In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 14-236V

Filed: March 4, 2021

VICTORIA NIFAKOS, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	TO BE PUBLISHED Dismissal; Hepatitis A Vaccine; Meningococcal Vaccine; Varicella Vaccine; Human Papillomavirus (HPV) Vaccine; Primary Mediastinal Large B-Cell Lymphoma (PMBCL); Non-Hodgkin's Lymphoma.

Mark Theodore Sadaka, Mark T. Sadaka, LLC, Englewood, NJ, for Petitioner
Ida Nassar, U.S. Department of Justice, Washington, DC, for Respondent

DECISION ON ENTITLEMENT[1]

Oler, Special Master:

On March 27, 2014, Victoria Nifakos ("Petitioner") filed a petition for compensation under the National Vaccine Injury Compensation Program, 42 U.S.C. § 300aa-10, *et seq*.[2] (the "Vaccine Act" or "Program"). Petitioner alleges that she developed primary mediastinal large B-cell lymphoma ("PMBCL") which was caused-in-fact or was significantly aggravated by the Hepatitis A ("Hep A"), meningococcal, varicella, and human papillomavirus ("HPV") vaccines[3] she

[1] This Decision will 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 (2012). **This means the Decision will be available to anyone with access to the internet**. As provided in 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the Decision's inclusion of certain kinds of confidential information. To do so, each party may, within 14 days, request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, this Decision will be available to the public in its present form. *Id.*

[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] Petitioner identifies the meningococcal and varicella vaccines she received by their tradenames, Menactra and Varivax. Menactra is a meningococcal polysaccharide diphtheria toxoid conjugate vaccine

received on June 29, 2011. Petition at 1, ¶¶ 2, 23, ECF No. 1.

Upon review of the evidence in this case, I find that Petitioner has failed to show that the vaccines she received on June 29, 2011 caused or significantly aggravated her PMBCL. The petition is accordingly dismissed.

I. Procedural History

Victoria Nifakos filed her Petition on March 27, 2014.[4] Over the subsequent six-month period, she filed the affidavit and medical records required by the Vaccine Act. Exs. 1-10, ECF Nos. 6, 14, 18-19, 23 (Notice of Filing by CD);[5] *see* Section 11(c). On November 7, 2014, Respondent filed a Rule 4(c) Report, setting forth his objections to compensation. ECF No. 24.

During a status conference held telephonically on November 18, 2014, Petitioner expressed her intention to provide expert reports from an immunologist and/or oncologist to support her claim. ECF No. 25. On October 21, 2015, Petitioner filed an expert report from Yehuda Shoenfeld, M.D. Ex. 11, ECF No. 45. More than two months later, she filed medical literature said to "represent Petitioner's vaccine related injury." Notice of Filing at 1 (describing Exs. 12-58, 60-77),[6] filed Jan. 4, 2016, ECF No. 51. On March 8, 2016, Petitioner filed an expert report and curriculum vitae ("CV") from Jeffrey Alan Gordon, M.D. Exs. 78-79, ECF No. 57.

In response, Respondent filed an expert report and CV from Kenneth McClain, M.D. Exs. A-B, filed June 6, 2016, ECF No. 59. In this first expert report, Dr. McClain addressed several of the points made by Dr. Shoenfeld. Ex. A at 8-10. Approximately two months later, Respondent filed medical literature and a supplemental expert report from Dr. McClain which focused on the opinion provided by Dr. Gordon. Exs. A.1-A.7, C, filed Aug. 15, 2016, ECF No. 62. During this time, Petitioner filed updated medical records. Ex. 80, filed June 30, 2016, ECF No. 60.

Thereafter, the parties discussed potential dates for an entitlement hearing with Special Master Hastings, but the case was reassigned before a hearing could be scheduled. Status Report,

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manufactured by Sanofi Pasteur, Inc. https://www.fda.gov/vaccines-blood-biologics/vaccines/menactra (last visited Jan. 22, 2021). Varivax is a live virus varicella vaccine manufactured by Merck Corp. https://www.fda.gov/vaccines-blood-biologics/vaccines/varivax (last visited Jan. 22, 2021).

[4] Initially assigned to Special Master Moran, this case was reassigned to now-retired Special Master George Hastings on March 1, 2016. ECF No. 54. It was reassigned to my docket on December 5, 2017. ECF No. 69.

[5] Exhibit 10, which was filed by CD in early September 2014, was refiled electronically on December 14, 2020 at ECF No. 134.

[6] When labeling and filing her exhibits, Petitioner mistakenly skipped the number 59. Thus, there is no Exhibit 59 in the record of this case. *See, e.g.,* Exhibit List, filed June 13, 2019, at 7, ECF No. 100. Additionally, Ex. 72 was filed a second time as Ex. 73. Exhibit List at 8. Approximately 20 percent of the medical literature filed by Petitioner contains only the article title or title and abstract. *See* Exs. 23-25, 32, 37-39, 43-44, 50, 52-54, 56-58, 64-65, 74, 90. Exhibits 12-58 and 60-77, which were filed by CD in early January 2016, were refiled electronically on December 14, 2020 at ECF Nos. 135-137.

filed Apr. 18, 2017, ECF No. 65. After the case was assigned to my docket, an in-person entitlement hearing was set for June 18-19, 2019. *See* Non-pdf Scheduling Order, issued Apr. 9, 2018. On July 24, 2018, I established a schedule for pre-hearing submissions. ECF No. 75.

After several requests for additional time, Petitioner filed her pre-hearing brief and additional medical literature on May 10, 2019. Petitioner's Prehearing Submission (referred to hereinafter as "Pet. Pre-Hearing Brief"), ECF No. 86; Exs. 81-87, ECF No. 85. She filed a supplemental expert report from Dr. Shoenfeld approximately one week later. Ex. 88, filed May 16, 2019, ECF No. 88.

On May 30, 2019, I held a telephonic status conference with the parties to address Respondent's concerns regarding the timing of Dr. Shoenfeld's supplemental expert report, filed approximately one month before the entitlement hearing. Scheduling Order at 1, ECF No. 89. Respondent's counsel indicated that Respondent's expert, Dr. McClain believed he could provide a third expert report, filed with Respondent's pre-hearing submissions, if allowed several additional weeks. In response to questioning from Respondent's counsel, Petitioner's counsel indicated Petitioner planned no further filings. *Id.* at 1-2. Respondent's counsel then requested that Petitioner file textbook chapters referenced by Dr. Shoenfeld and an affidavit from Petitioner's mother. *Id.* at 2.

On June 4, 2019, the parties confirmed agreement regarding the following: 1) the timeliness of Petitioner's claim, 2) the accuracy of vaccines received, and 3) the accuracy of Petitioner's PMBCL diagnosis. Joint Status Report at 1, ECF No. 91. The parties added that, although they generally agreed with the events and treatment as set forth in the medical records, their experts "may disagree over the medical significance to be placed on the medical facts." *Id.* As expected, Petitioner maintained she has established causation, and Respondent disputed that assertion. *Id.*

On June 12, 2019, Petitioner filed the textbook excerpts and affidavit from Petitioner's mother which were requested by Respondent, as well as additional medical literature. Exs. 89-100, ECF Nos. 93-95. The same day, Respondent filed his pre-hearing briefing and Dr. McClain's third expert report, updated CV, and referenced medical literature. Respondent's Pre-Hearing Brief ("Res. Pre-Hearing Brief"), ECF No. 96; Exs. D, D.1-D.13, E, filed June 12, 2019, ECF Nos. 96-97. The next day, he filed an additional article and his exhibit list. Ex. D.14, Exhibit List, filed June 13, 2019, ECF Nos. 98-99.

The first day of the entitlement hearing, Petitioner filed two additional articles. Exs. 101, 102, filed June 18, 2019, ECF No. 101. During the two-day entitlement hearing, I heard testimony from Petitioner, her experts Dr. Shoenfeld and Dr. Gordon, and Respondent's expert Dr. McClain.

Approximately one month later, Respondent filed additional medical literature. Exs. F-H, filed July 19, 2019, ECF No. 106. On August 2, 2019, the parties indicated that they believed the record was complete. Joint Status Report, ECF No. 107.

Despite this representation, Petitioner filed an additional article on December 2, 2019. Ex. 103, ECF No. 110. The next day, he filed his post-hearing brief. Petitioner's Post-Hearing Brief ("Pet. Post-Hearing Brief"), filed Dec. 3, 2019, ECF No. 113. Four months later, Respondent filed

his post-hearing brief. Respondent's Post-Hearing Brief ("Res. Post-Hearing Brief"), filed Apr. 10, 2020, ECF No. 117.

In early May 2020, Petitioner filed a CV for Dr. Schoenfeld and reply to Respondent's post-hearing brief. Ex. 104, filed May 7, 2020, ECF No. 118; Petitioner Reply Brief ("Pet. Reply Brief"), filed May 8, 2020, ECF No. 119. On May 28, 2020, both parties filed additional briefs. Respondent's Sur-Reply in Support of His Post-Hearing Briefing ("Res. Sur-Reply Brief"), ECF No. 122; Petitioner's Sur-Sur Reply in Support of Her Post-Hearing Brief ("Pet. Sur-Sur Reply Brief"), ECF No. 123. On July 10, 2020, the parties filed a joint status report indicating that the record is complete for a ruling on the record. ECF No. 125.

This matter is now ripe for adjudication.

II. Factual History

As stated in the joint status report filed prior to the entitlement hearing, the parties generally agree that the events and treatment set forth in Petitioner's medical records are accurate. Although specific details may be disputed, for example the exact weight lost by Petitioner in the year prior to vaccination, these differences do not impact my analysis in this case. Thus, there is no factual issue about Petitioner's health which requires adjudication.

A. Medical Records

Petitioner was born in early 1994. *E.g.*, Ex. 2 at 13. Prior to 2011, she was a healthy child who suffered the usual childhood illnesses. *Id.* Medical records from her well child visits reveal she was consistently in the upper 50th percentile for weight and height. *Id.* at 26-30.

Approximately one month prior to vaccination, Petitioner was seen by a dermatologist for a growth on her left knee, tag on her neck, and mole on her back which were either removed, shaved, or treated with cryotherapy.[7] Ex. 6 at 1, 3. In a follow-up phone call on June 14, 2011, the dermatologist recommended removal of the left knee growth by a plastic surgeon. *Id.* at 2; *see* Ex. 2 at 24 (additional notation regarding this phone call in pediatric records).

At her well child visit on June 29, 2011, Petitioner received the vaccinations alleged as causal. Ex. 2 at 31-33. At this visit, it was noted that Petitioner's potassium was low, and she had lost 50 pounds in the past year. *Id.* at 31-32. Petitioner requested a referral to a plastic surgeon who could excise the growth on her knee. *Id.* at 31; *see id.* at 25 (referral provided on July 1, 2011).

Petitioner returned to her pediatrician on August 3, 2011, complaining of facial swelling, nausea, dizziness, and an itchy throat which began one day earlier. Ex. 2 at 34. She also reported that she had experienced lower back, neck, and shoulder pain for the last month. Petitioner's

[7] Cryotherapy is "the therapeutic use of cold." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY (hereinafter "DORLAND'S") at 438 (32th ed. 2012).

pediatrician ordered testing and instructed her to drink fluids and to take antipyretics.[8] Ex. 2 at 35.

