] maybe even some hives." Tr. 106:15–16. This same person, "if they happen to exercise around the same time they're eating that food, they may have a life-threatening allergic reaction." Tr. 106:16–19. The combination of those two stressors on the body, the allergic reaction and the exercise, "can cause an entirely different reaction than if they just had the food and sat back and watched a movie." Tr. 106:20–23. Similarly, Dr. Gershwin opined that Petitioner's chILD developed due to immune system dysregulation "caused by the vaccine and an underlying viral infection" acting in combination on the immune system. Tr. 109:11–12.

According to Dr. Gershwin, the logical sequence of cause and effect in this case began with Petitioner's "underlying predisposition" due to her prematurity. Tr. 109:18. He testified that "chILD is extremely rare[,] and we should discuss that, but . . . it is true that being born premature will make you more susceptible." Tr. 109:19–22. Dr. Gershwin noted "that the use of steroid cream and ointment [from approximately 2011 to 2014] did lead to some T cell suppression in [Petitioner] and likely a dysregulation, and also would have been a predisposing factor if she faced the right challenge to getting interstitial [lung] disease in the future." Tr. 110:1–6. Dr. Gershwin continued that Petitioner "had a really intense innate immune response against the vaccine." Tr. 110:7–9. He characterized Petitioner's swollen arm as a local reaction. Tr. 110:9. Petitioner's fever, however, he did "not believe [was] a response [to vaccination]," and stated that "it[was] part of the interstitial lung disease." Tr. 110:12. Dr. Gershwin noted Petitioner's sore throat, "pharyngitis and some evidence of a viral infection." Tr. 110:13–14. He explained that "[Petitioner] had her own innate immune response against that virus, as you would expect it," but he added that "this occurred in combination with a really high intense first responder response against the vaccine." Tr. 110:17–20. Specifically, in "a regional lymph node [there was] an intense up-regulation of molecules involved in the innate response to vaccination." Tr. 110:22–24. According to Dr. Gershwin, Petitioner was "a predisposed host [with] a viral infection" in an instance of "an incredibly fast onset of [chILD]." Tr. 110:25, 111:1–4. He added that this process "[wa]s being driven and

amplified by the bystander events by the cognate cells of [Petitioner's] immune system." Tr. 111:5–6.

In his written report, Dr. Gershwin likened this concept to sterile inflammation, which was discussed in the McDonald et al.[63] article. Pet'r's Ex. 8 at 5; *see also* Pet'r's Ex. 48. He wrote, "[i]n other words, [there is] inflammation in the absence of infection to a tissue injury which leads to chronic perpetuation of an immune response." Pet'r's Ex. 8 at 5. Later in this report, Dr. Gershwin explicitly incorporated the process of sterile inflammation into his theory. He wrote that Petitioner, "more likely than not, was undergoing a mild drug or viral-induced reaction that should have been reversible were it not for the sterile inflammation and abnormal healing characterized by fibrosis that was induced by her vaccinations." *Id.* During his testimony, Dr. Gershwin again analogized Petitioner's case to "acute sterile inflammation [that] is activated in response to podocyte death during [hepatitis]." Tr. 299:17–19. When discussing the migration of innate cells to a bodily injury, he noted that "[c]ells will go to areas of injury. Whether it's a sterile splinter, whether it's a nonbacterial infection, a viral infection, they will go there." Tr. 299:24–25, 300:1.

Dr. Gershwin noted that Petitioner "didn't have an underlying connective tissue disease," and "[s]he didn't have a family history of [ILD]." Tr. 111:21–23. Therefore, the quick progression of Petitioner's chILD "was guided and driven by cognate immune cells that result from the vaccination as bystanders pushing ahead what her own immune response was to [the] virus." Tr. 111:24–25, 112:1–2. He concluded, "[s]o it's not the virus that produced the [ILD]. It's her own immune system." Tr. 112:3–4. When asked what role the virus or Petitioner's Bactrim regiment had on the development of her chILD, Dr. Gershwin stated that the viral or Bactrim process would be the same. He explained that Petitioner "produced an innate or bystander response." Tr. 113:20. This "response became incredibly magnified [and] produced large numbers of cytokines because [Petitioner] got three vaccines." Tr. 113:23–25. Dr. Gershwin stated that he was unable to identify the cytokines produced in Petitioner's case because there was a virus involved and "they didn't do any cytokine measurements[,] and they didn't do immunohistochemistry of her lung tissue during the biopsy of August 15th." Tr. 114:3–6. He conceded that he was more familiar with the functions of specific cytokines in mice than in humans. However, Dr. Gershwin named TGF beta, IL-1 alpha and IL-17 as cytokines that could have been upregulated in response to Petitioner's vaccinations. Tr. 114:12–24.

In Petitioner's case, Dr. Gershwin opined that these and other cytokines acted as inflammatory mediators from macrophages to myofibroblasts that then "produce[d] scarring" and "release[d] connective tissue disease" in Petitioner's lung. Tr. 116:16–18. He explained that a fibroblast, or the "cell that wreaks havoc on the alveolar epithelial cell," can be found all over the body to heal damaged tissue and produce scars. Tr. 122:24–25, 123:1. These scars "will push out any [healthy or damaged] cells or tissue in the area and destroy it." Tr. 123:6–7. In the case of chILD, "the lung thinks it's got an injury that requires a scar." Tr. 116:18–19. He continued that the "scarring pushes out and removes the alveolar epithelial cells, which are the air sacs that we depend on to breathe." Tr. 123:7–9. This can occur because the cells "become[] susceptible to [inflammatory] mediators produced by macrophages, T cells, and to a lesser extent to neutrophils, including for example, IL-1, TGF beta, IL-13, and TNF." Tr. 116:10–13. Dr. Gershwin testified that "[t]he end result is [that] the lung turns basically to scar tissue. Instead of alveolar cells, it ends

[63] *See* McDonald, et al., *supra* note 60.

up with basically a wound." Tr. 118–21. Dr. Gershwin noted that due to the rare occurrence rate of chILD, "[s]o much of this data is based on our understanding of pulmonary fibrosis in other diseases." Tr. 117:13–14. He concluded that when this occurs "there has to be an abnormality in cytokines in the inflammatory response." Tr. 118:1–2.

Dr. Gershwin made the argument that the body mounts "an intense response" to vaccination that is analogous to "a civil war." Tr. 118:24. He referred to the Chatziandreou et al.[64] article that seeks to "examine the role of lymph node macrophages in the induction of the cytokine storm triggered by [an] inactivated influenza virus vaccine." Pet'r's Ex. 51 at 1, ECF No. 45-3. This article is a study of the influenza vaccine, but Dr. Gershwin argues that the authors illustrate an "intense cytokine response and chemokine response following vaccination." Tr. 119:1–2. In the present case, Petitioner "had an intense local response, an extremely intense fever following response, in very close proximity to a viral infection." Tr. 119:8–10. Dr. Gershwin explained that "[i]t's not the virus that's wiping out her lung. It's the immune response." Tr. 119:17–18. He described the "autoinflammatory response" as "extremely intense" and "very short-lived." Tr. 119:19–22. Dr. Gershwin asserted that the response is "going to all be over in three to four days." Tr. 119:23–24. He noted that Petitioner was vaccinated on July 29, 2014, and had a fever and swollen arm the next day. Tr. 119:24–25. By July 31, 2014, Petitioner had developed a cough and "[b]y the 2nd of August, she's got further evidence of a viral infection and even a higher fever." Tr. 120:1–3. Dr. Gershwin asserted that a biopsy during this period would have revealed "inflammatory cells in the lung." Tr. 120:10. Petitioner's deterioration continued, and Dr. Gershwin testified that Petitioner had pulmonary effusion by August 5, 2014, and nothing but "scar tissue" left by August 15, 2014. Tr. 120:4, 11–12.

Dr. Gershwin explained that while "[t]he FDA requires [a showing] that vaccines produce cytokines," the over production of cytokines in this case is indicative of a pathological, intense immune response. Tr. 121:16–17. Dr. Gershwin stated by way of example, "[i]f you get infected with [the] Ebola virus . . . and die, it's not because the virus has taken over the lungs." Tr. 124:1–3. Rather, "[i]t's because your immune system has gone astray[,] and it's become dysregulated . . . it's not as if you find sheets of virus there. It's our own immune response, . . .which has gone astray." Tr. 124:3–8. He noted that he did not find any analogous case studies, because Petitioner's course is "an extremely rare event." Tr. 122:15. She is, he concluded, "a perfect storm where someone who happens to be born premature, who has a cold, has an infection, also has a very intense reaction to a vaccine . . . all within that same short period of time." Tr. 122:16–20.

Petitioner's prematurity, according to Dr. Gershwin, may have affected "the matrix of her lung," and resulted in "lower levels of molecules known as trefoils, which are found in tissue repair." Tr. 124:14–15. He did not believe that her prematurity had resulted in surfactant defects, because that would have manifested "much earlier in [her] life." Tr. 125:3–4. Dr. Gershwin did not identify any other predisposing factors aside from Petitioner's prematurity. Tr. 125:10–11. In response to my questioning, Dr. Gershwin stated that as a practical matter, Petitioner's prematurity is not a significant factor for predisposition. Tr. 159:14. He confirmed that there was no indication that Petitioner suffered from any illness that was associated with prematurity, and it had not played

[64] N. Chatziandreou, et al., *Macrophage Death Following Influenza Vaccination Initiates the Inflammatory Response that Promotes Dendritic Cell Function in the Draining Lymph Node,* 18 CELL REPORTS 2427–40 (2017).

any role in her development up until the point that she developed chILD. Tr. 159:2–5. He reasoned that Petitioner's vaccinations were a substantial factor in causing her injury. Tr. 126:7–8. He added that he did not "believe that vaccinations will produce pulmonary fibrosis," and Petitioner's condition was multifactorial. Tr. 126:9–11.