When seen again by her pediatrician on August 5, 2011, Petitioner reported that her facial swelling had decreased, but that she continued to experience "general aches, muscle soreness, [a] deep, productive cough, [and] mid sternal chest pain." Ex. 2 at 36. Petitioner was diagnosed with acute bronchitis and prescribed a Zithromax Tri-Pak. *Id.* at 37.

Petitioner returned on August 10, 2011, complaining of abdominal and mid sternal pain and difficulty breathing, especially when laying down. Ex. 2 at 38. Petitioner's sore throat had improved but she continued to cough and was sleeping all day. *Id.* Assessed as having a slight fever and elevated heart rate with increased trouble breathing, Petitioner's pediatrician instructed her to go directly to the emergency room ("ER"). *Id.* at 39; *see also* Ex. 5 at 148.

After she visited the ER at Palms West Hospital, Petitioner was diagnosed with pleural effusion[9] and admitted to the PICU[10] that evening. Ex. 5 at 148, 156-57. Testing was ordered to rule out pericardial effusion.[11] Ex. 5 at 157. Results of testing revealed an elevated C-reactive protein level of 11.2 milligrams per liter.[12] Ex. 5 at 148. According to the history provided, Petitioner had experienced chest pain and difficulty breathing for two days. *Id.* at 148, 157. Her facial swelling and nausea began a week ago. *Id.* at 156.

By the time Petitioner was assessed in the PICU, test results revealed she also was suffering from pericardial effusion. Ex. 5 at 238. "[A] chest tube was placed, and the fluid was sent for culture." *Id.* at 148. Petitioner received temporary relief from fluid drainage from chest and pericardial tubes. *E.g., id.* at 149. A CT scan, performed on August 11, revealed a large mediastinal mass, indicative of lymphoma and measuring 13 x 6 x 10.4 centimeters. *Id.* at 421. When no diagnosis was obtained from the cytology of the pleural fluid, a CT-guided biopsy under local anesthesia was performed. *Id.* at 239. The biopsy results confirmed the mass was "a large B-cell lymphoma of the mediastinum." *Id.* at 240. Imaging performed on August 18, 2011 revealed thrombosis[13] in Petitioner's left jugular and subclavian veins, and Petitioner was transferred to a larger facility to begin chemotherapy. Ex. 5 at 240.

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[8] Antipyretics are agents which reduce or relieve fever. DORLAND'S at 109.

[9] Pleural effusion is "the presence of fluid in the in the pleural space." DORLAND'S at 596. Pleural is an adjective referring to "the serous membrane investing the lungs and lining the thoracic cavity, completely enclosing a potential space known as the pleural cavity." DORLAND'S at 1460.

[10] PICU stands for "pediatric intensive care unit." MEDICAL ABBREVIATIONS at 468 (16th ed. 2020).

[11] Pericardial effusion is "the accumulation of more than 50 mL of pericardial fluid in the pericardium." DORLAND'S at 596. Pericardium is "the fibroserous sac that surrounds the heart." DORLAND'S at 1412.

[12] C-reactive protein "is the most predominant of the acute phase proteins." DORLAND'S at 1532. Acute phase proteins are "any of the non-antibody proteins, produced mainly in the liver, found in increased amounts in serum during the acute phase response." DORLAND'S at 1531.

[13] Thrombosis is "the formation, development, or presence of a thrombus" which is "a stationary blood clot along the wall of a blood vessel." DORLAND'S at 1923.

Petitioner was admitted to the Arnold Palmer Hospital for Children from August 19 through September 8, 2011. Ex. 10 at 6. The histories found in the medical records from this facility are consistent with information contained in prior records. Regarding the weight loss she experienced prior to vaccination, Petitioner "reported a 20-pound intentional weight loss from January to July with exercise and appropriate dietary modification." *Id.* In a later record, it was noted that Petitioner was "a fit and trained athlete who works out regularly." *Id.* at 13.

On August 22, 2011, prior to the start of her chemotherapy, Petitioner underwent another CT scan which showed the anterior mediastinal mass "[wa]s overall not significantly changed in size, . . . measuring approximately 13.8 centimeters at the level of the carina.[14]" Ex. 10 at 533. The same day, Petitioner received a PICC[15] line in her left arm. Ex. 10 at 242. On August 23, 2011, she began chemotherapy which included multiple compounds including prednisone.[16] Following chemotherapy, she remained on prednisone. Ex. 10 at 242.

Petitioner's pericardial tube was removed on August 26, and her chest tube was removed on August 28. Ex. 10 at 6. She was moved to the hematology and oncology floor to continue her chemotherapy and given salt and soda mouth rinses for mouth care and a sore throat. *Id.* at 6, 244. X-rays performed on September 6 revealed the "mediastinal mass had decreased in size." *Id.* at 6-7. An ultrasound of Petitioner's left jugular and subclavian veins showed no thrombosis. Petitioner was discharged home on September 8, 2011. *Id.* at 7.

Petitioner returned to the Arnold Palmer Hospital for Children for three more rounds of chemotherapy in September, October, and November 2011. Ex. 1 at 6-20; Ex. 3 at 1-79. Between rounds of chemotherapy, Petitioner was seen by her local hematologist and oncologist. *See generally*, Ex. 4.

When Petitioner was seen on January 16, 2012, she was told she was in remission. Ex. 3 at 81. It was determined that Petitioner would undergo a PET scan and echocardiogram in February 2012 and could have her port removed if all test results were normal. *Id.* Petitioner's PET scan was normal, and she was instructed to follow-up in three months. *Id.* at 83-84. Throughout the remainder of 2012, Petitioner had follow-up visits at the Arnold Palmer Hospital for Children and with her local hematologist and oncologist. *Id.* at 85-93; Ex. 7 at 1-18. While physically well, Petitioner continues to experience panic attacks which are triggered by doctor visits. *E.g.*, Ex. 80 at 12 (medical record from June 29, 2016 visit).

B. Petitioner's Affidavit and Testimony

In her affidavit and testimony, Petitioner echoed the history contained in her medical

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[14] Carina is "a ridge or ridgelike structure." DORLAND'S at 296.

[15] PICC stands for "peripherally inserted central catheter." MEDICAL ABBREVIATIONS at 468.

[16] Prednisone is "a synthetic glucocorticoid derived from cortisone, administered orally as an inflammatory immunosuppressant in a variety of disorders." DORLAND'S at 1509.

records, adding additional detail regarding the difficulties she experienced throughout her illness. Ex. 9 at ¶¶ 6-53; Transcript ("Tr.") at 147-68. She described headaches beginning on July 10, 2011 and increasing neck and back pain and dizziness throughout the month. Ex. 9 at ¶¶ 9-11. When asked about the June 29, 2011 entry indicating she lost 50 pounds in the year prior to vaccination, Petitioner characterized her weight loss as closer to 30 pounds. Tr. at 148. She also provided information regarding the reason for her weight loss, attributing it to a concerted effort to exercise and eat healthier. *Id.* at 148-49; *see also* Ex. 9 at ¶ 6.

Petitioner's assertions regarding her efforts to exercise and to eat a healthy diet are supported by entries in the contemporaneously created medical records. *E.g.*, Ex. 10 at 6 (an August 2011 medical record chronicling a 20-pound weight loss from exercise and healthy eating during the prior six months). Thus, it appears Petitioner lost approximately 20 pounds in the six months prior to her illness and between 30 to 50 pounds during the full year. An exact finding regarding the amount of weight lost by Petitioner prior to her illness is not germane to the issue of causation in this case.

C. Affidavit from Petitioner's Mother

In her affidavit, Mary Nifakos contrasted her daughter's good health prior to vaccination with the deterioration of her health thereafter. Ex. 89 at ¶¶ 4-7. Like her daughter, she accurately recounted specific events, providing additional information regarding the effects of her daughter's illness on her life. *Id.* at ¶¶ 6-10. Ms. Nifakos indicated that her daughter continues to see "multiple doctors including a therapist for her anxiety, which is an ongoing thing." *Id.* at ¶ 9.

III. Expert Opinions

Petitioner submitted two expert reports from Dr. Yehuda Shoenfeld, an internist and immunologist, and one expert report from Dr. Jeffrey Alan Gordon, a hematologist and oncologist. Exs. 11, 88, 104 (hereinafter "First Shoenfeld Rep.", "Second Shoenfeld Rep.", and "Shoenfeld CV"); Exs. 78-79 (hereinafter "Gordon Rep." and "Gordon CV"). In response, Respondent's submitted three expert reports from Dr. Kenneth McClain, a pediatric hematologist and oncologist. Exs. A-D (hereinafter "First McClain Rep.", "McClain CV", "Second McClain Rep.", and "Third McClain Rep."). All experts testified at the entitlement hearing.

A. Qualifications

1. Petitioner's Expert: Dr. Yehuda Shoenfeld

Dr. Shoenfeld received his medical training at Hadassah Medical School, Hebrew University and Medical School, Tel-Aviv University. Shoenfeld CV at 2. Following fellowships in the United States, he returned to Israel where he concentrated on research and teaching. *Id.*; Tr. at 6. In 1985, he founded the Center for Autoimmune Diseases. First Shoenfeld Rep. at 1; Tr. at 6. He continues to see patients and teach as an emeritus professor at the Tel-Aviv University. Tr. at 6. Additionally, he is the Incumbent of the Laura Schwarz-Kipp Chair for Research of Autoimmune Diseases at Tel-Aviv University. Shoenfeld CV at 6; First Shoenfeld Rep. at 2. He is certified in internal medicine, clinical immunology, and allergy. First Shoenfeld Rep. at 1.

A member of numerous professional societies and editorial boards, Dr. Shoenfeld has helped organize numerous meetings and has received multiple awards. Shoenfeld CV at 4-11. Focusing on autoimmune and rheumatic diseases, he has performed extensive research and has authored chapters, books, and over 1800 peer reviewed papers. *Id.* at 21-129; First Shoenfeld Rep. at 2. In his first expert report, Dr. Shoenfeld emphasized the 15 articles he has published on vaccines and autoimmunity and 11 articles on lymphomas. First Shoenfeld Rep. at 3-5. He indicated he formulated the theory of Autoimmune Syndrome Induced by Adjuvants (known by the acronym ASIA)[17] in 2011. First Shoenfeld Rep. at 3.

2. Petitioner's Expert: Dr. Jeffrey Alan Gordon

Dr. Gordon received his M.D. from the University of Massachusetts Medical School in 1993. Gordon CV at 2; Tr. at 176. After a residency in internal medicine, he received fellowship training in hematology and oncology. Gordon CV at 2; Tr. at 176. He is board certified in hematology and oncology and has practiced medicine at the New London Cancer Center since 2012. Gordon CV at 1-2; Tr. at 176.

Having previously held teaching positions, Dr. Gordon testified that currently "nearly all of [his] time is spent on clinical care." Tr. at 177; *accord.* Gordon CV at 3. In his 20-year practice, he treats patients "with blood disorders, blood cancers, or what they call solid cancers, other types of cancers." Tr. at 193-94. Dr. Gordon explained that he performed the lung cancer research indicated on his CV during his fellowship because that was the focus of the work being performed by his mentor in the program. Tr. at 194; *see* Gordon CV at 4-5.

3. Respondent's Expert: Dr. Kenneth McClain

Dr. McClain attended the dual M.D./Ph.D program at the University of Chicago School of Medicine from 1963 to 1973. McClain CV at 1; Tr. at 208. While a predoctoral trainee, he worked in the Department of Pathology, focusing on tumor biology, specifically viral cause of cancers. *Id.* He earned his Ph.D. in 1972 and his M.D. in 1973. McClain CV at 1; Tr. at 209. He completed a pediatric residency at The Johns Hopkins Hospital in 1976, postdoctoral training at the National Institutes of Health in 1979, and a Hematology/Oncology Fellowship at the Department of Pediatrics, University of Minnesota in 1981. McClain CV at 1; Tr. at 209-10.

Certified in general pediatrics with a specialty in hematology-oncology, Dr. McClain is currently a Professor of Pediatrics in the Pediatric Hematology Oncology section at the Texas Children's Cancer Center. McClain CV at 3; Tr. at 211. He is the clinical director of the

[17] To date, the ASIA theory has not been found to be a valid theory, sufficient to satisfy *Althen* prong one. *See D'Angiolini v. Sec'y of Health & Hum. Servs.*, 122 Fed. Cl. 86, 101 (affirming the special master's rejection of the theory as "still developing and currently incomplete"), *aff'd*, 645 Fed.Appx. 1002 (Fed. Cir. 2016); *Garner v. Sec'y of Health & Hum. Servs.*, No. 15-0063V, 2017 WL 1713184, at *15 (Fed. Cl. Spec. Mstr. Mar. 24, 2017); *Johnson v. Sec'y of Health & Hum. Servs.,* No. 10-0578V, 2016 WL 4917548, at *8-9 (Fed. Cl. Spec. Mstr. Aug. 18, 2016) (describing this theory as overbroad, generalized, and vague and finding this expansive theory logically unpersuasive); *Rowan v. Sec'y of Health & Hum. Servs.*, No. 10-0272V, 2014 WL 7465661, at *12 (Fed. Cl. Spec. Mstr. Dec. 8, 2014).

histiocytosis program and co-director of the lymphoma program. Tr. at 211. Dr. McClain testified that the Texas Children's Cancer Center is the largest pediatric cancer center in the United States and one of the largest referral centers. *Id.* at 213. The lymphoma program is "the only designated lymphoma program among the pediatric oncology centers in the United States." *Id.* at 212. Dr. McClain estimated he spends 75 percent of his time seeing patients and 25 percent of his time performing clinical research. *Id.* at 214. Dr. McClain has published almost 200 articles, many regarding non-Hodgkin's and Hodgkin's lymphoma. McClain CV at 13-28. In his first expert report, Dr. McClain indicated he "ha[s] been especially interested in the care of children with lymphomas and those who have lymphoproliferative diseases caused by Epstein Barr Virus." First McClain Rep. at 1. He listed the 26 articles and book chapters he has authored on the topic of lymphomas. *Id.* at 1-3.

B. Expert Reports

1. Dr. Shoenfeld's First Expert Report

In his first report, Dr. Shoenfeld postulated the two theories of causation relied upon by Petitioner. Noting that Petitioner received four vaccinations on June 29, 2011, two of which contain an aluminum adjuvant, he posited that Petitioner's PMBCL "was caused by consistent stimulation of her immune system caused by the adjuvant, a cross reaction, or likely a combination of the two." First Shoenfeld Rep. at 25. He also theorized a cross reaction at the molecular level could have occurred between the HPV L1 protein and human proteins, damaging human proteins which play a role in suppressing the formation of lymphomas. *Id.* at 30-31.

Regarding his first theory, Dr. Shoenfeld described two stages he believes are involved in this process. The first stage consists of the attraction of lymphocytes to the stimulation provided by the adjuvants. First Shoenfeld Rep. at 28. Dr. Shoenfeld labeled this stage "pseudo lymphoma." *Id.* He then theorized "[t]he pseudo lymphoma (a benign condition) . . . can progress into a malignant condition, named lymphoma." *Id.* (emphasis in original removed). While Dr. Shoenfeld provided extensive medical literature regarding the development of cutaneous pseudo lymphoma at the site of vaccination, the first stage of this theory,[18] none of the medical literature filed by Petitioner addresses the second stage. When asserting "pseudolymphomas . . . can be transformed in time to malignant condition," he cited one article which was not filed by Petitioner. *Id.* at 30 (citing reference 15: Arai, et al., *A review of 55 cases of cutaneous lymphoid hyperplasia: reassessment of the histopathologic findings leading to reclassification of 4 lesions as cutaneous marginal zone lymphoma and 19 as pseudolymphomatous folliculitis,* 36 HUM. PATHOL. 505-11 (2005) (hereinafter "Arai")). This article was later filed by Respondent. *See* Arai (filed as Exhibit A.6). As the title suggests, the Arai article addresses only instances of incorrect classification. *Id.* at 6.

When discussing his second theory, Dr. Shoenfeld theorized that peptide matching between

[18] *E.g.,* Cerroni et al., *Cutaneous B-cell Pseudolymphoma at the Site of Vaccination,* 29 AM J DERMATOPATHO 538-42 (2007) (filed as Ex. 19); Hernandez et al., *B-cell Pseudolymphoma Caused by Aluminium Hydroxide Following Hyposensitization therapy,* 99 ACAD. DERMOSIFILIOGR. 213-16 (2008) (filed as Ex. 20). Petitioner did not present evidence that she experienced a pseudolymphoma.

different HPV L1 proteins and lymphoma-associated proteins in humans may trigger cross-reactions which suppress or alter the human proteins, interfering with their ability to prevent the formation of lymphoma or lymphomagenesis. First Shoenfeld Rep. at 24. This specific theory involves the process of molecular mimicry.[19] First Shoenfeld at 21-24. Dr. Shoenfeld then provided specific examples of human proteins, which if affected, could allow lymphomagenesis and listed multiple peptides which are shared by both HPV L1 and those and other human proteins. First Shoenfeld Rep. at 21-25. He provided numerous articles regarding human proteins whose mutation may be related to the formation of lymphoma or other cancers. *E.g.* Shin, et al., *Inactivating mutations of CASP10 gene in non-Hodgkin lymphomas,* 99 BLOOD, 11: 4094-99, 2002 (filed as Ex. 36).

To support both theories that vaccines can cause lymphoma through adjuvant stimulation and/or molecular mimicry, Dr. Shoenfeld relied upon what he described as the well-established association between autoimmune disease and lymphoma. First Shoenfeld Rep. at 20. He referenced several articles which discuss this association.[20] However, in at least one of the articles offered by Dr. Shoenfeld, the authors stated, "it may be hard to determine whether the autoimmune disease preceded the malignancy." Goldin at 1501. "[I]t could be that immune-related disorders are reflections of a pre-ceding precursory state on the pathway to full-blown malignancy." *Id.*

Furthermore, when discussing the possible mechanisms involved in any causal relationship between autoimmune diseases and lymphoma, factors provided by the autoimmune disease which may not be present for a vaccine, such as a sustained antigen drive, are required. *See* Cuttner at 793-94. Presumably to address this deficiency, on several occasions Dr. Shoenfeld quoted an online article stating that "[a] wide spread belief has been that alum exerts a depot effect whereby the emulsion retains antigen at the site of injection and releases it slowly to promote sustained antigen presentation." First Shoenfeld Rep. at 20-21, 27 (quoting B. Pulendran, *Immunological mechanisms of vaccination,* 12 NATURE IMMUNOLOGY, 6: 511, 509-17 (filed as Ex. 72) (hereinafter

[19] "[M]olecular mimicry has been suggested to explain the etiology of some autoimmune diseases. The molecular mimicry hypothesis posits that autoimmune diseases arise when the structure of the foreign invader resembles (or mimics) the structure of cells in the body. This similarity confuses the adaptive immune system and leads antibodies produced by B cells and/or T cells to attack the host, a process sometimes known as 'breaking tolerance.'" *Tullio v. Sec'y of Health & Hum. Servs.*, No. 15-0051V, 2019 WL 7580149, at *12 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), *aff'd,* 149 Fed. Cl. 448 (2020); Special masters have recognized molecular mimicry as the method by which streptococcus bacteria can develop into Sydenham's chorea and c. jejuni infection can cause Guillain-Barré syndrome. *W.C. v. Sec'y of Health & Hum. Servs.*, No. 07-456V, 2011 WL 4537877, at *11 (Fed. Cl. Spec. Mstr. Feb. 22, 2011), *mot. for rev. denied in relevant part,* 100 Fed. Cl. 440, 451-53 (2011), *aff'd,* 704 F.3d 1352 (Fed. Cir. 2013); *Isaac v. Sec'y of Health & Hum. Servs.*, No. 08-601V, 2012 WL 3609993, at *4 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for rev. denied,* 108 Fed. Cl. 743 (2013), *aff'd without op.*, 540 Fed. App'x 999 (Fed Cir. 2013).

[20] First Shoenfeld Rep. at 20 (citing J. Cuttner, *Autoimmune Disease Is a Risk Factor for the Development of Non-Hodgkin's Lymphoma*, 32 THE JOURNAL OF RHEUMATOLOGY, 10: 1884-87 (2005) (filed as Ex. 69) (hereinafter "Cuttner"); Mackay & Rose, *Autoimmunity and lymphoma: tribulations of B cells*, 2 NATURE IMMUNOLOGY 9: 793-95 (filed as Ex. 70) (hereinafter "Mackay"); Goldin & Landgren, *Autoimmunity and lymphomagenesis*, 124 INT. J. CANCER 1497-1502 (2009) (filed as Ex. 71) (hereinafter "Goldin").

"Pulendran")).[21] Relying on this sentence, he postulated that vaccines can cause a "[s]ustained antigen drive" similar to that created by autoimmune diseases and sufficient to create lymphoma. First Shoenfeld Rep. at 20, 26.

When opining that the four vaccines Petitioner received in this case caused her PMBCL, Dr. Shoenfeld relied upon Petitioner's lack of symptoms prior to vaccination, the temporal relationship between vaccination and Petitioner's first symptoms, and existence of the two theories he proposed. First Shoenfeld Rep. at 25-26. He concluded that "[t]he lack of prior disease, the time sequence and the plausible mechanism in which vaccine can induce pseudolymphoma and the later can progress to a malignant lymphoma (as in Sjogren's syndrome[22]) point to the fact that mo[re] probabl[y] than not that the four vaccine[s] were the sole cause to the emergence of the B cell lymphoma in Victoria." *Id.* at 32. He also theorized that, prior to vaccination, Petitioner "might have harbored a benign lymphoproliferation in her anterior chest, which did not cause any inconvenience" but developed into a malignancy "[u]pon being 'bombarded' by four vaccines, with all their constituents (adjuvant i.e. Aluminum), synthetic ingredients of the vaccines, diluents, yeast (i.e. saccharomyces)." *Id.*

2. Dr. Gordon's Expert Report

In his expert report, Dr. Gordon relied upon the theory of antigen stimulation postulated by Dr. Shoenfeld. Gordon Rep. at 5-7. After describing abnormalities in lymphocytes which occur with low levels of antigen stimulation over time, Dr. Gordon posited that "[s]ometimes, a potent exposure, such as a virus or a vaccination, can cause enough of an antigen stimulation that abnormalities within a lymphocyte occur quickly." *Id.* at 6. He provided examples when "[a] number of viruses have been implicated in lymphomagenesis, such as human immunodeficiency virus (HIV), hepatitis C (HCV), Epstein Barr virus (EBV), cytomegalovirus (CMV), human T-cell leukemia virus (HTLV), and Kaposi's sarcoma herpes virus (KSHV)." *Id.* While observing that it is more unusual for bacteria to contribute to the formation of lymphomas, Dr. Gordon noted that the *Helicobacter pylori* bacteria "ha[s] been implicated in the development of certain types of lymphomas." *Id.* He also theorized that pseudolymphomas "can over time become true lymphomas if continued antigen stimulation occurs or potent antigen stimulation occurs" (*id.*) but provided no evidence to support that assertion.