Dr. Gershwin ended his direct testimony by noting that "part of this serendipit[ous,] very rare event is that these two events, the vaccination and the viral infections, were very, very close in proximity to each other." Tr. 127:8–11. He noted the immune response to the virus would have been elicited at the same time as the response to the vaccine. Tr. 127:11–13. Ultimately, "the injury to [Petitioner's] lung [wa]s caused by her own innate immune system involving cytokines which ultimately [] target[ed] fibroblasts, which [] lead [sic] to scarring." Tr. 127:15–18. Dr. Gershwin noted that the progression of events in this case occurred "much more rapidly than the average patient in the literature with this symptomatology[.]" Tr. 127:19–21. Specifically, "that within days [Petitioner] had evidence of respiratory involvement, [and] ultimately within a period of a month or so[,] into end[-]stage respiratory failure." Tr. 127:21–24.

On cross examination, Dr. Gershwin broke down his theory into steps. First, Petitioner mounted an innate immune response against components of the vaccine that "occur[ed] at the local site to the regional lymph node and it [] spread." Tr. 132:10–11. He continued that the lymphocytes were activated and "cytokines [] travel[ed] through the blood." Tr. 132:16–17. This all happened while Petitioner was "having the same response at the same time to the virus." Tr. 134:5–6. He explained that the immune response to the virus was happening "in [Petitioner's] respiratory tract." Tr. 134:8–9. Dr. Gershwin noted he has "never testified that a vaccine by itself is going to produce a [specific organ injury]." Tr. 135:10–11. He continued, that patients "can get lymphadenopathy all over the body if [they] get a different kind of reaction known as serum sickness where you can get a diffuse lymphadenopathy all over the body if you happened to have that." Tr. 135:12–16. Dr. Gershwin testified that cytokines were being produced in multiple areas of the body and that Petitioner's pulmonary fibrosis proved they were being produced in the lung. Tr. 135:22–23. He opined that Petitioner's fever is proof that cytokines were also being produced in her blood and brain. Tr. 136:2–3.

When asked to identify the vaccine responsible for Petitioner's cytokine response, Dr. Gershwin stated that "it's more likely the tetanus [vaccine] that produced it because [he] suspects she received a tetanus vaccination early in life." Tr. 136:13–15. He would not rule out Petitioner's other vaccinations and stated that "the HPV [vaccine] would have also produced cytokine[s], meaning that all of [her vaccines] would have been involved." Tr. 137:7–9. "The quantitative nature of which might have been more involved than others will depend on the intensity of the innate first responder response against the vaccines." Tr. 139:14–17. Dr. Gershwin was then asked what cytokines were produced by this intense immune response. He responded that cytokine responses differ by age, individual, time of measurement, and other factors. Tr. 141:25, 142:1–3. He also noted that "there are different units, sub-units, that may be produced, for example, to each of these vaccines." Tr. 142:5–6. Dr. Gershwin was unable to opine as to an appropriate timeframe "on an epidemiologic perspective" for his theory, "because this [wa]s such an unusual event." Tr. 146:2–4. He stated that Petitioner's timeframe "occurred a lot more rapidly than the average survival of children with chILD." Tr. 146:5–6. Dr. Gershwin testified that "the onset [of

Petitioner's chILD] would be when she began to have worsening pulmonary symptoms, which looks to be [on] approximately the 3rd of August." Tr. 149:20–22.

Dr. Gershwin conceded that it is possible that Petitioner could have developed chILD without her vaccinations. Tr. 151:15. He noted the accelerated progression and late age of onset of her injury compared to other cases as evidence that the vaccines played a role. Tr. 151:16–22. Dr. Gershwin clarified that this is not an autoimmune response, but an autoinflammatory one. Tr. 165:24. I asked Dr. Gershwin if he routinely checks for the presence of cytokines to detect inflammation. He noted it was not practical to test for cytokines as a clinician. Tr. 159:23–24. However, he did reiterate that there is a relationship between cytokine upregulation and inflammation. He explained that cytokines are upregulated by the vaccines and they "further activate the mononuclear cells in the lung that are responding to the virus." Tr. 162:12–16. He added that they "produce other inflammatory bystander cells that will traffic into the lung and further amplify the response." Tr. 162:16–18. Dr. Gershwin summarized his position by noting that the "virus is in her respiratory tract." Tr. 164:6–7. "If the virus wasn't there, there wouldn't be mononuclear cells in the lung." Tr. 164:9–11. He concluded,"[i]f the mononuclear cells were not in the lung, there'd be nothing for the cytokines produced by the vaccination to amplify." Tr. 164:11–13.

Dr. Gershwin referred to the Kashiwagi et al.[65] article to establish that cytokine production increases post vaccination. Pet'r's Ex. 54 at 1, ECF No. 45-6. He noted that cytokine levels "are anywhere from a few hundred to nearly 1,000 percent higher than [in] unvaccinated people," depending on the number of vaccines an individual receives. Tr. 288:1–2. He then noted that Petitioner received one viral and four bacterial vaccines. Tr. 288:6–7. She was also suffering from a virus severe enough to "develop a clinically significant immune response." Tr. 307:9–10. Dr. Gershwin contended that Petitioner had a local response to her vaccines that "proceed[ed] to the lymph node," and "travel[ed] throughout the lymphatics and [entered] the lung as [an] activated cell in response to an injury." Tr. 308:12–15. Dr. Gershwin explained that cytokines produced as a result of one specific injury can adapt and respond to a different injury that occurred in a different area of the body, despite a different cause. Tr. 309:25. The combination of vaccinations and infection generated an immune response that ultimately caused Petitioner's case to be the fastest progressing chILD Dr. Gershwin has ever seen. Tr. 304:16.

Lastly, Dr. Gershwin clarified the effect of introducing multiple immune stimuli at one time. In theory, if a child that is already infected with a virus is vaccinated, "you would enhance the immune response to [the] virus and the child would get better faster against the virus." Tr. 315:19–22. He then cautioned that "[i]f your immune response to that virus cross-reacted with a self-antigen and you enhance that response, you'd enhance whatever molecular mimicry is taking place." Tr. 316:3–6. Because "there are some viruses that just have other properties that may cause other diseases," it is not worth enhancing the chance that a boosted immune response could prompt the development of an autoimmune disease. Tr. 318:1–3.

[65] Y. Kashiwagi, et al., *Production of Inflammatory Cytokines in Response to Diphtheria-Pertussis-Tetanus (DPT), Haemophilus Influenzae Type B (Hib), and 7-valent Pneumococcal (PCV7) Vaccines,* 10:3 HUMAN VACCINES & IMMUNOTHERAPEUTICS 677–85 (2014).

2. Respondent's Expert, Dr. Gary S. Rachelefsky, M.D.

Dr. Rachelefsky did not testify but he provided a written expert report that Respondent relied on, at least in part, to defend against Petitioner's claim. Resp't's Ex. A. Dr. Rachelefsky began his report with a chronological summary of Petitioner's relevant medical history pre vaccination. *Id.* at 1. He then provided a detailed account of Petitioner's symptoms, medical examinations, and treatment immediately prior to her vaccinations, and thereafter. *See id.* at 2–11. Dr. Rachelefsky noted that he was unable to review "the actual report of the lung biopsies and the CAT scans and chest X-rays performed at [Petitioner's] initial evaluations in Atlanta," because they were unavailable. *Id*. at 1.

For background, Dr. Rachelefsky conducted a review of the VAERS and VSD databases and found "no literature or epidemiologic investigations that associated the administration of [the] HPV [vaccine] to children and the development of interstitial lung disease." *Id.* at 12. Dr. Rachelefsky did note "one case report in an adult with [a] questionable association of [the] HPV vaccination and interstitial lung disease." *Id.* He concluded that "[v]accines are rarely associated with ILDs, except some cases of influenza or [Bacillus Calmette–Guérin] vaccines." *Id.*

Dr. Rachelefsky wrote that ILD is "characterized by inflammatory and fibrotic changes that affect alveolar walls." *Id.* at 13. He continued that "[i]diopathic interstitial pneumonias are diffuse parenchymal lung diseases, of which IPF is the most common type of fibrotic lung disease." *Id.* Dr. Rachelefsky conceded that "the exact nature of the initiating injury and the subsequent cascade of mechanistic events needs to be elucidated." *Id.* He explained IPF pathogenesis to the extent it is known:

> [I]t is now clear that the interaction of growth factors, cytokines, and other mediators with cells resident in the lung[,] is important to the evolution of the fibrotic response in IPF. Resident epithelial cells, fibroblasts, and endothelial cells within the lung produce an array of cytokines and growth factors that stimulate fibroblast proliferation and matrix synthesis. Following epithelial injury, fibrosis is believed to progress due to an imbalance between many groups of molecules that include pro-inflammatory and anti-inflammatory cytokines, fibrogenic and antifibrogenic polypeptides, oxidant-antioxidants, and angiogenic and angiostatic molecules.

Id.

He asserted that "[t]rue idiopathic pulmonary fibrosis, defined pathologically by the characteristic fibroblastic foci and temporal heterogeneity of usual interstitial pneumonia, has not been reported in children." *Id.* He reiterated, "IPF, a common idiopathic interstitial pneumonia in adults that has a very poor prognosis, does not occur in children." *Id.* at 14. He noted that "there are forms of diffuse lung disease (DLD) that are either unique to young children or having differing manifestations as compared with adults." *Id.* These conditions fall under the umbrella term chILD, which "differs from ILD in adults in that it is much rarer and, includes pathologies that are unique to infants and young children (e.g., pulmonary interstitial glycogenosis [or] genetic abnormalities that cause ILD in childhood." *Id.* at 15. "Conversely," he added, "common adult ILD[,] such as

usual interstitial pneumonia[,] is rarely described in children." *Id.* ChILDs "are divided into three subtypes according to the origin of the primary condition involving pulmonary conditions: ILD specific to infancy []; ILD related to a primary systemic disease; and exposure-related ILDs." *Id.* Dr. Rachelefsky estimated that the frequency of chILD is estimated as low, at 1.3 cases per 1,000,000 in one study of children less than seventeen years old. *Id.* He noted, however, that "it is difficult to fix a precise number for the frequency of chILD." *Id.* Ultimately, ILD can progress "to severe irreversible fibrosis of the lung. In such cases, lung transplantation can be used as a final option in children of all ages." *Id.* As such, chILD "has been associated with considerable morbidity and mortality." *Id.*

Dr. Rachelefsky opined that Petitioner suffered from an acute interstitial pneumonia ("AIP"), otherwise known as Hamman-Rich syndrome. *Id.* at 16. AIP is a type of idiopathic acute respiratory distress syndrome that "is classified as an idiopathic interstitial pneumonia" with the "most acute onset and rapidly progressive course." *Id.* Dr. Rachelefsky acknowledged that "[c]ontrolled prospective studies on the treatment of AIP are not available[, which is] not surprising since AIP is so uncommon." *Id.* He noted that AIP "generally affect[s] previously healthy individuals without a prior history of lung disease," and "has the histopathologic appearance of diffuse alveolar damage ("DAD")." *Id.* at 16–17.

Accelerated IPF is a potential differential diagnosis for AIP, however, Dr. Rachelefsky explained that in the former, there is evidence of "bilateral ground-glass opacities." *Id.* at 17. In AIP, "[t]he rapid onset of a widespread injury pattern suggests a single insult as an initiating factor." *Id.* at 18. He continued, "[a]lveolar epithelial cell damage and death lead to elaboration and release of mediators. Recruitment of neutrophils into the alveolar spaces and alveolar septal leads to further cellular damage, possibly via [the] release of toxic oxygen radicals and proteases." *Id.* The symptoms of AIP appear quickly, "with a prodromal illness that typically lasts 7 to 14 days prior to presentation, the most common presenting signs and symptoms are fever, cough, and progressive, severe shortness of breath." *Id.* Biopsy results will show "an acute and/or organizing form of [DAD]." *Id.* at 19. Dr. Rachelefsky wrote that "[t]he diagnosis of [AIP] is based upon two findings: the presence of a clinical syndrome of idiopathic acute respiratory distress syndrome [] and pathologic[al] confirmation of diffuse alveolar damage." *Id*. at 20.

Dr. Rachelefsky then discussed chILD in the context of Petitioner's condition and responded to Dr. Gershwin's report. He began by asserting that Dr. Gershwin's IPF discussion is misplaced because it does not relate to the disease that Petitioner has, "which is acute interstitial pneumonia." *Id.* In fact, Dr. Gershwin has also improperly lumped the diseases together, because "[t]he literature is quite clear that [ILD] in infants (and related to prematurity) is different than in childhood, which is then different from what one sees in adults." *Id.* at 22. He continued "the lack of evidence in the literature of association [between the HPV vaccine and ILD] is ample evidence that there is no relationship whatsoever between the two. This also relates to meningococcal vaccination and to TDaP." *Id.*; *see also* Resp't's Ex. D.[66] Dr. Rachelefsky also opined that "[Petitioner's] onset of [her] pulmonary disease at age [eleven] has nothing to do with her premature birth." Resp't's Ex. A at 24. Dr. Rachelefsky acknowledged that "it's plausible that the intravenous administration of the Bactrim may have enhanced its pulmonary toxicity," but

[66] Y. Yamamoto, et al., *Interstitial Lung Disease Associated with Human Papillomavirus Vaccination,* 16 RESPIRATORY MED. CASE REPORTS 15–17 (2015).

maintained that "[t]he unknown factor is whether [Petitioner] was exposed to some infectious agent or toxic substance that caused her disease [] prior to the onset of her symptoms." *Id.* at 23.

As to Dr. Gershwin's theory of causation, Dr. Rachelefsky asserted "the predominant response to the non-live vaccines is B-cell induced [] and has nothing to do with [sterile inflammation or a similar immune response]." *Id.* Dr. Gershwin's explanation, according to Dr. Rachelefsky, is "an overstatement of the actual immunologic response to the vaccines." *Id.* As support, he noted that the "lessons learned from the skin or kidney are not necessarily applicable to the liver microvasculature." *Id.*

3. Respondent's Expert, Dr. McCusker

Dr. McCusker was admitted as an expert in the fields of pediatric immunology, pediatric clinical allergy and immunology, and pediatrics. Tr. 175:8–11. She began with a general overview of interstitial lung disease. She explained that the clinical diagnosis is based on a patient presenting with "low oxygen saturation [and] an X-ray picture that is quite specific." Tr. 175:22–23. Dr. McCusker also identified associated risk factors including, prematurity, "mutations in the genes involved in formation and functioning of surfactant," and "telomeres which [have] to do with factors affecting cell life." Tr. 177:3–8. Specific to chILD, Dr. McCusker noted that patients "will have a history and a relatively recent antecedent history of infection." Tr. 177:13–15. She added that it is not clear why some patients will develop chILD and others do not, but "[w]e know that there are certain immunodeficiencies" and "particulates in the airway [that] are associated with the development of interstitial lung disease." Tr. 177:16–19.

Dr. McCusker testified that there is no literature that relates the HPV vaccination and chILD, aside from a temporal association. Tr. 178:12–14. The Yamamoto et al.[67] study referenced by Dr. Rachelefsky is not analogous to this case, according to Dr. McCusker. *See* Tr. 178–79; *see also* Resp't's Ex. D. She noted that the patients were not the same age, and in the case study, "the responsiveness to corticosteroids was clear in this patient whose symptoms resolved completely." Tr. 179:20–23. Petitioner did not respond similarly to corticosteroid treatment, and Dr. McCusker concluded that the patient in the case study was an adult suffering from a different disease. Tr. 179:24–25.

Dr. McCusker also wanted to clarify that "the gold standard for a vaccine is clinical protection from disease. It doesn't matter how many cytokines you produce." Tr. 182:19–22. The outcome measures used as the gold standard for vaccine clinical protection are the "levels of protective antibodies and/or evidence of [a] protective adaptive T cell response." Tr. 183:1–2. Dr. McCusker explained that "[t]he cytokines – the purpose of the inflammatory response at the site is to attract cells to the area." Tr. 183:9–11. These cells, she continued, "contain the inflammation at the site and for the antigen presenting cells to pick up those antigens and travel back to the draining lymph node." Tr. 183:14–17. This process continues for approximately four days, before there is "[m]ovement outside of the lymph node." Tr. 184:12. The cells will then circulate "back to the site of the original inflammation," thereby triggering an adaptive immune response. Tr. 184:16–19. Dr. McCusker testified "that there's actually very little cytokines that circulate in the peripheral circulation post vaccination." Tr. 184:24–25, 185:1.

[67] *See* Yamamoto, et al., *supra* note 66.

Turning to the Boyce et al.[68] study, Dr. McCusker explained that the authors sought to answer, "does [receipt of a vaccination] worsen the acute viral infection in a real[-]world study." Tr. 186:11–13. The authors looked at children who were hospitalized with RSV "proximal to getting the pertussis vaccination." Tr. 186:20–21. Ultimately, "what they found was that a recent immunization with pertussis was not a risk factor for hospitalization." Tr. 187:3–5. Additionally, Dr. McCusker testified that the study found that "pertussis in the arm does not worsen what's going on in the lungs." Tr. 187:24–25. She continued that line of reasoning to note another study that revealed "no increased episodes of inflammatory events post vaccination in patients who have underlying autoimmune [autoinflammatory] disease." Tr. 188:21–24 (citing Resp't's Ex. WW, ECF No. 46-6).[69]

Dr. McCusker also sought to clarify the concept of sterile inflammation. She defined the term as "an inflammatory event that would occur in the absence of – technically it's an exogenous antigenic trigger." Tr. 191:19–20. She then referenced the McDonald et al.[70] article, submitted by Petitioner, that discusses how sterile inflammation leads to tissue injury, followed by normal healing. Tr. 192:22–24. Dr. McCusker explained that "inflammation and healing are two sides of the same coin." Tr. 192:8–9. In cases where there is "an inflammatory event and there's a problem or disconnect between inflammation and then healing, you end up with damage." Tr. 192:12–14. In the McDonald et al. article, there is localized sterile inflammation that stays at the initial site. Tr. 193:5–6. Dr. McCusker noted "it's not like you get sterile inflammation of the liver[,] and the kidney inflames." Tr. 193:6–7. There is "no evidence here in this article that there's trafficking to other organs." Tr. 193:10–11. Furthermore, Dr. McCusker asserted that "[b]ecause vaccine[s] provide antigen[s]," they are not sterile. Tr. 193:18–21. Cell damage is the usual trigger for sterile inflammation and "when a cell dies by necrosis, the wrong way, and it releases its cellular contents, those cellular contents are actually inflammatory." Tr. 194:4–6. In Petitioner's case, "the signaling for the inflammation [wa]s the release of self-molecules that are normally not seen [outside of the cell by the immune system]." Tr. 194:11–12. This concept, Dr. McCusker asserted, is completely different from vaccinations. She stated that the vaccine components are "foreign in the first place, . . . and [are] also designed to activate the immune system in the form of the microbes themselves and the adjuvants that go with. So that's not sterile." Tr. 194:15–19.

Next, Dr. McCusker discussed cytokines. She defined them as small communication molecules with different functions, different receptors, and "each with their own regulatory pathway." Tr. 195:4–5. She noted that "[t]here are at least 80-plus, probably over 100 now[,] cytokines that have been defined." Tr. 195:2–3. They can vary wildly in origin, function, and form. Tr. 195:15–17. One type of cytokine, Dr. McCusker explained, is released by epithelial cells when they are damaged. Tr. 195:22. Those "cytokines tell the local area that cells are being damaged." Tr. 195:22–23. She described preformed mediators, which are "formed inside cells and they're ready to — ready to rock when the cell opens up." Tr. 196:2–3. Cells can also signal to other cells signaling for additional cytokines as needed to address the damage. Tr. 196:4–7. When asked how this happens when chILD develops, Dr. McCusker admitted that "we don't know." Tr. 196:25. She noted that TGF-beta is one cytokine that is released by epithelial cells and has also "been

[68] *See* Boyce, et al., *supra* note 58.
[69] J. Westra, et al., *Vaccination of Patients with Autoimmune Inflammatory Rheumatic Diseases,* 11 NATURE REVIEWS RHEUMATOLOGY 135–46 (2015).
[70] *See* McDonald, et al., *supra* note 60.

implicated in the development of fibrosis." Tr. 197:1–2. Specifically, TGF-beta is released by some types of T cells and myofibroblasts. Tr. 197:6–7. Dr. McCusker cautioned that animal models show "excessive amounts of TGF[-]beta in addition to an inflammatory insult," but "it is not clear who's the boss in terms of getting that TGF[-]beta released." Tr. 197:10–15.