Regarding causation in this case, Dr. Gordon relied upon one of the factors mentioned by Dr. Shoenfeld, specifically Petitioner's lack of symptoms prior to vaccination, and the alleged

[21] This article was filed twice as Exs. 72 and 73. *Supra* at note 6.

[22] Sjogren's syndrome is "a symptom complex of unknown etiology usually occurring in middle-aged or older women" implicating "an abnormal immune response." DORLAND'S at 1848. Dr. Shoenfeld filed several exhibits regarding Sjogren's syndrome. Exs. 22-24. Two exhibits consist of only the article title. Exs. 23-24. The other involves a case study of a 74-year old patient with Sjogren's syndrome complicated by cutaneous tumors. Y. Horiuchi, *Massive cutaneous follicular lymphoid hyperplasia in a patient with the Sjogren syndrome: 7-year follow-up and immunohistochemical study*, 26 RHEUMATOL INT. 1044-49 (2006) (filed as Ex. 22) (hereinafter "Horiuchi"). However, the patient's condition was deemed to be benign and the lesions disappeared after several months of topical steroid treatment. Horiuchi at 1044.

absence of a cause other than her vaccinations. Gordon Rep. at 6-7. To account for the short time period between vaccination and Petitioner's first symptoms, Dr. Gordon emphasized that PMBCL is an aggressive lymphoma. *Id.* at 6. He concluded that "the lymphoma experienced by [Petitioner] was caused more probably than not by a strong, immune mediated, antigen response from the multiple vaccinations she received." *Id.* at 7.

In forming this opinion, Dr. Gordon did not provide or cite to any medical literature. He indicated he had reviewed Petitioner's affidavit and medical records filed to date (Exs. 1-3, 5-10)[23] and Dr. Shoenfeld's first expert report. *Id.* at 1.

3. Dr. McClain's First Expert Report

In his first expert report, Dr. McClain opined "[t]he progression of [Petitioner's] symptoms [wa]s characteristic of all young people who have large mediastinal masses from lymphoma and [he] believe[s] there is no data to suggest the vaccinations had anything to do with the onset of her lymphoma." First McClain Rep. at 6. Stressing the amount of weight loss Petitioner experienced in the year prior to vaccination, he suggested the weight loss could have been an early sign of Petitioner's lymphoma. He indicated that he believes the back, neck, and shoulder pain which Petitioner experienced in July 2011, the month following vaccination, "may have been secondary to the mediastinal mass which could have been developing." *Id.*

Stating that PMBCL is no longer considered a subset of diffuse large B-cell lymphomas ("DLBCL") but rather a distinct entity, Dr. McClain described the differences in these lymphoma types. First McClain Rep. at 7. He explained that DLBCLs "have surface markers which identify the malignant cells as originating in the germinal center of a lymph node." *Id.* In contrast, PMBCL "arises from thymic B-cells in the mediastinum." *Id.* Dr. McClain provided several articles indicating PMBCL is "demographically, clinically, and ecologically distinct from other DLBCL [(diffuse large B-cell lymphoma)] subtypes [with] clinical and biological features more closely resemble[ing] those of nodular sclerosing Hodgkin lymphoma (NSHL) arising in the mediastinum." K. Dunleavy, *Primary mediastinal B-cell lymphoma: biology and evolving therapeutic strategies,* AMERICAN SOCIETY OF HEMATOLOGY EDUCATION BOOK 2017(1): 298-303 (2017) (filed as Ex. D.5) (hereinafter "Dunleavy"). According to Dr. McClain, "[t]he cause of PMBCL is rooted in characteristic DNA mutations and rearrangements . . . [and] [t]here is no known connection with viral infections, environmental exposure, or vaccines." *Id.*

Dr. McClain also delivered a critique of the theories posited by Dr. Shoenfeld. First McClain Rep. at 8-10. Stressing "a fundamental lack of knowledge of the biology of lymphoma" on the part of Dr. Shoenfeld, he maintained that Dr. Shoenfeld's opinion is "built upon an unsound foundation of faulty biologic associations that he incorrectly claims support a conclusion of vaccine causation. *Id.* at 8. He characterized Dr. Shoenfeld's theories as "only confabulations of loosely associated, and often misquoted 'facts' which make no biologic sense." *Id.* (internal quotes in original).

[23] When identifying the medical records which he reviewed in this case, Dr. Gordon did not include records from the local hematologist and oncologist who treated Petitioner following her initial hospitalization in late August through early September 2011, Ex. 4. From his description of Petitioner's medical history, it appears he has not seen these records. *See* Gordon Rep. at 1-4.

Specifically, Dr. McClain criticized Dr. Shoenfeld's reliance on a connection between autoimmune disease and lymphoma, proclaiming it irrelevant in this case as Petitioner has no history of autoimmune disease. First McClain Rep. at 8. He also criticized Dr. Shoenfeld's claim that the expected collection of lymphocytes at the site of vaccination (a normal event) and development of the benign inflammatory response of pseudolymphoma can progress to the malignant condition of lymphoma as untrue. *Id.* at 9-10 (observing that the Arai article cited by Dr. Shoenfeld does not support this assertion). He stressed that "pseudo lymphomas are NOT real lymphomas." *Id.* at 9 (emphasis in original).

Regarding Dr. Shoenfeld's theory of molecular mimicry, Dr. McClain insisted it "is totally without experimental support." First McClain Rep. at 9. He declared "[m]olecular similarity does NOT mean the presence of these peptides would CAUSE cancer." *Id.* (emphasis in original). He posited Dr. Shoenfeld's theory as another example of true but unrelated occurrences. *Id.*

4. Dr. McClain's Second Expert Report

In his second expert report, Dr. McClain criticized Dr. Gordon's opinion as lacking detail and scientific proof. Dr. McClain's Second Expert Report ("Second McClain Rep.") filed as Ex. C at 1. Regarding Dr. Gordon's discussion of a relationship between autoimmune disease and lymphoma, he reiterated his observation, made when critiquing Dr. Schoenfeld's expert report, that Petitioner had no history of autoimmune disease. *Id.* He opined that there is no connection between the PMBCL Petitioner suffered and the vaccines she received. *Id.* at 2.

5. Dr. Shoenfeld's Second Expert Report

In his second expert report, Dr. Shoenfeld characterized the opinions expressed by Dr. McClain as a denial of a causal link between immune attacks and the formation of lymphomas. Second Shoenfeld Rep. at 1. Regarding Dr. McClain's discussion of the differences in lymphomas, he criticized this act of "meticulously classifying the disease" as distracting from a discussion of the "root cause(s) of the disease." *Id.*

In response to Dr. McClain's criticism of his theories, Dr. Shoenfeld argued that Dr. McClain misunderstood and misrepresented those theories. He characterized Dr. McClain's use of the term "upregulation" as a misrepresentation of the suppression he described. Second Shoenfeld Rep. at 2. He stressed that he "used NFKB2 protein as an example but obviously cross-reactive mechanism can apply to all the lymphoma-related proteins sharing peptides with the viruses contained in vaccines." *Id.* at 3. Noting that Dr. McClain described his theory as "a very wordy discussion of correlations without proof of causation," Dr. Shoenfeld again stressed the "high extent of peptide identities between Gardasil HPV L1s and human proteins that are related, when altered, to lymphoma." *Id.* at 3 (quoting First McClain Rep. at 10). He provided a table of multiple shared peptides (Table 1) and asserted this data showed that "a potentiating cross-reactive synergy appears more than possible." Second Shoenfeld Rep. at 4. After providing tables regarding the matching peptides contained in Hep A and Varicella virus (Table 2-3), he maintained these tables showed "scientific data that actually do represent the concrete possibility that HPV

cross-reactivity [along with that of Hep A and varicella viruses] may well have implemented a powerful and unfortunately successful lymphomatogenic synergy." *Id.* at 5.

Regarding Dr. McClain's opinion that Petitioner's PMBCL most likely had a genetic etiology, he insisted "cancer is not exclusively a genetic disease." Second Shoenfeld Rep. at 6. He accused Dr. McClain of refusing to accept the fact that Petitioner's lymphoma could have had multiple etiologies including an autoimmune etiology. *Id.* at 6. To support his assertion that it did, he cited the remission obtained by the chemotherapy drugs Petitioner received which he described as "among the most potent known inhibitors of the immune response." *Id.* at 7. He claimed Dr. McClain's opinion that PMBCL had a genetic cause would not account for the remission Petitioner experienced in January 2012, stating this would have to be caused by the "DNA alterations . . . magically disappear[ing]." *Id.* at 10.

To further support his opinion, Dr. Shoenfeld provided a list of more than 40 cases in which a VAERS[24] report was filed alleging lymphoma following receipt of one or more vaccines. Second Shoenfeld Rep. at 8-10.

6. Dr. McClain's Third Expert Report

In his third expert report, Dr. McClain responded to Dr. Shoenfeld's latest assertions. Regarding his use of the term "upregulation," he explained that "inactivating the repressor domain is the same as upregulation." Third McClain Rep. at 1 (internal quotations omitted). He observed that none of the medical literature cited by Dr. Shoenfeld related to the type of cancer Petitioner suffered, PMBCL. *Id.* He maintained "the underlying premise of Dr. Shoenfeld's arguments that an antibody response can induce PMBCL has no reliable foundation in the scientific literature." *Id.* at 2.

Regarding the tables of shared peptides provided by Dr. Shoenfeld, Dr. McClain asserted they are irrelevant for several reasons. Third McClain Report at 2. First, he explained that "vaccines induce antibodies to the entire 485 amino acid HPV L1 protein, NOT to just the 7 amino acid SLVDTYR peptide." *Id.* He insisted Dr. Shoenfeld had provided no experimental proof that the vaccine would specifically bind to the seven amino acids identified or "even if it did, that such binding would induce a mutation that would trigger the onset of the particular type of lymphoma Victoria has." *Id.*

Observing that "the degree of homology overlap identified by Dr. Shoenfeld is not unique," Dr. McClain offered a paper which found that the overlap between viral and human proteomes was rarely less than 90 percent. Third McClain Rep. at 2 (citing Kanduc, et al., *Massive peptide sharing between viral and human proteomes,* 29 PEPTIDES 1755-66 (2008) (filed as Ex. D.8) (hereinafter "Kanduc"). He maintained the authors of this paper as well as one discussing comparing bacteria to the human proteome, concluded their research undermines any role of

[24] "Established in 1990, the Vaccine Adverse Event Reporting System (VAERS) is a national early warning system to detect possible safety problems in U.S.-licensed vaccines, . . . co-managed by the Centers for Disease Control and Prevention (CDC) and the U.S. Food and Drug Administration (FDA)." https://vaers.hhs.gov/about.html (last visited on Feb. 19, 2021). Although healthcare providers are required to report certain events, "[a]nyone can report an adverse event to VAERS." *Id.*

molecular mimicry in the genesis of autoimmunity because, due to the extensive instance of overlap, the incidence of autoimmunity should occur at a rate of almost 100 percent. *Id.* (citing Kanduc at 1765; B. Trost, *Bacterial peptides are intensively present throughout the human proteome,* 1 SELF/NONSELF 1: 73, 71-41).