Dr. Gershwin and Dr. McCusker agree that animal models show "the inciting event leading to pulmonary fibrosis is epithelial cell damage." Tr. 199:20–22. During the healing process, "you end up restricting the lung differently from the original lung and you end up with a lung that is no longer able to do its job, which is to exchange air." Tr. 199:24–25, 200:1–2. Dr. McCusker explained that adult literature is used for comparison due to the rarity of chILD. Tr. 200:4–5. She testified that "there is some evidence" that ILD responds to corticosteroids, which "implies that it's inflammatory." Tr. 200:6–8. The best immune response following vaccination is a regulatory response that does not involve inflammation. Tr. 201:14–17. Dr. McCusker characterized Dr. Gershwin's discussion of pro-inflammatory and anti-inflammatory T cells as "concepts in the early 2000s[and noted that] we've moved on from there a long time ago." Tr. 201:25, 202:1–2.

In response to Dr. Gershwin's reliance on medical literature to establish that "exogenous cytokines com[e] from someplace else . . . and act as factors to promote more inflammation," Dr. McCusker walked through some of the same articles he used. Tr. 205:17–19. She noted that the article by Wynn[71] provides "an overall big picture about how you end up with pulmonary fibrosis." Tr. 203:8–9 (citing Pet'r's Ex. 47). The "first step in pulmonary fibrosis is epithelial cell injury." Tr. 203:10. That leads directly to "the release of inflammatory mediators" coming from the inside of the injured cells. Tr. 203:11–14. Dr. McCusker continued that these "inflammatory mediators induce migration of cells from the periphery into the area of cell damage." Tr. 203:20–21. They are "now in the milieu looking at or being triggered or stimulated by the inflammatory mediators and by whatever else is in the environment." Tr. 203:24–25, 204:1. They are also producing cytokines. Tr. 204:1–2. These cytokines would normally initiate the repair response; however, the repair does not go as it should. Tr. 204:6. Dr. McCusker explained that the first stage of lung repair is to lay down the "extracellular matrix." Tr. 204:20–21. Everything is great "[i]f all this is done in a relatively short order where you kind of rebuild the structure, reset everything up[,] and stop the repair[.]" Tr. 204:23–25. Fibrosis occurs when "that matrix continues to be laid and you don't actually get that stop. So now instead of having relaying of the matrix and them allowing [] everything to heal, you end up with cement in the lung." Tr. 205:9–11. Dr. McCusker testified that "the problem with fibrosis isn't more inflammation. It's more repair." Tr. 205:20–21. She agreed that "while TGF-beta is one of the cytokines . . . it's a cytokine that's being released and acting locally and the dysregulation is local." Tr. 205:21–24. She asserted that "in the case of chILD, at least in theory, you would have that inflammation, that cell death of the epithelial cells, and then just ongoing progression of fibrosis instead of the stop." Tr. 206:12–15. Respondent filed the Kolahian et al.[72] article to support Dr. McCusker's contention that the idiopathic pulmonary fibrosis is not the result of too much inflammation or stimulation. Tr. 220:21–23 (citing Resp't's Ex. UU). She stated, "once you switch to healing the process [] — that's where the fibrotic process take[s] hold and takes off." Tr. 220:23–25. Dr. McCusker added that premature infants and babies with genetic variations in surfactant [may be] particularly at risk [because] their pulmonary vasculature and the structure of their regulatory tree never fully forms." Tr. 206:17–20.

[71] *See* Wynn, *supra* note 48.
[72] *See* Kolahian, et al., *supra* note 55.

The Chatziandreou et al.[73] article that Dr. Gershwin referenced was not thoroughly explained according to Dr. McCusker. Tr. 208:4–6 (citing Pet'r's Ex. 51). She noted this article tried "to understand how the influenza vaccine can craft an influenza-specific response" by injecting mice with the flu vaccine. Tr. 208:6–12. The lymph nodes from the mice were then isolated so that researchers could "watch the cells talk to one another in the lymph node and try to figure out what [wa]s going on." Tr. 208:16–18. Dr. McCusker explained that "you could maybe translate this — vaccinate [] mice in their muscle, the components of the vaccine are taken up and brought to the local lymph node[,] and there's a lot of activity in that lymph node." Tr. 209:19–22.

Turning next to the Kashiwagi et al.[74] article, Dr. McCusker stated the researchers found that blood samples taken from children within 24 hours of vaccination revealed the production of cytokines; but she noted, "[t]hat is not evidence that cytokines circulate at 24 hours." Tr. 210:15–23 (citing Pet'r's Ex. 54). In fact, when looking at "circulating serum cytokine profiles" in vaccinated children that were febrile vs. non febrile, "there was actually very little cytokine[s] that circulated." Tr. 211:3–8. Dr. McCusker stated that she "was not able to find literature that would say that inflammation in the arm would lead to upregulation of cytokines in the lung." Tr. 212:4–7. She asserted that the immune system, even when exposed to a vaccine, "works in a compartmental fashion." Tr. 212:7–9. She conceded that while there are "'systemic symptoms' such as fever and sickness behaviors, the mechanisms of those are not through the circulation of cytokines through the blood stream." Tr. 212:11–14. Dr. McCusker could not reconcile how to "walk the cytokines from the arm to the lung." Tr. 212:14–15.

Petitioner's typical clinical presentation of chILD was another factor that Dr. McCusker identified as evidence that Petitioner's vaccination had nothing to do with how her condition developed and progressed. Tr. 212:16–19. She testified that:

> [b]ecause I can't walk the cytokines to the lungs from the arm or the draining lymph node, and I don't — I can't — I do not have any literature that says that that happens. And the disease in and of itself occurs in the sequence of events that it occurred in this case in the absence of vaccination. It's exactly what happens. This is chILD.

Tr. 213:1–7.

When asked about Dr. Gershwin's concept of concurrent processes, Dr. McCusker asserted that this theory doesn't work by using Dr. Gershwin's analogy of exercise and food allergies. Tr. 213:25. She explained that "the mechanism by which exercise increases the severity of [a] food allergy is not related to the circulation of cytokines." Tr. 213:25, 214:1–2. That mechanism is completely different and "has to do with the activation of mast cell mediators and the increase in the basal metabolic rate." Tr. 214:2–4.

[73] *See* Chatziandreou, et al., *supra* note 64.
[74] *See* Kashiwagi, et al., *supra* note 65.

Dr. McCusker then continued her discussion of Petitioner's filed literature. She noted that the Tempark et al.[75] article describes "adrenal suppression and [asserts] that there's increased risks for difficultly of the immune system to generate a good response to [an] infection" that is "associated with the use of topical corticosteroids." Tr. 218:12–18 (citing Resp't's Ex. SS, ECF No. 46-2). Dr. McCusker then addressed the Galati et al.[76] article. Resp't's Ex. TT. This article suggests that "in idiopathic pulmonary fibrosis, there's evidence of T cell dysregulation." Tr. 219:18–20. Taken together, Dr. McCusker asserted that "corticosteroids could affect T cells and T cell development and that idiopathic pulmonary fibrosis might be a disease of T cell dysregulation." Tr. 219:21–23. However, Dr. McCusker also conceded that there is some debate regarding this theory. Tr. 219:23–25.

She discussed these articles in the context of Petitioner's case. Dr. McCusker noted that Petitioner "was using a fairly high potency corticosteroid . . . from eight years to [eleven.]" Tr. 218:24–25, 219:1. Dr. McCusker explained that Petitioner's steroid use could have led to her "immune dysregulation." Tr. 219:4. She also noted that Petitioner showed evidence of dysregulation, specifically that "her NK cells were low[,] and she had 'lowish' T cells." Tr. 220:4–6. This is especially possible in Petitioner's case because her infection could have served as an exciting event. Tr. 220:19–20. Dr. McCusker concluded that Petitioner's infection, "coupled with the recent history of the chronic topical steroid use, you put those together and you have your perfect situation for dysregulation." Tr. 220:12–15.

The biggest contention Dr. McCusker had with Dr. Gershwin's theory is that it would require a "change in how the immune system works." Tr. 221:15. She gave the example of a cut on a patient's thumb in tandem with a virus. According to Dr. Gershwin, "if I have a cut on my thumb, I'm going to have inflammation in my thumb and I'm going to have inflammation in my nose because I've got, you know, some stimulation of the immune system in my nose." Tr. 221:17–21. Dr. McCusker asserted that it "doesn't work that way because if the signal in my nose is saying, yeah, you got a little cold, don't worry about it, but my thumb is saying, listen this is going to get infected; you want to focus your attention to the thing that's more dangerous." Tr. 221:23–25, 222:1–2. This, Dr. McCusker explained, is "the containment concept." Tr. 222:7. Dr. Gershwin's example of serum sickness is a systemic immune response. However, Dr. McCusker clarified that it is "a Type III hypersensitivity reaction." Tr. 222:12–15. This type of reaction involves "antibodies that are floating around bound to antigen[s] and they get caught in small capillaries and create inflammation." Tr. 222:16–18. The circulation of these antibodies "isn't the same as a cytokine being produced in one lymph node[,] circulating[,] and affecting the immune response in the lung." Tr. 222:20–23. She testified that it is "really not the same." Tr. 222:23. Dr. McCusker continued that even if "these two things connected, which I can't connect in my mind, then you still need [to get to] the fibrosis." Tr. 223:15–17.

Dr. McCusker identified three factors to explain why cytokines do not circulate. First, she stated that they "act over short distances." Tr. 269:4–5. Cytokines look for and find their receptors immediately. Tr. 269:7–8. Those receptors hold them, and cytokines don't then "bounce from one receptor to another." Tr. 269:9–10. Second, "there's a regulation loop" that "doesn't really allow

[75] T. Tempark, et al., *Exogenous Cushing's Syndrome due to Topical Corticosteroid Application: Case Report and Review Literature,* 38 ENDOCR. 328–34 (2010).
[76] *See* Galati, et al., *supra* note 52.

for significant . . . amplification." Tr. 269:13–18. Lastly, the half-life of cytokines would not support that process. Tr. 269:21–23. Dr. McCusker noted that "one of the cytokines that keeps getting discussed is IL-1 beta." Tr. 269:22–23. With a half-life of nineteen minutes, "they do their thing and then they're deactivated." Tr. 269:25, 270:1. Dr. McCusker mentioned signal transduction, whereby a fever can result from a localized inflammatory event because "the nerves that are innervated are triggered at the site of the lymph node by the release of those cytokines." Tr. 270:10–16. She went on to say that the trigger that moves to the hypothalamus and "says turn on fever" does not involve the movement of cytokines. Tr. 270:16–18. She identified other examples of systemic signs of inflammation but noted that "the circumstances that are predicated to occur with a vaccination under this case scenario does [sic] not — allow for it." Tr. 271:10–12. She also noted literature that studied the interaction between the pertussis vaccination and RSV. *See* Resp't's Ex. VV.[77] The literature indicated that "if there was an interaction, it would be to sort of tamp down the immune response." Tr. 279:3–5.