Noting that Dr. Shoenfeld criticized his lack of evidence of the specific genetic mutation, Dr. McClain observed that Dr. Shoenfeld, likewise, had performed no DNA sequencing to show the lack of DNA mutation. Third McClain Rep. at 4. He stressed that "it is generally accepted in the oncology community that the types of genomic abnormalities in a given type of lymphoma are caused by spontaneous mutations." *Id.*

Regarding Dr. Shoenfeld's discussion of Petitioner's treatment and remission, Dr. McClain argued that remission was obtained because all lymphoma cells, which were the only ones carrying the DNA mutation, were destroyed by chemotherapy. Third McClain Rep. at 4. While acknowledging that the chemotherapy drugs Petitioner received are immune-suppressive, he explained that "those same medications are used in chemotherapy protocols in lymphoma because they kill lymphoma cells." *Id.* (emphasis in original). He added that Dr. Shoenfeld had not provided nor was he aware of any literature to explain that these medications play a different role in this instance. *Id.* at 5. He again reiterated that there was no evidence indicating Petitioner had an autoimmune disease and stressed that VAERS reports have not been found to be evidence of causation. *Id.* at 4-5.

C. Testimony

1. Dr. Shoenfeld

During his direct testimony, Dr. Shoenfeld repeated the theories he advanced in his first expert report. Tr. at 4-46. He confirmed that, other than the mechanisms he described, he continued to rely on Petitioner's lack of symptoms prior to vaccination and the temporal association between vaccination and Petitioner's PMBCL. *Id.* at 144-45.

Dr. Shoenfeld also discussed two articles filed earlier that day.[25] He claimed the second article, which involved biopsies of cats showing the presence of cutaneous lymphomas at commonly used injection sites (Roccabianca at 832), was evidence that pseudolymphoma can transform into lymphoma. Tr. at 51. Dr. Shoenfeld also discussed the list of VAERS reports

[25] The first article was a population-based study which indicated the herpes zoster infection is an independent risk marker for subsequent lymphoid malignancies. Lui, et al., *Herpes zoster is associated with an increased risk of subsequent lymphoid malignancies – A nationwide population-based matched-control study in Taiwan,* posted on an Open Access website (filed as Ex. 101). The second article purported to show an increased presence of cutaneous lymphomas arising in areas commonly used for injection. Roccabianca, et al., *Cutaneous Lymphoma at Injection Sites: Pathological, Immunophenotypical, and Molecular Characterization in 17 Cats,* 53 VETERINARY PATHOLOGY 4: 823-32 (2016) (filed as Ex. 102) (hereinafter "Roccabianca"). Respondent's counsel objected to any consideration of these articles as they were published in 2012 and 2016 but only introduced into the record the morning of the first day of the entitlement hearing. Tr. at 47, 50. I indicated I would consider the articles but allowed Respondent's counsel time to first review the articles with her expert. Tr. at 47-48.

included in his second expert report, claiming these were proof of vaccine included lymphomas. *Id.* at 54

During cross examination, Respondent's counsel attempted to elicit, from Dr. Shoenfeld, an estimate of the percentage of time he spends diagnosing patients with cancer, specifically PMBCL. Tr. at 61-65. She also questioned him about his relationship to Claire Dwoskin, the founder of Children's Medical Safety Research Institute, considered an anti-vaccine organization.[26] *Id.* at 66-67. While acknowledging that he is listed as a member of the Scientific Advisory Board for this organization, Dr. Shoenfeld testified that he "never attended a board [meeting], and . . . was not involved in any decision of the board." *Id.* at 76. When asked about funding from Ms. Dwoskin and her organization, Dr. Shoenfeld acknowledged that one of his colleagues and co-authors, Miri Blank, had received funding from this source but denied accepting any such financial support himself. *Id.* at 67, 70-73.

Regarding Petitioner's case, Dr. Shoenfeld confirmed that Petitioner's diagnosis was PMBCL and that she had never been diagnosed with an autoimmune disease, pseudolymphoma, or any other type of lymphoma. Tr. at 85. When asked about his extensive discussion regarding autoimmune disease in his expert reports and testimony, despite the lack of autoimmune disease in this case, Dr. Shoenfeld testified that the purpose of these discussions was to provide examples of the mechanism by which lymphomagenesis occurs. *Id.* at 88-90. He stated, "I brought [up] Sjogren's disease as an example to show how chronic stimulation can stimulate and increase lymphocyte infiltration, progress to pseudolymphoma and then also develop lymphoma." *Id.* at 90. When related to stimulation by vaccines, as opposed to autoimmune diseases, Dr. Shoenfeld testified that "chronic means intensive stimulation," . . . not necessarily the timing, but the intens[ity] of the stimulation." *Id.* at 92.

Dr. Shoenfeld often provided confusing and conflicting testimony. When asked to provide the appropriate timing between vaccination and tumor formation under his theories of causation, Dr. Shoenfeld based his answer on the specific facts in this case. He stated "[i]n this case, in my opinion, due to the facts, which are very clear, one month." Tr. at 97. He attributed the facial swelling Petitioner experienced on August 3 to her tumor but not the neck and back pain she experienced in July. *Id.* at 96-99. He theorized that these July symptoms may have been due to a vaccine site injury but then admitted there was no evidence of such an injury in the medical records. *Id.* at 97-99. He then seemed to reverse his opinion on this point, indicating that while "not directly related," these symptoms would have drawn the attention of a treating physician "that something unusual [wa]s going [on] there." *Id.* at 98-99. He then reiterated his claim that Petitioner's facial swelling would have been the first symptom of her PMBCL. *Id.* at 99.

Throughout his testimony, Dr. Shoenfeld continued to insist that the only difference between PMBCL and other lymphomas was its location. He testified that "B large cell lymphoma

[26] Children's Medical Safety Research Institute is a 501(c)(3) non-profit organization which highlights what it deems to be "serious concerns raised by the scientific and medical community about the acknowledged significant increases in immune and inflammatory diseases in children and adults during the past three decades" and advocates that the study of "[t]he effect of vaccines on the immune and neurological systems must also be assessed in association with cognitive function as it is related to academic performance and systemic effects on the educational system." https://www.cmsri.org/about (last visited Feb. 17, 2021).

[in] the mediastinum is the same if it appears in the abdomen" (Tr. at 109) and that "the location in lymphoma is not important," [l]ymphoma is lymphoma" *Id.* at 136. He claimed his theories of causation would apply to "any kind of lymphoma." *Id.* at 89.

2. Dr. Gordon

During his testimony, Dr. Gordon explained that he is not a researcher, but a clinician involved in direct patient care. Tr. at 177. Describing PMBCL, he testified "it is a distinct lymphoma entity . . . recognized as its own subcategory of lymphoma." *Id.* at 179. However, he added that as a subcategory of non-Hodgkin's lymphoma, "it does have a lot of similarities in general to non-Hodgkin's lymphoma with regard to certain etiologies . . . and some commonality in the types of treatments that we general[ly] consider." *Id.* at 181.

When discussing the two-stage theory of sustained antigen simulation advanced by Dr. Shoenfeld, Dr. Gordon was asked if "there is a reason to believe that a pseudolymphoma could not eventually progress to lymphoma." Tr. at 186. He initially replied, "Classically, it's not described as an entity that in and of itself has a high risk of turning into a lymphoma." *Id.* After being asked, however, if it could happen, he replied in the affirmative. *Id.*

Regarding the timing of Petitioner's PMBCL, Dr. Gordon testified that a 30-day period between vaccination and the symptoms Petitioner experienced would be "consistent with an abnormal response to one or more of the vaccinations" she received. Tr. at 189. In reaching this conclusion, he emphasized that "it is an aggressive, fast-growing type of lymphoma." *Id.* Regarding a comparison of the CT scans performed on August 11 and 22, 2011, Dr. Gordon noted that the results of the second CT scan listed only the tumor's two dimensional measurement of 13.8 centimeters, which still was .8 centimeters greater than the largest of the three dimensional measurements reported on August 11. *Id.* at 280-82. Upon cross-examination, Dr. Gordon admitted that he had no information regarding the doubling rate of PMBCL. *Id.* at 200.

During cross-examination, Dr. Gordon also testified that "to a certain degree," he agreed with the scientific community's belief that the development of PMBCL "is triggered by genetic mutations in the cells." Tr. at 195. He also acknowledged that he could point to nothing atypical about the presentation of Petitioner's PMBCL. *Id.* at 201.

In closing, Dr. Gordon confirmed that the bases for his opinion in this case, that the vaccines Petitioner received caused her PMBCL, was the lack of an alternative cause and the timing of her symptoms and diagnosis. Tr. at 204-06.

3. Dr. McClain

During the first portion of his direct testimony, Dr. McClain described the two major categories (Hodgkin's and non-Hodgkin's) and various types of lymphomas. Tr. at 220-30. He testified that PMBCL "was once thought to be a part of the diffuse large B cell lymphomas but is now understood through genetic research to be a separate category." *Id.* at 222. He then discussed an article showing the DNA characteristics which he indicated showed, "in a very dramatic way, . . . the complete uniqueness of PMB[C]L versus the other type of lymphoma." *Id.* at 227

(discussing Wessendorf et al., *Further delineation of chromosomal consensus regions in primary mediastinal B-cell lymphomas: an analysis of 37 tumor samples using high-resolution genomic profiling (array-CGH),* LEUKEMIA 21: 2463-69, (2007)) (filed as Ex. D-10).

When asked about the connection between autoimmune disease and lymphoma, Dr. McClain opined that he was unaware of any autoimmune disease linked to the formation of PMBCL. Tr. at 234. He acknowledged, however, that this could be due, in part, to the rarity of PMBCL. *Id.*

Discussing further this theory of chronic stimulation, Dr. McClain emphasized the need for and correlation between the constant stimulation over time, like that provided by autoimmune disease. He noted that rheumatoid arthritis patients with the highest disease activity were at greatest risk of developing lymphoma. Tr. at 235-36. He explained that the type of inflammation produced by an autoimmune disease can occur for weeks and months. In contrast, inflammation at the site of vaccination "might happen for a few days or a week or two at most." *Id.* at 237.