Turning to Petitioner's medical record, Dr. McCusker discussed what she identified as the "wide net of ideologies" that Petitioner's treaters explored. Tr. 227:1–2. She noted that on August 18, 2014, "they talked about [an] idiosyncratic reaction to Bactrim, . . . the potential for an infectious ideology . . . an inflammatory ideology or rheumatologi[c] ideology but found no significant persistent elevation in the inflammatory markers of the body." Tr. 227:2–7 (citing Pet'r's Ex. 4 at 2472). Although Petitioner exhibited an elevated C-reactive protein ("CRP"), which is indicative of systemic inflammation when Petitioner was admitted to the hospital, by that time, treaters were more concerned about addressing Petitioner's failing lungs. Tr. 227:8–10.

Dr. McCusker noted that Petitioner's treaters took "into account the family's concerns that the vaccines may have played a role[]" in her condition. Tr. 227:19–20. Although there are disadvantages with relying on VAERS reporting that Dr. McCusker acknowledged, she stated that they "found there was no reported association" between the HPV vaccine and ILD. Tr. 227:21–25. Instead, an immunological examination revealed a "decrease in total T cells and the decrease in — specifically in T helpers and NK cells for age, which is consistent with other children or other individuals who have interstitial lung disease." Tr. 228:14–17. Looking at her entire medical record, Dr. McCusker concluded that Petitioner "followed a clinical course that was consistent with other children who had chILD[,] and [she] did not have features that would distinguish her [case] as [a] vaccine-mediated event as opposed to anybody else who developed chILD." Tr. 228:21–15. This is a rare disease, Dr. McCusker admitted, but she opined that Petitioner's case was classic. Tr. 229:1.

Dr. McCusker stated that redness, swelling, and site pain are common symptoms of a "large local reaction" to a vaccination. Tr. 229:5–7. A fever lasting 24 hours and "an elevation in the C-reactive protein" are also symptoms of a large local reaction. Tr. 229:14–17. Petitioner in the present case suffered from a fever and localized arm inflammation, which Dr. McCusker characterized as "normal responses to her vaccine." Tr. 182:11–12. However, Dr. McCusker noted that during Petitioner's July 31, 2014 medical visit, there was no mention of arm swelling upon her physical examination. Tr. 212:19 (citing Pet'r's Ex. 2 at 57–58). This suggests that Petitioner's immune stimulus "that had started locally was gone." Tr. 233:8–9. Dr. McCusker testified that a strep screen would have been her first course of action given Petitioner's symptoms of "swollen

[77] *See* Boyce, et al., *supra* note 58.

tonsils, the sore throat, big tonsils, swollen lymph nodes[,] and high fever." Tr. 276:2–3. Following a negative strep test, "most likely the reason for this constellation of symptoms is that your child has a virus." Tr. 276:9–10. She identified Epstein-Barr virus ("EBV")[78] because it is "one of the factors that is associated with chILD." Tr. 277:7–8. Dr. McCusker was unable to identify an etiology. She also admitted that it was unclear "when [Petitioner] presented with the cough and the hypoxia and the real story of hardcore [symptoms]." Tr. 281:8–10. Dr. McCusker was unable to unequivocally identify an onset date for Petitioner's chILD. Tr. 234:10. She reasoned that based on an account of Petitioner's mild cough, July 31, 2014, would be a good estimate. Tr. 235:3. She admitted her uncertainty, but stated that "on the 31st, . . . there were already signs, which means that you kind of have to back up — yeah, probably pre vaccine in order for the series of events to reach symptomatic by the 31st." Tr. 283:1–5. Immediately following that statement, she noted that she was "very hesitant to time out the pathophysiology because, yeah, it is apparently very sudden onset." Tr. 283:10–12. Dr. McCusker described a recent patient who went from healthy, to having a fever with cough two days later, and then needed ventilation by day four. Tr. 283:15–22. In that case, Dr. McCusker noted that the patient "grew two viruses on her culture . . . , so of course people sa[id], oh, it must [have] be[en] the virus that caused all this." Tr. 283:23–25, 284:1. That patient notwithstanding, Dr. McCusker asserted that "the process that led to [Petitioner's respiratory distress] was not 24, 48, 72, or even 96 hours in going. It was probably a much longer process before you g[o]t to that." Tr. 281:15–18. As support, she explained that "the lungs of children are generally healthy," and that "it takes a significant amount of compromise for the child to deteriorate." Tr. 281:25, 282:1–2.

IV. Applicable Legal Standards

A. Causation

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

To receive compensation under the Act, a petitioner must demonstrate either that: (1) the petitioner suffered a "Table injury" by receiving a covered vaccine and subsequently developing a listed injury within the time frame prescribed by the Vaccine Injury Table set forth at 42 U.S.C. § 300aa-14, as amended by 42 C.F.R. § 100.3; or (2) that petitioner suffered an "off-Table injury," one not listed on the Table, as a result of his receiving a covered vaccine. *See* 42 U.S.C. §§ 300aa-11(c)(1)(C); *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1319–20 (Fed. Cir. 2006). Petitioner does not allege a Table injury in this case; thus, she must prove that her injury was caused-in-fact by a Table vaccine.

[78] Epstein-Barr is also referred to as human herpesvirus 4. *Dorland's* at 2061. Human herpesvirus 4 is a virus of the genus lymphocryptovirus that causes infectious mononucleosis[.]" *Id.* at 852–53.

To establish causation-in-fact, a petitioner must demonstrate by a preponderance of the evidence that the vaccine was the cause of the injury. 42 U.S.C. § 300aa-13(a)(1)(A). A petitioner is required to prove that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321–22 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)). *Shyface* clarifies "[i]t is not necessary that it be the cause, using the word "the" as meaning the sole and even the predominant cause." 165 F.3d at 1352.

In the seminal case of *Althen v. Sec'y of the Dept. of Health & Hum. Servs.*, the Federal Circuit set forth a three-pronged test used to determine whether a petitioner has established a causal link between a vaccine and the claimed injury. *See* 418 F.3d 1274, 1278–79 (Fed. Cir. 2005). To that end, the Circuit noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279–80. A special master may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Id.* at 1280.

The *Althen* test requires petitioners to set forth: "(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." *Id.* at 1278. To establish entitlement to compensation under the Program, a petitioner is required to establish each of the three prongs of *Althen* by a preponderance of the evidence. *See id.*

A petitioner who satisfies all three prongs of the *Althen* test has established a prima facie showing of causation. *Hammitt v. Sec'y of Health & Hum. Servs*., 98 Fed. Cl. 719, 726 (2011). A petitioner who demonstrates by a preponderance of the evidence that he suffered an injury caused by vaccination is entitled to compensation unless the respondent can demonstrate by a preponderance of the evidence that the injury was caused by factors unrelated to the vaccination. *See Althen*, 418 F.3d at 1278; *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 547 (Fed. Cir. 1994). Consequently, when and if a petitioner establishes a prima facie case, the burden then shifts to the government to prove that an alternative cause, unrelated to the administration of the vaccine, was the "sole substantial factor" in causing the alleged injury. *See de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1354 (Fed. Cir. 2008); *see also Hammitt*, 98 Fed. Cl. at 726 (explaining that the respondent's burden is to show that the "factor unrelated" was the "sole substantial factor" in causing the injury). Additionally, a factor unrelated "may not include 'any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness or condition.'" 42 U.S.C. § 300aa-13(a)(2); *see also Doe v. Sec'y of Health & Hum. Servs.*, 601 F.3d 1349 (Fed. Cir. 2010) (opining that an idiopathic diagnosis cannot be a "factor unrelated," as it is idiopathic).

B. Significant Aggravation

Petitioners must establish causation in all off-Table cases; however, petitioners may establish they are entitled to compensation based on a claim that a vaccination significantly aggravated a pre-existing condition. The Vaccine Act 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 of health." § 300aa-33(4). When a petitioner makes this argument, the evidentiary burden is expanded. *See Loving v. Sec'y of Health & Hum. Servs.*, 86 Fed. Cl. 135, 144 (2009). In *Loving*, the Court of Federal Claims set forth a six-factor test, which requires establishing the following:

> (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 significantly 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 *Loving* analysis requires the special master to "evaluat[e] whether the vaccine made the person worse than the person would have been but for the vaccination. In doing so, the natural course of the disease must be considered." *Locane v. Sec'y of Health & Hum. Servs.*, No. 99-589V, 2011 WL 3855486 at *10 (Fed. Cl. Spec. Mstr. Feb. 17, 2011), *mot. for review den'd*, 99 Fed. Cl. 715 (2011), *aff'd*, 685 F.3d 1375 (Fed. Cir. 2012); *see also Hennessey v. Sec'y of Health & Hum. Serv.*, No. 01-190V, 2009 WL 1709053, at *41–42 (Fed. Cl. Spec. Mstr. May 29, 2009), *mot. for review den'd*, 91 Fed. Cl. 126 (2010). However, a petitioner is not required "to demonstrate an expected outcome and that her current post vaccination condition was worse than such expected outcome." *Sharpe v. Sec'y of Health & Hum. Servs.*, 964 F.3d 1072, 1081 (Fed. Cir. 2020).

V. Discussion

Petitioner's theory of causation must generally establish that one or more of the vaccines at issue is the but-for cause of the type of injury alleged. Her petition sought relief for two related injuries, IPF and acute respiratory failure. ChILD syndrome covers a wide range of conditions that includes IPF to the extent that it occurs in children. However, there is so much that remains unknown about the etiology and pathogenesis of IPF, especially in the extremely rare pediatric cases. Furthermore, the literature filed in this case does not paint a clear picture of Petitioner's diagnosis. After careful consideration of Petitioner's medical history, expert reports, and filed medical literature, Petitioner has provided preponderant evidence that she suffered from IPF that ultimately lead to acute respiratory failure. Given her age, Petitioner's condition would fall under the umbrella syndrome of chILD. I will consider Petitioner's causation theory in light of this injury.

Petitioner's expert's argument that her otherwise mild, viral illness was worsened by vaccination and ultimately developed into chILD is reconcilable with Respondent's expert's argument that Petitioner was likely suffering from a viral infection pre vaccination and that was the cause of her acute respiratory failure. Both experts characterize Petitioner's clinical course as a worsening of an otherwise manageable infection. The heart of the issue then becomes whether one or more of her vaccines was a substantial cause of the worsening. This analysis requires

consideration of the *Shyface* "substantial factor" standard in bringing about the harm, and the significant aggravation factors detailed in the *Loving* decision. Petitioner has not explicitly identified her claim as one of significant aggravation, but Dr. Gershwin made that argument. He testified that the onset of her chILD "would be when she began to have worsening pulmonary symptoms." Tr. 149:20–21. Furthermore, Respondent's expert indicated that was her understanding of Petitioner's theory. She testified, "[Dr. Gershwin] feels that those two things came together in the lungs because cytokines worsened her pulmonary disease leading to her chILD." Tr. 181:14–16. I must consider the evidence presented to reach my decision in conjunction with counsel's framing of the claim in Petitioner's filings. Therefore, I find that there is preponderant evidence of a post-vaccination change for the worse in Petitioner's condition, which resulted in markedly greater illness accompanied by a substantial deterioration of her health.

In addition to preponderant evidence of a worsened condition, a significant aggravation claim must still establish by a preponderant standard all three *Althen* factors: general causation, specific causation, and timing. It is not entirely clear if Petitioner's condition is the result of an aberrant immune response to multiple stimuli including a wild virus and vaccinations (causation-in-fact). Alternatively, Petitioner's condition could be the result of vaccine-caused dysregulation of the immune system's response to a respiratory virus that had already begun to cause lung damage (significant aggravation). In either instance, Petitioner has established by a preponderant standard that her vaccinations were a substantial, but not necessarily the sole or predominant cause of her IPF, acute respiratory failure, and need to undergo a bilateral lung transplant. *See Shyface*, 165 F.3d at 1352–53.

A. *Loving* Prong One – Condition Prior to Vaccination

There is no dispute that Petitioner was generally healthy in the days leading up to her vaccination. Her prematurity had not resulted in any chronic respiratory condition, and her wellness check immediately prior to vaccination did not reveal any pulmonary concerns. Petitioner did have a years-long history of chronic corticosteroid use for dermatological conditions that lasted up until the month of her vaccinations. She was also prescribed antibiotics for a viral infection in mid-to-late July of 2014, but there were no indications of sequela post treatment. Petitioner's medical record also does not include symptoms or a diagnosis of lung disease prior to July 29, 2014. Instead, the medical record illustrates how quickly Petitioner's condition worsened from symptoms consistent with a mild viral infection that manifested just hours post vaccination.

Dr. Gershwin's theory begins with the premise that Petitioner's "vaccination(s) provided a mechanism of exacerbation of an already ongoing 'starter' cause." Pet'r's Br. at 6. Her expert Dr. Gershwin asserted in his written expert opinion that although vaccinations were the but-for cause of Petitioner's ILD, "more likely than not, [she] was undergoing a mild drug or viral-induced reaction that should have been reversible were it not for the sterile inflammation and abnormal healing characterized by fibrosis that was induced by her vaccination." Pet'r's Ex. 8 at 5. He admitted that Petitioner could have developed chILD without her vaccinations but noted the severity and rapid progression of her case to support his opinion on vaccine-causation.

Respondent's expert testified that "children who present with chILD will have a history and a relatively recent antecedent history of infection." Tr. 177:13–25. Dr. McCusker also noted

the sudden onset of Petitioner's symptoms and testified that "you kind of have to back up yeah, probably pre vaccine in order for the series of events to reach symptomatic by the 31st." Tr. 283:2–5. Both experts explained the clinical progression of ILD with supporting literature that identified infection as a possible trigger.

Traditionally, the *Loving* factors have been applied to cases where, pre vaccination, the petitioner has symptoms consistent with the ultimate diagnosis or where the petitioner has already been diagnosed. *See Tomsky v. Sec'y of Health & Hum. Servs.*, No. 17-1132V, 2020 WL 5587365 (Fed. Cl. Spec. Mstr. Aug. 24, 2020) (applying the *Loving* analysis in a case where the petitioner's alleged vaccine-caused injury was chronic inflammatory demyelinating polyneuropathy ("CIDP") and where he exhibited symptoms consistent with CIDP, including lower extremity and facial weakness, pre vaccination); *Maciel v. Sec'y of Health & Hum. Servs.*, No. 15-362V, 2018 WL 6259230 (Fed. Cl. Spec. Mstr. Oct. 12, 2018) (applying the *Loving* analysis in a case involving a petitioner who had already been diagnosed with multiple sclerosis and was alleging the significant aggravation of the same); *see also L.Z. v. Sec'y of Health & Hum. Servs.*, No. 14-920V, 2018 WL 5784525 (Fed. Cl. Spec. Mstr. Aug. 24, 2018); *Bubb v. Sec'y of Health & Hum. Servs.*, No. 01-721V, 2005 WL 1025707 (Fed. Cl. Spec. Mstr. Apr. 29, 2005).

In this case, Petitioner does not present evidence that she was suffering from chILD at the time of vaccination. Dr. McCusker suggested this during her testimony, but her explanation was limited to the timing of Petitioner's progression. She was unable to point to any evidence in the medical record that Petitioner had begun to develop lung disease prior to vaccination. However, given the immediacy of Petitioner's respiratory symptoms following vaccination, it is reasonable that some latent period must be accounted for. Assuming that infection and symptom onset are not instantaneous, Petitioner's assertion that she had developed a mild respiratory illness that would not have worsened and led to severe chILD absent vaccination, is consistent with her medical presentation prior to vaccination. Petitioner has established by a preponderance of the evidence that she had been infected with a virus and was asymptomatic or exhibiting mild symptoms immediately prior to or around the time of vaccination.

B. *Loving* Prongs Two and Three – Post-Vaccination Condition/Significant Aggravation

While there are sub-classifications of chILD syndrome, the urgent need for treatment in some cases prevents the comprehensive testing needed for diagnostics. Petitioner's medical records are not in dispute in this case, but her rapid clinical progression did not allow for differential exclusions. Petitioner was asymptomatic or exhibiting mild symptoms at the time of her vaccinations. She was coughing later that day, seen by a doctor two days later, admitted to the hospital four days later, and completely unable to use her lungs two weeks later. When Petitioner was transported to Kentucky for her lung transplant in late August of 2014, she had been diagnosed with acute respiratory failure. Her record also listed idiopathic pulmonary fibrosis and interstitial pneumonia as diagnoses.

The heterogenous nature of chILD makes sub-classification extremely difficult. Petitioner's condition shares some features with adult IPF, but there is disagreement within the medical community regarding whether IPF is seen in children at all. Petitioner's condition does

not answer that question as it does not neatly fit into either category. Petitioner's test results included evidence of active bleeding, small hemorrhagic areas, interstitial fibrosis, collagen deposition, alveoli destruction, diffuse petechiae, interstitial opacities, pneumomediastinum, and subcutaneous air. Some of these are commonly seen in chILD, while some symptoms are very rare in children, but common with adult IPF. The medical personnel at CHOA realized fairly quickly that identifying Petitioner's specific condition would be of no consequence absent immediate treatment. They secured her a place at a lung transplant facility, and Petitioner ultimately received a life-saving bilateral lung transplant. The hospital where Petitioner received her transplant did note her diagnosis, but her admission paperwork generally lists "acute lung failure."

The medical literature filed by both parties details how ILD generally and IPF specifically result from the immune system's unsuccessful attempt to repair injury to the lung. The majority of patients then experience a gradual deterioration over several years, but there are some exceptions where onset is acute and severe. Petitioner and Respondent both filed medical literature that sets the life expectancy post diagnosis between two and six years without a lung transplant. Even on the shorter end of the range, treatment was discussed in terms of months. Petitioner's medical history, when compared with the filed medical literature, would place her in an extremely rare class of chILD cases characterized by a high mortality rate, the failure to respond to treatment, and an absolute inability to recover absent lung transplantation. The Clement et al.[79] article, filed by Respondent, explains that the "outcome [for chILD] is highly variable with a mortality rate around 15%," but "[a]n overall favorable response to corticosteroid therapy is observed in around 50% of cases." Resp't's Ex. H at 1. In this case, the experts testified that Petitioner's deterioration was rapid and extreme. The rapid deterioration of Petitioner's condition, measured in days and weeks, was noted by her treaters and both experts.

In Petitioner's case, her medical records note that test results, including her lung biopsy, could not identify the cause of Petitioner's extensive fibrosis. Her treaters noted that additional testing would be of no use to determine etiology and their focus shifted to life-saving treatment. The difference between Petitioner's initial mild viral symptoms and later need for ECMO, underscores the disparity between her pre vaccination and post vaccination condition. While chronology alone is not sufficient to prevail, it is necessary to establish an appropriate timeline. Dr. Gershwin, in arguing that Petitioner's respiratory illness was worsened by her vaccinations, made a significant aggravation argument. He asserts explicitly that Petitioner would have recovered if not for the amplified immune response that was partly due to her vaccines. I find there is preponderant evidence that Petitioner's condition post vaccination constitutes a significant aggravation of both her asymptomatic status and her mild viral symptoms at the time of or immediately preceding her vaccinations.

C. *Loving* Prong Four/*Althen* Prong One – Medical Theory

Under the first prong of *Althen*, 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), *aff'd*, 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

[79] *See* Clement, et al., *supra* note 42.

or scientific explanation." *Knudsen*, 35 F.3d at 548. 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). However, 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). 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. In general, "the statutory standard of preponderance of the evidence requires a petitioner to demonstrate that the vaccine more likely than not caused the condition alleged." *LaLonde,* 746 F.3d at 1339.