Dr. McClain also stressed the importance of the location of a tumor in relationship to the chronic stimulation. He explained that any lymphoma caused by inflammation would occur close to the origin of the inflammation. Tr. at 253. As examples, he discussed the lymphoma which develops in the parotid gland in response to the accumulation of lymphocytes due to Sjogren's disease and the lymphoma which develops in the stomach in reaction to the *Helicobacter pylori*, bacteria which causes constant stimulation, inflammation, and ulcers in that area. *Id.* at 238-39. He maintained that the location of Petitioner's tumor undermined the possibility that it was caused by the vaccinations she received as any related lymphoma would have formed physically much closer to the site of vaccination. *Id.* at 253.

Regarding the theory of cross reactivity posited by Dr. Shoenfeld, Dr. McClain testified that molecular mimicry had been debunked as a cause of cancer. Tr. at 176-77. When asked about the human proteins identified by Dr. Shoenfeld as lymphoma-related, he testified that he was unaware of any association between these protein sequences and the development of PMBCL. *Id.* at 240-41. He also explained that any antibody attack would be against the whole protein not just the smaller groups of peptides identified by Dr. Shoenfeld. *Id.* at 246-47.

Dr. McClain also disagreed with Dr. Gordon's characterization of PMBCL as an aggressive and therefore fast-growing lymphoma. He testified that the term aggressive does not automatically equate to fast-growing. Tr. at 256. While asserting that the neck and back pain Petitioner experienced in July 2011 could have been related to her PMBCL, he theorized that Petitioner's tumor could have been there for quite a long time before it actually caused [any] . . . symptoms." *Id.* at 255. Dr. McClain acknowledged that a fast-growing lymphoma, like Burkitt's[27] could have produced a tumor the size seen on the August 11, 2011 CT scan within a month. *Id.* at 256-57. However, he pointed to the results of Petitioner's second CT scan performed on August 22, 2011

[27] Burkitt's lymphoma is a type of non-Hodgkin's lymphoma that is further classified as a mature B-cell lymphoma. First McClain Rep. at 6. Dr. McClain described as Burkitt's lymphoma as "the fastest growing lymphoma that we know." *See* Tr. at 254.

which showed no significant change in size from what was observed on the August 11 CT scan, to show that the growth of Petitioner's tumor was slow. *Id.* at 258-59.

IV. Applicable Law

A. Overall Burden in Vaccine Program Cases

Under the Vaccine Act, a petitioner may prevail on her claim if she has "sustained, or endured the significant aggravation of any illness, disability, injury, or condition" set forth in the Vaccine Injury Table (the Table). § 11(c)(1)(C)(i). The most recent version of the Table, which can be found at 42 C.F.R. § 100.3, identifies the vaccines covered under the Program, the corresponding injuries, and the time period in which the particular injuries must occur after vaccination. § 14(a). If a petitioner establishes that she has suffered a "Table Injury," causation is presumed.

If, however, a petitioner suffered an injury that either is not listed in the Table or did not occur within the prescribed time frame, she must prove that the administered vaccine caused injury to receive Program compensation. § 11(c)(1)(C)(ii) and (iii). In such circumstances, petitioner asserts a "non-Table or [an] off-Table" claim and to prevail, a petitioner must prove her claim by preponderant evidence. § 13(a)(1)(A). This standard is "one of . . . simple preponderance, or 'more probable than not' causation." *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274, 1279-80 (Fed. Cir. 2005) (referencing *Hellebrand v. Sec'y of Health & Hum. Servs.*, 999 F.2d 1565, 1572-73 (Fed. Cir. 1993). The Federal Circuit has held that to establish an off-Table injury, a petitioner must "prove . . . that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury." *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1351 (Fed. Cir 1999). *Id.* at 1352. The received vaccine, however, need not be the predominant cause of the injury. *Id.* at 1351.

The Federal Circuit has indicated that a petitioner "must show 'a medical theory causally connecting the vaccination and the injury'" to establish that the vaccine was a substantial factor in bringing about the injury. *Shyface*, 165 F.3d at 1352-53 (quoting *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992)). The Circuit Court added that "[t]here must be a 'logical sequence of cause and effect showing that the vaccination was the reason for the injury.'" *Id.* The Federal Circuit subsequently reiterated these requirements in its *Althen* decision. *See* 418 F.3d at 1278. *Althen* requires a petitioner demonstrate by preponderant evidence that the vaccinations she received caused her injuries by providing: "(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.* All three prongs of *Althen* must be satisfied. *Id.* "Unlike an on-Table case, proof of causation in an off-Table case must comprise more than just a literal temporal association between the onset of the injury and the vaccination." *Pafford v. Sec'y of Health & Hum. Servs.*, 64 Fed. Cl. 19, 24 (Fed. Cl. 2005); *see also Grant*, 956 F.2d at 1148.

The Federal Circuit has instructed that a petitioner may satisfy her evidentiary burden by relying either on "medical records or medical opinion." *Althen*, 418 F.3d at 1279 (emphasis in original). Any offered expert testimony must be scientifically reliable and may be analyzed using

the four factors enumerated by the Supreme Court in *Daubert*. *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1301, 1316 (Fed. Cir. 1999) (referring to *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579 (1993)). Circumstantial evidence also might be used. *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1325-26 (Fed. Cir. 2006). Evidence that satisfies one prong might assist in proving another prong as well. *Id.* at 1326.

Petitioner is not required to eliminate alternative causes when establishing his prima facie case. *Doe 11 v. Sec'y of Health & Hum. Servs.*, 601 F.3d 1349, 1357-58 (Fed. Cir. 2010); *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). To support an argument regarding causation, a petitioner may, however, introduce evidence of the lack of an alternative cause. *Walther v. Sec'y of Health & Hum. Servs.*, 485 F.3d 1146, 1149-50 (Fed. Cir. 2007). Respondent also may introduce evidence of the presence of an alternative cause to rebut evidence regarding causation. *Doe 11*, 601 F.3d at 1358; *de Bazan*, 639 F.3d at 1353.

Once a petitioner has established a prima facie case, the burden shifts to respondent to show by preponderant evidence that petitioner's injury was "due to factors unrelated to the administration of the vaccine." § 13(a)(1); *see also DeBazan*, 639 F.3d at 1352-54; *Walther*, 486 F.3d at 1150.

B. Analysis of Expert Testimony

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). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert*, 509 U.S. at 594-96. *See Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (*citing Terran*, 195 F.3d at 1316). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592-95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora. *Daubert* factors are employed by judges to exclude evidence that is unreliable and potentially confusing to a jury. In Vaccine Program cases, these factors are used in the weighing of the reliability of scientific evidence. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g., Snyder*, 88 Fed. Cl. at 743. In this matter, (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts of his own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)). A "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1324 (Fed. Cir. 2010). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Id.* at 1325-26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs.*, 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

C. Consideration of Medical Literature

Although this decision discusses some but not all of the medical literature in detail, I reviewed and considered all of the medical records and literature submitted in this matter. *See Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though [s]he does not explicitly reference such evidence in h[er] decision."); *Simanski v. Sec'y of Health & Hum. Servs.*, 115 Fed. Cl. 407, 436 (2014) ("[A] Special Master is 'not required to discuss every piece of evidence or testimony in her decision.'" (citation omitted)), *aff'd*, 601 F. App'x 982 (Fed. Cir. 2015).

V. Analysis

A. Credibility of the Experts

I will note at the outset that while all of the experts were qualified to testify in this proceeding, I found Dr. McClain to possess the best qualifications with respect to the disease at issue in this case: PMBCL. Dr. McClain serves as the clinical director of the histiocytosis program and co-director of the lymphoma program at Texas Children's Hospital. Tr. at 211-12. This facility is the only designated lymphoma program among the pediatric oncology centers in the United States. *Id.* at 212. Further, Dr. McClain has seen or consulted with over 300 lymphoma patients during his lengthy career. *Id.* at 215. He has numerous publications relevant to this field. *See* McClain CV. These impressive qualifications render him especially qualified to opine on the issues germane to this case. Special masters may consider the relative expertise of testifying experts when weighing the value of their opinion. *See Depena v. Sec'y of Health & Hum. Servs.*, No. 13-675V, 2017 WL 1075101 (Fed. Cl. Spec. Mstr. Feb. 22, 2017), *mot. for rev. denied*, 133 Fed. Cl. 535, 547-48 (2017), *aff'd without op.*, 730 Fed. App'x 938 (Fed. Cir. 2018); *Copenhaver*

v. Sec'y of Health & Hum. Servs., No. 13-1002V, 2016 WL 3456436 (Fed. Cl. Spec. Mstr. May 31, 2016), *mot. for rev. denied*, 129 Fed. Cl. 176 (2016).

B. Three-Pronged *Althen* Test

In order to receive compensation under the Vaccine Act, a petitioner must prove causation by satisfying the three-pronged test set forth in *Althen* by the preponderance of evidence standard required in the Vaccine Act. 418 F.3d at 1278. In *Althen,* the Federal Circuit described this standard "as one of proof by a simple preponderance, of 'more probable than not' causation." *Id.* at 1279.

Although the first and second prongs of *Althen* appear to be similar, these analyses involve different inquiries. *See Doe 93 v. Sec'y of Health & Hum. Servs.*, 98 Fed. Cl. 553, 566-67 (2011). The first prong focuses on general causation, whether the administered vaccine can cause the particular injury suffered by the petitioner, and the second prong focuses on specific causation, whether the administered vaccine did cause the injury. *Pafford v. Sec'y of Health & Hum. Servs.*, 451 F.3d 1352, 1355-56 (Fed. Cir. 2006). This distinction "has been described as the 'can cause' vs. 'did cause' distinction." *Stapleton v. Sec'y of Health & Hum. Servs.*, No. 03-234V, 2009 WL 1456441, at *18 (Fed. Cl. Spec. Mstr. May 1, 2009).

1. *Althen* Prong One

Under the first prong of *Althen*, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford,* 451 F.3d at 1355-56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs*., 35 F.3d 543, 548 (Fed. Cir. 1994). Proof that the proffered medical theory is reasonable, plausible, or possible does not satisfy a petitioner's burden. *Boatmon v. Sec'y of Health & Hum. Servs*., 941 F.3d 1351, 1359-60 (Fed. Cir. Nov. 7, 2019).

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). However, special masters are "entitled to require some indicia of reliability to support the assertion of the expert witness." *Boatmon*, 941 F.3d at 1360, *quoting Moberly*, 592 F.3d at 1324. Special Masters, despite their expertise, are not empowered by statute to conclusively resolve what are complex scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Hum. Servs.*, 121 Fed. Cl. 230, 245 (2015), *vacated on other grounds*, 844 F.3d 1363 (Fed. Cir. 2017); *see also Hock v. Sec'y of Health & Hum. Servs.*, No. 17-168V, 2020 U.S. Claims LEXIS 2202 at *52 (Fed. Cl. Spec. Mstr. Sept. 30, 2020).

Petitioner in this case proposed two theories of causation which she maintained establish,

either separately or collectively, that the multiple vaccines she received can cause PMBCL. In her pre-hearing brief, she averred "[t]here is considerable overlap between our two positions as they both deal with stimulation brought about by vaccination." Pet. Pre-Hearing Brief at 7. Both theories are described in detail in Dr. Shoenfeld's first expert report and discussed in further detail in Petitioner's pre- and post- hearing briefs. In his expert report, Dr. Gordon advanced the first of Dr. Shoenfeld's theories but added no accompanying evidence.

When presenting both theories, Dr. Shoenfeld provided evidence of associations which do not equate to a causal relationship. Additionally, much of his discussion was not relevant to Petitioner's case but was presented only to illustrate how Dr. Shoenfeld's theories are potentially substantiated in other circumstances. He focused on the validity of his theories in these other circumstances but failed to establish how they translate to the facts of Petitioner's case.

Both theories offered by Dr. Shoenfeld are unsupported and incomplete. While petitioners are not required to provide the exact mechanism involved in any general theory of causation, there must be some support for their assertions. *Knudsen*, 35 F.3d at 548-49. When discussing his theories, Dr. Shoenfeld provides details based upon assumptions and conjecture.

a. *Chronic Stimulation*

With respect to his first theory, Dr. Shoenfeld posited that vaccines can cause PMBCL in the same manner that autoimmune disease has been shown to cause non-Hodgkin's lymphoma, through chronic stimulation. When advancing this theory, he sometimes focused on the aluminum adjuvant alone and, at other times, the vaccine antigen supported by the included adjuvant. First Shoenfeld Rep. at 28-30. In forming his opinion of causation, Dr. Gordon relied upon the same theory, referring to the chronic stimulation provided by vaccine antigens. Gordon Rep. at 5-7. However, there are several problems with this theory.

Dr. Shoenfeld described chronic stimulation as follows:

> What I mean by chronic stimulation, it's a strong repetitive stimulation. There are two kinds of strong stimulations. One is repetitive with small amounts, and one which is repetitive with huge amounts with different kinds of antigens. This case is unique. There are four different vaccines given at the same day, at the same injection, with huge amounts of aluminum. So in this case, the chronic means intensive stimulation.

Tr. at 91-92.

First, none of the evidence Dr. Shoenfeld provided to support the relationship between autoimmune disease and non-Hodgkin's lymphoma pertains to the specific type of lymphoma Petitioner suffered, PMBCL. As Dr. McClain testified, PMBCL "is a very unique form of lymphoma." Tr. at 227. According to literature supplied by Dr. McClain, PMBCL actually more closely resembles a subtype of Hodgkin's lymphoma. Dunleavy at 298.

Second, even if applicable to the formation of PMBCL, Petitioner has not provided sufficient evidence to show that the vaccines Petitioner received would have resulted in the chronic stimulation induced by autoimmune disease. The medical literature provided by Dr. Shoenfeld discussed sustained antigen drive. Mackay at 793-94. Citing the Pulendran article, Dr. Shoenfeld seemed to theorize that the inclusion of alum adjuvant would increase the duration of the effect of the vaccine antigen. First Shoenfeld Rep. at 20-21, 27; *see* Pulendran at 511. He further testified as followed regarding aluminum: "So the aluminum, being a strong stimulant of the immune system, is toxic to many organs in our body, including the brain. So in this case, she got one gram in one shot with multiple antigens. This is a strong stimulation which lasted -- in this case didn't need more than one month to arise or to stimulate to get the emergence of the aggressive lymphoma." Tr. at 93. Dr. Shoenfeld later conceded that Petitioner received one milligram of aluminum in the four vaccines and not one gram. *Id.* at 94. However, he continued to call this dose "a huge amount." *Id.* Dr. Shoenfeld acknowledged that he had not submitted evidence in this case that the amount of aluminum in vaccines constitutes a toxic amount. *See* Tr. at 94-95.

Dr. McClain contrasted the autoimmune stimulation provided by vaccines which is lesser in duration than what would be provided by autoimmune disease, calling them "markedly different". Tr. at 237; First McClain Rep. at 8. Specifically, Dr. McClain stated that "inflammation that happens at the site of an injection might happen for a few days or a week or two at most" whereas the inflammation from an autoimmune condition can go on for "months and months and months." Tr. at 237.

Finally, as discussed by Dr. McClain, it is illogical to assume that chronic stimulation provided at the site of vaccination would cause the type and location of tumor Petitioner experienced. During his testimony, Dr. McClain stressed the importance of the location of a tumor in relationship to the chronic stimulation, explaining that any lymphoma caused by inflammation would occur close to the origin of the inflammation. Tr. at 253. I find Dr. McClain's testimony on this point to be persuasive.

Examining the two-stage explanation advanced by Dr. Shoenfeld further underscores the weakness of this theory. While Dr. Shoenfeld supplied extensive medical literature showing that benign lymphomas can form at the site of vaccination, he provided no support for the proposition that these benign pseudolymphomas can progress to cutaneous lymphomas. Dr. Shoenfeld claimed the Roccabianca article regarding biopsies in cats supported this assertion, but that article only indicates cutaneous lymphomas can form at common injection sites. It does not suggest a transformation from benign to malignant tumor occurs. Furthermore, there is no evidence Petitioner experienced cutaneous pseudo lymphoma in this case. Certainly, there is no support for the proposition that any response which occurred at the site of vaccination would affect lymphocytes in the chest cavity.

Petitioner has failed to provide preponderant evidence that this theory of chronic stimulation is a reliable medical theory applicable to Petitioner's case.

b. *Cross Reactivity - Molecular Mimicry*

Dr. Shoenfeld next proposed a theory of cross reactivity following the process of molecular mimicry. In additional to being an accepted means by which certain viral and bacterial infections can cause autoimmune disease (*see supra* note 19), the theory of molecular mimicry has been used to persuasively show a causal link between the HPV and MMR vaccines and immune thrombocytopenic purpura ("ITP"). *Johnson v. Sec'y of Health & Hum. Servs.*, No. 14–113V, 2017 WL 772534 (Fed. Cl. Spec. Mstr. Jan. 6, 2017) (finding petitioner presented sufficient evidence to conclude the HPV vaccine can cause ITP); *Ebenstein v. Sec'y of Health & Hum. Servs.*, No. 06–573V, 2010 WL 5113185, at *21 (Fed. Cl. Spec. Mstr. Sept. 1, 2010) (accepting that molecular mimicry links the MMR vaccine and ITP). However, the fact that these theories have been found to provide sufficient evidence of prong one general causation, does not equate to an acceptance of the theory of molecular mimicry in every instance. As the special master in *Isaac* stated,

> The fact that molecular mimicry exists as a biological phenomenon does not automatically mean that vaccines can cause autoimmune disease by that process. Applicable law instructs that special masters need not accept unsupported theories of vaccine causation without some indicia of reliability, and that a temporal association is not sufficient in itself. I accept the theory of molecular mimicry in some cases and reject it in others, depending on the particular vaccine, the injury, the reliability of the expert testimony supporting and opposing causation, and the weight of the other evidence in the record.

2012 WL 3609993, at *4; *accord. Caves v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 119, 135 (June 24, 2011) (indicating the theory of molecular mimicry must be held applicable to the specific case at hand), *aff. per curiam*, 463 Fed. Appx. 932 (Fed. Cir. 2012). To date, the theory of molecular mimicry has not been accepted as a reputable theory of general causation when used to link vaccines to cancers, including lymphoma.

I will note that lymphoma is not an autoimmune disease and is not considered to be an antibody-mediated condition. Tr. at 246. Based on that, Dr. McClain testified that the vaccines that Petitioner received could not have triggered an autoantibody response that in turn caused PMBCL. *Id.* Dr. McClain further testified that there is no evidence in the scientific community that PMBCL has an infectious or an autoimmune etiology. *Id.* at 250. There is additionally no evidence in the scientific community that PMBCL can be caused by vaccination. *Id.* Further, Dr. McClain, in his 42 years of treating cancer patients, has not seen a case of vaccination causing a lymphoma. First McClain Rep. at 7.

In this case, Dr. Shoenfeld relied solely upon the similarities between the proteins found in the HPV, Hep A, and Varicella-Zoster vaccines and human proteins which he theorized are involved in lymphomagenesis. First Shoenfeld Rep. at 20-25, 30-31; Second Shoenfeld Rep. at 2-5. The medical literature Petitioner filed addressed these similarities but provided no evidence to show these vaccines would initiate the cross reactivity (molecular mimicry) Dr. Shoenfeld presumes would occur. Neither does he provide any evidence to establish that alteration or mutation of these human proteins would result in the formation of lymphoma.

Dr. McClain succinctly described the flaws in Dr. Shoenfeld's theory when he wrote "[m]olecular similarity does NOT mean the presence of these peptides would CAUSE cancer." First McClain Rep. at 9 (emphasis in original). He emphasized the lack of scientific evidence showing that the antibodies induced by vaccines would bind to the specific peptides identified by Dr. Shoenfeld as proposed or that such binding would produce a mutation that would trigger the type of lymphoma Petitioner had, PMBCL. Third McClain Report at 2. Dr. McClain also asserted that if the similarity that Dr. Shoenfeld relied upon were sufficient by itself to ensure the cross-reactivity Dr. Shoenfeld described, the expected outcome, be it autoimmune disease or lymphoma would occur much more often. First McClain Rep. at 2 (citing Kanduc at 1765; Trost at 73). I find Dr. McClain's criticisms to be persuasive.

I will also note that Petitioner has provided no medical literature which supports a connection between the vaccines at issue in this case and the development of PMBCL. As Dr. McClain observed, there is no evidence that wild type HPV infection, Hepatitis A infection, or Varicella infection cause PMBCL. Third McClain Rep. at 2. "Thus, if the antigens associated with these viral infections had any capacity to induce PMBCL, it would have likely been noted in the scientific literature as PMBCL is an extensively studied disease." *Id.* While support in the medical literature is not required in order for Petitioner to establish a reputable prong one theory, the absence of such evidence does not serve to advance Petitioner's case. "[A] scientific theory that lacks any empirical support will have limited persuasive force." *Caves*, 100 Fed. Cl. at 134.

Petitioner has failed to provide preponderant evidence that her theory of cross reactivity or molecular mimicry is a reputable medical theory connecting vaccinations to the formation of PMBCL.

2. *Althen* Prong Two

To satisfy the second prong of the *Althen* test, a petitioner must establish a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." *Althen*, 418 F.3d at 1278. The sequence of cause and effect need only be "logical and legally probable, not medically or scientifically certain." *Knudsen*, 35 F.3d at 548-49; *accord. Capizzano*, 440 F.3d at 1326. In establishing that a vaccine did cause the injury in question, the opinions and views of treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280).

A review of the medical records in this case reveals no entry which supports Petitioner's claim that the vaccines she received on June 29, 2011 caused her PMBCL. None of her treating physicians implicated, or even discussed the possibility of a causal link, and Petitioner does not argue that this evidence exists.

Additionally, the medical records themselves do not provide evidence linking Petitioner's PMBCL to her vaccination. Dr. Shoenfeld testified that after vaccination "I believe that the stimulant will go immediately at the same very day, which will be exemplified quite often by fever,

by feeling unwell, et cetera, which quite often the vaccinee would complain." Tr. at 95. Yet as Dr. McClain points out in his report, "from June to early August [Petitioner] had no fevers or cervical or axillary adenopathy, which one would expect if an injection in the deltoid muscles of both arms were to excessively activate the immune system." First McClain Rep. at 6. Indeed, there is no evidence in Petitioner's medical records that she developed an aberrant immune response to her vaccinations.