Furthermore, establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of her claim. *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). The Supreme Court's opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), requires that courts determine the reliability of an expert opinion before it may be considered as evidence. "In short, the requirement that an expert's testimony pertain to 'scientific knowledge' establishes a standard of evidentiary reliability." *Id*. at 590 (citation omitted). Thus, for Vaccine Act claims, a "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly*, 592 F.3d at 1324. The *Daubert* factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted."). Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). And nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder v. Sec'y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 743 (2009) (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)).

Petitioner is placed in a difficult position in this case. She must establish a theory that cannot be systemically tested, due to the uncommon nature of the disease, nor can it be methodically observed, due to the speed at which irreversible and fatal damage occurs following onset. Petitioner's expert has presented a causation theory that has evolved over time. Throughout this case, however, Petitioner's expert never suggested that the vaccines at issue were the sole cause of the alleged condition. Petitioner's theory depends on multiple immune triggers, including long-term corticosteroid use, antibiotic treatments, viral illness, and, finally, vaccines. Had Petitioner's explanation of vaccine causation ended here, Respondent would be correct that Petitioner's claim fails. This overview of Petitioner's theory must be supported by indicia of reliability. I have cautioned petitioners in the past that the mere mention of upregulated cytokines is not the same as an articulated biological mechanism. *See, e.g.*, *Nunez v. Sec'y of Health & Hum.*

Servs., No. 14-863V, 2019 WL 2462667, at *41 (Fed. Cl. Spec. Mstr. Mar. 29, 2019) (finding that the petitioners failed to present a biological mechanism connecting the vaccination to the alleged injury because their theory involving the increase in cytokine production levels did not involve evidence of an active transportation mechanism to cause said injury.). This case involves a condition (like others in the Program) that medical professionals have classified as idiopathic. Indeed, it is not surprising that Petitioner's expert was unable to provide a detailed and exact biological mechanism to explain how one or more of the vaccines at issue in this case can cause chILD. That is not the standard. Dr. Gershwin was ultimately able to articulate a medical theory that causally connects the vaccinations at issue to IPF and acute respiratory failure. Therefore, I find that Petitioner has met her burden with respect to *Althen* prong one/*Loving* prong four.

Respondent's expert asserts that Dr. Gershwin's theory must fail, because it involves a rare disease that cannot be studied epidemiologically. Furthermore, Petitioner's theory lacks a practical testing methodology, and it has not been proposed by anyone in the medical community. Both experts repeatedly agreed that IPF is an extremely rare form of the already rare chILD. Its high mortality rate compounds that. In fact, some of the literature submitted argued that children do not suffer from IPF. As a result, there are no studies that have been done that explicitly study vaccinations and IPF in children. Petitioner submitted literature that provided varying perspectives on ILD generally, chILD, and IPF. Petitioner's submitted literature explained the role of cytokines in the development of lung disease. Petitioner also submitted literature that successfully established that there is an increase in cytokine production post vaccination. The conclusions from these studies, when put together, support Petitioner's theory of causation.

The ineffectiveness of autoinflammatory therapies has fueled significant debate within the medical community about whether IPF is the result of a systemic inflammatory response. Dr. McCusker explained that IPF does not develop as a result of inflammation or the body's disarming of an offending antigen. The dysregulation that leads to IPF occurs during the repair phase. She likened the relationship between inflammation and repair to opposites sides of the same coin. If that is the case, however, it would stand to reason that the two would be directly correlated to each other. An intense immune response could cause severe damage and increase the possibility for something to go wrong during a substantial repair phase. Dr. Gershwin does not undertake to explain how cytokines produced as a response to vaccination miscommunicate with cells in the lung. He does, however, identify some of the relevant proteins and explain their intended role. Specifically, TNF-beta and several interleukins are instrumental in fibroblast proliferation and the development of ECM. It is reasonable that these cytokines, if improperly upregulated or dysregulated, could prevent tissue repair following lung damage. Dr. Gershwin argues that the inciting agent (a virus), vaccinations, and potentially Bactrim, could all overload the immune system resulting in cytokine miscommunication. He has presented preponderant evidence that this process could occur. The remaining piece of his causation theory is how these cytokines that are responding to immune stimuli in other parts of the body are able to migrate to the lung.

Petitioner's mechanism is based on the concept of bystander activation and circulation. Dr. Gershwin argues that Petitioner's IPF developed due to the migration of bystander cells summoned by circulating cytokines that called because they were reacting to a multifactorial, immune stimulus event. Petitioner has presented preponderant evidence of cytokine upregulation following

vaccination, cytokine migration to injured tissue, and cytokine involvement in disease development.

Dr. McCusker was asked to respond to Dr. Gershwin's description of the role of cytokines, specifically TFG-beta, and she agreed with his explanation. Her dissent lies in Dr. Gershwin's assertion that the cytokines migrate. Dr. McCusker testified that she "can't walk the cytokines from the arm to lung." Tr. 212:14–15. Despite this, Dr. McCusker later testified that in a systemic immune response, there are antibodies "floating around bound to antigen[s] and they get caught in small capillaries and create inflammation," but, she noted that this is not the same as migrating cytokines. *See* Tr. 222:15–23.

Dr. Gershwin's explanation of sterile inflammation in this context is confusing. At one point, he incorporated sterile inflammation directly into his causation theory. At another point, he testified that this reference is an analogy to explain the concept of cell migration. Sterile inflammation was defined in the literature as cell death in the absence of inflammation. Pet'r's Ex. 48 at 1. Petitioner filed literature that described IPF as a "highly progressive fibrotic disease in the absence of detectable inflammation." Pet'r's Ex. 47 at 3. Dr. McCusker clarified that sterile inflammation occurs in the absence of "an exogenous antigenic trigger." Tr. 191:19–20. There is no evidence in the record, however, that IPF or acute respiratory failure can develop from sterile inflammation pursuant to Dr. Gershwin's theory. Vaccines, viral infections, and even Bactrim exposure are all exogenous antigens. Furthermore, as Dr. McCusker noted, the McDonald et al.[80] article cited by Dr. Gershwin does not discuss multi-system injury where there are simultaneous immune system responses. The article does, however, explain how "[r]ecent studies of models of sterile injury in the liver have uncovered cellular and molecular mechanisms of immune cell recruitment to damaged tissues as well as the cell types that mediate tissue repair and homeostasis." Pet'r's Ex. 48 at 3. Dr. Gershwin appears to be using this article to provide an example of immune cells 'figuring out' where the damage is and that they are needed in the absence of inflammation. It may not be a perfect analogy, but it is an exception to Dr. McCusker's blanket rule of 'no migration.' The potential migration of neutrophils and monocytes via intravascular channels to tissue that has been injured can be supported potentially by evidence of vasculitis. Furthermore, evidence of severe diffuse fibrosis tracks the process in the McDonald et al. study of monocytes producing cytokines and chemokines to summon other immune cells and stimulate extracellular matrix production. This can result in the overproduction of ECM and the dysregulation of lung repair.

Indeed, Petitioner may have taken a "kitchen sink approach" with a mechanism that involves cytokine production, bystander activation, and molecular mimicry. Ultimately, Dr. Gershwin's theory narrowed subject to cross-examination and further questioning. Dr. Gershwin shifted his theory and provided vague and extremely tentative answers. It is noteworthy that Dr. McCusker was likewise vague and tentative at times. Petitioner has therefore met her burden with respect to *Althen* prong one/*Loving* prong four.

D. *Loving* Prong Five/*Althen* Prong Two – Actual Causation

[80] *See* McDonald, et al., *supra* note 60.

Under the second prong of *Althen*, 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. The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). 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). The Court 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). Nevertheless, "[r]equiring epidemiologic studies . . . or general acceptance in the scientific or medical communities . . . impermissibly raises a claimant's burden under the Vaccine Act and hinders the system created by Congress . . . ." *Capizzano*, 440 F.3d at 1325–26. "[C]lose calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F.3d at 1280.

In Program cases, contemporaneous medical records and the opinions of treating physicians are favored. *Capizzano*, 440 F.3d at 1326 (citing *Althen*, 418 F.3d at 1280). 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." 42 U.S.C. § 300aa-13(b)(1). Rather, when "evaluating the weight to be afforded to any such . . . [evidence], the special master . . . shall consider the entire record . . . ." *Id.* The record often includes "evidence of possible sources of injury" that can show alternate causes for the alleged vaccine-related injury. *See Stone v. Sec'y of Health & Hum. Servs.,* 676 F.3d 1373, 1379 (Fed. Cir. 2012).

In order to apply Petitioner's presented causation theory (*Loving* prong four/*Althen* prong one) to Petitioner's clinical presentation and condition (*Loving* prongs 1–3), my analysis pursuant to *Loving* prong five/*Althen* prong two must begin with the specifics of Petitioner's condition. Because it is difficult to align IPF histology with typical chILD cases, it is necessary to determine, based on Petitioner's history, where her condition fits within the expert opinions and the medical literature.

During Petitioner's initial urgent care visit on July 31, 2014, her symptoms were not indicative of lung disease. Petitioner's medical history included no signs of asthma or other respiratory distress. Initially, medical personnel believed Petitioner was suffering from a viral illness, or possibly an adverse vaccine reaction. By the time the severity of Petitioner's condition was discovered, she was unable to breathe on her own. Both experts in this case testified that while

prematurity is a risk factor for ILD, Petitioner had no known respiratory issues resulting from her prematurity. Petitioner's Bactrim course in the days prior to her vaccinations had not led to any respiratory issues, and her lung examination at the time of her vaccinations on July 29, 2014, was normal. Dr. Gershwin and Dr. McCusker agreed that Petitioner was suffering a viral infection at the end of July of 2014, but neither expert was able to definitively identify Petitioner's symptom onset. Because Petitioner's July 31, 2014 complaints of fever, vomiting, sore throat, and fatigue are all potential symptoms of a Bactrim reaction, virus, and/or ILD, and one or more of these conditions all manifested at the same time, it is impossible to assign any specific symptom to any one condition. Furthermore, treaters never ruled out a reaction to the HPV vaccine. Petitioner's medical record also indicates she suffered swollen tonsils and bilateral anterior cervical lymphadenopathy following vaccination. This is all evidence that Petitioner's immune system had initiated a strong response to one or more of these possible triggers.