Further, during his testimony, Dr. McClain stressed the importance of the location of a tumor in relationship to the chronic stimulation, explaining that any lymphoma caused by inflammation would occur close to the origin of the inflammation. Tr. at 253. Dr. McClain testified as follows:

> If a person has some inflammatory infectious condition of the shoulder, the lymph nodes of the armpit, the axilla, would be the recipients of that information, whether it's cancer cells or inflammation. So if she had had inflammation from, or if the lymphoma had started in her vaccine site, it would have gone to her axillary lymph nodes. She did not have axillary lymphadenopathy....

Id. Petitioner's medical records make it clear that her PMBCL did not develop close to the origin of her purported vaccine-induced inflammation. In short, Petitioner's medical records are bereft of evidence connecting her June 29, 2011 vaccinations to her subsequent development of PMBCL.

When asserting that causation-in-fact has been proven, Petitioner and her experts relied upon her lack of symptoms prior to vaccination, the timing of her symptoms post-vaccination, along with a lack of an alternative cause. First Shoenfeld Rep. at 32; Gordon Rep. at 6-7; Tr. at 144-45, 204-06; Pet. Brief at 12; Pet. Post-Hearing brief at 9-12. Although presented as two separate bases, the first two assertions (made by Dr. Shoenfeld) are simply variations of the argument that the timing of Petitioner's symptoms is temporally appropriate to vaccination, in essence the focus of *Althen* prong three. Proper timing may be considered as evidence to establish the second *Althen* prong, but timing alone is not sufficient. *Grant*, 956 F.2d 1148 (Fed. Cir. 1992). Furthermore, as discussed below, I do not find the temporal relationship between Petitioner's PMBCL and the vaccines she received to be medically appropriate.

In his expert report, Dr. Gordon also discussed the lack of an alternative cause. Gordon Rep. at 6-7. He maintained that "[n]o other plausible etiology has been identified in the provided medical records." *Id.* at 7. At the end of her post-hearing brief, Petitioner argued that Respondent failed to provide "a cogent argument for alternative cause."[28] Pet. Post-Hearing Brief at 12.

In this case, Dr. Gordon claimed there was no alternative cause for petitioner's PMBCL but offers no evidence to support that assertion. Gordon Rep. at 7. In contrast, Dr. McClain asserted PMBCL has a genetic etiology. Tr. at 225. In his expert report, Dr. McClain stated that

[28] To support causation, a petitioner may introduce evidence of the lack of an alternative cause. *Walther*, 485 F.3d at 1149-50. Respondent is not required to provide preponderant evidence of a viable alternative cause until Petitioner has established her *prima facie* case. *Walther*, 485 F.3d at 1150; *see* § 13(a)(1).

"[t]he cause of PMBCL is rooted in characteristic DNA mutations and rearrangements." First McClain Rep. at 7; *accord.* Third McClain Rep. at 3. Petitioner's other expert, Dr. Shoenfeld, does not dispute this fact but rather asserts that Dr. McClain failed to recognize that multiple etiologies could be involved. Second Shoenfeld Rep. at 6. During his testimony, Dr. Gordon expressed a level of agreement asked when about the scientific community's view that PMBCL has a genetic basis. Tr. at 195. Even combined with Petitioner's assertions regarding appropriate timing, this assertion of the lack of an alternative cause is not sufficient to satisfy *Althen* prong two, especially when considered in the context of her medical records and the lack of treater support for vaccine causation.

Petitioner has not provided preponderant evidence of a logical sequence of cause and effect between the vaccines she received and the PMBCL she developed. She has therefore failed to sustain her burden under the second prong of *Althen*.

3. *Althen* Prong Three

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* The timing prong contains two parts. First, a petitioner must establish the "timeframe for which it is medically acceptable to infer causation" and second, she must demonstrate that the onset of the disease occurred in this period. *Shapiro v. Sec'y of Health & Hum. Servs.,* 101 Fed. Cl. 532, 542-43 (2011), *recons. denied after remand on other grounds*, 105 Fed. Cl. 353 (2012), *aff'd without op.,* 503 F. App'x 952 (Fed. Cir. 2013). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Shapiro*, 101 Fed. Cl. at 542; *Koehn v. Sec'y of Health & Hum. Servs*., No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

a. *The Timeframe for which it is Medically Appropriate to Infer Causation*

Petitioner and her experts posited that a 30-day time frame between vaccination and Petitioner's first symptoms constituted a medically appropriate temporal relationship under the theories they advanced. Pet. Pre-Hearing Rep. at 12; Tr. at 97, 189. They did not, however, provide a persuasive explanation regarding why this is the case or what supported this temporal window. In fact, the experts all acknowledged that the doubling rate for a PMBCL tumor is unknown. *See e.g*., Tr. at 100, 200, 254, 283. Given this point, it is difficult to understand how Petitioner's experts could opine that preponderant evidence establishes the development and growth of Petitioner's tumor in this case is medically appropriate.

b. *The Onset of Petitioner's Disease*

Focusing on the facial swelling and dizziness that Petitioner reported on August 3, 2011, Petitioner's experts maintained that the onset of Petitioner's symptoms was consistent with that 30-day time frame. Pet. Pre-Hearing Brief at 1; Tr. at 101-02; *see* Ex. 2 at 34 (report from August 3, 2011 visit). However, they ignore the lower back and shoulder pain Petitioner reported

experiencing throughout July. *See* Ex. 2 at 34. Moreover, in her affidavit, Petitioner indicated that her dizziness occurred, along with headaches and back and neck pain earlier, in July 2011. Petitioner stated, "Around July 10, I started getting frequent headaches. As the month progressed, I also started having neck and back pains, and I felt dizzy a lot." Ex. 9 at 9.

Dr. McClain stated that in July 2011, Petitioner "noted back, neck, and shoulder pain which I believe may have been secondary to the mediastinal mass". First McClain Rep. at 6. He also testified that "the tumor could have been there for quite a long time before it actually caused any pain symptoms." Tr. at 255. In her affidavit, Petitioner indicated the dizziness she reported on August 3, 2011 began in July 2011, prior to the facial swelling she had experienced for a few days. Ex. 9 at ¶ 9.

Dr. Gordon does not address these earlier occurring symptoms, but Dr. Shoenfeld appears to consider they could be connected to Petitioner's PMBCL. In his testimony, he stated these earlier symptoms "would have to draw the attention of the physician, the treating physician, that something unusual is going [on] there." Tr. at 98-99. Additionally, Petitioner included the symptoms of back and chest pain which occurred in July 2011, as symptoms of PMBCL in her post-hearing brief. Post-Hearing Brief at 9-11. However, when doing so, she shortened the medically appropriate time frame previously supplied, stating "within 30-days after exposure is within the timeframe the medical community would expect from an aggressive tumor like PMBCL." *Id.* at 10 (emphasis added); *see* Pet. Pre-Hearing Brief at 12 (describing "the development of symptoms a little over 30-days after exposure" as appropriate for comparison (emphasis added)).

Petitioner offers little support for the 30-day time frame she initially proposed. And the evidence she did supply is less potent when applied to the shorter window, less than 30 days. Despite being asked to "set[] Petitioner's clinical course aside" and provide a timeline for tumor formation under the theories he advanced, Dr. Shoenfeld referenced the facts in Petitioner's case to opine that a one-month time frame was appropriate. Tr. at 97. Dr. Gordon offered at least some additional basis for his opinion when he described PMBCL as an aggressive cancer, and Petitioner echoed this argument in her briefs. Gordon Rep. at 6; Tr. at 189; Pet. Pre-Hearing Brief at 12; Pet. Post-Hearing Brief at 10-11. Dr. Gordon theorized that Petitioner's tumor could have grown to the size observed in a CT, performed on August 11, 2011, even if it originated after vaccination in late June 2011. Tr. at 204-06.

Respondent's expert, Dr. McClain agreed that a fast-growing tumor, such as a Burkitt tumor, could grow to the size observed on August 11, 2011 even if formed six weeks earlier. Tr. at 255-57. However, he also testified that labeling a cancer as aggressive did not mean it was fast growing. *Id.* at 256.

However, there is evidence in the medical records showing Petitioner's tumor was not fast-growing. A CT performed on August 11 showed the tumor measured 13 x 6 x 10.4 centimeters at that time. Ex. 5 at 421. While a second CT scan performed on August 22 was only two dimensional, the report indicated the "anterior mediastinal mass [wa]s overall not significantly

changed in size." Ex. 10 at 533. Dr. McClain surmised from these CT scans that Petitioner's tumor had a "very slow" growth rate.[29] Tr. at 259-60.

Ultimately, there is persuasive evidence that Petitioner's first symptoms of PMBCL occurred, at latest two weeks after vaccination, and there is some evidence that Petitioner's tumor formed prior to vaccination. Ultimately, it is unnecessary for me to determine the precise onset of Petitioner's disease because she has failed to establish that a time frame of 30 days or less between vaccination and the first symptoms of PMBCL is medically appropriate to infer vaccine causation. Accordingly, Petitioner has failed to provide the preponderant evidence needed to satisfy the third prong of *Althen.*

C. Significant Aggravation

In her petition, Ms. Nifakos advanced claims of both causation-in-fact and significant aggravation. Petition at 1. However, other than that one mention, she provided no further discussion of or evidence for a claim of significant aggravation.

Petitioner's expert Dr. Shoenfeld briefly mentioned that Petitioner's mass may have been present prior to vaccination. First Shoenfeld Rep. at 32. However, he then hypothesized that the mass was benign until "bombarded" by the four vaccines Petitioner received. *Id.* Thus, his discussion was still focused on a causation-in-fact claim.[30]

If Petitioner had pursued a significant aggravation claim further, it would be appropriate to discuss the legal standards for such a claim as articulated in *Loving ex rel. Loving v. Sec'y of Health & Hum. Servs.*, 86 Fed. Cl. 135, 144 (2009). Because Petitioner effectively abandoned this argument by not discussing significant aggravation in her briefs, no further discussion is required.[31]

VI. Conclusion

Upon careful evaluation of all the evidence submitted in this matter, including the medical records, the testimony, as well as the experts' opinions and medical literature, I conclude that Petitioner has not shown by preponderant evidence that she is entitled to compensation under the

[29] Although Dr. Gordon's disagreed with this position because three-dimensional imaging had not been performed on August 22, I find that argument unpersuasive. Tr. at 281-82. Dr. McClain effectively testified that when a tumor changes in one dimension, it generally changes in the other dimensions as well. Tr. at 262. Conversely, when one dimension of a tumor "doesn't change, you have to assume that it's not changing in other dimensions, also." *Id.*

[30] Even assuming that Petitioner had advanced a significant aggravation theory, I find that theory would have been unpersuasive for the reasons articulated earlier in this decision. Namely, any significant aggravation theory would have necessarily relied on the same unpersuasive causal mechanism articulated in Petitioner's causation-in-fact claim.

[31] In fact, in her brief, Petitioner stated "There is absolutely no evidence that petitioner had large B cell lymphoma prior to the development of facial swelling, back, and chest pain within 30-days of administration of 4 biologic products." Pet. Post-Hearing Brief at 9.

Vaccine Act. **The petition is therefore DISMISSED. The clerk shall enter judgment accordingly.**[32]

IT IS SO ORDERED.

s/ Katherine E. Oler
Katherine E. Oler
Special Master

[32] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by each filing (either jointly or separately) a notice renouncing their right to seek review.