Petitioner's rapid deterioration hindered her treaters' ability to rule out differential diagnoses of ILD. In essence, Petitioner's lungs were destroyed by a force similar to a fire in speed and severity. The damage was total, irreversible, and opaque. A chest scan performed on August 6, 2014, showed ground-glass opacities consistent with Dr. Rachelefsky's description of accelerated IPF. Pet'r's Ex. 4 at 2341; *see also* Resp't's Ex. A. Her biopsy also revealed severe, advanced diffuse alveolar damage with little indication of the stages of injury and fibrosis. Pet'r's Ex. 4 at 2472. According to Dr. Rachelefsky, this is consistent with acute interstitial pneumonia. Her treaters specifically listed IPF as a diagnosis on August 18, 2014. *Id.* at 2407. And, Petitioner's medical records note diffuse fibrosis with no other findings. Petitioner did have some inflammatory markers. However, they were slight. Furthermore, she was treated with steroids that are designed to fight inflammation. The rapid progression of Petitioner's condition makes it difficult to determine how all of these factors affect each other. Because her condition deteriorated so quickly, Petitioner's treaters were forced to shift their focus entirely from pathogenesis to treatment. As with many cases where patients experience acute and irreversible respiratory failure, it is difficult, if not impossible, to retroactively determine etiology in Petitioner's case. Based off the opinions of Petitioner's treaters as documented in her medical records, the expert opinion evidence, and the medical literature filed in this case, I find there is preponderant evidence that Petitioner suffered from IPF and subsequent acute respiratory failure.

i. Immune Response

Dr. Gershwin asserts that in the wake of her vaccinations, Petitioner's immune system was dysregulated, and her lungs were unable to recover following a mild respiratory illness, due to the immune system's over-production of cytokines needed to initiate tissue healing and regulate repair. Dr. McCusker relied on two factors to argue that vaccinations did not lead to Petitioner's immune system dysregulation and her development of chILD. First, Petitioner's immunological testing revealed decreased T and NK cells. This finding is consistent with the Galati et al.[81] article's conclusion that because IPF patients in severe cases have a decreased number of NK cells, the disease itself it not the result of an overactive immune system upregulating the production of killer cells. Additionally, Petitioner's rheumatological testing did not uncover significantly elevated inflammatory markers, they were merely slightly elevated. Petitioner's treaters noted the presence of fever and severe lung tissue damage, but they determined that there was little evidence of

[81] *See* Galati, et al., *supra* note 52.

systemic inflammation. Dr. Gershwin countered that Petitioner's persistent fever and CRP elevation is some evidence of systemic inflammation. He further argued that Petitioner's treatment course, including an extended course of anti-inflammatory drugs, had severely impacted the integrity of any testing to identify inflammation.

Dr. Gershwin's theory does not rely on a sustained, heightened immune response in the face of anti-inflammatory or immuno-suppressive treatment. I do not find here any evidence of cytokine storm. Petitioner's disease, as both testifying experts pointed out, resulted from an error in repair facilitated by the immune system. The immune system is regulated by cytokines. In this case, Petitioner's immune response is evidenced by her local immune reaction at the vaccination site and her fever that exceeded 102 degrees Fahrenheit. Dr. McCusker did not rebut Dr. Gershwin's contention the Petitioner's body was attempting to develop antibodies pursuant to vaccination, fight off her mild viral illness, stave off further cell damage, and initiate lung tissue repair. Even acting in a compartmentalized manner, these stressors more likely than not had an additive, if not synergistic, effect on Petitioner's immune system.

In accordance with *Shyface*, I find that all of these competing factors: Bactrim; viral infection; and TDaP, HPV, and meningococcal vaccines, collectively played a role in this child's development of IPF. The vaccinations were a substantial factor in the severity of her condition. If not for the vaccines Petitioner received on July 29, 2014, she would not have suffered a rapid and life-threatening condition requiring a bilateral lung transplant. I must emphasize that the causation in this case is extremely fact specific. It is difficult to imagine how Petitioner's theory would be applicable to another individual, given her age, the rarity of her condition, the rapid progression of her disease following vaccination, her contemporaneous illness, and her prior antibiotic use.

ii. Rapid Progression of Disease

All agree that by July 31, 2014, Petitioner was exhibiting signs of respiratory distress. Approximately two weeks later, her treaters had determined that she would need a bilateral lung transplant immediately to save her life. By all measures, this would appear to be an extremely rapid progression of disease. Respondent's expert testified that she had a similar patient who went from healthy to ventilator in four days. However, Dr. McCusker did not file any literature to support her contention that a range from 4–14 days from time of diagnosis to respiratory failure is expected. In fact, Dr. McCusker stated plainly that she did not know what an appropriate timeframe is. She described Petitioner's case as "classic" and "very sudden" without additional context from the medical literature. She then testified that chILD takes longer than several days to process and hypothesized that Petitioner likely began to develop chILD prior to vaccination. Ultimately, Respondent was unable to provide persuasive evidence to counter the medical literature provided by both parties, and Dr. Gershwin's testimony regarding the timeframe for a chILD patient to advance to respiratory failure. Therefore, I find that Petitioner has provided persuasive evidence that her rapid progression is evidence there were compounding triggers for her disease.

Petitioner and Respondent also agree that Petitioner was born premature but that her medical records to do not reveal a history of respiratory issues. Both experts testified at some point that Petitioner's prematurity is a risk factor, but also likely played no role in the pathogenesis of her disease. Lastly, both parties noted that Petitioner's Bactrim use and upper respiratory infections

are known triggers of some forms of interstitial lung disease. Petitioner asserts that her predisposition and additional causal factors led to an exacerbated version of her disease and severe outcome. Respondent counters that vaccinations do not cause chILD, and any one of Petitioner's other issues could be the sole cause of her chILD; alternatively, it could be idiopathic.

I do not accept Respondent's contention that any of Petitioner's other immune stimuli could be the trigger, but due to the rarity of the disease, we cannot include vaccines in that list. Petitioner's clinical course is truly one in a million, but the mechanism submitted by Dr. Gershwin is consistent with the facts in this case. Therefore, I find that Petitioner has met her burden with respect to *Althen* prong two/*Loving* prong five.

E. *Loving* Prong Six/*Althen* Prong Three – Temporal Relationship

Under the third prong of *Althen*, 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,* 956 F.2d at 1148; *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) ("Without more, [a] proximate temporal relationship will not support a finding of causation.").

Petitioner exhibited symptoms consistent with an errant reaction immediately following her vaccinations. She described swelling on her arm at the injection site and fever the same day. She began to experience respiratory issues within 48 hours of vaccination and was diagnosed with acute respiratory failure two weeks later. Dr. Gershwin explained that the stress on Petitioner's innate immune system due to the virus and the culmination of vaccinations happened during the peripheral circulation of proinflammatory cytokines. The testimony by both experts established that there was a window of up to four days for this to occur. The onset of Petitioner's chILD around July 31, 2014, is within this timeframe. Therefore, I find that Petitioner has established by a preponderance of the evidence that the temporal relationship between her July 29, 2014 vaccinations and symptoms is appropriate based on her causation theory. She has therefore met her burden with respect to *Althen* prong three/*Loving* prong six.

F. Alternative Causation

If a petitioner presents a prima facie case, the Federal Circuit has held that the burden of proof shifts to the government, and Respondent must prove that the "'injury . . . described in the petition is due to factors unrelated to the . . . vaccine.' 42 U.S.C. § 300aa-13(a)(1)(b)." *Knudsen,* 35 F.3d at 547. Yet, a petitioner's failure to prove any element of his prima facie case mandates that the Court deny entitlement. *See id.* Under such circumstances, the burden of proof does not shift to the respondent to establish an alternate cause for the petitioner's claimed injury. *Althen,* 418 F.3d at 1278; *see also Bradley v. Sec'y of Health & Hum. Servs.,* 991 F.2d 1570, 1575 (Fed. Cir. 1993).

In this case, Petitioner has established a prima facie case for compensation under *Loving* and *Althen.* Therefore, Respondent has the burden to prove Petitioner's injury was caused by something other than her July 29, 2014 vaccinations. *See LaLonde,* 746 F.3d at 1340. However, Respondent has been unable to do so. Dr. McCusker contends that Petitioner's chILD developed because her corticosteroid treatment may have somehow disrupted her immune system and then she got sick. This process, according to Dr. McCusker, was unaffected by Petitioner's multiple vaccines, which are designed to engage the immune system. There is no biological mechanism articulated here. Respondent argues that Petitioner is an isolated case with no known cause and no cure. Petitioner is, according to Dr. McCusker, "the perfect situation for dysregulation," and her fibrosis is the result of the inability of the immune system to properly shift from fighting infection to tissue repair. Dr. Gershwin goes a step further than Dr. McCusker and offers a logical explanation as to why Petitioner's immune system was unable to shift. The immune system's signalers were unable to properly relay a message of repair. This explanation is reasonable and persuasive. Dr. McCusker did not identify a biological mechanism of causation, a potential trigger for Petitioner's ILD, or an appropriate symptom-onset date to counter Dr. Gershwin's theory. Therefore, Respondent has failed to show by preponderant evidence that Petitioner's acute respiratory failure has an alternative cause.

VI. Conclusion

Petitioner has suffered an unimaginable injury that brings with it life changing effects. She is to be commended for her bravery and resolve. The determination of her immediate family is undoubtably the reason she is here today, and their continued support is a ray of light in stormy weather. As I stated during the entitlement hearing in this case, I do not allow sympathy to sway the outcomes in these cases. However, it is endearing on those occasions when the Program is used as it was intended, to provide compensation with certainty and generosity, to the rare few who establish that they suffered a vaccine-caused injury. This is one such occasion. Petitioner has shown by a preponderance of the evidence that one or more of her vaccinations was a substantial factor and a but-for-cause of her IPF and acute respiratory failure. She is therefore entitled to compensation and a subsequent damages order will issue.

IT IS SO ORDERED.

s/Herbrina D. Sanders
Herbrina D. Sanders
Special Master